HERBAL DRUG TECHNOLOGY

B.Pharm, Semester-VI

According to the syllabus based on 'Pharmacy Council of India'

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Herbal Drug Technology

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PGP Group of Educational and Research Institutions"

- Dr. G. Arunachalam

"Dedicated
to

my ***Almighty God***
and
my ***Family****"*

- Dr. V. E. Ida Christi

"Dedicated
to
my ***Parents***
Sh. Kishori Lal *&* ***Smt.Krishna Kumari****"*

-Dr. Prashant Kumar

Preface

It gives us immense pleasure to place before the **B.Pharm Sixth Semester** pharmacy students the book on **"Herbal Drug Technology"**.

This book has been written strictly in accordance with the current syllabus prescribed by Pharmacy Council of India, for B.Pharm students. Keeping in view the requirements of students and teachers, this book has been written to co ver all the topics in an easy -to-comprehend manner within desired limits of the prescribed syllabus, and it provides the students fundamentals of biodynamic agriculture, Indian medicine systems, nutraceuticals, herb -drug and herb -food interactions, drug e valuation, patenting and regulatory requirements, herbal industry, and Schedule T which are required by them during their pharmaceutical career.

All efforts have been made to keep the text error -free and to present the subject in a student friendly and e asy to understand. However, any suggestions and constructive comments would be highly appreciated and incorporated in the future edition.

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Acknowledgement

First and foremost, I would like to thank **Almighty God**. In the process of putting this book together in front of you, I realised how precious gift God has given to me by giving me the capability and the power to believe in my passion and pursue my dreams.

I would also like to thank the **Management of PGP College of Pharmaceutical Science & Research Institute**, for their constant motivation and support.

I owe a deep sense of appreciation for my academic Colleagues and Students, for their whole hearted cooperation and support. I would like to extend my gratitude towards my Family Members, for their cooperation and blessings.

- Dr. G. Arunachalam

First and foremost, praises and thanks to **God**, the Almighty, for His showers of blessings throughout work to complete this work successfully. I would like to express my deep and sincere gratitude to our Principal **Dr. S. Mohan.** M. Pharm., Ph.D. (Karpagam college of Pharmacy, Coimbatore) for giving me the opportunity, providing invaluable guidance and encouragement. His dynamism, vision, sincerity and motivation have deeply inspired me.

It was a great privilege and honour to work in Karpagam College of Pharmacy, Coimbatore. I am extremely grateful for the management & the Managing Director, **Dr. R. Vasanthakumar**. I would also like to thank him for his empathy, and great sense of humor. I am extending my heartfelt thanks to his son, **Mr. V. Karthick**, for his support and encouragement during my job, my professional progressing as well as to give me an opportunity to work in this institution.

- Dr. V. E. Ida Christi

First of all I bow to **Maa Saraswati** and **Almighty** who blessed me with courage to carry out this work. I also express my deep gratitude to **Almighty** for blessed the people in my life so helpful and kind, without all these, this work was not possible. I hope this work will be helpful for the society. I tried to focus all the important aspects of Herbal Drug Technology in this Book.

Likewise due recognition is given in this book to **Ms. Tuhina Banerjee (Copy Editor), Mr. Vinod Awathi (Marketing Head)** and **Mr. Anoop Kumar (Marketing Co -ordinator)** of **Thakur Publications Pvt. Ltd.** for their encouragement and advice in reviewing the manuscripts and also obliged the staff of **Thakur Publications Pvt. Ltd**. for their co -operation for finalising this volume and their efforts in keeping this project on schedule.

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-Dr. Prashant Kumar

Syllabus

Module 01 **11 Hours**

Herbs as Raw Materials

- Definition of herb, herbal medicine, herbal medicinal product, herbal drug preparation.
- Source of Herbs.
- Selection, identification and authentication of herbal materials.
- Processing of herbal raw material.

Biodynamic Agriculture

- Good agricultural practices in cultivation of medicinal plants including Organic farming.
- Pest and Pest management in medicinal plants: Biopesticides/Bio Insecticides.

Indian Systems of Medicine

- Basic principles involved in Ayurveda, Siddha, Unani and Homeopathy
- Preparation and standardization of Ayurvedic formulations viz Aristas and Asawas, Ghutika, Churna, Lehya and Bhasma.

Module 02 **07 Hours**

Nutraceuticals

- General aspects, Market, growth, scope and types of products available in the market. Health benefits and role of Nutraceuticals in ailments like Diabetes, CVS diseases, Cancer, Irritable bowel syndrome and various Gastro intestinal diseases.
- Study of following herbs as health food: Alfaalfa, Chicory, Ginger, Fenugreek, Garlic, Honey, Amla, Ginseng, Ashwagandha, Spirulina

Herbal-Drug and Herb-Food Interactions

- General introduction to interaction and classification.
- Study of following drugs and their possible side effects and interactions: Hypercium, kava-kava, Ginkgo biloba, Ginseng, Garlic, Pepper & Ephedra.

Module 03 **10 Hours**

Herbal Cosmetics

- Sources and description of raw materials of herbal origin used via, fixed oils, waxes, gums colours, perfumes, protective agents, bleaching agents, antioxidants in products such as skin care, hair care and oral hygiene products.

Herbal Excipients

- Herbal Excipients – Significance of substances of natural origin as excipients – colorants, sweeteners, binders, diluents, viscosity builders, disintegrants, flavors & perfumes.

Herbal Formulations

- Conventional herbal formulations like syrups, mixtures, tablets, and Novel dosage forms like phytosomes.

Module 04 **10 Hours**

Evaluation of Drugs

- WHO & ICH guidelines for the assessment of herbal drugs
- Stability testing of herbal drugs.

Patenting and Regulatory Requirements of Natural Products

- Definition of the terms: Patent, IPR, Farmers right, Breeder's right, Bioprospecting and Biopiracy
- Patenting aspects of Traditional Knowledge and Natural Products. Case study of Curcuma & Neem.

Regulatory Issues

- Regulations in India (ASU DTAB, ASU DCC), Regulation of manufacture of ASU drugs - Schedule Z of Drugs & Cosmetics Act for ASU drugs.

Module 05 **07 Hours**

General Introduction to Herbal Industry

- Herbal drugs industry: Present scope and future prospects.
- A brief account of plant based industries and institutions involved in work on medicinal and aromatic plants in India.

Schedule T – Good Manufacturing Practice of Indian systems of Medicine

- Components of GMP (Schedule – T) and its objectives.
- Infrastructural requirements, working space, storage area, machinery and equipments, standard operating procedures, health and hygiene, documentation and records.

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Module 2

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Module 3

Chapter 6: Herbal Cosmetics

CHAPTER 1

Herbs as Raw Materials

1.1. HERBS

1.1.1. Introduction

The term **herb** has been originated from the Latin term ***herba*** and an old French term ***herbe***; and was used for non-woody plants, including those that come from trees and shrubs. But at the present time, the term **herb** is used for any part of the plant such as fruit, seed, stem, bark, flower, leaf, stigma, root, or a non-woody plant. Herbs are also used as food, flavonoid, medicine, perfume, etc.

Medicinal use of plants has started long before pre-historic period, and can be seen in ancient Unani manuscripts, Egyptian papyrus, and Chinese writings. There are many evidences which verify that Unani Hakims, Indian Vaids, and European and Mediterranean cultures were using herbs as medicine from past 4000 years. In various indigenous cultures, like Rome, Egypt, Iran, Africa and America, herbs were used for healing purposes; while in other developed traditional medical systems such as Unani, Ayurveda and Chinese Medicine, herbal products were used systematically.

Use of traditional systems of medicine has been increased due to many reasons such as population rise, inadequate drug supply, prohibitive cost of treatments, side effects of several synthetic drugs, and resistance development to currently used drugs for infectious diseases. These reasons have increased the dependency on plant materials as a source of medicines for various human ailments.

1.1.2. Definition of Some Important Terms Related to Herbal Medicine

Some important terms related to herbal medicine are explained below:

1) **Herbs:** These are any crude plant material or product, like leaves, flowers, fruits, seeds, stems, wood, bark, roots, rhizomes, or other plant parts that may be entire, fragmented, or powdered.
2) **Herbal Materials:** These include either whole plants or parts of medicinal plants in crude state, such as herbs, fresh juices, gums, fixed oils, essential oils, resins, and dry powders of herbs. Sometimes, herbal materials are obtained by various local procedures, such as steaming, roasting, or stir baking with honey, alcoholic beverages, or other materials.
3) **Herbal Medicines:** These are herbs, herbal materials, herbal preparations, and finished herbal products.
4) **Herbal Preparations:** These are finished herbal products such as comminuted or powdered herbal materials, or extracts, tinctures and fatty

oils, expressed juices and processed exudates of herbal materials. They are obtained by various methods like extraction, distillation, expression, fractionation, purification, concentration, fermentation or other physical or biological processes. Herbal preparations also include those obtained by steeping or heating herbal materials in alcoholic beverages and/or honey, or in other materials.

5) **Finished Herbal Products:** These are medicinal products which contain herbal drugs or herbal drug preparations as active substances. They include herbal preparations made from one or more herbs. In case more than one herb is used, the term **mixed herbal product** can also be used. These products may have excipients along with the active ingredients.

   In some countries, herbal medicines include traditional, natural organic or inorganic active ingredients, which are not of plant origin (**e.g.,** animal materials and mineral materials). However, those finished or mixed products to which chemically defined active substances (such as synthetic compounds and/or isolated constituents from herbal materials) have been added, are not considered herbal.

6) **Medicinal Plants:** These plants are used for medical purposes, and are either grown wild or cultivated.

7) **Herbal Medicinal Products:** These are medicinal products which contain one or more herbal substances, or herbal preparations, or combination of both as active substances.

8) **Herbal (Drug) Preparations:** These preparations are obtained by subjecting the herbal substances to procedures like extraction, distillation, expression, fractionation, purification, concentration, or fermentation. Examples of herbal (drug) preparations are comminuted powdered herbal substances, tinctures, extracts, essential oils, expressed juices, and processed exudates.

9) **Herbal Remedies:** These are herbal products used for therapeutic purposes. The only difference between herbal remedy and herbal medicinal product is that the former one is subjected to drug regulations.

1.1.3. Source of Herbs

Various diseases have been treated by using plant products since ages. Plants and other natural substances have been employed in the traditional Indian systems of medicine (Ayurveda, Siddha, and Unani systems). The species of flowering plants ranges from 200,000-250,000, belonging to 10,500 genera, and around 300 families. The **genera** are spread into plant families like Solanaceae, Compositae, Papaveraceae, Scrophulariaceae, Leguminosae, Rutaceae, Rubiaceae, Umbelliferae, Dioscoreaceae, Gentaceae, Bromeliaceae, Apocynaceae, Rhamnaceae, Caricaceae, Plantaginaceae, Sterculiaceae, Ericaceae, Liliaceae, and Gramineae.

Drugs from plant origin when analysed, revealed that most of them have been derived from seed-bearing plants (spermatophytes), among which the angiosperms (flowering plants) compared to gymnosperms (non-flowering plants) have produced many useful medicinal plants.

Gymnosperms are rich in oils, resins, and alkaloids (like ephedrine). Amongst the angiosperms, monocotyledons as well as dicotyledons, yield purposeful drugs. In dicotyledons, cinchona, ipecac, rauwolfia, belladonna, and vinca are drugs obtained from higher plants. The entire plant or sometimes a part of it is beneficial and termed as **crude drugs**. The plant part with maximum content of active constituents is selected and collected for marketing. Therefore, seeds, fruits, leaves, flowers, roots, stems, and barks make crude drugs. Wood of a tree is also at times considered a crude drug.

1.1.4. Selection, Identification and Authentication of Herbal Materials

The specifications for herbal starting materials, herbal preparations , and finished herbal products are intended to establish full characterisation, to define the quality, and to focus on th e characteristics that ensure safety and efficacy. The quality of herbal medicines or finished herbal products can be assured only if the starting herbal materials are defined in a rigorous and detailed manner.

Herbal quality is also affected by v arious operations such as harvesting, drying, storage, transportation, and processing (**e.g.,** mode of extraction, polarity of the extracting solvent, instability of constituents, etc.).

Proper identification and appropriate quality indicates lack of adulteration, sophistication, or substitution, and are highly significant steps in the field of herbal medicines.

The quality of a herb also depends on the environmental conditions under which it is allowed to grow. Therefore, soil fertility, length of growing season, temperature, moisture content, and harvest time are some considerable factors:

1) Sometimes more detailed information is required for collection or agricultural production of medicinal plants. **For example,** for the production of a reproducible quality of herbal medicines , the selection of seeds and conditions of cultivation and harvesting are some important factors. Therefore, characterisation and a detailed evaluation of the botanical and phytochemical aspects of the medicinal plant s, manufacture of the herbal preparations and the finished herbal product s is important for establishing comprehensive and relevant specifications.
2) The family and botanical name of the plant should be used as per the binomial system (genus, species, variety , and the authority, i.e., reference to the originator of the classification , **e.g.,** Linnaeus). It is also suitable to add the vernacular name and the therapeutic use in the country or region of origin of the plant.
3) Other details about the plant source , such as origin country and/or region (state and province, if relevant), whether it was cultivated as per WHO GMP (updated supplementary guidelines for manufacturing herbal medicines) or collected from the wild , cultivation method, dates and conditions of harvesting (**e.g.,** whether there was extreme weather), collection procedures,

collection area, and brand, quantity and date of pesticide application, should be provided as per the requirement of WHO guideline on good agricultural and collection practices.

4) It is also essential to mention whether the whole plant or only a part is being used. If a part of plant is used, it should be mentioned that which part is used along with its state (**e.g.,** whole or reduced). For dried plant material s, the drying system used should be mentioned.
5) The plant materials should be described on the basis of macroscopic (i.e., visual) and/or microscopic examination.
6) Identification tests (such as TLC or other chromatographic fingerprint) for known active ingredients or markers should be performed as and when required. These tests should be performed with respect to a reference sample.
7) If required, the details of assay of active constituents or markers should be mentioned. Limit tests such as dry residue of liquids, ash value (total ash and ash insoluble in hydrochloric acid), water-soluble extractives, moisture/water content, and loss on drying (considering the presence of essential oils) should also be performed and briefly mentioned.
8) It is also important to determine pesticide contamination that may occur and the acceptable limits for such contamination in herbal materials or herbal preparations used for manufacturing herbal medicines.
9) Tests for toxic metals, contaminants, foreign materials , and adulterants should be performed.
10) Tests for fungal and/or microbiological contamination, fumigant residues, mycotoxins, pest-infestations, radioactivity and their acceptable limits should be conducted.
11) Tests for particle size, swelling index and residual solvents in herbal preparations and biological fingerprints (**e.g.,** induced fluorescent markers) should also be performed.
12) If required, the tests like uniformity of weight (**e.g.,** for tablets, single-dose powders, suppositories, capsules , and herbal tea in sachets), disintegration time (for tablets, capsules, suppositories , and pills), hardness and friability (for uncoated tablets), viscosity (for internal and external fluids), consistency (semisolid preparations), and dissolution (for tablets and capsules) should be performed. Physical appearance (colour, odour, form shape, size , and texture), loss on drying, or water content should be studied.
13) Identity tests, qualitative determination of relevant substances of the plants (**e.g.,** fingerprint chromatograms) should be performed.
14) If any relevant active ingredient is identified, its quantification should be performed using the available analytical methods.
15) Limit tests for residual solvents should be performed.

1.1.5. Processing of Herbal Raw Material

If drugs are found to be rich in active ingredients, it is believed that the collection of crude drugs was carried out efficiently, regardless of the crude drug type and area of collection. During the collection process of crude drugs, the advantage of prevailing environmental conditions is also considered.

After the crude drugs are collec ted, they are processed for marketing. This is done to maintain the stability of finished products during transport and storage, and to ensure that no foreign organic matter and substitutes are present.

These methods include appropriate methods of **collection**, **harvesting**, **drying**, and **garbling**. **Coating** and **bleaching** are also sometimes performed to transform the drug into a suitable form for the market.

Before preserving crude drugs, a complete knowledge about their physical and chemical properties is necessary. Adequate preservation of crude drugs maintains their quality. The drugs should be preserved in well -closed and filled containers, and stored in water-proof, fire-proof, and rodent-proof places.

1.1.5.1. Collection of Different Parts of Plant

Given below are the different plant parts collected in different conditions:

1) **Leaf and Flowering Tops:** These are collected before their maturity (i.e., flowering stage), **e.g.,** senna, digit alis, vinca, belladonna, etc.; while aloe leaves are collected when they have become adequately thick.
2) **Flowers:** These are collected in the morning hours of dry weather during pollination, or before their full expansion, **e.g.**, saffron, clove buds, chamomile, arnica, etc.
3) **Barks:** These are collected in spring or early summer when cambium is active, so that they can be easily detached from the stem. **For example**, wild cherry is collected in autumn; cinnamon in the rainy season. Barks can be collected by the following **three methods**:
   i) **Felling:** This method involves cutting the tree at base and peeling out the bark.
   ii) **Uprooting:** This method involves digging out the roots and stripping off the barks from roots and branches.
   iii) **Coppicing:** This method involves cutting the tr ees repetitively for obtaining bark.
4) **Fruits:** These are collected either ripe or half ripe, but fully grown. **For example**, cardamom fruits are collected before dehiscence; bael and tamarind are collected after full maturity; caraway, fennel, and coriander ar e collected after full ripening.
5) **Roots and Rhizomes :** Roots are collected in spring before the vegetative process stops, and then are transversely or longitudinally sliced for easy drying. Rhizomes are collected when they have a rich amount of food material and chemical constituents.
6) **Resins, Gums, and Lattices:** These unorganised drugs are collected when they start oozing out of the plants. **For example**, acacia gum is collected when it gets adequately hard after 2-3 weeks of making incisions on bark; opium an d papaya lattices are collected after the latex coagulates; turpentine oleo -resin and Peru balsam are collected from 8 -10 years old plant.

1.1.5.2. Harvesting

Harvesting is important as it reflects on the economic aspects of crude drugs. The type of drug to be harvested and the Pharmacopoeial standards to be achieved should also be considered.

An efficient harvesting is done by the skilled workers only. Selectivity is advantageous as the similar looking non -genuine drugs can be rejected during collection. But it is a strenuous job and also not economical.

Techniques of Harvesting

1) **Binders:** These are used for harvesting drugs which constitute all aerial parts.
2) **Seed Stripper:** This device is used for harvesting flowers, seeds, and small fruits.
3) **Beating with Bamboo:** This technique is used for harvesting cloves.
4) **Brushing:** This technique is used for collecting cochineal insects from branches of cacti.
5) **Handled Forks:** These are used for harvesting seaweeds producing agar.
6) **Mowers:** These are used for harvesting peppermint and spearmint.
7) **Reaping Machines:** These are used for harvesting fennel, coriander, and caraway plants which are uprooted, dried, beaten, or the fruits are separated by winnowing.

1.1.5.3. Drying

Drying involves removing sufficient moisture from the crude drug for obtaining a good quality finished product, which is also resistant to microbial growth. Drying also inhibits partially enzymatic reactions. Dryin g eases pulverising or grinding of a crude drug.

Some drugs demand specialised methods for matching the specified standards, **e.g.**, *Cinnamomum zeylanicum* bark and gentian roots demand fermentation. Drugs like glycyrrhiza, squill, and calumba are sliced an d cut into smaller pieces to enhance drying. For the flowers to retain their colour and volatile oil content, they are dried in shades.

Types of Drying

The collected drugs can be dried by the following methods:

1) **Natural Drying (Sun -Drying or in Shed):** Drying in direct sunlight is preferred i f the drug contents are stable to high temperature and sunlight (**e.g.,** gum acacia, seeds, and fruits). Drying in shed is preferred if the natural colour of the drug (**e.g.,** digitalis, clove, and senna) and its volatile ingredients (**e.g.,** peppermint) are to be retained.
2) **Artificial Drying:** This involves drying the drugs by using any of the available dryers:
   i) **Tray Dryers:** These are used for drugs not containing volatile oils, which are stable to heat, or which need deactivati on of enzymes. In tray

drying method, hot air of desired temperature is circulated through the dryers to remove the water content of drugs . Belladonna roots, cinchona bark, tea and raspberry leaves, and gums are **examples** of drugs dried by using tray dryers.

ii) **Vacuum Dryers:** These are used for drugs sensitive to higher temperature, **e.g.**, tannic acid and digitalis leaves.

iii) **Spray Dryers:** These are used for drugs highly sensitive to atmospheric conditions and to vacuum -drying temperature. Spray drying method is not suitable for drying crude drugs; but can be used for quick drying of economically important plant or animal constituents , **e.g.**, papaya latex, pectin, tannins, etc.

1.1.5.4. Garbling (Dressing)

After drying th e crude drug preparation, garbling is carried out to remove sand, dirt, and foreign organic parts of the same plant from the drug. A few available methods are practiced at the site of drug preparation for removing this foreign organic matter (extraneous ma tter). Otherwise, the quality of crude drugs gets altered and they fail to achieve the Pharmacopoeial standards.

1.1.5.5. Packing

During packaging of drugs, their morphological and chemical nature, uses, and effects of climatic conditions during transportation and storage should be considered. Given below are some **packing conditions** of different drugs:

1) Goatskin is used for packing aloe.
2) Kerosene tins are used for packing colophony and Tolu balsam.
3) Well-closed containers are used for asafoetida to prevent volatile oil loss.
4) Containers which remain unaffected by sunlight are used for packing sunlight-sensitive cod liver oil.
5) Leaf drugs like senna, vinca, etc. are pressed and baled.
6) In the presence of moisture, dr ugs like squill becomes flexible, ergot becomes prone to microbial growth, and digitalis loses its potency due to glycoside decomposition; thus these d rugs being moisture -sensitive demand costly and specialised packing requirements.

1.1.5.6. Storage of Drugs of Natural Origin

The physical and chemical properties of crude drugs should be well -known in order to preserve them. Adequate preservation of crude drugs improves their quality. **Well-closed** and **filled containers** should be used for preserving the drugs. The **premises** for storing the drugs should be **water-proof**, **fire-proof**, and **rodent-proof**.

Many drugs become **vulnerable to microbial growth** during their storage period by absorbing moisture. Some of them absorb moisture up to 25% of their weight, thus increasing the bulk of crude drugs, and also damaging their quality. Many **enzymatic reactions** occur due to the presence of **excessive moisture** ; these reactions further **decompose the active in gredients** of the drug as observed in

digitalis leaves and wild cherry bark. In plants like gentian and ergot, **mould infestation** is seen due to excessive moisture. In ergot, cod liver oil, and digitalis, the **active ingredients are destroyed** by radiation due to **direct sunlight**.

Preservation of crude drugs is also influenced by their form or shape. **Colophony** in its entire form (big masses) remains unchanged during the storage period; its **powdered form** , however, undergoes **oxidation** or becomes **insoluble in petroleum ether**.

Powdered form of squill during storage turns **hygroscopic** and **forms a rubbery mass** when exposed to air for a long time.

Powdered form of ergot contains a **fixed oil** which turns **rancid** during storage. A **good quality of ergot** can be maintained by **defatting it with lipid solvent** before its storage.

Lard (purified internal fat of hog's abdomen) can be **prevented from turning rancid** by **adding siam benzoin**.

Shark liver oil, papain, etc. are **destroyed by atmospheric oxygen** , thus are stored in **well-closed containers** , or the **container's air is replaced with an inert gas** (nitrogen).

The drugs should not only be protected against **adverse physical and chemical changes**, but also against **insect or mould attacks** as the drugs can get infested by various insects, nematodes, worms, moulds, and mites during storage.

Coleoptera (*Stegobium paniceum* and *Calandrum granarium*), **Lepidoptera** (*Ephestia kuehniella* and *Tinea pellionella*), and **Arachnida** or mites (*Tyroglyphus farinae* and *Glycophagus domesticus*) are some of the **pests** found in drugs.

Either proper drying or by treating with fumigants before storage can prevent infestation by these pests. **Methyl bromide** , **carbon disulphide** , and **hydrocyanic acid** are the commonly used **fumigants** for drug storage.

Sometimes drugs require **special treatments**, **e.g.,** liming of ginger, coating of nutmeg, etc.

Temperature also plays a crucial role in drug storage, as it can decompose the active constituents by initiating some chemical reactions. Thus, the drugs are preferred to be stored at a **very low temperature** . The costly **phytopharmaceuticals** are stored at **refrigerated temperature** in **well-closed containers**.

Small quantities of drugs should be stored in **air-proof**, **moisture-proof**, and **light-proof containers** (like tin, cans, covered metal tins, or amber glass containers). Drugs should **not** be stored in **wooden boxes** and **paper bags**.

1.2. SUMMARY

The details given in the chapter can be summarised as follows:

1) The term **herb** has been originated from the Latin term, ***herba*** and an old French term ***herbe***.
2) **Herbs** are any crude plant material or product, like leaves, flowers, fruits, seeds, stems, wood, bark, roots, rhizomes, or other plant parts that may be entire, fragmented, or powdered.
3) **Herbal materials** include either whole plants or parts of medi cinal plants in crude state, such as herbs, fresh juices, gums, fixed oils, essential oils, resins, and dry powders of herbs.
4) **Herbal medicines** are herbs, herbal materials, herbal preparations, and finished herbal products.
5) **Herbal preparations** are finished herbal products such as comminuted or powdered herbal materials, or extracts, tinctures and fatty oils, expressed juices and processed exudates of herbal materials.
6) **Finished herbal products** contain herbal drugs or herbal drug preparations as active substances.
7) **Medicinal plants** are used for medical purposes, and are either grown wild or cultivated.
8) **Herbal medicinal products** contain one or more herbal substances, or herbal preparations, or combination of both as active substances.
9) **Herbal (drug) preparation s** are obtained by subjecting the herbal substances to procedures like extraction, distillation, expression, fractionation, purification, concentration, or fermentation.
10) **Herbal remedies** are herbal products used for therapeutic purposes. The only difference between herbal remedy and herbal medicinal product is that the former one is subjected to drug regulations.
11) The entire plant or sometimes a part of it is beneficial and termed as **crude drugs**.
12) **Leaf and flowering tops** are collected before their m aturity (i.e., flowering stage).
13) **Flowers** are collected in the morning hours of dry weather during pollination, or before their full expansion.
14) **Barks** are collected in spring or early summer when cambium is active, so that they can be easily detached from the stem.
15) **Felling** method involves cutting the tree at base and peeling out the bark.
16) **Uprooting** method involves digging out the roots and stripping off the barks from roots and branches.
17) **Coppicing** method involves cutting the trees repetitively for obtaining bark.
18) **Fruits** are collected either ripe or half ripe, but fully grown.
19) **Roots** are collected in spring before the vegetative process stops, and then are transversely or longitudinally sliced for easy drying.

20) **Rhizomes** are collected when they have a rich amount of foo d material and chemical constituents.
21) **Resins, gums, and lattices** are collected when they start oozing out of the plants.
22) **Binders** are used for harvesting drugs which constitute all aerial parts.
23) **Seed stripper** device is used for harvesting flowers, seeds, and small fruits.
24) **Beating with bamboo** technique is used for harvesting cloves.
25) **Brushing** technique is used for collecting cochineal insects from branches of cacti.
26) **Handled forks** are used for harvesting seaweeds producing agar.
27) **Mowers** are used for harvesting peppermint and spearmint.
28) **Reaping m achines** are used for harvesting fennel, coriander, and caraway plants which are uprooted, dried, beaten, or the fruits are separated by winnowing.
29) **Drying** involves removing sufficient moisture from the crude drug for obtaining a good quality finished product, which is also resistant to microbial growth.
30) **Tray dryers** are used for drugs not containing volatile oils, which are stable to heat, or which need deactivation of enzymes.
31) **Vacuum dryers** are used for drugs sensitive to higher temperature.
32) **Spray dryers** are used for drugs highly sensitive to atmospheric conditions and to vacuum-drying temperature.
33) **Garbling** is carried out to remove sand, dirt, and foreign organic parts of the same plant from the drug.

1.3. EXERCISE

1.3.1. True or False

1) Herbal remedies are herbs, herbal materials, herbal preparations, and finished herbal products.
2) Finished herbal products contain herbal drugs or herbal drug preparations as active substances.
3) Fruits are collected before their maturity.
4) Uprooting method involves cutting the tree at base and peeling out the bark.
5) Rhizomes are collected when they have a rich amount of food material and chemical constituents.
6) Brushing technique is used for harvesting cloves.
7) Tray dryers are used for drugs sensitive to higher temperature.

1.3.2. Fill in the Blanks

8) The term herb has been originated from the Latin term, _____ and an old French term _____ .
9) _____ contain one or more herbal substances, or herbal preparations, or combination of both as active substances.

10) _____ are collected in the morning hours of dry weather during pollination, or before their full expansion.
11) _____ method involves cutting the trees repetitively for obtaining bark.
12) _____ are used for harvesting drugs which constitute all aerial parts.
13) _____ are used for harvesting seaweeds producing agar.
14) _____ are used for harvesting peppermint and spearmint.

Answers

1) False	2) True	3) False
4) False	5) True	6) False
7) False	8) *herba* and *herbe*	9) Herbal medicinal products
10) Flowers	11) Coppicing	12) Binders
13) Handled forks	14) Mowers	

1.3.3. Very Short Answer Type Questions

1) Define herbs and herbal materials.
2) What are finished herbal products?
3) Give any two techniques of harvesting.
4) What do you understand by garbling?
5) Enlist the types of dryers that may be used for processing of herbal drugs.

1.3.4. Short Answer Type Questions

1) Discuss the sources of herbs.
2) Write about the selection, identification and authentication of herbal materials.
3) Explain how the drugs of natural origin are stored.

1.3.5. Long Answer Type Question

1) Discuss briefly about the processing of herbal raw materials.

CHAPTER 2

Biodynamic Agriculture

2.1. BIODYNAMIC AGRICULTURE

2.1.1. Introduction

Biodynamic farming was introduced by **Rudolf Steiner** (the late Australian philosopher, architect, playwright, educator, and anthroposophist) and developed in popularity since **1922**. He first formulated the organic approach to agriculture in the western world by linking unhealthy agriculture and an unhealthy social and spiritual life. In **1924**, the bio-dynamic movement went under way from 8 lectures given by **Rudolf Steiner** in Koberwitz, Poland.

Biodynamic farming (means biological dynamics) is a **method of organic agriculture** that considers farm as a living system where one activity is affected by the other. The term **biodynamic** has been derived from the Greek term ***bios*** meaning **life** and ***dynamic*** meaning **energy**. Hence, biodynamic farming indicates **working with energies that create and maintain life**.

Biodynamic agriculture in other words is an organic farming method that treats farm as an individual organism, balances the holistic development and interrelationship of the soil, plants, and animals as a closed self-nourishing system.

2.1.2. Principles of Biodynamics

Biodynamics is ecologically oriented on a wider scope and includes sun, moon, planets, subterranean features, and mental factors. All natural things of the world are formed by the transformation and intimate combinations of four elements that include fire, earth, water, and air. Each element has one principle characteristic and one specific characteristic that serves as a connecting medium to the other elements.

1) **Harvesting Cosmic Forces:** The earthy forces of Moon, Mercury and Venus soak into earth from the air above, and the cosmic forces of Mars, Jupiter and Saturn upwards soak into earth from the rocks below. They interact in the clay region so the plants are in regular rhythms. Each contributes to the life growth and farm of the plant. By understanding the gesture and effect of each rhythm, agricultural activities like soil preparation, sowing, intercultural operations, and harvesting can be programmed.
2) **Biodynamic Calendar:** If agricultural practices are performed as per constellation, they prove to be more effective and beneficial as each constellation has dominant elemental effects.
3) Biodynamic farming restores the humus status of soil eco system to retain its fertility and productivity.

4) Soil is a living system wherein the microbes can be fully established and maintained; thus, biodynamic farming also restores the soil for a balanced functioning of flora and fauna.
5) Biodynamic farming does n ot deny the importance of mineral nutrients of soil (like nitrogen, phosphate, potash, calcium, magnesium, etc.) and also considers the use of organic matter as the factor for soil life.
6) A plant grows under the influence of abiotic factors (like temperatur e, oxygen, CO_2 light, water, etc.), thus biodynamic farming involves the application of these factors to soil life and health. These energies are transformed in the plant systems by photosynthesis into chemically active energies.
7) Biodynamic farming conside rs a plant as living entity consisting of mineral elements (like N, P, K, Ca, Mg, Cl, Fe, etc.) and organic matter (like proteins, carbohydrates cellulose, and starch).
8) Biodynamic farming gives importance to enzymes and growth substances.
9) It follows proper crop rotation in which soil exhausting crops are cultivated alternatively with fertility restoring crops to restore soil fertility.
10) It also restores the soil environmental conditions, forests, wind protection, and water regulation.
11) It maintains the soil structure, i.e., the physical characters (like, bulk density, pore space, water holding capacity, and texture).

2.1.3. Characteristics of Biodynamic Farming

Biodynamic farming has two characteristics. **Firstly**, it allows the inputs from various herbal, mineral and manual raw materials to be processed in complex ways and applied in small doses on soil and crops. **Secondly**, it observes the rhythms in nature that go beyond the influences of sun, weather and season, but include lunar, planetary and stellar constellations.

2.1.4. Biodynamic Preparations

To aid fertilisation , **Steiner** recommended the use of **eight different preparations** in biodynamic agriculture. These prepared substances are numbered 500 to 507; the first two are used for preparing fields and the remaining six ar e used for making compost. These eight preparations are discussed below:

1) **Field Preparations (500 and 501)**
   i) **Field Preparations for Stimulating Humus Formation - Preparation 500 (Horn Manure):** A humus mixture is prepared by filling the horn s of 9 cows with co w manure and burying them 46-69cm below the surface of fertile soil. The horns are placed in descending moon during autumn for incubating the whole winter. The horns are taken out in March-April in descending period and stored in earthen pots at a cooler place. Cow is an earthly creature with a very strong digestive system, and cow horns absorb life energies during decomposition of the dung.

   ii) **Preparation 501 (Horn Silica):** It is crushed powdered quartz prepared by stuffing in a cow horn, burying into the ground in spring, and taking out in

autumn. It can be mixed with preparation 500, but is generally prepared on its own (1 tablespoon of quartz powder is mixed in 250 litres of water). During the wet season, this mixture is sprayed under low pressure over the crops to prevent fungal diseases. It should be sprayed on an overcast day or early in the morning to prevent the leaves from burning.

2) **Compost Preparations (502-507):** Composting involves putting the organic substances together for rotting them in order to o btain a high-quality natural fertiliser agent.
   i) **Yarrow Preparation 502:** Yarrow blossoms (*Achillea millefolium*) are stuffed in the urinary bladder of red deer (*Cervus elaphus*), which is then placed in the sun during summer, buried in earth during winter, and taken out in the spring. This preparation stimulates potassium -, silica - and selenium-activating bacteria, combines sulphur with other substances, cures weaknesses, strengthens the flowering and fruiting plants against insect attack, and connects the soil to the planetary rhythms.
   ii) **Chamomile Preparation 503:** Chamomile blossoms (*Matricaria recutita*) are stuffed in the small intestine of cattle, which is then buried in humus-rich earth in the autumn, and taken out in the spring.
   iii) **Stinging Nettle Preparation 5 04:** Fully bloomed stinging nettle plants (*Urtica dioica*) are stuffed together underground and are surrounded on all sides by peat for a year.
   iv) **Oak Bark Preparation 505:** Oak bark (*Quercus robur*) is cut into small pieces, placed inside the skull of a domestic ated animal, surrounded by peat, and buried in a place where lots of rain water runs by.
   v) **Dandelion Preparation 506:** Dandelion flowers (*Taraxacum officinale*) are stuffed in the peritoneum of cattle, which is then buried in earth during winter, and taken out in the spring.
   vi) **Valerian Preparation 507:** Valerian flowers (*Valeriana officinalis*) are extracted in water.

2.1.5. Lunar Effects

Steiner proposed that the fact moon reflects light and has a gravitational effect on earth affects plant growth. Moon has a roughly el liptical orbit so the gravitational pull varies throughout its 28 day cycle. Root growth is improved when moon moves further out causing a decreased pull on the earth and *vice versa*. This force also causes the ocean tides. Planting flower, fruit and vegeta ble seeds are best done 2 days before a new moon because light and gravitational forces are favourable in the following 7 days. In the next 7 days, moon appears larger each night and approaches a full moon. The increased light stimulates foliage growth, bu t the increased gravitational pull is less favourable to root growth. As a result, young shoots thrive and the roots rest.

Seven days after the full moon, the light decreases thus slowing foliage growth. The gravitational pull also decreases but it helps the roots to develop. Therefore, this is a good time to transplant seedlings as the roots get better conditions to

flourish. In the last 7 days of the lunar cycle, the light decreases but the gravitational pull increases. As a result, foliage as well as the roots rest in the run up to the new moon of the next lunar cycle.

The different **phases of lunar cycle** are:

1) **Ascending Period:** During this period, a greater emphasis is laid on the energy flow from the centre of the earth to the cosmic periphery. This phenomenon is observed in spring tides, and has a correspondence to strength the sap flow in a plant that can be harnessed by the gardener.
2) **Descending Period:** During this period, lunar energy flows down from the cosmic periphery towards the centre of the earth. These forces work more strongly on the plant parts in the soil.

Table 2.1: Difference between the Ascending and Descending Period of Lunar Cycle

Ascending Moon	Descending Moon
The earth is breathing out; upper parts of the plant, **e.g.,** shoots, undergo development.	The earth is breathing in; ground parts of the plant, **e.g.,** roots, undergo development.
Cosmic energy works above the rhizosphere.	Cosmic energy works below the rhizosphere.
Spring and summer seasons.	Autumn and winter seasons.
Suitable for foliar applications, propagation activities, harvesting, and sowing.	Suitable for root development, transplanting, manure application, and harvesting of tuber crops.

3) **Perigee (Poornima):** At perigee, the moon is nearest to the earth, and plants are more prone to fungal diseases because of high atmospheric moisture.
4) **Apogee:** At apogee, the moon is farthest from the earth, and this time is suitable for sowing tuber crops.
5) **Rahu:** This is the lunar node in ascending period of moon, and is not suitable for agricultural activities.
6) **Ketu:** This is the lunar node in descending period of moon, and is not suitable for agricultural activities.

2.1.6. Practices for Biodynamic Production for Vegetables

Given below are the practices that should be followed for biodynamic production of vegetables:

1) **Nutrient Management:** This involves:
   i) Green manuring with sunhemp/sesbania.
   ii) Soil preparation and application of 5-10 tonnes of organic manures through NADEP, Vermi, Biodynamic Compost (BD), or microbe mediated compost in descending moon period.
   iii) Spraying cow horn manure before sowing/transplanting in descending period of moon.
   iv) Sowing in ascending moon period (i.e., 48 hours before the full moon) and on constellation based on the part of the crop to be harvested.
   v) Transplanting seedlings in descending moon period and on constellation based on the part of the crop to be harvested.

vi) Soaking seeds/seedlings in cow pat pit solution (1:7 ratio stirred for 30 minutes) before sowing.
vii) Spraying twice biodynamic liquid manure prepared from cow dung, co w urine, leguminous leaves, or Vermi-wash for better growth and fruiting.
viii) Intercultural operation/peppering/mulching for weed management and root development in soil.
ix) Harvesting and storage as per constellation.

2) **Disease Management:** This involves:
   i) Spraying twice cow horn silica (BD -501) at two leaf stage and fruit development stage.
   ii) Base spraying horsetail (*Equisetum arvensis*)/casuarina extract for controlling fungal diseases.
   iii) Spraying fresh cow dung/biodynamic liquid manures prepared from cow urine, neem an d karanj a (*Pongamia glabra*) for controlling bacterial diseases.

3) **Treatment of Pests and Weeds:** Biodynamic agriculture understands the necessity of pest and disease management for a healthy balanced farm organism. Where this is not achieved, techniques analo gous to fertilisation are used for pe st and weed control. These techniques include using the ashes of a pest or weed that has been picked from the fields and burnt.

   Steiner observed that weeds and plants are vulnerable to pests due to soil imbalance. Inse cts or field mice (Apodemus) have complex processes associated with them, depending on what pest is to be targeted.

   For example field mice are to be counted by developing ashes prepared from field mice skin when Venus is in the Scorpius constellation. We eds are combated by collecting seeds from the weeds, burning them on a wooden flame, and then spreading the seed ashes on the fields which are intended to block the influences from the full moon on the particular weed and make it unfertile.

   It is carried by:
   i) Spraying biodynamic liquid pesticides prepared from cow urine, neem, karanja (*Pongamia glabra*), c alotropis, datura, castor, *Thevetia nerrifolia*, Vitex spp. leaves, etc., or
   ii) Spraying nettle leaves extract to control pests.

2.1.7. Advantages

Biodynamic farming has the following advantages:

1) Its yield potentials are equal or better than those harvested after application of recommended doses of agrochemicals.
2) It shows continuous improvement in physical, chemical and biological properties of soil.
3) It produces qua lity with respect to nutrition and appearance, and improves shelf-life.
4) It is eco-friendly.

2.1.8. Interferences from Biodynamic Systems

Biodynamic system is almost new, but the preliminary observations show encouraging responses, based on which the following interferences are drawn:

1) It appears to be sustainable, economic, and eco-friendly.
2) It poses a minimum risk of residual toxicity.
3) It shows improvement in soil fertility with quality produce including shelf life.
4) It effectively employs microquantities of cow pit (BD-500 and BD-501) only if the soil is rich in organic matter content.
5) It maintains the organic matter content of the soil by incorporation of compost prepared locally from the organic waste by NADEP, Vermi, BD or micro mediated compost.

2.2. GOOD AGRICULTURAL PRACTICES IN CULTIVATION OF MEDICINAL PLANTS

2.2.1. Introduction

The general guidelines on good agricultural practices, and technical details for the cultivation of medicinal plants are discussed here. Different quality control measures and their applications are also mentioned.

2.2.2. Identification/Authentication of Cultivated Medicinal Plants

Selection of Medicinal Plants

The species or botanical variety selected for cultivation should be the same as specified in the National Pharmacopoeia or recommended by other authoritative national documents of other countries. If such national documents are not present, selection of species or botanical varieties is done as specified in the Pharmacopoeia or other authoritative documents of other countries. In newly introduced medicinal plants, the species or botanical variety selected for cultivation should be identified and documented as the source material used or should be described in traditional medicine of the original country.

Botanical Identity

The botanical identity, i.e., scientific name (genus, species, sub-species/variety, author, and family), of each medicinal plant being cultivated should be verified and recorded. The local and English common names (if available) should also be recorded. The cultivar name, ecotype, chemotype, or phenotype should also be provided as per the requirement. The name of cultivar and supplier should be provided for commercially available cultivars. For landraces collected, propagated, disseminated and grown in a specific region, the locally named line, including the origin of source seeds, plants or propagation materials should be recorded.

Specimens

A voucher botanical specimen should be submitted to a regional or national herbarium for identification in case of the first registration of a medicinal plant in a producer's country or in case of a doubt regarding the identity of a botanical species. If possible, a genetic pattern should be compared to that of an authentic specimen. The botanical identity should be documented in the registration file.

2.2.3. Seeds and Other Propagation Materials

Seeds and other propagation materials should be specified, and their suppliers should present information related to the identity, quality, performance, and breeding history of the products. For promoting healthy plant growth, the propagation or planting materials should be of appropriate quality, free from contamination and diseases, and resistant or tolerant to biotic or abiotic factors. Seeds and other propagation materials used for organic production s hould be certified as organically derived.

The quality of propagation material, including genetically -modified germplasm, should comply with regional and/or national regulations and should be labelled and documented. During production, the extraneous spec ies, botanical varieties and strains of medicinal plants should be excluded, and use of counterfeit, sub - standard and adulterated propagation materials should be avoided.

2.2.4. Cultivation

Cultivation of medicinal plants requires intensive care and management. The necessary conditions and duration of cultivation vary depending on the quality of medicinal plant materials. Traditional cultivation methods should be followed if scientific published or documented cultivation data are unavailable. Principles of good p lant husbandry and appropriate rotation of plants selected as per environmental suitability should be followed, and tillage should be adapted to plant growth and other requirements. Techniques of conservation agriculture should be followed in the build -up of organic matter and conservation of soil humidity. This agriculture also includes no-tillage systems.

Site Selection

Medicinal plant materials derived from the same species may differ in their quality when cultivated at different sites, due to the influence of soil, climate, and other factors. These differences may relate to physical appearance or variations in their constituents, the biosynthesis of which may be affected by extrinsic environmental conditions (including ecological and geographical variab les), and thus should be considered. Contamination risks due to soil, air or water pollution by hazardous chemicals should be avoided. The effect of past land uses and planting of crops on cultivation site, and any applications of plant protection products, should be evaluated.

Ecological Environment and Social Impact

Cultivation of medicinal plants affects the ecological balance and the genetic diversity of the flora and fauna in surrounding habitats. On the contrary, other plants, living organisms, and h uman activities can affect the quality and growth of medicinal plants.

Using non-indigenous medicinal plant species in cultivation can adversely affect the biological and ecological balance of the region. Wherever possible, the ecological impact of cultiv ation activities with time should be monitored. To avoid the negative impacts of cultivation on local livelihood, the social impact of

cultivation on local communities should be examined. If small -scale farmers jointly market their products, small -scale cu ltivation is considered superior to large-scale production in terms of local income -earning opportunities. In case of large-scale medicinal plant cultivation, it should be ensured that the local communities are directly benefited from fair wages, equal emp loyment opportunities, and capital reinvestment.

Climate

The physical, chemical and biological qualities of medicinal plants are affected by climatic conditions, like length of day, rainfall (water supply), and field temperature. The physiological and bio chemical activities of plants are also affected by duration of sunlight, average rainfall, average temperature, and daytime and night -time temperature differences, thus prior knowledge of these parameters should be considered.

Soil

Nutrients, organic matt er, and other elements should be present in soil in appropriate amounts so that the medicinal plants are of optimum growth and quality. Optimal soil conditions, like soil type, drainage, moisture retention, fertility, and pH, will be dictated by the select ed medicinal plant species and/o r target medicinal plant parts.

For obtaining large yields of medicinal plants, fertilisers of correct types and quantities should be used. Organic and chemical fertilisers are most widely used. Use of human excreta as a fe rtiliser should be avoided as they may have infectious microorganisms or parasites. Composting of animal manure is required to meet the safe hygienic standards of acceptable microbial limits and destroyed by the germination capacity of weeds. If animal man ure has been used, it should be documented.

Only the chemical fertilisers approved by the countries of cultivation and consumption should be used. The fertilising agents should be applied carefully as per the needs of the particular medicinal plant speci es and supporting capacity of the soil. Fertilisers should be applied to reduce leaching.

The growers should implement such practices that lead to soil conservation and reduce erosion, **for example**, creation of streamside buffer zones and planting of cover crops and green manure (crops grown to be ploughed in), such as alfalfa.

Irrigation and Drainage

Irrigation and drainage should be carried out and controlled as per the needs of the particular medicinal plant species during its various stages of growth. Water used for irrigation should meet the local, regional and/or national quality standards. It should be ensured that the plants being cultivated are neither over -watered nor under -watered. While deciding the irrigation method, the health impact of diffe rent types of irrigation (various forms of surface, sub -surface or overhead irrigation) on the risks of increased vector -borne disease transmission, should be considered.

Plant Maintenance and Protection

Growth and development characteristics of individua l medicinal plants and the plant parts meant for medicinal use should govern the field management practices. Application of measures such as topping, bud nipping, pruning, and shading can be used to control the plant growth and development; and this improves the quality and quantity of the medicinal plant material being produced.

Minimum amount of agrochemicals should be used when no alternative measures are available to promote the growth of or to protect the medicinal plants. Integrated pest management s hould be followed wherever required. Only approved pesticides and herbicides should be applied at the minimum effective level, as per the labelling and/or package insert guidelines of the individual product and the regulatory requirements for the grower an d the end -user countries. Pesticides and herbicides should be applied by qualified staff using approved equipment; and all the applications should be documented.

A constant minimum interval should be maintained between such treatments and harvest with the labelling and/or package insert instructions of the plant protection product, and such treatments should be carried out by consulting and with agreement of the buyer of medicinal plants or plant materials. The growers and producers should follow the limit s of maximum pesticide and herbicide residue as specified by local, regional and/or national regulatory authorities of the growers' as well as the end -users' countries and/or regions. International agreements such as the International Plant Protection Conv ention and Codex Alimentarius should also be consulted on pesticide use and residues.

2.2.5. Harvest

Harvesting of medicinal plants should be done during the optimal season or time period so that the production of medicinal plant materials and finished herbal products are of the best quality. The harvest time depends on the plant part to be used. Information on appropriate timing of harvest can be easily found in National Pharmacopoeias, published standards, official monographs, and major reference books. However , it is known that the concentration of biologically active constituents depends on the stage of plant growth and development. This applies to non-targeted toxic or poisonous indigenous plant ingredients also. The best time for harvest (i.e., quality peak season/time of day) should be determined as per the quality and quantity of biologically active constituents.

During harvesting, foreign matter, weeds or toxic plants should not be mixed with the harvested medicinal plant materials. Medicinal plants shoul be harvested under optimum conditions, avoiding dew, rain or high humidity. If harvesting has been done in wet conditions, the harvested material should be immediately transported to an indoor drying facility for drying. This is done to avoid the harmfu effects due to increased moisture levels or else it will facilitate microbial fermentation and mould. Clean cutting devices, harvesters, and other machines should be used to reduce damage and contamination from soil and other materials. These devices shoul be stored in an uncontaminated, dry place that is free from insects, rodents, birds and other pests, and unreachable to livestock and domestic animals.

The microbial load of harvested medicinal plant materials can be reduced by avoiding contact with soil. If required large and clean muslin drop cloths should be used as an interface between the harvested plants and soil. If underground parts (roots) are used, the adhering soil should be removed from the medicinal plant materials after their harvesting. The harvested raw medicinal plant materials should be transported under clean, dry conditions in clean baskets, dry sacks, trailers, hoppers or other well-aerated containers to a central point for transporting to the processing facility.

Clean containers should be used during harvest. These containers should not be contaminated with previously harvested medicinal plants and other foreign matter. If plastic containers are used, any retention of moisture that could lead to growth of mould should be removed. The containers not being used should be kept under dry conditions in an area free from insects, rodents, birds and other pests and unreachable to livestock and domestic animals.

Occurrence of any mechanical damage or compacting of the raw medicinal plant materials (such as overfilling or stacking of sacks or bags) that may compost or lessen the quality should be prevented. Decomposed medicinal plant materials should be identified and discarded during harvest, post-harvest inspections and processing to avoid microbial contamination and loss of product quality.

2.2.6. Personnel

The growers and producers should be adequately knowledgeable concerning the medicinal plants, including their botanical identification, cultivation, characteristics, environmental requirements (i.e., soil type, soil pH, fertility, plant spacing, and light requirements), and the means of harvest and storage.

The personnel (even the field workers) involved in the propagation, cultivation, harvest and post-harvest processing stages of medicinal plant production should maintain appropriate personal hygiene and should be trained regarding their hygiene responsibilities. Agrochemicals should be applied by properly trained personnel, wearing protective clothing (overalls, gloves, helmet, goggles, and face masks). The growers and producers should receive instruction on the issues related to environment protection, conservation of medicinal plant species, and proper agricultural stewardship.

2.3. ORGANIC FARMING

2.3.1. Introduction

The USDA study team defined organic farming as "**a system which avoids or excludes the use of synthetic inputs (such as fertilisers, pesticides, hormones, feed additives, etc.) and to the maximum extent feasible rely on crop rotations, crop residues, animal manures; off-farm organic waste, mineral grade rock additives and biological system of nutrient mobilisation and plant protection**".

FAO defined organic farming as "**a unique production management system that promotes and enhances agroecosystem health, including biodiversity, biological cycles and soil biological activity, by using on-farm agronomic, biological and mechanical methods in exclusion of all synthetic off-farm inputs**".

1939 – First Use of the Term "Organic Farming"
The term **organic farming** was first used by **Lord Northbourne**. The term was derived from his concept of "**the farm as organism**", which he explains in his book, "Look to the Land" (1940). Influenced by Sir Albert Howard's work, **Lady Eve Balfour** did first scientific, side-by-side comparison of organic and conventional farming.

2.3.2. Goals

Given below are the important goals of organic farming:
1) A high level of productivity.
2) Compatibility of cultivation with the natural cycles of the production system.
3) Maintaining and increasing the long-term fertility and biological activity of the soil.
4) Maintaining and increasing the natural diversity and agro-biodiversity.
5) Maximum use of renewable resources.
6) Creating a harmonic balance between crops and animal husbandry.
7) Creating such conditions for the animals that correspond to their natural behaviour.
8) Protecting and learning indigenous knowledge and traditional management systems.

2.3.3. Steps

Organic farming involves the following steps:
1) Conversion of land from conventional management to organic management.
2) Management of the entire surrounding system to ensure biodiversity and sustainability of the system.
3) Crop production by using alternative sources of nutrients (such as crop rotation, residue management, organic manures, and biological inputs).
4) Management of weeds and pests by better management practices, physical and cultural means, and biological control system.
5) Maintenance of livestock along with organic concept and make them an integral part of the entire system.

2.3.4. Principles

Given below are the four major principles of organic farming:
1) **Principle of Health:** Health is the wholeness and integrity of living systems. Organic farming should sustain and enhance the health of soil, plant, animal, human, and planet as a whole. Healthy soils yield healthy crops that nurture the health of animals and humans. Organic farming, whether in farming, processing, distribution, or consumption, sustains and enhances the health of ecosystem and organisms ranging from the smallest in the soil to human beings.

2) **Principle of Ecology:** Organic farming should be based on living ecological systems and cycles, should work with them and sustain them. Production should be based on ecological processes and recycling. Nourishment and well-being are achieved through the ecology of specific p roduction environment. Organic management should be adapted to local conditions, ecology, culture , and scale. Use of inputs should be avoided by reusing, recycling and efficient management of materials and energy to maintain and improve environmental quali ty and conserve resources. It should attain ecological balance by designing farming systems, establishing habitats, and maintaining genetic and agricultural diversity.

3) **Principle of Fairness:** Organic farming should be based on relationships that ensure fair ness with regard to common environment and life opportunities. This principle states that those involved in organic farming should conduct human relationships to ensure fairness at all levels and to all farmers, workers, processors, distributors, traders, and consumers.

   This is done with the goal of producing a sufficient supply of good quality food and other products. Natural and environmental resources used for production and consumption should be managed such that it is socially and ecologically fair an d trusted for future generations. Fairness requires open and equitable systems of production, distribution and trade accounting for real environmental and social costs.

4) **Principle of Care:** This principle states that precaution and responsibility are the key concerns in management, development and technology choices in organic agriculture. Organic farming should be managed in a cautionary and responsible way to protect the health and well -being of current and future generations and the environment. It is a li ving and dynamic system that responds to internal and external demands and conditions.

2.3.5. Advantages

Organic farming has the following advantages:

1) **Nutritional, Poison-Free and Tasty Food:** The nutritional value of food is a function of its vitamin and minera l content. The mineral content of organically-grown food is more than that of the food grown by modern conventional methods. The consumers of organic food are benefitted as it is not contaminated with health -harming chemicals such as pesticides, fungicides, and herbicides.

2) **Lower Growing Cost:** The economics of organic farming is characterised by increasing profits by reducing water use, lowering expenses on fertiliser and energy, and increasing top soil retention. The increased demand for organic produce makes organic farming a profitable option for farmers.

3) **Enhances Soil Nourishment:** Organic farming effectively addresses soil management. Damaged, saline and eroded soil feed on micronutrients via crop rotation, inter-cropping techniques, and extensive use of green manure. Since use of chemicals is avoided in organic farming, the microbes which increase soil nourishment are not killed.

Biodynamic farms have better soil quality, greater organic matter content and microbial activity, better soil structure, low er bulk density, easier penetrability, and thicker top soil agricultural productivity due to the use of soil fertility techniques, compost application, and introduction of leguminous plants into the crop sequence.

4) **More Energy Efficiency:** Growing organic ri ce was much more energy efficient than the conventional method. Organic farming in comparison to conventional chemical -based agriculture reduces energy requirements for production systems by 25-50%.

5) **Carbon Sequestration:** German organic farms annually seque ster 402kg Carbon/ha, while conventional farms had losses of 202kg.

6) **Less Water Pollution:** In conventional farms, 60% more nitrates are leached into groundwater in 5 years.

7) **Environment-Friendly Practices:** Green pesticides (**e.g.,** neem, compost tea, and spino sad) are environment -friendly and non -toxic. They help in identifying and removing diseased and dying plants, thus, increase the crop defence systems. The biodiversity of organic farms increases resilience to climate change and weather unpredictability. Or ganic agriculture reduces erosion caused by wind, water, and overgrazing at a rate of 10 million hectares annually.

8) **Organic Farming as a Source of Productivity for Labours:** In rural areas, agriculture is the main employer, and wage labour provides an impor tant income source for the poor. Thus organic farming, being labour intensive, creates employment and improves returns on labour, fair wages and non - exploitive working conditions. New sources of livings, especially once market opportunities are exploited, in turn rejuvenate rural economies and enable their incorporation into national economies.

2.3.6. Disadvantages

Organic farming has the following disadvantages:

1) **Lower Productivity:** The yield or productivity of an organic farm is not as much as that of a conventi onal or industrialised farm. A survey and study conducted by the UN Environmental Programme in 2008 established that organic farming methods, compared to conventional farming techniques, result in small yields in developing areas. However, this point is controversial as the productivity and soil quality of an industrialised farm rapidly decreases with time.

2) **Requires Skill:** An organic farmer should have a greater understanding of the crops and should closely watch them as pesticides or chemical fertilisers cannot be used as quick fixes. Sometimes it is difficult to meet all the strenuous requirements and experience required for organic farming.

3) **Time-Consuming:** Time and energy are required in significant amounts to execute the detailed techniques of organic farming. If a farmer fails to comply with any of these requirements, he loses his certification that can be regained

only after 3 years, thus making it more time-consuming. Organic farming increases soil fertility by composting and use of organic fertilisers and mulch. As with control by botanicals, horticultural oils, and insecticidal soaps, organic fertilisers need several applications to obtain the desired results.

4) **More Labour-Intensive:** Organic farming can be more labour-intensive as the biological, cultural and mechanical responses to production challenges are considered. It focuses on plant and soil health through proper aeration, drainage, fertility, structuring, and watering. Organic farming methods are not as established and prevalent as conventional methods. So, organic control by botanicals (such as pyrethrin) can be more expensive than conventional controls by the longer established, more available, and wider ranging artificial, commercial, and synthetic chemical pesticides.

2.3.7. Organic Farming Practices

Organic farming methods involve the following:

1) **Crop Rotation:** This involves **planting different crop species on the same field**, but **at different times** and **locations**. Rotating crops improve the soil structure. This practice reduces erosion of soil and build-up of pests, promotes soil fertility, and spreads out financial risk if a crop fails. Crop rotation increases soil's microbial activity, which in turn increases nutrient availability (including phosphorus). Yields with the practice of crop rotation are 10-15% higher than with monoculture.

2) **Cover Cropping:** In this practice, a cover crop is grown to **provide a cover for the soil**. This crop can be annual, biennial, or perennial herbaceous plants grown in a pure or mixed stand throughout the year. The practice of cover cropping loosens the compacted soil through root growth, improves water filtration, prevents soil erosion by wind and water, suppresses weeds by keeping the sun from reaching weed seeds, and reduces insects, pests and diseases.

3) **Green Manure:** It is a **cover crop that is tilled into the soil while still green**. It adds organic matter and nutrients to the soil. When a green plant is incorporated into the soil, it contains high amounts of nitrogen and moisture, and becomes a food source for soil micro organisms and earthworms. Green manure also suppresses weeds and soil-borne diseases.

4) **Animal Manures:** Manures can be applied to the field in either a raw or composted form. Raw manure provides nutrients and organic matter to the soil, and encourages biological processes in the soil. Composted manure is the most suitable since the heat generated during composting kills most of the contaminants, reduces or completely eliminates the risk of pathogens related to food safety. Composted manure also reduces biomass volume, thus facilitates transportation.

5) **Weed Management:** This involves crop rotations, removing weeds before seed set and reproduction, and not allowing weeds on the farm. Mulches prevent light from reaching the weeds or decrease the amount or quality of light reaching the weed seeds or leaves, thus suppress them. Certain mulches with naturally occurring chemicals prevent the germination of weed seeds.

6) **Pest Management:** Maintaining an ecological balance is the major goal under the organic system. Ecol ogical balance is maintained by using beneficial insects, predatory or parasitic mites, and spiders to keep pest population down. Beneficial insects include lady beetles, various wasps, and some nematodes that are used for insect control. In case of severe infestations, farmers use non -toxic pesticides, such as soaps, pheromones (used as bait for traps and to disrupt mating cycles), botanical plant extracts (like neem, and sulphur) for control of foliar diseases, and mites (in rare cases). These non-toxic pesticides are not harmful as conventional pesticides.

7) **Livestock Management:** Livestock feed should be organically produced (including pasture and forage), contain no urea or manure, and have no animal slaughtered by -products. It should provide suitable hou sing, pasture conditions, and sanitation practices to animals to reduce the occurrence and spread of diseases and parasites. It should regularly move animals to fresh pasture and use other preventative methods instead of routinely dosing the animals with drugs to control parasite in farm animals. Livestock may not be treated with antibiotics and any animal drugs used to promote growth, including hormones. Animals should be provided with access to outdoors, shade, shelter, exercise areas, fresh air, and dire ct sunlight based on the type of animal, stage of production, climate, and environment.

2.4. PEST AND PEST MANAGEMENT IN MEDICINAL PLANTS

2.4.1. Introduction

An **undesired plant** or **animal species** is termed as a **pest**; and chemicals obtained from synthetic and natural sources used against these pests in small concentrations are **pesticides**.

2.4.2. Types of Pests

Medicinal plants are infested by fungi, viruses, weeds, insects, and some non -insect pests like rodents. Some **examples** of pests are discussed below:

1) **Fungi:** The **examples** of different types of fungi attacking medicinal plants are:
   i) *Ascochyta atropae* forms greyish -white irregular spots, which further cause **leaf necrosis**.
   ii) *Cercospora atropae* causes **leaf-spot** in which round to angular brown spots having chestnut coloured m argins are formed on both sides of the leaves.
   iii) *Phytophthora nicotianae* causes **phytophthora root -rot**, which is a dreadful disease occurring in belladonna and other plants. In this disease, dropping of young leaves and branches, yellowing of older leaves, a nd drying of whole apical portion occurs.
   iv) *Fusarium solanii* and *Pythium butleri* together causes damping off in young seedlings. They mainly affect the isolated branches of the roots of older plants.

v) *Phytophthora erythroseptica* causes **phytophthora rot disease** in which the roots turn black. It also causes damping off in young seedlings and wilt in matured plants.

vi) *Pythium spinosum* (pythium rhizome rot), *Curvularia prasadii* (leaf blight), *Colletotrichum fuscum* (anthracnose) on digitalis, *Septoria digitalis* and *Phyllosticta digitalis* (leaf spot), and *Ascochyta kashmeriana* (leaf spot) are some other pathogenic fungi which cause diseases by attacking the medicinal and aromatic plants.

2) **Viruses:** The **examples** of different types of viruses attacking medicinal plants are:

i) **Tobacco mosaic virus**, **cucumber mosaic virus**, and **tobacco ring spot virus** attack digitalis and a strain of cucumber mosaic virus attack hyoscyamus. These viruses cause necrosis of leaves, petioles, and stem of different plants belonging to family Solanaceae.

ii) Viruses cause disease symptoms on rauwolfia, tobacco, datura, vinca, and eucalyptus.

iii) Yellow vein mosaic, graft transmissible virus, distortion mosaic, rugose leaf curl, and *Ruga tabaci* are other viruses attacking the medicinal plants.

3) **Insects:** Total number of insect species in the world is larger than the total number of species of all other life forms. Plants should be provided protection against insects which cause a drastic problem. The **examples** of different types of insects attacking medicinal plants are:

i) *Diaphania nilagirica, Indomia cretaceus, Plantia viridicolis,* and various beetles attack rauwolfia.

ii) *Papilio machaon* and *Hyadaphis coriandri* attack dill.

iii) *Gonocephalum* species and *Agrotis flammatra* cause loss of belladonna leaves.

iv) Caterpillar, lepidopterus larvae, cutworms, termites, weevil, Hessian fly, aphids, pyrilla, grass-hoppers, locusts, spiders, ticks, mites, etc. are other insects damaging the plants.

4) **Weeds:** These undesired plants are dreadful pests because the loss caused by them is much more than the combined loss caused by other pests and diseases. If weeds are not controlled, problems like loss of nutrients, water, light and space, increase in labour and equipment cost, low product quality, problems in marketability, enhanced chances of attacks by bacteria, fungi, viruses, and insects arises. The **examples** of different types of weeds which grow along with the plants and attack them are:

i) Some allergy-causing, weeds, **e.g.**, ragweed, mexican tea, yellow dock, parthenium, etc. cause hay fever.

ii) Corn cockle contains cyanophore glycosides and the seeds of this plant have fatal effects.

iii) Poison ivy, western poison oak, varnish tree, poison sumac, etc. cause dermatitis.

iv) Datura and monospermous species, etc. are poisonous plants which grow as weeds.

5) **Non-Insect Pests:** These pests are of **two types**:
   i) **Vertebrates:** Rats, monkeys, birds, rabbits , hares, squirrels, antelopes, deer, pigs, etc.
   ii) **Invertebrates:** Nematodes, crabs, snails, mites, and symphylids.

   The rodents with their sharp and gnawing incisor teeth cause a huge spoilage to stored crude drugs. Their faecal matter also contaminates the crude drugs extensively.

2.4.3. Pest Management

Control or management of an undesired animal or plant species is termed as **pest management**. Given below are the various **methods of pest management**:

1) Mechanical methods,
2) Agricultural methods,
3) Biological methods,
4) Chemical methods,
5) Environmental methods or integrated pest management programme,
6) Natural pest control agents, and
7) Biopesticides/bioinsecticides.

2.4.3.1. Mechanical Methods

Mechanical methods collect and destroy pests using different devices. **Hand-picking**, **pruning**, **burning**, and **trapping of pests** are some of the simple mechanical methods by which eggs, larvae, pupae, and adults of insects are collected and destroyed suitably. Concrete warehouses having metal reinforcement corners on window frames are prepared for protection against rodents, like rats. Devices for trapping rats and mouse can also be used. Flavoured attractants (prepared by mixing rose oil, anise oil, etc. with sawdust) are placed in funnel-shaped containers for trapping flying insects, which easily enter the trap but could not come out.

2.4.3.2. Agricultural Methods

Agricultural methods involve advanced techniques of plant breeding , which produce pest-resistant species by **genetic manipulations** . Hybrid varieties resistant to fungal and bacterial attack have also been produced by this technique. Systemic insecticides are also applied, which get absorbed through the roots and reach the leaves to distaste the foliage portion for insects.

2.4.3.3. Biological Methods

Biological methods involve combating the pests (insects especially) with other living organisms (often parasites). If properly designed, this pest control method proves to be effective, safe, and economic. Some female insects produce and release **sex pheromones** (a chemical substance which induces sexual response in male insects); **for example,** 7,8-epoxy-2-methyloctadecane from gypsy-moth can be used for controlling pests. Another approach involves using Australian lady beetle (ladybug) to eat the cottony cushion scale insect on citrus crop, rat terriers to eat rats, and various birds to eat the insect pests. The larger harmful insects are often destroyed by hatching the eggs of certain types of flies and wasps.

2.4.3.4. Chemical Methods

Chemical methods involve controlling pests by using che mical **pesticides**, **e.g.,** insecticides, fungicides, herbicides, and rodenticides. The chemical pesticides are sub-categorised into:

1) **Rodenticides:** Warfarin, strychnine, arsenic trioxide, thallium sulphate, red squill, etc.
2) **Insecticides:** DDT, gammexine, methoxychlor, parathion, malathion, sodium arsenate, pyrethroids, rotenoids, carbamates, etc.
3) **Acaricides (Miticides):** Tetradifon, chlorobenzilate, etc.
4) **Fungicides:** Bordeaux mixture, chlorophenols, antibiotics, quaternary ammonium compounds, etc.
5) **Herbicides:** 2,4-Dichlorophenoxy acetic acid, calcium arsenate, sulphuric acid, etc.

2.4.3.5. Environmental Methods or Integrated Pest Management Programme

Environmental methods are more effect ive in controlling pests. By using the multi-faceted control procedures selectively and carefully, resistance development, effects on non-target organisms, and environmental damage can be reduced. This technique of integrated control demands thorough knowl edge of ecological principles and of the life history and population dynamics of pests.

Altering the environmental conditions under which the pests are prevailing is another approach. It is brought about either by eradicating the food supply or by obstructing their life cycle. **For example,** mosquito larvae in water can be killed by spreading an oil layer.

2.4.3.6. Natural Pest Control Agents

The following natural agents are employed for controlling pests:

1) **Leaf T obacco:** The leaves of *Nicotiana tabacum* gives tobacco, which contains **nicotine** (a pyridine alkaloid, pale yellow coloured liquid, acrid burning in taste, having odour of pyridine, oily in nature, highly hygroscopic, turns brown when exposed to air or light , volatile with steam, and poisonous being a local irritant and paralyzent).

   Nicotine is an insecticide and fumigant. Being a contact poison, it is effectively used as a soap (i.e., as laurate, oleate, or naphthenate form). Soap solution of nicotine decom poses the sulphate into free alkaloid , which produces more toxic effects to the insects. Nicotine is also used as a stomach poison along with bentonite. 40% Nicotine sulphate solution (bl ack leaf 40) is toxic to aphids, and its toxicity increases on alkalising this solution.

2) **Pyrethrum Flowers:** These are dried flower heads of *Chrysanthemum cinerariaefolium* or *C. mars hallii* of Compositae family. 0.5% of total pyrethrins (pyrethrin I and pyrethrin II) constitute pyrethrum. Pyrethrum obtains its insecticidal property from **pyrethrins I and II** and **cinerins I and II**. These are four complex esters of chrysanthemum carboxylic acid and the

monomethyl ester of chrysanthemum dicarboxylic acid with pyrethrolones and cinerolones. The **pyrethroids** (or rethroids), like allethrin, furethrin, and cyclethrin, are synthetic compounds of structure similar to that of pyrethrins.

3) **Derris and Lonchocarpus:** The roots of several species of derris and lonchocarpus (of Leguminosae family) possess insecticidal activity. The powdered roots mixed with water or with organic solvents (like ethylene dichloride, trichloroethylene, or chlorobenzene) are sprayed over plant species. Extracts of **rotenone** prepared with oil and emulsifying agents and extracts dissolved in paraffin oil are effective household and cattle sprays. Rotenone decomposes on exposure. If large doses of it are inhaled or ingested, a number of oral mucous membrane problems, nausea, vomiting, muscle tremors, and tachypnoea develop.

4) **Ryania:** The roots and stems of *Ryania speciosa* contain 0.16 -0.2% of insecticidal alkaloids. **Ryanodine** (the chief alkaloid) is a complex ester having 1-pyrrole-carboxylic acid. This plant is used for controlling various lepidopterous larvae which attack fruits.

2.4.3.7. Biopesticides/Bioinsecticides

Biopesticides are naturally occurring substances of living organisms (natural enemies), their products (microbial products and phytochemicals) or by-products (semiochemicals) that can control pest by non-toxic mechanisms. They cover a wide range of microbial pesticides and biochemicals obtained from microorganisms and natural sources. Traditionally, biopesticides have been associated with the biological control and by implication, the manipulation of living organisms as indicated in **table 2.2**.

Table 2.2: Some Successful Experimental Uses of Bio-Pesticides against Various Diseases

Bioagents	Pathogens	Hosts (Crops)
1) *Trichoderma viride* and *T. harzianum*	*Macrophomina phaseolina*	Sunflower
2) *T. viride*	*Fusarium oxysporum f. sp. udum*	Pigeon pea
3) *T. harzianum*	*Phytophthoracapsici* and *Fusarium oxysporum f. sp. lycopersici*	Chilli and tomato
4) *Bacillus subtilis*	*Monilinia fructicola* and *M. laxa*	Peaches
5) *T. harzianum*	*Fusarium moniliforme*	Maize
6) *T. vride*	*Colletotrichum truncatum*	*In vitro*
7) *T. viride*	*Colletotrichum capsici*	Chilli
8) *T. viride*	*Phytophthora capsici*	Black pepper
9) *Tricihoderma spp.*	*Botrytis cinerea*	Tomato
10) *B. subtilis*	*Peronosclerospora sorghi*	Maize
11) *Trichoderma spp.*	*Rhizoctonia solani*	*In vitro*
12) *Pseudomonas aeruginosa*	*Sclerotinia sclerotiorum*	Tomato
13) *B. subtilis*	*Ralstonia solanacearum*	Tomato
14) *Streptomyces spp.*	*Xanthomonas oryzae pv. Oryzae*	Rice
15) *T. harzianum*	*Alternaria alternata*	Tobacco
16) *T. harzianum*	*Puccinia sorghi*	Rice
17) *T. viride*	*Colletotrichum capsici*	Chilli
18) *T. viride*	*Alternaria porri*	*In vitro*
19) *T. harzianum*	*Pyricularia oryzae*	Rice

Types

1) **Microbial Pesticides:** These pesticides consist of microorganisms (such as bacterium, virus, fungus, and protozoan) as active ingredients, and are used for the biological control of plant pathogens, pestiferous insects, and weed. The insect pathogenic bacterium, *Bacillus thuringiensis* (Bt), is the most commonly used microorganism in biopesticide development. This bacterium serves as an insecticide for most Lepidoptera, Coleoptera, and Diptera. It produces protein crystals or toxin during spore formation of the bacterium that can cause lysis of gut cells when consumed by specific or susceptible insects.
2) **Biochemical or Herbal Pesticides:** These pesticides are naturally occurring and are used for controlling pests through a non-toxic mechanism. Since it is difficult to evaluate whether a natural pesticide can control pests by a non-toxic mechanism, Environmental Protection Agency (EPA) has established a committee to determine whether or not a pesticide meets the specified standards for being a biochemical pesticide. Plants producing secondary metabolites are also considered as biopesticides.
3) **Plant-Incorporated-Protectants (PIPs):** PIPs are also known as **Genetically Modified Crops** (GMCs). They are biopesticidal substances produced by plants from genetic material added or incorporated into their genetic makeup. Use of Bt protein to develop PIP in genetic engineering process is a common **example**. Bt toxin is host-specific and can cause death within a period of 48 hours. It is safe for beneficial organisms, human, environment, and vertebrates.
4) **Semiochemicals:** These are chemical signals produced by an organism (usually insects), which causes a behavioural change in an individual of the same or different species. Insect pheromones are the most commonly used semiochemicals for crop protection. They serve as a signal to communicate with others in their species. They are synthesised for pest control by mating disruption, Lure-and-Kill systems, and mass trapping.

Mechanism of Action

Biopesticides act by any of the following mechanisms:

1) **Antibiosis:** This mechanism occurs when biopesticides interact with other microorganisms under the influence of specific microbial metabolite, volatile compounds, lytic enzymes, or other toxic substances. The microorganisms produce antibiotics, bacteriocin, volatile compounds, and metabolites.
2) **Competition:** In this mechanism, biopesticides aggressively compete to grow rapidly and colonise substrate to exclude pathogens.
3) **Hyperparasitism:** This mechanism is the lysis of the death by other microorganisms or direct parasitism. **For example,** *T. lignorum* parasitise the hyphae of *R. solani*, and therefore soil inoculation with Trichoderma spores control damping off disease in citrus seedlings.
4) **Synergism:** This mechanism is the ability of some bioagents to combine actions of hydrolytic enzymes and antibiotic secondary metabolites. **For example,** the effectiveness of *Trichoderma* spp. as a biocontrol agent and its fitness in the environment is the result of synergistic effects of antimicrobial compounds (like, pyrones, coumarins, etc.).

Formulations

Depending on the physical states (dry or liquid forms) of the biopesticide formulation, the active ingredients are produced by addition of stabilisers, synergists, spreads, stickers, surfactants, colouring agents, anti-freezing compounds, additional nutrients, dispersants, and melting agents (**table 2.3**). Biopesticides are generally formulated as dry formulations (for direct applications) and liquid formulations:

1) **Dry Formulations for Direct Applications**
   i) **Dustable Powders (DPs):** The concentration of active ingredients in dust formulations is usually 10%. These are formulated by sorption of active ingredient on finely ground, solid mineral powder (talc, clay, etc.) with particle size ranging from 50-100mm. The inert ingredients for dust formulations are UV protectants, adhesive materials (i.e., stickers) to enhance adsorption, and anticaking agents.

   ii) **Granules (GRs):** The concentration of active ingredients for granules is 2-20%. The ingredients are either coated outside the granule or are absorbed into the granules. The granules can be coated with resins or polymers for controlling the rate of effectiveness of active ingredients after application. Granules are mostly applied to control insects in soils, weeds, and nematodes for uptake by roots. Granules of coarse size particles (ranging from 100-600 microns) are made up of kaolin, silica, starch, polymers, groundnut plant residue, dry fertilisers, etc. Some granules release their active ingredients after getting exposed to soil moisture.

   iii) **Seed Dressing (SDs):** This biopesticide formulation is obtained by mixing powdered active ingredient carrier and accompanying inert so that the end product adheres to seed coats. Powders for seed dressing are applied by tumbling the seeds with the product designed to adhere to them. Colouring agents as a red pigment can be added as a safety marker for treated seeds.

   iv) **Wettable Powders (WPs):** These dry formulations are finely grounded and applied after making a suspension in water. They are obtained by blending active ingredients with melting and dispersing agents, synergists, surfactants, and inert fillers. Strict safety measures are taken because of their dustiness that can lead to serious health problems to manufacturers and during application. Wettable powders have long stability during storage, good miscibility with water, and can be applied with conventional spraying equipment.

   v) **Water Dispersible Granules (WDGs):** They are suspended in water before application. They are designed to overcome problems associated with WPs, to be dust-free, and have good storage stability.

2) **Liquid Formulations**
   i) **Emulsions:** These liquid formulations are mixed with water before application. They can be normal o/w emulsion or an inert w/o emulsion. Suitable emulsifiers should be chosen for stabilisation to avoid instability. In w/o emulsion, in which oil is in the external phase of the formulation, losses due to evaporation and spray drift are minimal.

ii) **Suspension Concentrates (SCs):** These liquid formulations are obtained by dispersing finely grounded, solid active ingredient in liquid phase (usually water). Agitation is required before application so that t he particles remain uniformly distributed because the solid particles are not dissolved in liquid phase. Particle size distribution is 1-10µm; and due to such small particle size, the active ingredients easily penetrate the plant tissues and also bioeffici ency is improved. Suspension concentrates are safer to the operator and environment also.

iii) **Suspo-Emulsions (SE s):** These highly demanding liquid formulations are a mixture of emulsion and suspension concentrate. A homogenous emulsion component should be pre pared with a particle suspension component so that the final product remains stable.

iv) **Oil Dispersions (OD s):** These liquid formulations are produced in the same ways as SCs. By proper selection of inert ingredients, instability problems can be avoided.

v) **Capsule Suspensions (CS s):** In these liquid formulations, the active ingredients are formulated in micro -encapsulated stable suspension that should be diluted with water before application. Capsules made from gelatin, starch, cellulose, and other polymers are used to encapsulate the bioagents. Thus, the bioagents are protected from harsh environmental conditions. Interfacial polymerisation principle is the most frequently applied encapsulation method to obtain smaller size and highly efficient formulations. Fungal biopesticides are prepared by this technique.

vi) **Ultra Low Volume Liquids (ULV s):** These liquid formulations need not to be diluted in water before application and have concentration of active ingredients. They can be easily transported and can be formula ted using a suspended biocontrol agent as an active ingredient.

Table 2.3: Some Biopesticide Formulations Available in Commercial Quantity

Product Name	Active Ingredients (Bioagents)	Targets
Antagon*	*Trichoderma viride*	*Rhizoctonia solani* and *Macrophomina phaseolina*
Biocon*	*T. viride*	Root and stem diseases of tea.
Bioderma*	*T. virid e and T. harzianum*	Pathogens of vegetables, pulse and cereals.
Defence-SF*	*T. viride*	Soil-borne diseases of crops.
Biogaurd*	*T. viride*	Soil-borne diseases of ve getables and pluses.
Biotok*	*Bacillus subtilis*	*Corticium invisum* and *C. theae*
Bisoheld	*Pseudomonas fluorescens*	Fungal pathogens of cereals , pulses and vegetables.
Regaila*	*Reynoutria sachalinensis*	*Botrytis sp.,* downy mildew, powdery mildew, Phytophthora infestans.
Contans WG*	*Coniothyrium minitans*	*Sclerotia spp.*
Serenade ASO*	*Bacillus subtilis QST713*	*Botrytis spp.*
Nema-Q**	*Quillaja saponaria*	Plant parasitic nematodes
MeleCon WG**	*Paecilomyces lilacinus*	Plant parasitic nematodes in soil.

Pasteuria usage**	*Pasteuria usage*	Sting nematodes
Curbit ***	Zucchini yellow mosaic virus, weak strain.	Zucchini yellow mosaic virus
Chontrol****	*Chondrostereum purpureum*	Cut stumps of hardwoods trees shrubs
DeVine****	*Phytophthora palmivora*	*Morrenia odorata*
Biomite*****	Citronellol	Tetranychid mites
Exosex CM******	(E,E)-8,10 dodecadienlol	Codling moth
Cyd-X[7]	Cydiapomonella GV	Codling moth
Azatin XL[7]	Azadirachtin	Aphids, scale, thrips, weevil, and leafhoppers

* = Fungicides, ** = Nematicides, *** = Antiviral, **** = Herbicides, ***** = Attractants, ****** = Semiochemicals, and [7] = Insecticides.

Applications

Pests can be effectively controlled by selecting suitable application techniques/methods and an appropriate time and/or frequency of biopesticides application. Given below are some methods of biopesticides applications:

1) **Seed Treatment:** This means application of biopesticides on seeds. This method is the most effective. Powder formulations are applied on seeds by tumbling them with the product designed to adhere to the seeds.

2) **Foliar Application:** This means application of biopesticides on surface of leaves in the form of sprays. **For example,** application of *B. subtilis* to bean leaves reduce the occurrence of bean rust caused by *Uromyce sphaseoli.*

3) **Seedling Dipping:** In this method, roots of the seedlings are dipped in biopesticide suspensions for a few minutes or hours before transplanting. **For example,** *Trichoderma* spp. are applied in this way.

Advantages

1) Biopesticides are inherently less harmful or toxic and cause less environmental load or pollution.
2) They are designed for a specific pest, or a few target pests as opposed to chemical having a broad spectrum of activity.
3) Cost of their development is significantly lower tha n those of synthetic chemical pesticides.
4) Their nature of control is preventive (not curative) and their effects on flower is less.

Disadvantages

1) Due to their high specificity, it is necessary to identify the exact target pest or pathogen.
2) Due to their slow speed of action, they are often unsuitable if there is an immediate pest outbreak that becomes a threat to crops.
3) They are not suitable for a stand -alone treatment, and should have to be with a compatible method for high efficacy.
4) Living organisms evolve and increase their resistance to biological, chemical, physical and any other form of control.

2.5. SUMMARY

The details given in the chapter can be summarised as follows:

1) Biodynamic farming was introduced by **Rudolf Steiner**.
2) The term **biodynamic** has been derived from the Greek term ***bios*** meaning **life** and ***dynamic*** meaning **energy**.
3) **Biodynamic agriculture** is an organic farming method that treats farm as an individual organism, balances the holistic development and interrelationshi p of the soil, plants, and animals as a closed self-nourishing system.
4) **Steiner** recommended the use of **eight different preparations** in biodynamic agriculture. These prepared substances are numbered 500 to 507; the first two are used for preparing fields and the remaining six are used for making compost.
5) **Preparation 501 (horn silica)** is crushed powdered quartz prepared by stuffing in a cow horn, burying into the ground in spring, and taking out in autumn.
6) **Rahu** is the lunar node in ascending period of moon, and is not suitable for agricultural activities.
7) **Ketu** is the lunar node in descending period of moon, and is not suitable for agricultural activities.
8) The USDA study team defined **organic farming** as "a system which avoids or excludes the use of synthetic inputs (such as fertilisers, pesticides, hormones, feed additives, etc.) and to the maximum extent feasible rely on crop rotations, crop residues, animal manures; off -farm organic waste, mineral grade rock additives and biological system of nutrient mobilisation and plant protection".
9) FAO defined **organic farming** as "a unique production management system that promotes and enhances agro-ecosystem health, including biodiversity, biological cycles and soil biological activity, by using on -farm agronomic, biological and mechanical methods in exclusion of all synthetic off-farm inputs".
10) The term **organic farming** was first used by **Lord Northbourne**.
11) **Crop rotation** involves planting different crop species on the same field, but at different times and locations.
12) In **cover cropping**, a cover crop is grown to provide a cover for the soil.
13) **Green manure** is a cover crop that is tilled into the soil while still green.
14) **Weed management** involves crop rotations, removing weeds before seed set and reproduction, and not allowing weeds on the farm.
15) An **undesired plant** or **animal species** is termed as a **pest**; and chemicals obtained from synthetic and natural sources used against these pests in small concentrations are **pesticides**.
16) *Ascochyta atropae* forms greyish-white irregular spots, which further cause **leaf necrosis**.
17) *Cercospora atropae* causes **leaf-spot** in which round to angular brown spots having chestnut coloured margins are formed on both sides of the leaves.
18) *Phytophthora nicotianae* causes **phytophthora root -rot**, which is a dreadful disease occurring in belladonna and other plants.
19) *Fusarium solanii* and *Pythium butleri* together causes damping off in young seedlings.
20) *Phytophthora erythroseptica* causes **phytophthora rot disease** in which the roots turn black.
21) **Tobacco mosaic virus**, **cucumber mosaic virus**, and **tobacco ring spot virus** attack digitalis and a strain of cucumber mosaic virus attack hyoscyamus.

22) *Diaphania nilagirica*, *Indomia cretaceus*, *Plantia viridicolis* and various beetles attack rauwolfia.
23) *Papilio machaon* and *Hyadaphis coriandri* attack dill.
24) *Gonocephalum* species and *Agrotis flammatra* cause loss of belladonna leaves.
25) Control or management of an undesired animal or plant species is termed **pest management**.
26) Agricultural methods involve advanced technique s of plant breeding, which produces pest-resistant species by **genetic manipulations**.
27) Pyrethrum obtains its insecticidal property from **pyrethrins I and II** and **cinerins I and II**.
28) **Ryanodine** is a complex ester h aving 1 -pyrrole-carboxylic acid, used for controlling various lepidopterous larvae which attack fruits.
29) **Biopesticides** are naturally occurring substances of living organisms (natural enemies), their products (microbial products and phytochemicals) or by-products (semiochemicals) that can control pest by non-toxic mechanisms.
30) **Microbial pesticides** consist of microorganisms (such as bacterium, virus, fungus, and protozoan) as active ingredients, and are used for the biological control of plant pathogens, pestiferous insects, and weed.
31) The insect pathogeni c bacterium, *Bacillus thuringiensis* (Bt), is the most commonly used microorganism in biopesticide development.
32) **Biochemical or herbal pesticides** are naturally occurring and are used for controlling pests through a non-toxic mechanism.
33) **Plant-Incorporated-Protectants (PIPs),** also known as **Genetically Modified Crops** (GMCs), are biopesticidal substances produced by plants from genetic material added or incorporated into their genetic makeup.
34) **Semiochemicals** are chemical signals produced by an organism which causes a behavioural change in an individual of the same or different species.
35) **Antibiosis** mechanism occurs when biopesticides interact with other microorganisms under the influence of specific microbial metabolite, volatile compounds, lytic enzymes, or other toxic substances.
36) In **competition** mechanism, biopesticides aggressively compete to grow rapidly and colonise substrate to exclude pathogens.
37) **Hyperparasitism** mechanism is the lysis of the death by other microorganisms or direct parasitism.
38) **Synergism** mechanism is the ability of some bioagents to combine actions of hydrolytic enzymes and antibiotic secondary metabolites.

2.6. EXERCISE

2.6.1. True or False

1) Biodynamic farming was introduced by Lord Northbourne
2) Preparation 503 is crushed powdered quartz prepared by st uffing in a cow horn, burying into the ground in spring, and taking out in autumn.
3) Green manure is a cover crop that is tilled into the soil while still green.
4) *Phytophthora erythroseptica* causes phytophthora rot disease in which the roots turn black.
5) *Papilio machaon* and *Hyadaphis coriandri* attack digitalis.
6) Antibiosis is the ability of some bioagents to combine actions of hydrolytic enzymes and antibiotic secondary metabolites.
7) Biopesticides are used for controlling pests through a non-toxic mechanism.

2.6.2. Fill in the Blanks

8) The term biodynamic has been derived from the Greek term _____ meaning life and _____ meaning energy.
9) In _____, a cover crop is grown to provide a cover for the soil.
10) _____ forms greyish-white irregular spots, which further cause leaf necrosis.
11) Plant-incorporated-protectants are also known as _____.
12) _____ are chemical signals produced by an organism which causes a behavioural change in an individual of the same or different species.
13) _____ is the lysis of the death by other microorganisms or direct parasitism.
14) _____ is used for controlling various lepidopterous larvae which attack fruits.

Answers

1) False 2) False 3) True
4) True 5) False 6) False
7) False 8) *bios* and *dynamic* 9) Cover cropping
10) *Ascochyta atropae* 11) Genetically modified crops 12) Semiochemicals
13) Hyperparasitism 14) Ryanodine

2.6.3. Very Short Answer Type Questions

1) Define biodynamic agriculture.
2) What are the characteristics of biodynamic agriculture?
3) Give the advantages of biodynamic agriculture.
4) What do you understand by organic farming?
5) Enlist the goals of organic farming.
6) Define pests and pesticides.
7) Give two examples each of insect and non-insect pests.
8) Name any four chemical used for pest management.

2.6.4. Short Answer Type Questions

1) Discuss the principles of biodynamics.
2) Write about the different biodynamic preparations.
3) Explain the principles of organic farming.
4) Discuss the merits of organic farming.
5) Write about different types of pests.
6) Write a short note on mechanical and biological methods of pest management.
7) What are the different natural pest control agents?

2.6.5. Long Answer Type Questions

1) Discuss briefly about biodynamic agriculture.
2) Write an exhaustive note on organic farming.
3) Give a brief review on different pest management techniques.
4) Briefly discuss about the biopesticides or bioinsecticides used for pest management.
5) Write about the different good agricultural practices in cultivation of medicinal plants.

CHAPTER 3

Indian Systems of Medicine

3.1. INDIAN SYSTEMS OF MEDICINE

3.1.1. Introduction

Many civilisations in different parts of the world were developed and they perished; however the medicine systems developed by them became popular as **alternative systems of medicine** and are still in practice. The modern allopathic system has been considered worldwide the principal system of medicine; thus all the other medicine systems existing in different parts of the world are its alternatives. The philosophy and basic principles of these alternative medicine systems are different from each other; they have served the humankind by treatment and management of diseases and by maintaining good health.

These alternative systems of medicines are referred to as **traditional systems of medicines**, which are still in use by about 80% of the world population. The traditional Chinese, Unani, Ayurvedic, Amchi, and Homoeopathy medicine systems in ancient times were practiced only in China, Greece, India, Tibet, and Germany, respectively; but at the present time worldwide population rely on them.

The major systems of medicines that are used alternatively are as follows:

1) Ayurvedic system,
2) Unani system,
3) Siddha system, and
4) Homeopathic system.

3.1.2. Ayurveda System of Medicine

Ayurvedic medicine system was established by the Hindus in India several thousand years ago. The Vedic period started with the Aryans. The **four holy books** (in Sanskrit) written with divine inspiration were included in the **Vedas** (meaning **wisdom**). These Vedas were initially conveyed verbally to the students by their teachers. But during the period of 2500-1500 B.C., the Vedas were available in written forms on birch bark. Later, they were written on papers.

Rig Veda (the oldest Veda) has drugs and diseases mentioned in it. **Atharva Veda** (the fourth Veda) has ideologies for maintaining health and the medicinal effects of health mentioned in it.

3.1.2.1. History

Indian medicine is one of the oldest organised medicine systems, thus has a long history. Given below are some historical views about Ayurveda medicine system:

1) Its most primitive concepts are available as sacred writings in the **Vedas**, especially in the metrical passages of the Atharva Veda, which dates back to 2nd millennium B.C.

2) **Dhanvantari** was idolised as the **God of Medici ne** as he received the medicine system from **Brahma**. Later his status started to decline, until when he was credited with having been an earthly king.
3) Knowledge in ancient times was transmitted verbally in **Sanskrit**. It is the Vedic language of 2000-500 B.C. A dissertation named **Sushruta Samhita** carries the most authentic collection of teachings and work of **Dhanvantari**. This treatise has 184 chapters and 1,120 illnesses, 700 medicinal plants, 64 preparations from mineral sources, and 57 preparations from anim al sources described in it.
4) **Sushruta** (the physician) was the first one to perform **cataract surgery** in the 1st millennium B.C. using **jabamukhi salaka** (a curved needle used for loosening the lens and pushing the cataract out of the vision field). After surgery, he used to soak the eye with warm butter and then bandage it.
5) **Charaka Samhita**, attributed to Charaka is another work of Ayurveda of ancient time.
6) **Bower Manuscript** is the most basic persisting written material which dates back to the 4th century A.D. Thi s book contains the works of Sushruta, description of Indian medicine and its concepts in Central Asia; thus is of special interest to the historians.
7) **Vagbhata** (son of a senior doctor, **Simhagupta**) also compiled his works on traditional medicine.
8) Early Ayurveda had separate schools for physicians and surgeons. **Agnivesh** (a student of the sage, **Bharadwaja**) wrote the text **Agnivesh tantra** which influenced the writings of Ayurveda.
9) **Fa Hsien** (the Chinese traveller) wrote about the health care system of Gupta Empire (320-550). He also gave a description on the institutional approach of Indian medicine. This is still available in the works of **Charaka**, who mentioned a clinic and its equipment.
10) **Madhava**, **Sarngadhara**, and **Bhavamisra** also compiled their works on Indian medicine.
11) During the **Abbasid Caliphate**, the medical works of **Sushruta** and **Charaka** were translated in Arabic language. These Arabic works were transferred to Europe through intermediaries.
12) The Branca family of **Sicily** and **Gaspare Tagliacozzi** (Bologna) in Italy got acquainted with the techniques of **Sushruta**.
13) British physicians moved to India to see how rhinoplasty was performed by native methods, and the reports on Indian rhinoplasty were published in **1794** in the **Gentleman's Magazine**.
14) **Joseph Constantine Carpue** lived in India for 20 years and studied local plastic surgery methods; and finally performed the first major surgery in **1815** in the western world.

3.1.2.2. Basic Principles Involved

The development of Ayurvedic medicine system is based on the following **5 pharmacological principles of a drug**, i.e., **Panchsheel**:

1) **Rasa:** It denotes the drug's taste (i.e., **Dravya**), action, and properties. In the table below, **6 types of rasa** are enlisted:

Sweet	Solid + Liquid	Pitta ↑ and Kapha ↓
Sour	Solid + Energy	Pitta ↑
Saline	Liquid + Energy	Kapha and Pitta ↑
Pungent	Air + Energy	Vata ↑
Bitter	Air + Space	Vata Pitta ↑
Astringent	Air + Solid	Vata ↑

2) **Guna:** It denotes the drug's physical properties. In total **2 pairs of guna** are available, and each pair has opposite activity. In th e table below, **10 types of guna** are enlisted:

Guru (Heavy)	**Laghu** (Light)
Sukshma (Subtle)	**Sthula** (Gross)
Sthira (Stable)	**Sara** (Unstable)
Snigdha (Unctuous)	**Rooksha** (Ununctuous)
Sandra (Dense)	**Dense** (Liquid)
Sheetal (Cold)	**Ushna** (Hot)
Manda (Dull)	**Tikshna** (Sharp)
Mridu (Soft)	**Kathina** (Hard)
Visuda (Non-slime)	**Picula** (Slime)
Slakshan (Smooth)	**Khara** (Rough)

3) **Virya:** It denotes the drug's potency and shows two intrinsic properties, i.e., **Sheeta Virya** (kapha group) and **Ushna Virya** (pitta group).

4) **Vipaka:** Also known as **nishthapak**, it denotes the end product of digestion. It is different from the **awasthapak prapk** (the stage of initial transformation in digestion). The **3 types of vipaka** which influence **kapha**, **pitta**, and **vata** are **madhur**, **amla**, and **katu**, respectively.

5) **Prabhava:** It denotes the drug's power. A drug's rasa, guna, virya, and vipaka may be the same, but its prabhava is always different because of its specificity in chemical composition and site of action.

Five Elements

The **Sankhya theory** of cosmology (an ancient theory on which Ayurveda is based) stated that the world is made up of a combination of different proportions of the following **5 elements**, i.e., the **Panchamahabhuta**:

1) Akasha (space), 2) Vayu (air), 3) Tejas or Agni (fire),
4) Apa or Jala (water), and 5) Prithvi (earth).

Some authorities believed that the early concept of the 5 elements which the Europeans gave, originated from the Ayurvedic medicine system. When a human body (a complex and a multicellular organism) is taken as an **example**, the 5 elements signify the following:

1) **Akasha:** It denotes the spaces within the body, i.e., mouth, nostrils, abdomen, etc.
2) **Vayu:** It denotes the muscular movement.
3) **Tejas or Agni:** It denotes the functions of enzymes, i.e., intelligence, digestion, and metabolism.
4) **Apa or Jala:** It denotes the body fluids, i.e., plasma, saliva, and digestive juices.
5) **Prithvi:** It denotes the body structure, i.e., bones, teeth, flesh, and hair.

Thus, it is concluded that in Ayurvedic medicine system, the base of all diagnosis and treatment pu rpose is the **Panchamahabhutas**. The physicians also gave it importance and considered it for successful treatment of the body and mind disorders.

Doshas

It is believed that all the processes occurring within a body are governed by a balance of the **3 types** of doshas. The dosha which dominates a person's behaviour and body is called his **constitution type**, having particular strengths and susceptibilities. The **3 types of doshas** are discussed below:

1) **Vata:** It is composed of **air** and **space**. All the movements in mind and body are controlled by it, thus should be maintained in a good balance. Worries, insomnia, cramps, and constipation are the result of too much vata. It also controls blood flow, waste elimination, breathing, and movement of thoughts across the mind. It activates the nervous system, hearing, and speech, and expresses them in the form of enthusiasm and creativity. Vata also controls pitta and kapha (other two principles), and is the first cause of disease.

2) **Pitta:** It is composed of **fire** and **water**. All heat, metabolism, and transformation within the mind and body are controlled by pitta. It controls food digestion, metabolism of sensory perceptions, and judgement between right and wrong. It should also be maintained in a good bala nce. Anger, criticism, ulcers, rashes, and thinning hair result from too much pitta.

3) **Kapha:** It is composed of **earth** and **water**. It cements the elements in the body, providing the material for physical structure. It maintains resistance of the body. It cause s joint lubrication, provides moisture to the skin, helps in wound healing, fills the spaces in body, provides biological strength, vigour and stability, supports memory retention, provides energy to heart and lungs, and maintains immunity. Kapha also cont rols the emotions of attachment, greed, and envy. It is also expressed in tendencies toward calmness, forgiveness, and love. Lethargy, weight gain, congestion, and allergies result due to too much kapha.

Ayurveda medicine system considers the states of mi nd as well as the body in its diagnosis and treatment. Ayurveda believed in the fact that foreign agents and small organisms cause many illnesses, which may require aggressive intervention.

3.1.2.3. Diagnosis Process

Imbalance that occurs in doshas and their progression towards a disease is termed **Samprapti** (pathogenesis). A complete knowledge related to diseases help in their early detection before they progress in other stages.

Therefore, Ayurvedic medicine system gave a description on **Kriya** (action) **Kal** (time) which is a diagnostic process of 6 stages. An individual having sound knowledge about **Sanchaya** (various stages of pathogenesis accumulation), **Prakopa** (provocation), **Prasara** (spread or migration), **Sthana Samshaya** (deposition or augmentation), **Vyakti** (manifestation), and **Bheda** (differentiation) is qualified to be a physician.

3.1.2.4. Stages of Pathogenesis

Pathogenesis is divided into the following **6 stages**:

Stage One: Accumulation (Sanchaya)

1) Weak digestive power and too much dosha are responsible for this condition.
2) Toxins (ama) produced by improper digestion accumulate in the GIT.
3) Toxins produced due to an imbalance in kapha accumulate in the stomach, those produced due to an imbalance in pitta accumulate in small intestine, and those produced due to an imbalance in vata accumulate in the colon.
4) Presence of one of these toxins causes mild and ill-defined symptoms.
5) The cause should not be ignored or suppressed, but should be identified and removed.
6) Cause dislikes similar things and attracts to opposites.

Stage Two: Provocation (Prakopa)

1) The accumulated, stagnant doshas get excited by factors like ahara, vihara, and seasons.
2) The toxins accumulate in such amount that they get provoked in the production site in the GIT.

Stage Three: Spread or Migration (Prasara)

In th is stage, the toxins accumulated in GIT start overflowing. Spontaneous Prashama (remission) occurs due to seasonal changes; Sanchaya of pitta occurs in the rainy season, Prakopa in fall, and Prasara in early winter. Based on the excitation degree, the toxins may even pass the stages of Prashama or Prasara.

Stage Four: Deposition or Augmentation (Sthana Samshaya)

1) The toxins overflowing migrate and settle in localised, weak or defective dhatus, thus causing malfunction and structural damage.
2) Now specific deg enerating diseases and susceptibilities to serious infections start occurring.

Stage Five: Symptom Manifestation (Vyakti)

1) Differentiated symptoms start appearing from the location.
2) Manifested symptoms are observed by modern medicine to identify and diagnose the disease.

Stage Six: Complications or Differentiation (Bheda)

1) The disease which took years or even decades to reach the final stage becomes chronic.
2) The appearingsymptoms offer detailed understanding of the nature of a disease.
3) Complications may occur, giving rise to other diseases.

3.1.2.5. Qualities of Ayurvedic System

The principle of Ayurveda is knowledge and awareness of the qualities of nature called **gurvadi gunah** . If a person understands the qualities inherent in environment, foodstuffs, activities, etc., he/she can gain an appreciation of their effects on the individual constitution through the principle of similarities (i.e., similarities cause increase while dissimilarities cause decrease). Thus, the hot qualities in an environment or diet increase the hot qualities in body.

The gurvadi gunah are listed in **Vagbhata's Astanga Hrdayam** as follows:
1) **Guru** (heavy) – **Laghu** (light),
2) **Manda** (slow) – **Tikshna** (quick, sharp),
3) **Hima** (cold) – **Ushna** (hot),
4) **Snigdha** (unctuous) – **Ruksha** (dry),
5) **Slakshna** (smooth) – **Khara** (rough),
6) **Sandra** (solid) – **Drava** (liquid),
7) **Mrdu** (soft) – **Kathina** (hard),
8) **Sthira** (stable) – **Cala** (mobile),
9) **Sukshma** (subtle) – **Sthula** (gross), and
10) **Vishada** (non-slimy) – **Picchila** (slimy).

Everything in the material world possesses a combination of 20 qualiti es. Thus, Ayurveda assumes that each material process or object can either harm or benefit a person by influencing his/her original constitution (prakriti). An Ayurvedic practitioner before deciding the plan of treatment evaluates the qualities of a disorder, the patient's unique prakriti, and his/her influencing factors. The treatment plan consists of using herbs, therapies, diet, etc., producing opposite effect in order to re-establish the prakriti of a patient.

3.1.3. Siddha System of Medicine

Siddha medicine system was found by the **Dravidian** culture of the pre -Vedic period. It is the oldest medicine system, which utilises drugs obtained from vegetables. Siddha medicine system deals with the human body as well as with the inner soul. This medication system should not be used for earning money as it is a divine art based on truth.

3.1.3.1. History

Siddha medicine system is one of the ancient traditional systems practised in India. The word **Siddha** originated from **Siddhi** (an object to be a ttained or perfection of heavenly bliss). Siddhi signifies **8 supernatural powers** , i.e., **Ashtama Siddh**, and **Siddhars** are the people having such powers. The various works of the authors of Siddha treatises (Sattaimuni, Yugimuni, Macha Muni, Kakabusundar, etc.) are currently available and also practised.

3.1.3.2. Basic Principles Involved

The universe is made up of **matter** and **energy** (two essential entities). The Siddhas call them **Siva** (male) and **Shakti** (female, creation). Matter cannot exist without energy in-built in it and *vice versa.* Matter and energy co-exist and cannot be separated. There are **5 primitive elements** (**bhutas**), i.e., **Munn** (solid), **Neer** (fluid), **Thee** (radiance), **Vayu** (gas), and **Aakasam** (ether). These elements should not be confused with modern chemistry. Different proportions of them are present in every substance. Earth, water, fire, air, and ether are the manifestations of these elements. The human body is made up of different combinations of these elements. There are 3 substances (**dravyas**), i.e., **vatham**, **pitham**, and **karpam** which facilitate the body's physiological functions. The dravyas co-exist and function mutually in each and every cell of the body. The tissues are called **dhatus**. Imbalances in the equilibrium of these dravyas cause diseases.

Tridoshas According to Siddha Medicine

All the body functions (physical, mental, and emotional) are controlled by the tridoshas:

1) **Vatham**
   i) It is dry, light, cold, and motile.
   ii) It is formed by Aakasam and Vayu.
   iii) It controls the nervous actions (movement, activity, sensation, etc.).
   iv) It predominates in the bone.
   v) It dominates in first one -third phase of life when activities like growth and sharpness of function of sense are greater.

2) **Pitham**
   i) It indicates heat.
   ii) It is formed by Thee.
   iii) It controls the metabolic activity of the body, digestion, assimilation, warmth, luster, intellect, etc.
   iv) It predominates in the tissue blood.
   v) It dominates in the second one-third phase of life.

3) **Karpam**
   i) It is smooth, firm, viscid, and heavy.
   ii) It is formed by Munn and Neer.
   iii) It controls the stability o f body such as strength, potency, and smooth working of joints.
   iv) It predominates in other tissues.
   v) It dominates in the last one-third phase of life.

Given below are the **7 dhatus**:

1) **Rasa** (lymph),
2) **Kurudhi** (blood),
3) **Tasai** (muscle),
4) **Kozhuppu** (adipose tissue),
5) **Elumbu** (bone),
6) **Majjai** (marrow), and
7) **Sukkilam** and **Artavam** (male and female hormones).

3.1.3.3. Diagnosis

The diagnostic techniques practised in Siddha system rely on "clinical acumen" of the physicians, thus, is different. The physicians diagnose a patient by **eight types of examinations**, which involve observing the patient's tongue, complexion, speech, eyes, palpitation, urine, stool, and lastly the pulse. Physicians practicing Siddha medicine system also employ the modern diagnostic techniques.

3.1.3.4. Treatment

The drugs used for treating imbalance of tridoshas are made up of the 5 elements. Equilibrium is restored by substituting a drug of the same constituent (guna). The imbalance is corrected by substituting with a drug of opposite nature. Some **examples** are vatham imbalan ce is cold and dry, so the treatment involved will

be warm and oily; for inactivity of limbs, massage and activity are prescribed; warmth is produced due to increased pitham dosha, thus sandalwood is administered either internally or externally to decrease pitham.

Given below are the **5 types of vayus**:

1) **Prana:** Present in mouth and nostrils (inhaled); aids in ingestion.
2) **Apana:** Present at anal extremity (expelled); aids in elimination and expulsion.
3) **Samana:** Equaliser; aids in digestion.
4) **Vyana:** Aids in blood and nutrient circulation.
5) **Udana:** Present in the upper respiratory passages.

Materia Medica

Siddhas obtained clarified and instinctive intelligence from yogic powers. They used this knowledge to explore the nature and exploit the natural resources to serve h umanity. They worked on the characteristic features of the products obtained from plants, animals, metals, and minerals. They wrote their works in poetic forms for future use of children. The students of Siddha medicine obtain knowledge about drugs, purifi cation, processing, heat application, fixing dosage, toxicity, antidote, and clinical application from their Gurus, and this vast knowledge astounds the modern scientific world.

3.1.3.5. Therapeutics

Mercury

Mercury holds a significant importance in Siddha medicin e as it is used as a catalytic agent. Mercury is used in combination with sulphur; sulphur controls the fluidity of mercury so that it gets converted into mercuric sulphite (insoluble in mineral acids).

Mercury is used in Siddha medicine system in the following **5 forms**:

1) **Rasam** (mercury metal),
2) **Lingam** (red sulphide of mercury),
3) **Veeram** (mercury chloride),
4) **Pooram** (mercury subchloride), and
5) **Rasa chenduram** (red oxide of mercury is a poison, but when processed as **poorna chandrodayam** by practising Siddha becomes ambrosia).

Classification of Siddha Medicine

1) **Uppu (Lavanam):** These drugs dissolve in water and when put into fire gets decrepitated giving off vapours (water -soluble inorganic compounds). These have 25 varieties and are called **kara-charam**, salts, and alkalis.
2) **Pashanam:** These drugs do not dissolve in water and when put into fire give off vapours (water-insoluble inorganic compounds).
3) **Uparasam:** These drugs do not dissolve in water. They are chemically similar to pashanam but their actions differ. **Examples** include mica, magnetic iron, antimony, zinc sulphate, iron pyrites, and ferrous sulphate.

4) **Loham:** These drugs are insoluble in water, melt in fire, and solidify on cooling. **Examples** include metals and mineral alloys such as gold, silver copper, iron, tin, and lead.
5) **Rasam:** These drugs are soluble in water, when put in fire undergoes sublimation, and changes into small crystals. **Examples** include mercury amalgams, mercury compounds, and arsenic.
6) **Gandhakam:** These drugs are insoluble in water, and burns off when p ut into fire.
7) **Ratnas and Uparatnas:** These have 13 varieties, such as coral, *lapis-lazuli*, pearls, diamonds, jade, emerald, ruby, sapphire, opal, *vaikrantham*, *rajavantham*, and *spatikam harin mani*.

Some common **preparations of Siddha medicines** are:
1) **Bhasma** (calcined metals and minerals),
2) **Churna** (powders),
3) **Kashaya** (decoctions),
4) **Lehya** (confections),
5) **Ghrita** (ghee preparations) and **taila** (oil preparations),
6) **Chunna** (metallic preparations which become alkaline),
7) **Mezhugu** (waxy preparations), and
8) **Kattu** (a preparation that is impervious to water and flames).

Sulphur
Sulphur is solidified by the Siddha method of purification to obtain calcined sulphur or red oxide of sulphur. It conserves the body in small doses. It acts as a diaphoretic and alterative (a drug used to a lter the course of a disease). Therapeutically it is used as an external as well as an internal remedy against skin diseases, rheumatic arthritis, asthma, jaundice, and blood poisoning.

Arsenic
Arsenic in purified and consolidated form is used against all fevers, asthma, and anaemia according to Siddha Kalpa.

Gold
Gold is used as an alterative, nervine tonic, poison antidote, and a powerful sexual stimulant. Very little amount of it gets absorbed in the system. It should be taken care of that calcination of gold is freed from metallic state and luster; this ensures safe absorption in the system. Thus, screening of these drugs and metallic minerals for their antiviral, immune stimulant, and immune -modulatory activity can be done.

Many HIV patients have ta ken Kalpha drugs for rejuvenation and long life. Therefore, it is believed that by thorough investigations of Kaya Kalpa therapy using modern parameters one can determine whether or not these drugs can be used for preventing or curing AIDS or other diseases.

3.1.4. Unani System of Medicine

Unani (or **Yunani** or **Unani-Tibb**) is a traditional medicine system practised in India and Indian subcontinent. It refers to the practise of **Graeco-Arabic** medicine, which relies on the teachings of **Hippocrates** and **Galen** (physicians of Greece and Rome, respectively). The Unani medicine was developed into an elaborate medical system by **Rhazes** (Arab and Persian physicians). The base of Unani medicine system is formed by the concepts of four humours, i. e., **Phlegm** (Balgham), **Blood** (Dam), **Yellow bile** (Safra), and **Black bile** (Sauda).

3.1.4.1. History

The history of Unani healing started from **Claudius Galenus** of Pergamum (who lived in the 2nd century of Christian Era) and from Ancient Iranian Medicine. But Unani medicine as a healing system was introduced by the **Avicenna** in the west. **Hakim Ibn Sina** described the same in his medical encyclopaedia, **The Canon of Medicine**.

Unani medicine first arrived in India in the 12th-13th century of Christian Era when the Delhi Sultanate was established here (1206-1527 CE) and Muslim ruled over North India and then thrived under the Mughal Empire. **Alauddin Khilji** had many famous Hakims/Unani physicians in his royal courts. In further years, **Alauddin Khilji** took help from Indian Ayurvedic physicians and developed the Unani system and Unani literature in India.

3.1.4.2. Basic Principles Involved

The principles of **Hippocrates** formed the base of Unani medicine system. **Hippocrates** laid the facts that disease is a natural process, symptoms are the reactions that body produces towards the disease, and physician's role is to help the natural forces of the body. He introduced the method of checking patient's medical history. He also bought the **Humoral Theory**, which is his most essential contribution in the field of medicine. The components whose loss in a human body can cause a disease or even death are as follows:

1) **Al-arkan** or **al-anasir** (Elements), 2) **Al-mizaj** (Temperament),
3) **Al-akhalt** (Humours or body fluids), 4) **Al a'za'** (Organs or members),
5) **Al-arwah** (Pneuma or vital spirit), 6) **Al-quwa** (Faculties or Powers), and
7) **Al-at'al** (Functions).

Besides the above mentioned seven causes, given below are the **other causes** which influence the human body:

1) Atmospheric air,
2) Foods and drinks,
3) Physical or bodily movement and repose,
4) Mental or psychic movement and repose,
5) Sleep and wakefulness, and
6) Evacuation and retention.

Humoral Theory

As per the **Humoral Theory**, four humours, i.e., **Dam** (blood), **Balgham** (phlegm), **Safra** (yellow bile), and **Sauda** (black bile) make up the human body. Depending on the mass of these four humours in a human body, their nature is expressed by the terms **sanguine** (for blood), **phlegmatic** (for phlegm), **choleric** (for yellow bile), and

melancholic (for black bile). The nature of four humours is that bl ood is hot and moist, phlegm is cold and moist, yellow bile is hot and dry, and black bile is cold and dry. A person's health condition can be predicted by his/her humoral composition. **Quwwat-e-Mudabbira** (medicatrix naturae) is a power of self -preservation or adjustment present within the body to maintain humoral balance. Deterioration of this power causes an imbalance in the humoral composition, thus resulting in a diseased state. The Unani physicians rely on this power. A person's health can be put back to normal by using Unani medications which help the body to recover the power to its optimum level, and thus, re -balance the humoral composition. Proper diet and digestion also supports in maintaining humoral composition.

3.1.4.3. Diagnosis

Unani system emphasises on disease diagnosis through **Nabz** (pulse), which is a rhythmic expansion of arteries that can be felt by touching with fingers. The system also utilises diagnosis techniques through examination of **Baul** (urine), **Baraz** (stool), etc.

3.1.4.4. Treatment

Unani medicine system follows the treatments mentioned below:

1) **Ilaj-bil-tadbeer (Regimental Therapy):** This therapy involves venesection, cupping, diaphoresis, diuresis, Turkish bath, massage, cauterisation, purging, emesis, exercise, leeching, etc.
2) **Ilaj-bil-ghiza (Dietotherapy):** This therapy involves having proper diet or regulating the food quantity and quality for treating some particular diseases.
3) **Ilaj-bil-dawa (Pharmacotherapy):** This therapy involves the use of drugs of plant origin. However, drugs obtained from anim al or mineral sources can also be used.
4) **Ilaj-bil-yad or Jarahat (Surgery):** This therapy was used by the ancient physicians who developed this technique, and also various surgical instruments and techniques.

Raw form of single drugs or their combinations a re preferred over compound formulations by the Unani medicine system. The compound formulations treat many complex and chronic diseases; still Unani system prefers single drugs. Unani medications are easily available due to the vast Materia Medica of the U nani system. Since the crude natural or herbal drugs used in the Unani system are toxic in nature, they are processed and purified by various t echniques to eliminate the side effects they might produce; thus, Unani medications are representative of life. Unani medications have an advantage of patient compliance, thus the patients immediately recover and also the risk of drug reactions reduces.

3.1.5. Homeopathy System of Medicine

Homeopathic medications are prepared by succes sive dilutions with forcefully shaking and striking (**succussion**). It was believed by the Homeopaths that after each dilution the effect of medication is enhanced; and this preparation process was named **potentisation**. Dilution is carried on till the origina l substance completely fades away.

Before recommending any medicine, the Homeopaths ask the patients about their symptoms, physical and psychological state. Then they consult the **repertories** (homeopathic reference books) and select a medication based on the totality of the symptoms. Homeopathic medicines are considered safe and have no side effects. However, the patients are put at risk when Homeopaths advise them not to take conventional medicine (like vaccinations, anti-malarial drugs, and antibiotics).

3.1.5.1. History

Homeopathic medicine relies on the principle of ***Similia Similibus Curentur***, i.e., **like cures like**. **Dr. Samuel Hahnemann** (a German physician) is the founder of this medicine system which is a complete healing system.

Regulation and prevalence of Homeopathy medicine system are different for different countries. Some countries practicing Homeopathic system do not require any legal regulations; while some other countries demand licence or degree from approved universities. In several countries, Homeopathy is covered to different extents by the national insurance coverage; while in other countries it is fully integrated into the national healthcare system. In many countries, the laws governing the regulation and testing of conventional drugs are not applied to Homeopathic medications.

3.1.5.2. Basic Principles Involved

Every science guides the whole system by their some specific basic principles. Similarly, Homoeopathy being a science of medical treatment has its own philosophy, and its therapeutics relies on certain principles which are much different from those of other schools of medical science. **Hahnemann** discussed these fundamental principles in different sections of his medicine and philosophy as follows:

1) **Law of Similia:** Homoeopathy medicine system relies on the therapeutic law, ***Similia Similibus Curentur***, which means „**let likes be cured by likes**'. In this healing system, the patient is given such a medicine which will produce the same symptoms (as found in the patient) if given to a healthy person also. Thus, the symptoms of the patient are matched with the pathogenesis of the medicine; and the medicines which show a greater degree of similarity, i.e., *Simillimum*, are selected and administered to cure the patient.

2) **Law of Simplex:** As per this law, simple and single drugs should be prescribed at a particular time. Thus, medicines act on healthy human beings individually and in simple form without the addition of any other substance.

3) **Law of Minimum:** As per this law, drugs are administered in minimum quantity because of hypersensitivity to disease. The drug action is always directed towards normal as a result of altered receptivity of tissue to disease stimuli. The medicines are required in minimum amount only to stimulate a reaction within the body. If given in large doses, physiological actions will occur within the body which would lead to undesirable side effects and organic damage. The smallest quantity of medicine helps it to reach the disease, which is of very subtle nature. A drug's healing action can be estimated by using minimum quantity of medicine so that no undesirable aggravation occurs.

4) **Drug Proving:** Drugs can be used therapeutically only if their healing power is known. A drug's healing power is its ability to produce disease symptoms when given to a healthy individual. A drug's healing power and curative properties can be known by its pathogenesis and can be determined by proving its effect alone on a healthy individual.

5) **Drug Dynamisation or Potentisation:** A disturbance or deviation in the normal harmonious flow of dynamic life forces is termed a disease. Thus, the drug used for encountering a disease should also have a dynamic action to act on the dynamic disturbance of life force. For this purpose, the drugs are dynamised or potentised by the process of **trituration** (for insoluble substances) or **succussion** (for soluble substances). This redeems their dynamic curative power which was lying dormant within them.

Preparation of Potencies

Potency can be prepared by the following **3 different scales**:

i) **Decimal Scale: Dr. Constantine Hering** introduced this scale, in which the first potency should contain 1/10th part of the original drug; the second potency should contain 1/10th part of the first potency, and so on. In this scale, potency is denoted by suffixing the letter 'X' to the number indicating the potency, **e.g.,** the first potency is 1X, the second is 2X, and so on.

ii) **Centesimal Scale:** In this scale, the first potency should contain 1/100th part of the original drug; the second potency should contain 1/100th part of the first potency, and so on. In this scale, potency is denoted by suffixing the letter 'C' to the number indicating the potency. **For example**, it is generally denoted by a simple numerical 1C potency which is equivalent to 2X potency, 2C potency is equivalent to 4X, and so on.

iii) **Millesimal Scale:** In this scale, the first potency should contain 1/50,000th part of the original drug; the second potency should contain 1/50,000th part of the first potency, and so on. In this scale, potency is denoted by I, II, V, X, etc., or 0/1, 0/2, 0/5, 0/10, etc. **For example**, potency 0/2 is equivalent to 4C = 8X, 0/4 is equivalent to 8C = 16X, and so on.

Preparation of potencies by trituration is made either by decimal or centesimal, and the preparation of potencies by succussion is made by decimal, centesimal, and millesimal.

6) **Vital Force:** Disease is the disharmonious flow of the vital force, thus producing abnormal sensations and functions (symptoms and signs). For health restoration, the disordered vital force should be normalised. Disease and health are two quantitative states of this vital force of living being, and cure is to be affected here. Vital force is spiritual, autocratic, automatic, dynamic, unintelligent, and instinctive.

7) **Acute and Chronic Diseases:** The diseases are either acute or chronic depending on their onset, progression, and termination.

8) **Individualisation:** Since two individuals in the world are not the same, similarly diseases affecting them are also never same assuming the unique

individual pict ure in each diseased individual. Thus, medicines are not merely prescribed based on the disease name, but by individualising each disease case.

9) **Direction of Cure: Dr. Hering** stated that „cure takes place within outward from above to downward and the sympto ms disappear in the reverse of their appearance'. If the direction occurs in reverse to that stated, then it is not cure but suppression.

3.1.5.3. Miasms and Disease

Hahnemann gave the concept of **miasms** which denotes the fundamental causes of many diseases in **1828**. Miasms by the Homeopaths was defined as " **peculiar morbid derangement of vital force** ". **Hahnemann** related each miasm with a particular disease (of which it is the main cause). **Hahnemann** stated that local symptoms (skin or venereal diseases) develop when a person is exposed to miasm in the early stages. But on inhibiting these symptoms by medication, the miasm goes deeper to affect the internal organs with the same disease.

An assumption of Homeopathy medicine system is that directly opposing the symptoms of a disease (as in conventional medicine) does not treat the disease, since all disease can be traced to some latent, deep-seated, underlying chronic, or inherited tendency. The underlying miasm remains, and removing the deeper disturbance of the vital force cures the deeper illnesses.

Hahnemann firstly attributed only three miasms; **psora** (derived from the Greek word **itch** and associated with itching skin disorder) being the most significant one; it is believed to be originated from suppressed scabies and f orms the underlying cause of other diseases.

Hahnemann considered that psora causes diseases like epilepsy, cancer, jaundice, deafness, and cataracts. Some other miasms, which either replace one or more of psora's proposed functions (including tubercular miasms and cancer miasms) originated during the same period.

3.1.5.4. Homeopathic Remedies

A substance prepared by a specific procedure and used for treating patients is a **remedy**. The term **remedy** should not be confused with the medicine or therapy used for curin g disease or relieving pain. The **ones practising Homeopathy depend** on the following **two types of references**:

1) **Materia medica:** Drug pictures arranged in alphabetical order of remedies and also the related symptoms are included in this book.
2) **Repertories:** Symptoms of a particular disease and also the remedies of particular symptoms are included in this index.

Homeopathic medicine system utilises various plants, animals, minerals, and synthetic substances as remedies, **e.g.,** ***Arsenicum album*** (arsenic oxide), ***Natrum muriaticum*** (sodium chloride or table salt), ***Lachesis muta*** (the venom of bushmaster snake), **opium**, and **thyroidinum** (thyroid hormone).

Homeopaths used two specific type of treatment, first is **Nosodes** (derived from the Greek word **nosos**), meaning **preparations made from pathological products** such as faecal, urinary, and respiratory discharges, blood, and tissue collected from diseased patients).

Another type of treatment used is **Sarcodes** (a **Greek** word which means **fleshy**) and denotes medicines obtained fr om healthy endocrine or ductless glands or normal secretions of living human organs and lower animals.

Preparation

Homeopathic medications are prepared by grinding insoluble solids (quartz and oyster shells) in mortar and pestle. Homeopaths prepare medica tions by the process of **dynamisation** or **potentisation**. In this process, a substance is diluted with alcohol or distilled water, followed by vigorous shaking and forceful striking against an elastic body atleast 10 times; this process is termed **succussion**.

Hahnemann used substances which produce those symptoms in healthy individuals that occur in diseased individuals. These substances, however in some cases were found to be worsening the condition by strengthening the symptoms and thus further producing tox ic effects. Therefore, **Hahnemann** suggested the dilution of these substances as he believed that the vital energy of diluted substance can be activated by succussion process.

Dilutions

Homeopathic medicine system utilises **3 logarithmic potency scales** . **Hahnemann** invented the **centesimal** (**C**) **scale** for diluting substance s by a factor of 100 at each stage. First, a substance is diluted to one part in one hundred, followed by again diluting a portion of the diluted solution by a factor of 100 in case of 2C dilution.

This works out to be one part of the original substance in 10,000 parts of the solution. This step is repeated 6 times so that the original material gets diluted by a factor of $100^{-6} = 10^{-12}$ (one part in one trillion) (1/1,000,000,000,000) in case of 6C dilution.

The same dilution process is followed for higher dilutions. Homeopaths considered that the substances which are more diluted have a strong and deep action, because the potency of a highly diluted solution is high. If the end product is highly diluted, the end product and the dilutant (pure water, sugar, or alcohol) are mostly indistinguishable.

Hahnemann diluted a solution by a factor of 10^{60} in case of 30C dilutions. T he concept that **atoms or molecules are the smallest unit of a chemical substance** was about to be recognised, thus the fact that Homeopathy medications can be diluted indeterminately was practically accepted. A substance with 12C dilution contains one molecule of the original.

3.2. PREPARATION AND STANDARDIZATION OF AYURVEDIC FORMULATIONS

3.2.1. Introduction

Indian medicine comes from Ayurveda which is said to be the science of life and was originated by Brahma. Ayurveda contains knowledge of medicines and the healing art. Ayurvedic medicine system from the ancient era utilises many pharmaceutical dosage forms which are even practiced at the present time. These dosage forms are derived from vegetable drugs. Nowadays Allopathic and modern system of medicine is in genera l practice; however the pharmacists should be aware of the prevailing Ayurvedic dosage forms and their process of manufacturing. This is a point of consideration as Indian population in rural areas depend on Ayurvedic drugs. Interest has been developed aro und the world for Ayurvedic products, especially for herbal drugs and cosmetics. Ayurvedic dosage forms are also less expensive than the Allopathic dosage forms. Classification of Ayurvedic dosage forms is presented in **table 3.1**, and the English synonyms are mentioned in brackets:

Table 3.1: Classification of Ayurvedic Dosage Forms

Solids	Semisolids or Viscous Liquids	Liquids
Churna (powders)	Kalka (ointments and pastes)	1) Aqueous i) Swarasa (self-juices), ii) Kasaya (extracts): a) Shita-kasaya (cold infusions), b) Phanta-kasaya (hot infusion), c) Kwatha (decoction), and d) Paniya (weak decoctions) iii) Kshira-paka (milk decoctions), iv) Vasti (enemas), and v) Sugandhita jala (perfumed waters).
Vatika (pills)	Avaleha (soft extracts)	2) Oily i) Taila (medicated oils), ii) Ghrita (medicated clarified butter), and iii) Mantha (a kind of emulsions).
Modaka (boluses)	Khandapaka (confections)	3) Acetus i) Kanjika (vinegars), ii) Samkhadrav (mineral acids), and iii) Swalpadravaka (mineral acids).
Guggulu (plant exudations)	Yavagu (gruels)	4) Spirituous i) Sura (wines), ii) Asava (tinctures), and iii) Arishta (tinctures).
Netranjan (collyria) Nasya (snuffs) Phalavarti (suppositories) Dhumapana (inhalations) Kshara (alkalis)		

The preparation and standardisation of the following Ayurvedic for mulations are discussed below:

1) Arishtas, 2) Asavas, 3) Gutikas,
4) Churnas, 5) Lehyas, and 6) Bhasmas.

3.2.2. Arishtas

Arishtas are prepared by the process of fermentation for a specific time period after boiling the main decoction substance and adding other ingredients. Arishta is an ancient medicinal preparation mentioned in the Vedas, having Ayurvedic medicines.

Method of Preparation

The drug is coarsely powdered (javkut) to prepare kasaya, which is strained and transferred to the fermentation vessel. Req uired amount of sugar, jaggery, or honey are dissolved, boiled, and then added to the mixture obtained after straining the kasaya. An earthen lid is used to cover the mouth of the vessel, and clay-smeared cloth is used to seal the edges by winding it in se ven repeated layers. For the fermentation process, the temperature has to be kept constant; this can be achieved by placing the container in a special room, in an underground cellar, or in a heap of paddy. The jar is uncovered (lid is removed) after a prescribed time and the contents are inspected to determine whether or not complete fermentation has occurred. The fluid in the jar is decanted followed by straining after 2-3 days only when the fine suspended particles has settled at the bottom. The liquid obtained after straining is the product which is filtered and the filtrate is stored in a bottle.

This filtered Arishta has a characteristic, aromatic, and alcoholic odour.

Standardisation of Process

Standardisation refers to standardising a preparation as per the studied characters of plant. Standardisation of Arishtas is done in either of the **two ways**:

1) By using standardised raw material, and
2) By maintaining a definite time period, temperature, light, and humidity conditions.

The Arishta products are repro ducible since all the conditions are well -defined, thereby eliminating batch-to-batch variation.

Standardisation of Finished Product

The traditional analytical approach involving monographs like viscosity, density, refractive index, and polarity needs est imation for which uniformity is required. Total amount of alcohol the preparation holds is estimated. Other parameters include TLC, HPTLC, etc.

General Problems Associated with their Standardisation

During the standardisation of Arishta preparations, the following problems arise:

1) The preparation is polyherbal,
2) Active constituents are not identified, thus its specific action cannot be determined.

3) Any such pharmacological preparation has not been identified which can counteract a drug.
4) Activity of preparation is known, but information on dose and side effects is still unknown.
5) Clinical data is absent.

Examples
Abhyarista, Balarista, Khadirarishta, Dasmularista, Vidangarishta, etc.

3.2.3. Asavas

Asavas are a famous ancient medicinal preparation mentioned in the Vedas. Asavas are prepared by the process of fermentation for a prescribed time after mixing all the specified ingredients with required quantity of unboiled water.

Method of Preparation
The drug is soaked in the form of a decoction in a solution of either sugar or jaggery for a prolonged duration. Thereafter the mouth of the vessel is covered with a lid and edges are sealed with clay. During this time period, fermentation of Asava takes place; and as a result alcohol is produced which acts as a preservative. The product is filtered and the filtrate is stored in a bottle.

The filtered Asava should be clear and free of froth at the top. It should have a characteristic, aromatic, and alcoholic odour. It should not be sour. Asavas can be stored for a long duration in well-stoppered bottles or jars.

Examples
Kumaryasava, Madhukasava, Vasakasava, Arvindasava, Punarnavasava, etc.

Difference between Arishtas and Asavas
1) The preparation method of Arishtas is decoction and that of Asavas is infusion.
2) The fermentation time duration of Arishtas is much smaller than that of Asavas.

3.2.4. Gutikas

Gutikas are available as medicated pills, prepared by combining the vegetables, mineral or animal drugs together. Gutikas should be consumed within two years. The pill forms of Gutikas having mineral ingredients can be used for life long.

Method of Preparation
Drugs obtained from plants are separately dried and finely powdered. The minerals are made into **bhasmas** or **sindura**. When **parada** (mercury) and **gandhaka** (sulphur) are stated, **kajjali** is made first and added with other drugs one at a time as given in the formula. This mixture is grounded properly in **khalva** to yield a soft paste containing the prescribed fluids. The mass after reaching a condition that it can be casted as pills is again grounded with added **sugandha dravyas** (flavouring agents) like **kasturi** and **karpura**.

The mass obtained should not stick upon rolling between the fingers. The mass is shaped into many pills, which are dried in shade or in sun. If sugar or jaggery is added, **paka** is vigorously mixed. In warm state, **vatakas** should be rolled and shade dried. Pills of plant origin are stored in air -tight containers and should be consumed within two years. Pills of mineral origin can be used inde finitely. Gutikas should retain their original colour, odour, and taste after formulation. Gutikas containing salt or sugar should be prevented from moisture.

Examples
Lasunadi gutika, Marma gutika, Pranda gutika, Bilvadi gutika, Marma gutika, Mritsanjivni gutika, etc.

3.2.5. Churnas

Churnas are finely powdered drug(s). Drugs stated in patha are first cleaned, dried, pulverised, and then sieved. Churnas are stored in air -tight containers to maintain their potency and free flowing nature for a year.

Method of Preparation
The drug prescribed in the yoga is cleaned, dried, finely powdered, and sieved. In case of many drugs, each drug is separately powdered, sieved, and weighed, followed by mixing together all the resultant powder. For large scale pr oduction, all the drugs are cleaned, dried, powdered together in disintegrators, and then screened through mechanical sifters. The powder should be made fine enough to pass through 80 mesh sieve. The powder particles should not adhere or become moist. The therapeutic efficacy of fine powder is comparatively better.

Standardisation
Churnas are standardised by the following parameters:
1) Determination of sieve size,
2) Loss on drying/moisture content,
3) TLC,
4) Total ash,
5) Acid-insoluble ash,
6) Water-soluble ash,
7) Extractive value in water, alcohol, and other solvents,
8) Phytoconstituents,
9) Microbial contaminations,
10) Heavy metal limit test for mercury, arsenic, cadmium, and lead, and
11) Microscopic analysis.

Examples

Names of Medicine	Active Ingredients	Therapeutic Uses
Agnimukh Churna	Sonth, Jirak, Marich, Menthol, Bid, Lavan, Saindhava, Lemon juice, etc.	Expectorant, diuretic, and aperients; indicated in dyspepsia and loss of appetite.
Ashwagandhadi Churna	Ashwagandha and Bidhara	Alterative tonic, aphrodisiac, and anti-rheumatic; indicated in impotency, spermatorrh oea, old age debility, and leucorrhoea.

Bilwadi Churna	Bael, Mochras, Sonth, Bhang, Dhaiphool, Dhania, and Saunf.	Astringent and alterative; indicated in sprue, diarrhoea, and dysentery.
Chandanadi Churna	Chandan, Gum acacia, Priyangu, Jamun guthli, Aam guthli, Nagarmotha, Ajwain, Giloy, Indrajav, and Mochras.	Stimulant, demulcent, and urinary antiseptic; indicated in gonorrhoea, cystitis, genito -urinary infections, thirst, extreme heat, and coma.
Eladi Churna	Ela, Keshar, Bhringraj, Bansalochan, Munakka, Anardana, Dhania, Jeera, Pipalmool, Chitrak, Trikatu, Ajwain, and Amalbet.	Carminative and anti -emetic; indicated in vomiting, indigestion, and anorexia.
Haritaki Churna	Harad (*Terminalia chebula*)	Internal cl eanser and detoxifier; supports body tissues; improves body tissues and digestive functions.
Jatiphaladi Churna	Jaiphal, Lavang, Ela, Tejpatra, Cinnamon , Tagar, Amla, Citrak, Camphor, Banslochan, Bidang, Harre, Trikatu, etc.	Sedative, antispasmodic, and astringent; indicated in diarrhoea, sprue, spasmodic cough, migraine, mania, menorrhagia, spasmodic cough, dysmenorrhoea, etc.
Mahasudarshan Churna	Triphala, Trikatu, Chiraita, Bidang, Lavang, Kateri Kachur, Daruhaldi, Giloy, and other 40 items.	Diaphoretic and diuretic; indicated in fever, intermittent fever, liver and spleen enlargement, fatigue, and nausea.
Panchasakar Churna	Sanai, Harre, Sonth, Anisi, and Saindhava.	Purgative, carminative, and stimulant; indicated in constipation, colic, indigestion, and other intestinal disorders.
Sitopaladi Churna	Sugar candy, Dalchini, Ela, Pipal, and Banshlochan.	Stimulant, laxative, and expectorant; indicated in bronchitis, cough, excessive thirst, burning sensation, and respiratory complains.
Triphala Churna	Harre, Bahera, and Amla.	Alterative, astringent, laxative, and aperient; indicated in dyspepsia, diarrhoea, piles, blood impurity, eye irritation, and haemorrhage.

3.2.6. Lehyas

Lehyas (also known as **aveleha** or **leha**) is a semisolid drug product pr epared by adding sugar, jaggery (gur), or sugar candy to the drug and further boiling with drug juice or decoction.

Method of Preparation

Lehyas are prepared by dissolving jaggery or sugar candy in liquid, followed by moderate boiling and straining the obtained mixture to remove impurities. Boiling is stopped when the paka (phanita) becomes thready on pressing between two fingers or if it sinks in water without getting dissolved. Small quantities of the fine powdered drugs are added and stirred in a constant and vigorous manner to yield a homogeneous mass. The hot preparation is added and properly mixed with ghee or oil (if required); while if honey is to be added the preparation should be first cooled.

Lehyas have the following components:
1) Kasaya or other liquids,
2) Jaggery, sugar, or sugar candy,
3) Powders or pulps of certain drugs,
4) Ghee or oil, and
5) Honey.

Standardisation
Lehyas are standardised by the following parameters:
1) Loss of drying, 2) Ash values, 3) Extractive values,
4) pH, and 5) TLC.

Examples
Kutajavaleha, Draksavaleha, Vasavaleha, Bilvadileha, Surnavaleha, etc.

3.2.7. Bhasmas

Bhasmas are grey, whitish, yellowish, or black coloured powdered form of substances. These can be obtained from metals, minerals, or animal sources by a process named **calcination** carried out in closed crucibles or in pits covered with cow dung cakes (puta). They are typically stored in glass containers. Bhasmas are stable and retain their potency for a long time.

Method of Preparation
Bhasmas are prepared in two steps, n amely **sodhana** and **marana**. These are time-consuming processes and require attention:

1) **First Stage (Sodhana):** Bhasmas, as already known are obtained from minerals, metals, marine, and animal products. Sodhana is a purification process which is of the following **two types**:
   i) **Samanya Sodhana:** In this method, thin metal sheets are heated and immersed in taila, takra, gomutra, etc. This method can be used for large number of metals or minerals.
   ii) **Visesa Sodhana:** This method can be used for some drugs and preparations.
2) **Second Stage (Marana):** This second stage of bhasma preparation occurs in the following **steps**:
   i) The purified drug is grounded for a specified time with juices of particular plants or kasayas of drugs (stated for a specific mineral or metal) in a stone mortar and pestle (khalva).
   ii) Small cakes (cakrikas) are prepared from the obtained mixture.
   iii) These cakes are sun dried and arranged in a shallow earthern plate (sarava) as a single layer.
   iv) Thereafter, the plate is closed with another plate, edges are sealed by winding clay-smeared cloth in seven consecutive layers, and then it is dried.
   v) A pit is formed in an open space, and filled with cow dung cakes up to the half level.
   vi) The sealed earthen container (iv) is kept in the pit and more cow dung cakes are added to fill up the remaining space.

vii) All the four sides and the middle of the pit are put on fire.
viii) After complete burning, the pit is cooled, the earthen container is taken out, opened, and its contents are removed.
ix) The content if required is again grounded with juice in a khalva to yield a fine powder, from which cakes are made, and putas are obtained.

Bhasmas are yellowish, black, dark white, grey, red, or reddish black in colour, as per the major drug and the other drugs in the process of marana.

Standardisation

Bhasmas are standardised by the following parameters:

1) Determination of foreign organic matter,
2) Determination of ash value:
   i) Total ash value,
   ii) Acid-insoluble ash,
   iii) Water-soluble ash, and
   iv) Sulphated ash.
3) Determination of extractive value:
   i) Alcohol-soluble extractive value, and
   ii) Water-soluble extractive value.
4) Determination of moisture content,
5) Determination of physical constants:
   i) Melting point,
   ii) Boiling point,
   iii) Refractive index, and
   iv) Optical rotation.
6) Determination of specific gravity,
7) Determination of solid content, and
8) Determination of alcohol content.

Examples

Tamra bhasma, Godanti bhasma, Pravala bhasma, Mukta bhasma, Lauha bhasma, etc.

3.3. SUMMARY

The details given in the chapter can be summarised as follows:

1) The alternative systems of medicines are referred to as **traditional systems of medicine**.
2) The **four holy books** (in Sanskrit) written with divine inspiration were included in the **Vedas** (meaning **wisdom**).
3) **Rig Veda** (the oldest Veda) has drugs and diseases mentioned in it.
4) **Atharva Veda** (the fourth Veda) ha s ideologies for maintaining health and the medicinal effects of health mentioned in it.
5) **Dhanvantari** was idolised as the **God of Medicine** as he received the medicine system from **Brahma**.

6) A dissertation named **Sushruta Samhita** carries the most authentic collection of teachings and work of **Dhanvantari**.
7) **Sushruta** was the first one to perform **cataract surgery** in the 1st millennium B.C. using **jabamukhi salaka**.
8) **Agnivesh** (a student of the sage, **Bharadwaja**) wrote the text **Agnivesh tantra** which influenced the writings of Ayurveda.
9) The Branca family of **Sicily** and **Gaspare Tagliacozzi** (Bologna) in Italy got acquainted with the techniques of **Sushruta**.
10) **Rasa** denotes the drug's taste (i.e., **Dravya**), action, and properties.
11) **Guna** denotes the drug's physical properties.
12) **Virya** denotes the drug's potency and shows two intrinsic properties.
13) **Vipaka**, also known as **nishthapak**, denotes the end product of digestion.
14) **Prabhava** denotes the drug's power.
15) **Akasha** denotes the spaces within the body, i.e., mouth, nostrils, abdomen, etc.
16) **Vayu** denotes the muscular movement.
17) **Tejas or Agni** denotes the functions of enzymes, i.e., intelligence, digestion, and metabolism.
18) **Apa or Jala** denotes the body fluids, i.e., plasma, saliva, and digestive juices.
19) **Prithvi** denotes the body structure, i.e., bones, teeth, flesh, and hair.
20) Ayurvedic medicine system, the base of all diagnosis and treatment purpose is the **Panchamahabhutas**.
21) **Vata** is composed of **air** and **space**.
22) **Pitta** is composed of **fire** and **water**.
23) **Kapha** is composed of **earth** and **water**.
24) Imbalance that occurs in doshas and their progression towards a disease is termed **Samprapti** (pathogenesis).
25) The principle of Ayurveda is knowledge and awareness of the qualities of nature called **gurvadi gunah**.
26) There are **5 primitive elements** (**bhutas**), i.e., **Munn** (solid), **Neer** (fluid), **Thee** (radiance), **Vayu** (gas), and **Aakasam** (ether).
27) **Prana** is present in mouth and nostrils (inhaled) and aids in ingestion.
28) **Apana** is present at anal extremity and aids in elimination and expulsion.
29) **Samana** is an equalizer and aids in digestion.
30) **Vyana** aids in blood and nutrient circulation.
31) **Udana** is present in the upper respiratory passages.
32) **Uppu (Lavanam)** dissolve in water and when put into fire gets decrepitated giving off vapours.
33) **Pashanam** drugs do not dissolve in wat er and when put into fire give off vapours.
34) **Uparasam** drugs do not dissolve in water.
35) **Loham** drugs are insoluble in water, melt in fire, and solidify on cooling.

36) **Rasam** drugs are soluble in water, when put in fire undergoes sublimation, and changes into small crystals.

37) **Gandhakam** drugs are insoluble in water, and burns off when put into fire.

38) The base of Unani medicine system is formed by the concepts of four humours, i.e., **Phlegm** (Balgham), **Blood** (Dam), **Yellow bile** (Safra), and **Black bile** (Sauda).

39) As per th e **Humoral theory**, four humours, i.e., **Dam** (blood), **Balgham** (phlegm), **Safra** (yellow bile), and **Sauda** (black bile) make up the human body.

40) **Quwwat-e-Mudabbira** (medicatrix naturae) is a power of self -preservation or adjustment present within the body to maintain humoral balance.

41) **Ilaj-bil-tadbeer (regimental therapy)** involves venesection, cupping, diaphoresis, diuresis, Turkish bath, massage, cauterisation, purging, emesis, exercise, leeching, etc.

42) **Ilaj-bil-ghiza (dietotherapy)** involves having proper diet or r egulating the food quantity and quality for treating some particular diseases.

43) **Ilaj-bil-dawa (pharmacotherapy)** involves the use of drugs of plant origin.

44) **Ilaj-bil-yad or Jarahat (surgery)** was used by the ancient physicians who developed this technique, a nd also various surgical instruments and techniques.

45) Homeopathic medicine relies on the principle of ***Similia Similibus Curentur***, i.e., **like cures like**. **Dr. Samuel Hahnemann** is the founder of this medicine system which is a complete healing system.

46) As per **Law of Simplex** , simple and single drugs should be prescribed at a particular time.

47) As per **Law of Minimum** , d rugs are administered in minimum quantity because of hypersensitivity to disease.

48) **Dr. Constantine Hering** introduced **decimal scale** , in which the firs t potency should contain 1/10 th part of the original drug; the second potency should contain 1/10th part of the first potency, and so on.

49) In **centesimal scale** , the first potency should contain 1/100 th part of the original drug; the second potency should co ntain 1/100 th part of the first potency, and so on.

50) In **millesimal scale** , the first potency should contain 1/50,000 th part of the original drug; the second potency should contain 1/50,000 th part of the first potency, and so on.

51) **Hahnemann** gave the concept of **miasms** which denotes the fundamental causes of many diseases in **1828**.

52) Homeopaths prepare medications by the process of **dynamisation** or **potentisation**.

53) **Arishtas** are prepared by the process of fermentation for a specific time period after boiling the mai decoction substance and adding other ingredients.

54) **Asavas** are prepared by the process of fermentation for a prescribed time after mixing all the specified ingredients with required quantity of unboiled water.

55) The preparation method of Arishtas is decoct ion and that of Asavas is infusion.
56) **Gutikas** are available as medicated pills, prepared by combining the vegetables, mineral or animal drugs together.
57) **Churnas** are finely powdered drug(s).
58) **Lehyas** (also known as **aveleha** or **leha**) is a semisolid drug product prepared by adding sugar, jaggery (gur), or sugar candy to the drug and further boiling with drug juice or decoction.
59) **Bhasmas** are grey, whitish, yellowish, or black coloured powdered form of substances.

3.4. EXERCISE

3.4.1. True or False

1) Atharva Veda has drugs and diseases mentioned in it.
2) Agnivesh was the first one to perform cataract surgery in the 1 st millennium B.C. using jabamukhi salaka
3) Virya denotes the drug's potency and shows two intrinsic properties
4) Kapha is composed of fire and water.
5) Prana is present at anal extremity and aids in elimination and expulsion.
6) Pashanam drugs do not dissolve in water and when put into fire give off vapours
7) Ilaj-bil-ghiza involves having proper diet or regulating the food quantity and quality for treating some particular diseases.
8) The preparation method of Arishtas is infusion and that of Asavas is decoction.
9) Gutikas are grey, whitish, yellowish, or black coloured powdered form of substances.

3.4.2. Fill in the Blanks

10) _____ was idolised as the God of Medicine as he received the medicine system from Brahma.
11) _____ denotes the drug's taste, action, and properties.
12) Vayu denotes the _____.
13) Ayurvedic medicine system, the base of all diagnosis and treatment purpose is the _____ .
14) The principle of Ayurve da is knowledge and awareness of the qualities of nature called _____.
15) _____ aids in blood and nutrient circulation.
16) _____ drugs are insoluble in water, melt in fire, and solidify on cooling.
17) _____ involves the use of drugs of plant origin.
18) _____ gave the concept of miasms which denotes the fundamental causes of many diseases in 1828.

Answers

1) False	2) False	3) True
4) False	5) False	6) True
7) True	8) False	9) False
10) Dhanvantari	11) Rasa	12) Muscular movement
13) Panchamahabhutas	14) Gurvadi gunah	15) Vyana
16) Loham	17) Ilaj-bil-dawa	18) Hahnemann

3.4.3. Very Short Answer Type Questions

1) What are the different alternative medicine systems?
2) Give the six types of Rasa.
3) What are the five elements of Ayurveda medicine system?
4) Enlist the seven dhatus of Siddha medicine system.
5) What is humoral theory?
6) What do you understand by drug dynamisation or potentisation?
7) Differentiate between Arishtas and Asavas.
8) Give some examples of Churnas.

3.4.4. Short Answer Type Questions

1) Discuss the history of Ayurveda medicine system.
2) Write about the principles of Ayurveda medicine system.
3) Discuss the therapeutics of Siddha medicine system.
4) Give a short review on Unani medicine system.
5) Write about the principles involved in Homeopathy medicine system.
6) Write a short note on the preparation and standardisation process of Arishtas.
7) Discuss the preparation and standardisation of Bhasmas.

3.4.5. Long Answer Type Questions

1) Discuss briefly about Ayurveda medicine system.
2) Write an exhaustive note on Siddha medicine system.
3) Briefly discuss about the Homeopathy medicine system.
4) Write the preparation and standardisation of any three Ayurvedic formulations.

CHAPTER 4

Nutraceuticals

4.1. NUTRACEUTICALS

4.1.1. Introduction

Nutraceutical is a substance considered as a food or its part, which apart from its normal nutritional value provides health benefits, prevents diseases, or promotes health, **e.g.,** lycopene, β-carotene, etc. Thus, nutraceuticals are foods or food ingredients providing medical or health benefits.

The term **nutraceuticals** was coined from **nutrition** and **pharmaceutical** by **Stephen Defelice** in **1989**. He defined nutraceutical as "**a substance that is food or a part of food and provides medical or health benefits, including the prevention and treatment of disease s**". Such products range from isolated nutrients, dietary supplements, and specific diets to genetically engineered designer foods and herbal products.

4.1.2. Classification

Depending on various characteristics, nutraceuticals are classified into the following major classes:

1) Nutraceuticals according to their food source,
2) Nutraceuticals according to their mechanism of action,
3) Nutraceuticals according to their chemical nature, and
4) Nutraceuticals according to their higher content in specific food items.

4.1.2.1. Nutraceuticals According to their Food Source

Nutraceuticals are obtained from and restricted to plants, animals and microbi al resources **(table 4.1)**.

Table 4.1: Classification of Nutraceuticals Based upon Food Source

Food Sources	Examples
Plants	β-Glucan, Ascorbic acid, γ-Tocotrienol, Quercetin, Luteolin, Cellulose, Lutein, Gallic acid, Perillyl alcohol, Indole -3-carbonol, Pectin, Daidzein, Glutathione, Potassium, Allicin, δ-Limonene, Genestein, Lycopene, Hemicellulose, Lignin, Capsai cin, Geraniol, β-Lonone, α-Tocopherol, β-Carotene, Nordihydrocapsaicin, Selenium, Zeaxanthin, and Minerals.
Animals	Conjugated Linoleic Ac id (CLA), Eicosapentaenoic Acid (EPA), Docosahexenoic Acid (DHA), Sphingolipids, Choline, Lecithin, Calcium, Coenzyme Q10, Selenium, Zinc, Creatine, and Minerals.
Microbes	*Saccharomyces boulardii* (yeast), *Bifidobacterium bifidum*, *B. longum*, *B. infantis*, *Lactobacillus acidophilus* (LCI), *L. acidophilus* (NCFB 1748), and *Streptococcus salvarius* (subs, Thermophilus)

An interesting consideration with this classification system is that the food source may not be the point of origin for one or more substances. An **example** of such substance is Conjugated Linoleic Acid (CLA), which is added in the human diet as a component of beef and dairy foods. However, it is made by bacteria in the rumen of the cow. Therefore, issues involving the food chain or symbiotic relat ionships should be considered for some individuals working with this classification system.

Because of fairly conserved biochemical aspects across species, many nutraceuticals are found in plants, animals, and sometimes in microbes; **for example,** choline a nd phospha tidylcholine are found in microbes, plants, and animals; sphingolipids are also found in microbes, plants, and animals (however, the latter two are better sources); linolenic acid (18:3 ω-3 fatty acid) are found in various food resources includin g animal flesh, and even synthesised in plants and other lower members of food chain. The fact that few nutraceuticals are found in plants and animals, while others are found in all the three resources forms the demerit of this classification system.

4.1.2.2. Nutraceuticals According to their Mechanism of Action

Nutraceuticals can also be classified as per their mechanism of action. This system groups nutraceutical factors together, irrespective of their food source, based on their proven or claimed physiological properties. Such nutraceuticals include antioxidants, anti-bacterials, anti-hypertensives, anti-hypercholesterolemics, anti-aggregates, anti -inflammatories, anti -carcinogenics, osteoprotectives, etc. Some **examples** are given in **table 4.2**:

Table 4.2: Examples of Nutraceuticals Grouped by Mechanisms of Action

Anticancers	Positive Influence on Blood Lipid Profile	Antioxidant Activity	Anti-Inflammatories	Osteogenetics or Bone Protectives
Capsaicin	β-Glucan	CLA	Linolenic acid	CLA
Genestein	γ-Tocotrienol	Ascorbic acid	EPA	Soy protein
Daidzein	δ-Tocotrienol	β-Carotene	DHA	Genestein
α-Tacotrienol	MUFA	Polyphenolics	GLA	Daidzein
γ-Tocotrienol	Quercetin	Tocopherols		Calcium
CLA	ω-3 PUFAs	Tacotrienols	Capsaiein	Casein phosphopeptides
Lactobacillus acidophilus	Resveratrol	Indole-3-carbonol	Quercetin	FOS (Fructooligoaccharides)
Sphingolipids	Tannins	α-Tocopherol	Curcumin	
Limonene	β-Sitosterol	Ellagic acid		Inulin
Diallyl sulphide	Saponins	Lycopene		
Ajoene	Guar	Lutein		
α-Tocopherol	Pectin	Glutathione		
Enterolactone		Hydroxytyrosol		
Glycyrrhizin		Luteolin		
Equol		Oleuropein		
Curcumin		Catechins		
Ellagic acid		Gingerol		
Lutein		Chlorogenic acid		
Carnosol		Tannins		

4.1.2.3. Nutraceuticals According to their Chemical Nature

Nutraceuticals can also be cla ssified as per their chemical nature (**table 4.3**). Under this approach, nutraceuticals are categorised under molecular or elemental groups. This preliminary model includes several large groups, which provide a base for sub -classification or sub -groups, and so on. As scientific investigation continues, several hundred substances are deemed nutraceuticals, of which many compounds are found to be related in synthetic origin or molecular nature, thus, many of the substances can be grouped together.

Table 4.3: Classification of Nutraceuticals Based upon Chemical Nature

Classes/Components	Sources	Potential Benefits
1) Carotenoids		
i) α-Carotene	Carrots	Neutralises free radicals which may cause damage to cells.
ii) β-Carotene	Various fruits and vegetables.	Neutralises free radicals.
iii) Lutein	Green vegetables	Maintenance of healthy vision.
iv) Lycopene	Tomatoes and tomato products (ketchup, sauces, etc.).	Reduce the risk of prostate cancer.
v) Zeaxanthin	Eggs, citrus, and corn.	Maintenance of healthy vision.
2) Collagen Hydrolysate	Gelatin	Improve some symptoms associated with osteoarthritis.
3) Dietary Fibre		
i) Insoluble fibre	Wheat bran	Reduce risk of breast and/or colon cancer.
ii) β-Glucan	Oats	Reduce the risk of Cardiovascular Diseases (CVDs).
iii) Soluble fibre	Psyllium	Reduce the risk of CVDs.
iv) Whole grains	Cereal grains	Reduce the risk of CVDs.
4) Fatty Acids		
i) Omega-3-fatty acids (DHA/EPA)	Tuna fish and marine oils.	Reduce the risk of CVD s; and improve mental, visual functions.
ii) Conjugated Linoleic Acid (CLA)	Cheese and meat products.	Improve body composition; and decrease the risk of certain cancers.
5) Flavonoids		
i) Anthocyanidins	Fruits	Neutralise free radicals; and reduce the risk of cancer.
ii) Catechins	Tea	Neutralise free radicals; and reduce the risk of cancer.
iii) Flava nones	Citrus	Neutralise free radicals; and reduce the risk of cancer.
iv) Flavones	Fruits and vegetables	Neutralise free radicals; and reduce the risk of cancer.
6) Glucosinolates, indoles, isothiocyanates, and sulphoraphane	Cruciferous vegetables (broccoli and kale) and horseradish.	Induce detoxification enzymes; and reduce the risk of cancer.
7) Phenols		
i) Caffeic acid ii) Ferulic acid	Fruits, vegetables, and citrus.	Antioxidant-link activities; and reduce the risk of degenerative diseases, heart disease s, and eye diseases.
8) Plant s terols and stanol ester	Corn, soy, wheat, and wood oils.	Lower blood cholesterol levels by inhibiting cholesterol absorption.

9) Prebiotics/Probiotics		
i) Fructo-Oligosaccharides (FOS)	Jerusalem artichokes, shallots, and onion powder.	Improve gastrointestinal health.
ii) Lactobacillus	Yogurt and other dairy products.	Improve gastrointestinal health.
10) Saponins	Soybeans, soy foods, and soy protein - containing foods.	Lower LDL cholesterol; anti-cancer activity.
11) Soy protein	Soybeans and soy - based foods.	25 grams per day may reduce risk of heart disease.
12) Phytoestrogens		
i) Isoflavones-daidzein, genistein	Soybeans and soy - based foods.	Reduce menopause symptoms, such as hot flashes.
ii) Lignans	Flax, rye, and vegetables.	Protect against some cancers and heart diseases.
13) Sulphides/Thiols		
i) Diallyl sulphide	Onions, garlic, leeks, and scallions.	Lower LDL cholesterol; and maintain healthy immune system.
ii) Allyl methyl trisulphide, Dithiolthiones	Cruciferous vegetables	Lower LDL cholesterol; and maintain healthy immune system.
14) Tannins and proanthocyanidins	Cranberries, cranberry products, cocoa, and chocolate.	Improve urinary tract h ealth; and reduce the risk of CVDs.

4.1.2.4. Nutraceuticals According to their Higher Content in Specific Food Items

Nutraceuticals can be classified based on the relatively concentrated foods. This approach of classification is more appropriate when there is int erest in a particular nutraceutical compound or related compounds, or in a specific food for agricultural/geographic reasons or functional food -development purposes; **for example,** the interest may be in nutraceutical qualities of a local crop or a traditionally consumed food in a geographic region. Some nutraceuticals are found in higher concentrations in specific foods or food families; **for example**, capsaicinoids are mainly found in pepper fruit, and allyl sulphur (organosulphur) compounds are mainly concen trated in onions and garlic. **Table 4.4** represents some nutraceuticals that are considered unique to certain foods or food families.

Table 4.4: Examples of Foods with Higher Content of Specific Nutraceuticals

Neutraceutical Substances/Family	Foods of Remarkably High Content
Allyl sulphur compounds	Onion and garlic
Isoflavones (**e.g.,** genistein and daidzein)	Soybeans and other legumes, apios
Quercetin	Onion, red grapes, citrus fruit, broccoli, and Italian yellow squash
Capsaicinoids	Pepper fruit
FPA and DHA	Fish oils
Lycopene	Tomatoes and tomato products
Isothiocyanates	Cruciferous vegetables
β-Glucan	Oat bran
CLA	Beef and dairy
Resveratrol	Grapes (skin) and red wine

β-Carotene	Citrus fruit, carrots, squash, and pumpkin
Carnosol	Rosemary
Catechins	Teas and berries
Adenosine	Garlic and onion
Indoles	Cabbage, broccoli, cauliflower, kale, and Brussels sprouts
Curcumin	Turmeric
Ellagic acid	Grapes, strawberries, raspberries, and walnuts
Anthocyanates	Red wine
3-n-Butyl phthalide	Celery
Cellulose	Most plants (component of cell walls)
Lutein and zeaxanthin	Kale, collards, spinach, corn, eggs, and citrus
Psyllium	Psyllium husk
Monounsaturated fatty acids	Tree nuts and olive oil
Inulin and Fructooligosaccharides (FOS)	Whole grains, onions, and garlic
Lactobacilli and bifidobacteria	Yogurt and other dairy
Catechins	Tea, cocoa, apples, and grapes
Lignans	Flax and rye

Note: The substances listed in this table include those that are either accepted or purported nutraceuticals.

One consideration for this classification approach is that for several substances there is a short list of food s that are concentrated sources. However, the list of food sources for other nutraceuticals can be much longer and include many unrelated foods. **For example,** citrus fruits and onions are unrelated plant foods (as the former grow on trees and the latter is the edible bulb of a herb that develops at ground level), but both contain isoflavone quercetin.

4.1.3. Market, Growth and Scope of Products Available in the Market

In India, the healthcare costs need to be reduced because of the rising R and D costs, patent ex piration, volatile market scenarios, hikes in healthcare costs, and disease burden. There is also a shift towards wellness among educated and health-conscious patients. Any individual does not want to fall sick even if he/she is not aware of healthy habits and health benefits provided by a product. So, it is observed that consumers generally choose OTC products or counts on their experience, and revert to readily available and cost-effective traditional medicines.

Consumers are now bound to look towards pr evention. For good health , a patient/consumer should use medicines as well as food products considered as nutraceuticals. In cases of chronic diseases, doctors are creating awareness and advising the patients about changing lifestyle and food habits. A pro gress in scientific understanding of natural products from advertisements increased the market demand for nutraceuticals. Proteins, fibres, and various specialised functional additives have become the top-selling group of nutraceutical ingredients. The wide variety and complexity of nutraceuticals around the world have made

accurate estimation of their true market value and their sales very difficult. A report from Freedonia Group noted that "nutraceutical application is forecasted to reach $6.0 billion in 2015, up to 6.2% annually from 2010".

Based on the increasing demand for nutraceuticals in the Western world, it is predicted that China, Brazil, Japan, India, Mexico, Poland, Russia, and South Korea will evolve as the largest producers of nutraceuticals by 2020. Nutraceuticals as formulated beverages, foods, and dietary supplements are becoming mainstream in American households. A popular insight is that these products will prevent disease, enhance performance, and delay the onset of ageing, leading to a huge market share of nutraceutical products to over U.S$80 billion.

As per the results of a research from Freedonia global market, the nutraceutical and dietary supplement industry was found to be growing annually in excess of 7% to reach U.S. $24 billion in 2015. According to Global Industry Analysts, the global market for functional food and drinks was expected to reach U.S. $130 billion by 2015.

Global Business Intelligence (GBI) researchers estimated that the global nutraceutical market worth is around U.S. $128.6 billion, after increasing at a Compound Annual Growth Rate (CAGR) of 4.4% during 2002 through 2010. It was projected that the market will expand to about U.S. $180.1 billion by 2017, after growing at a CAGR of 4.9% from 2010 through 2017. GBI attributed the growth rates to an increase in the elderly population, the affluence of the working population, and increasing awareness of and preference for preventive medicine. These factors are in stimulating market growth in United States, Japan, the United Kingdom, Spain, Italy, Germany, and France, which are regarded the top seven markets of world.

According to Nutraceutical Product Market, Global Market Size, Segment and Country Analysis and Forecasts (2007-2017), the North America and Asia Pacific nutraceutical markets were found to be having market shares of 39.2% and 30.4%, respectively in 2017. In a recent study it was stated that the number of people above 60 years will be >1 billion by 2020 of which 70% will be from developed nations. It was expected that the increasing elderly population will drive the global nutraceutical market upward to about U.S. $250 billion by 2018.

In a report published by the BBC, the global nutraceutical market was estimated to reach about U.S. $207 billion in 2016. Functional beverages market was expected to experience the highest growth, at a CAGR of 8.8% from 2011 to 2016.

China is another market that is growing significantly, followed by Brazil (U.S. $881 million in 2006), Turkey (U.S. $200 million in 2006), and Australia, New Zealand, and Middle East and African countries (U.S. $300 million in 2006).

Indian Market

Another emerging worldwide market include India with U.S. $540 million in sales in 2006, and an expected annual rise of almost 38% crossing the billion mark by the end of 2009. The Indian nutraceutical market is estimated to grow

five times its current size by the end of the current decade. Currently, the market is growing at a double digit rate and may reach 195 billion (approximately $4.2 billion) mark in the current fiscal year. The growth of nutraceutical market in India is large because of the increased affluence and lifestyle diseases and change in consumer perception and mind-set. Increase in awareness about the extra supplements amon g consumers and an increase in health consciousness along with rising healthcare costs are paving the way for the growth of Indian nutraceutical market.

The market is becoming increasingly competitive with three different types of players in the market, i .e., pharma companies, FMCG companies, and pure nutraceutical manufacturers.

When nutraceuticals were introduced in India, it was not known by the industry leaders if nutritional supplements would gain acceptability in the Indian prescription-driven healt h and wellness industry. But, nutraceuticals were well-accepted, mostly by the upper -middle segment of the Indian population. However, the industry is in developing stage and still has many opportunities for further growth in future.

Scope of Indian Nutraceutical Markets

The Indian nutraceutical market valued at $1,480 million in 2011 was expected to grow to $2,731 million in 2016. As per the report of business research and consulting firm Frost & Sullivan, functional foods were the quickest growing category accompanied by dietary supplements until 2015. However, dietary supplements (specially, herbal and dietetic supplements) will form the greatest opportunity areas for nutraceutical manufacturers. The report also mentioned that dietary supplements are th e largest category accounting for 64% of the nutraceuticals market driven by the pharmaceutical sector in the form of vitamin and mineral supplements.

According to a study, the global nutraceutical market was estimated to be $149.5 billion in 2011 with U .S., Europe and Japan being the largest regional markets, accounting for 93% of the global nutraceutical demand. With maturity of these markets, with exceptionally high per capita spends on nutraceutical products, the nutraceutical manufacturers are looking towards developing countries (such as India and China) as the key growth regions. Besides the current low per capita spend on these products in India, increasing obesity in the population , and rising occurrences of diabetes and cardiovascular diseases are the other factors supporting nutraceutical growth in India.

The government is also chipping in by funding vitamin fortification initiatives due to increasing food security concerns in India and need for additional nutrition. With increasing sophistication among nutraceuticals, consumer demand for products with specific health benefits is increasing. Globalisation of nutraceutical and functional food industries challenges the stakeholders, not the least of which is the regulatory variance between countries active in the marketplace.

Nutraceuticals are important in the development of future therapeutics, but it depends on the control of purity, efficacy, and safety. Henceforth, whenever a new applicant wants to enter the Indian nutraceutical market, it is important to comply with the regulatory framework, so that the business runs smoothly. The focus areas should be product evaluation for each active ingredient in the context of permissibility, standards and dosage of vitamins/minerals allowed, product classification as per various Indian healthcare laws, India-specific label claims and advertising.

The recent happenings on regulatory front and the requirements of a business performance consultancy (giving an overview of the Indian nutraceuticals market) should be met by new entrants before entering it. The global nutraceutical market was estimated to be $140.1 billion in 2010; of which, U.S. and Europe formed the largest markets accounting to 36% and 25%, respectively. In 2010, the Indian nutraceutical market was estimated at $2 billion, which was only 1.5% of the global nutraceutical industry. Broad segments of Indian nutraceutical industry include dietary supplement (40%) and functional food and beverage market (60%). The total Indian nutraceuticals market was expected to be approximately $5 billion in 2015.

4.1.4. Types of Products Available in the Market

Nutraceuticals are non-specific, biological therapeutic agents that promote wellness, prevent malignancy, and maintain homeostasis. They can be grouped into the following categories:

1) **Nutrients:** These are substances with established nutritional functions, **e.g.,** vitamins, minerals, amino acids, and fatty acids.

Table 4.5: Nutrients Used and their Health Benefits

Nutrients	Health Benefits
Vitamin A	Antioxidant; essential for growth and development; helps in the treatment of certain skin disorders.
Vitamin E	Antioxidant; helps in forming blood cells, muscles, lung and nerve tissue; boosts the immune system.
Vitamin K	Essential for blood clotting.
Vitamin C	Antioxidant; essential for healthy bones, gums, teeth and skin; helps in wound healing; prevents common cold and attenuate its symptoms.
Vitamin B_1	Helps to convert food into energy; essential in neurologic functions.
Vitamin B_2	Helps in energy production and other chemical processes in the body; helps in maintaining healthy eyes, skin and nerve function.
Vitamin B_3	Helps to convert food into energy; maintains proper brain function.
Vitamin B_6	Produces the genetic material of cells; helps in the formation of RBCs; maintenance of central nervous system; synthesises amino acids; metabolism of fats, proteins and carbohydrates.
Folic acid	Produces the genetic materials of cells; in pregnancy for preventing birth defects; RBCs formation; protects against heart disease.
Calcium	Essential for development of bones and teeth; maintains bone strength; important in nerve, muscle and glandular functions.
Iron	Energy production; carries and transfers oxygen to tissues.
Magnesium	Healthy nerve and muscle function; bone formation; helps prevent Premenstrual Syndrome (PMS).
Phosphorous	Essential for development of strong bones and teeth; helps in formation of genetic material; energy production and storage.

Chromium	With insulin helps in converting carbohydrates and fats into energy.
Cobalt	Essential component of vitamin B_{12}, but ingested cobalt is metabolised *in vivo* to form the B_{12} coenzymes.
Copper	Essential for haemoglobin and collagen production; healthy functioning of heart; energy production; absorption of iron from digestive tract.
Iodine	Essential for proper functioning of thyroid.

2) **Herbals:** These are herbs or botanical products used as concentrated extracts.

Table 4.6: Herbals Used and their Therapeutic Activities

Herbals	Therapeutic Activities
Aloe vera gel *(Aloe vera L.N.L. Burm)*	Dilates capillaries; anti -inflammatory; emollient; wound healing properties.
Chamomile *(Matricaria recutita L.)*	Anti-inflammatory; spasmolytic; antimicrobial; wound healing properties.
Echinacea *(Echinacea purpurea L.)*	Immunostimulant; treatment of cold and flu symptoms.
Ephedra (*Ephedra sinica* Stapf.)	Bronchodilator; vasoconstrictor; reduces bronchial oedema.
Evening primrose oil *(Oenothera biennis L)*	Dietary supplement of linoleic acid; treatment of atopic eczema.
Feverfew *(Tanacetum parthenium L.)*	Treatment of headac he, fever, menstrual problem, severity and duration of migraine headaches.
Garlic *(Allium sativum L.)*	Antibacterial; antifungal; antithrombotic; hypotensive; anti-inflammatory.
Ginger *(Zingiber officinale Rosc.)*	Carminative; anti-emetic; cholagogue; positive inotropic.
Ginseng *(Panax ginseng)*	Adaptogen.
Ginkgo *(Ginkgo biloba L.)*	Vasodilation; increased peripheral blood flow ; treatment of post-thrombotic syndrome.
Goldenseal (*Hydrastis canadensis L.)*	Antimicrobial; astringent; anti-hemorrhagic; t reatment of mucosal inflammation dyspepsia, and gastritis.
Horehound *(Marrubium vulgare L.)*	Expectorant; antitussive; choleretic.
Licorice *(Glycyrrhiza glabra L.)*	Expectorant; secretolytic; treatment of peptic ulcer.
Melissa *(Melissa officinalis L.)*	Topical antibacterial and antiviral.
Plantago seed *(Plantago arenaria waldst)*	Cathartic
St. John's wort *(Hypericum perforatum L.)*	Anxiolytic; anti-inflammatory; antidepressant; monoamine oxidase inhibitor.
Valerian *(Valeriana officinalis L.)*	Spasmolytic; mild sedative; sleep aid.
Willow bark *(Salix alba L.)*	Anti-inflammatory; analgesic; antipyretic; astringent; treatment of rheumatic and arthritis.

3) **Dietary Supplements:** These substances are derived from other sources (**e.g.,** pyruvate, chondroitin sulphate, and steroid hormone precursors) that serve specific functions, **e.g.,** sports nutrition, weight loss supplements, and other dietary replacement.

Table 4.7: Dietary Supplements Used and their Significance

Dietary Supplements	Significance
Ketogenic diets	Comprised of foods with high fat and low p rotein and carbohydrate content; have been repo rted to improve seizure control; h owever, are widely ack nowledged to be unpalatable.
Minimally refined grains	Cereals and grains fortified with calcium ; may reduce the incidence of diabetes; prevent gastrointestinal cancers.
Phytoestrogens	Found in soya flour and linseeds; have been documented to enhance oestrogens levels when hormonal levels are low; this action may prevent hot flushes and breast cancer.
Several species of edible mushrooms	Tonnage, Lentinus, Pleurotus, Auricularia, Flammulina, Tremella, Hericium , and Grifola have vary ing degrees of immunomodulatory; lipid lowering and antitumor activity without any significant toxicity.
Glucosamine sulphate and chondroitin sulphate	Effective and safer to alleviate symptoms of osteoarthritis.
Peptides/Hydrolysates	Found in casein and whey protein ; have A CE inhi bitor activity; b uckwheat proteins used as flour reduces cholesterol, hypertension; improve constipation and obesity by acting similar to dietary fibres and interrupting *in vivo* metabolism.
Dairy foods	Contain friendly or probiotic bacteria claimed to promote gut health; bio -yoghurts containing *Lactobacillus acidophilus* and *Bifido* bacteria lead the sector.

Table 4.8 lists the nutraceutical products available in the market:

Table 4.8: List of Marketed Nutraceutical Products

Products	Categories	Contents
Coral Calcium	Calcium supplement	Calcium and trace minerals
Weightsmart	Nutritional supplement	Vitamins and trace elements
Omega Woman	Immune supplement	Antioxidants, vitamins and phytochemicals (**e.g.,** lycopene and resveratrol)
Appetite Intercept	Appetite suppressant	Caffeine, tyrosine, and phenylalanine
Chaser	Hangover supplement	Activated calcium carbonate and vegetable carton
Rox	Energy drink	Taurine, caffeine, and glucuronolactone
Mushroom Optimiser	Immune supplement	Mushrooms, polysaccharides, and folic acid
Biovinca	Neurotonic	Vinpocetine
Proplus	Nutritional supplement	Soy proteins
Snapple-a-day	Meal replacement beverage	Vitamins and minerals
WelLife	Amino acid supplement	Granulated-L-glutamine
PNer pfus	Neuropathic pain supplement	Vitamin and other natural supplement
Olivenol	Dietary supplement	Natural antioxidant, i.e., hydroxytyrosol
Threptin Diskettes	Protein supplement	Proteins and vitamin B
GRD	Nutritional supplement	Proteins, vitamins, minerals, and carbohydrates
Proteinex	Protein supplement	Pre-digested proteins, vitamins, minerals, and carbohydrates
Calcirol D-3	Calcium supplement	Calcium and vitamins

Nutraceuticals can be categorised as follows based on the foods available in the market:

1) **Traditional Nutraceuticals:**
   i) Chemical constituents:
      a) Nutrients,
      b) Herbals, and
      c) Phytochemicals.
   ii) Probiotic microorganisms, and
   iii) Nutraceutical enzymes.
2) **Non-Traditional Nutraceuticals:**
   i) Fortified nutraceuticals, and
   ii) Recombinant nutraceuticals.

4.1.4.1. Traditional Nutraceuticals

Traditional nutraceuticals are natural substances with no changes to the food. They contain several natural components that deliver benefits beyond basic nutrition, **e.g.,** lycopene in tomatoes, omega-3 fatty acids in salmon, or saponins in soy.

Table 4.9 illustrates the applications of traditional nutraceuticals in chronic disease control:

Table 4.9: Applications of Traditional Nutraceuticals in Chronic Disease Control

Nutraceuticals	Effects
Allenic carotenoid fucoxanthin (brown seaweeds)	Improves insulin resistance and decreases blood glucose levels through regulation of cytokine secretions from WAT (White Adipose Tissues).
n-3 PUFAs (Polyunsaturated Fatty Acids)	Prevents several disorders affecting lungs and airways.
ASU (unsaponifiable residues of avocado and soybean oils)	Stimulates synthesis of aggrecan and extracellular matrix component as type II collagen by reducing the production of catabolic (MMP-3) and pro-inflammatory (IL-8 and IL-6) mediators in OA (osteoarthritis) .
CLA (Conjugated Linoleic Acids)	Significantly improves AHR (Airway Hyper Responsiveness) associated with reduction in leptin/adiponectin ratio in mild asthma.
Siphonaxanthin, a marine carotenoid (green algae)	Induces apoptosis in H L-60 cells by decreasing Bcl -2; increases activation of caspase-3.
FPP (Fermented Papaya Preparation)	Unregulated TNF -α and Thioredoxin (Trx) in liver cirrhosis.
MUFAs(Monounsaturated Fats)	Lowers cardiovascular disease risk and metabolic syndrome.
$1,25(OH)_2D$, or calcitriol	Regulates the levels of p21 and p27 and increases expression of BRCA -1 and -2 tumour suppressor genes contributing in DNA repair mechanism .
Resveratrol	Chemosensitises tumour by modulating drug transporters, cell survival proteins, cell proliferative proteins, and members of the NF -kB and STAT3 signalling pathways.
Fortified wheat flour	Reduces prevalence of NTDs (Neural Tube Defects) at birth; increases blood folate concentrations .

Traditional nutraceuticals are categorised into:

1) **Chemical Constituents:** These are of the following types:
   i) **Nutrients:** These substances, **e.g.,** vitamins, minerals, amino acids , and fatty acids, have established nutritional functions. Most vegetables, wholegrain cereals, dairy products, fruits, and animal products (such as, meat and po ultry) contain vitamins and cure heart diseases, stroke, cataracts, osteoporosis, diabetes, and cancer. Plant, animal and dairy products contain minerals that are useful in osteoporosis, anaemia, building strong bones, teeth and muscles, and improving nerve impulses and heart rhythm. Flax seeds and salmon contain fatty acids and omega-3 PUFAs, and control the inflammatory processes, maintain brain functions, and reduce cholesterol deposition.

   ii) **Herbals:** Nutraceuticals are very useful in improving health and preventing chronic diseases with the help of herbals. Some **examples** of which are:
      a) Willow bark (*Salix nigra*) contains salicin, which is an anti - inflammatory, analgesic, antipyretic, astringent, and anti-arthritic.
      b) Parsley (*Petroselinum crispum*) contains flav onoids (apiol and psoralen) and is a diuretic, carminative, and antipyretic.
      c) Peppermint (*Mentha piperita*) contains menthol and cures cold and flu.
      d) Lavender (*Lavandula angustifolia*) contains tannin, which cures depression, hypertension, stress, cold, cough, and asthma.
      e) Cranberries (*Vaccinium erythrocarpum*) contain proanthocyanadin and are useful in cancer, ulcers, and urinary tract infections.

   iii) **Phytochemicals:** These nutraceuticals are c lassified on the basis of the chemical name given to them as per their phy tochemical properties. Some **examples** are:
      a) Carotenoids (isoprenoids) found in various fruits, vegetables and egg yolk, are anti -carcinogenic, boost natural killer immune cells , and protect cornea against UV light.
      b) Legumes (chickpeas and soybeans), grains, a nd palm oil contain non-carotenoids, which remove cholesterol and are anti - carcinogenic.
      c) Flavonoid polypheno lics, present in berries, fruits, vegetables, and legumes, are antioxidants, phytoestrogens, prevent breast cancer, prostate cancer, and control diabetes.
      d) Non-flavonoid polyphenolics, present in dark grapes, raisins, berries, peanuts, and turmeric roots ar e strong anti -inflammatories, anti-oxidants, and anti -clotting agents, and reduce cholesterol.
      e) Phenolic acids, present in blueberries, tomatoes, and bell peppers, are antioxidants, and reduce mutagenicity of polycyclic aromatic hydrocarbons.
      f) Seeds of *Barbarea verna* and broccoli contain isothiocyanates (glucosinolates) having anti-tumorigenesis activity.

2) **Probiotic Microorganisms:** The scientific interest in probiotics was encouraged from the work of **Metchnikoff.** To transform the toxic flora of large intestine into a host-friendly colony of *Bacillus bulgaricus* was found by **Hord**. **Probiotics** mean **for life** and are **live microorganisms, which on consuming in adequate amounts confer a healthy effect on the host**

Probiotics are friendly bacteria that promote healthy digestion and absorption of some nutrients. They crowd out pathogens, such as yeasts, bacteria, and viruses that may cause disease and develop a mutually advantageous symbiosis with human GIT. Probiotics exert an antimicrobial effect by modifying the microflora, preventing adhesion of pathogens to intestinal epithelium, competing for nutrients essential for pathogen survival, producing an antitoxin effect, and reversing some consequences of infection on intestinal epithelium, such as secretory changes and neutrophil migration. They can cure lactose intolerance by producing β-galactosidase enzyme that hydrolyses the offending lactose into its component sugars. Sources of probiotic microorganisms are enlisted in **table 4.10**:

Table 4.10: Sources of Probiotic Microorganisms

Milk	Yoghurt	Fermented Products	Human Breast Milk	GIT	Vegetables or Grains or Fruits
Lactobacillus acidophilus	*L. delbrueckii* subsp. *bulgaricus*	*L. casei* *L. cellobiosus* *L. curvatus* *L. fermentum* *L. helveticus* *L. farciminis*	*L. reuteri* *L. salivarius*	*L. gasseri* *L. johnsonii*	*L. brevis* *L. plantarum*
L. lactis	*Bifidobacterium adolescentis*	*B. thermophilum* *B. animalis*	*B. infantis* *B. longum* *B. breve* *B. lactis*		*Leuconostoc mesenteroides*
Propionibacterium freudenreichii	*Streptococcus thermophilus*	*Enterococcus faecium* *Pediococcus acidilactici*		*E. coli* Nissle 1917	*Saccharomyces cerevisiae* *S. boulardii* Mushrooms

3) **Nutraceutical Enzymes:** Enzymes are an essential part of life, without which our bodies would stop functioning. Individuals suffering from hypoglycaemia, blood sugar disorders, digestive problems, and obesity, are relieved from the symptoms by adding enzyme supplements to their diet. These enzymes are derived from microbial, plant and animal sources (**table 4.11**).

Table 4.11: List of Nutraceutical Enzymes from Microbes, Plants and Animals

Microbial Enzymes/Source	Plant Enzymes/Source	Animal Enzymes/Source
Hemicellulase (microorganisms and mushrooms)	Hemicellulase (plant walls)	OxBile (ox)
Catalase	Pectinase (cell wall)	Pancrelipase (pancreatic juice)
Amyloglucosidase (ascomycetes)	α- Galactosidase (beans, cabbage, Brussels sprouts, broccoli, asparagus, other vegetables, and whole grains)	Trypsin (pancreatic juice)

Glucoamylase (*Aspergillus niger*, *Saccharomycopsis fibuligera*)	β-Amylase (higher plants)	Chymotrypsin (all classes of vertebrates)
Cellulase (all living cells)	Bromelain (pineapple)	Pepsin (animals tracheal secretions)
Invertase – Sucrase (yeast)	Biodiastase (soybean)	Lysozyme (saliva, tears, egg white, and animal fluids)
Lactase-β-galactosidase (bacteria)	Glucoamylase (callus and suspension cultures of sugar beets and in mature roots)	α-Amylase (saliva)

4.1.4.2. Non-Traditional Nutraceuticals

Non-traditional nutraceuticals are artificial foods prepared with the help of biotechnology. Food samples contain bioactive components engineered to produce products for human wellness. These nutraceuticals are classified into:

1) **Fortified Nutraceuticals:** These nutraceuticals include fortified food from agricultural breeding or added nutrients and/or ingredients. Some **examples** are:
   i) Orange juice fortified with calcium,
   ii) Cereals with added vitamins or minerals,
   iii) Flour with added folic acid,
   iv) Milk fortified with cholecalciferol is used in vitamin D deficiency,
   v) Prebiotic and probiotic milk fortified with *Bifidobacterium lactis* HN019 is used in diarrhoea, respiratory infections, and severe illnesses in children, and
   vi) Banana fortified with soybean ferritin gene is used in iron deficiency.

2) **Recombinant Nutraceuticals:** These nutraceuticals include energy-providing foods, such as bread, alcohol, fermented starch, yogurt, cheese, vinegar, etc. These are produced with the help of biotechnology. Production of probiotics (**table 4.12**) and extraction of bioactive components by enzyme/fermentation technologies and genetic engineering technology are achieved through biotechnology.

Table 4.12: Products Produced by Recombinant Microorganisms, Plants and Animals

Recombinant Microorganisms		
Sources	**Enzymes**	**Products**
Acetobacter xylinum	β-glucuronidase	Kombucha beverage
E. coli K-12	Chymosin	Milk-coagulated products
Fusarium venenatum	Xylanase	Increased bran solubilisation
Aspergillus oryzae	Esterase-lipase, aspartic proteinase, glucose oxidase, lactase, lipase, pectin esterase	Alcoholic beverages (Sake, koji)
Saccharomyces cerevisiae	Stilbene synthase and 4-coumaroyl-CoA	Resveratrol
Spirulina pacifica	Indoleamine 2,3-Dioxygenase (IDO)	Increased haemoglobin
Recombinant Plants		
Sources	**Deficiency**	**Gene for Recombination**
Gold kiwifruit	Iron	High level of ascorbic acid, carotenoids lutein, and zeaxanthin

Potatoes	Protein	Tuber-specific expression of a seed protein, AmAl (Amaranth Albumin 1)
Golden mustard	Vitamin A	Soybean ferritin gene
Multivitamin corn	Multivitamin	Vitamins (β-carotene corn (Zea mays) phytoene synthase (psyl) cDNA), ascorbate (rice dehydroascorbate reductase (dhar) cDNA), and folate (*E. coli* folE gene encoding GTP cyclohydrolase (GCH1)
Maize	Vitamin A (retinol)	Bacterial genes (crtB and crtl)
Tomato	Folate	Aminodeoxychorismate synthase (AtADCS)
Golden rice	Vitamin A (retinol)	Two daffodil genes and one bacterial gene
Iron rice	Iron deficiency	Soybean ferritin gene
Recombinant Animals		
Fermented soya milk	Calcium deficiency	*Lactobacillus acidophilus* American Type Culture Collection (ATCC) 4962
Cattle	Human lysozyme	rHLZ expression vector pBC2 -HLY-NEOR
Yogurt	Probiotics microorganism	*Bifidobacterium lactis* Bb-12 and *Lactobacillus acidophilus* LA-5
Cows	Lactoferrin deficiency	Recombinant human Lactoferrin (rhLf)

4.1.5. Health Benefits of Nutraceuticals

Nutritional therapy is a healing system that uses dietary therapeutics or nutraceuticals as a complementary therapy.

This therapy relies on the belief that foods can not only be sources of nutrients and energy, but can also provide the following benefits:

1) Provide medicinal benefits,
2) Avoid side effects,
3) Increase the health beneficial effects,
4) Due to their natural dietary supplement, they do not have unpleasant side effects,
5) Increase the health value, diet and improve medical condition of humans, and
6) Easily available and economically affordable.

Most of the nutraceuticals possess numerous therapeutic benefits and are claimed to exhibit physiological benefits or provide protection against various diseases. Some of these products are:

1) Cardiovascular agents,
2) Anti-obese agents,
3) Anti-diabetic agents,
4) Anti-cancer agents,
5) Immune boosters,
6) Substances that manage chronic inflammatory disorders, and
7) Formulations to cure degenerative diseases.

Table 4.13: Some Diseases that can be Cured by Nutraceuticals

Diseases	Nutraceuticals
Eye health	Lutein and zeaxanthin.
Mental health	Phosphatidylserine, docosahexaenoic, and soy isoflavones.
Sleep enhancement	Melatonin.
Cancer prevention	Tea, lycopene, and flax seeds.
Bone health	Melatonin and L-carnitine.
Skin health	Tea, soy isoflavones, glycosamine, and melatonin.
Oral health	Pycnogenol.

4.2. ROLE OF NUTRACEUTICALS IN AILMENTS

4.2.1. Introduction

Nutraceuticals are getting recognised for being valuable in coronary heart disease, obesity, diabetes, cancer, osteoporosis, and other chronic and degenerative diseases like Parkinson's and Alzheimer's diseases. As per the evidences, the natural compounds act via various biological processes that include activation of antioxidant defences, signal transduction pathways, cell survival-associated gene expression, proliferation and differentiation of cell, and preservation of mitochondrial integrity. These processes have vital roles in providing protection against the pathologies of a wide array of age-related or chronic diseases. The nutrients found in many foods, fruits, and vegetables contribute to the many well-known health benefits. **For example**, lutein and zeaxanthin prevent cataracts and macular degeneration; β-carotene and lycopene protect the skin from UV light damage; lutein and lycopene benefit cardiovascular health; and lycopene helps preventing prostate cancer. Because of these and other health benefits, nutraceuticals should be regularly consumed, as they also reduce the risk factors of high cholesterol, high blood pressure, and diabetes.

There are many industries that manufacture and market nutraceutical products, and where the side effects of these nutraceuticals (especially when consumed in large quantities) are not reported or are still to be proved. In order to have scientific knowledge about the nutraceuticals, the consumers should be educated and should know the recommended daily doses. Since the interest in nutraceuticals is rapidly increasing, a nutraceutical research community should be established to convert the numerous potential nutraceuticals into established ones so that their enormous benefits can be offered to all. Herbal treatment with the active constituents obtained from different parts of herbs for treatment and utilisation in various health problems are presented in **table 4.14**.

Table 4.14: Different Types of Diseases and Nutraceuticals Used in their Treatment

Types of Diseases	Nutraceuticals Used
Cardiovascular diseases	1) Anti-oxidants, dietary fibres, omega -3 PUFAs, vitamins, minerals for prevention and treatment of CVD. 2) Polyphenol (in grapes) prevent and control arterial diseases. 3) Flavonoids (in onions, vegetables, grapes, red wine, apples, and cherries) block the ACE and strengthen the tiny capillaries that carry oxygen and essential nutrients to all cell 4) Ethyl esters of n-3 fatty acids may be beneficial in diabetic patients.

Diabetes	1) Docosahexaenoic acid modulates insulin resistance and is also vital for neurovisual development. 2) Lipoic acid (an antioxidant) is used for the treatment of diabetic neuropathy. 3) Dietary fibres from psyllium have been used for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia. 4) Herbal stimulants, such as ephedrine, caffeine, ma huang - guarana, chitosan and green tea, help in body weight loss. 5) Buckwheat seed proteins act similar to natural fibres present in food.
Obesity	1) 5-Hydroxytryptophan and green tea extract may promote weight loss, while the former decreases appetite, the lat ter increases energy expenditure. 2) A blend of glucomann an, chitosa n, fenugreek, *Gymnema sylvestre*, and vitamin C in dietary supplement significantly reduce body weight. 3) Conjugated Linoleic Acid (CLA), capsaicin, and Momordica Charantia (MC) possess potential anti -obese properties. 4) Flavonoids block the enzymes that produce estrogen , thus reduce estrogen-induced cancers. 5) A broad range of phytopharmaceuticals with a claimed hormonal activity, called phyto -estrogens prevent prostate/breast cancer. 6) Isoflavones from s oy foods and curcumin from curry possess cancer chemopreventive properties.
Cancer	1) Lycopene concentrates in the skin, testes, adrenal and prostate and protects these organs against cancer. 2) Saponins (found in p eas, soybeans, some herbs, spinach, tomatoes, potatoes, alfalfa , and clover) contain antitumor and anti-mutagenic activities. 3) Curcumin (a polyphenol of turmeric) possesses anti - carcinogenic, anti -oxidative and anti -inflammatory properties. 4) Top of beet roots, cucumber fruits, spinach leaves, and turmeric rhizomes, were reported to possess anti -tumour activity. 5) γ-Linolenic acid (found in green leafy vegetables, nuts, vegetable oils, i.e., evening primrose oil, blackcurrant seed oil, and hemp seed oil, and from spirulina, cyanobacteria) is used for treating problems related to inflammation and auto-immune diseases.
Anti-inflammatory activities	1) Glucosamine and chondroitin sulphate are used against osteoarthritis and regulate gene expression and synthes is of NO and PGE_2. 2) Cat's claw has 17 alkaloids, along with glycosides, tannins, flavonoids, sterol fractions, and other compounds , and work as a potent anti-inflammatory agent.
Allergy	Querect (found in onions, red wine , and green tea) reduce inflammation that results from hay fever, bursitis, gout, arthritis, and asthma.

Alzheimer's disease	β-carotene, curcumin, lutein, lycopene, turmerin, etc., may exert positive effects on specific diseases by neutralising the negative effects of oxidative stress, mitochondrial dysfunction, and various forms of neural degeneration.
Vision improving agents	1) Lutein (found in mangoes, corn, sweet potatoes, carrots, squash, tomatoes and dark, leafy greens) is used for the treatment of visual disorders. 2) Zeaxanthin (found in corn, egg yolks, and green vegetables and fruits, such as broccoli , green beans, green peas, brussel sprouts, cabbage, kale, collard greens, spinach, lettuce, kiwi and honeydew) is used in traditional Chinese medicine mainly for the treatment of visual disorders.
Osteoarthritis	Glucosamine (GLN) and Chondroitin Sulphate (CS) alleviate the symptoms.

4.2.2. In Diabetes

Diet therapy is the keystone for the management of gestational diabetes mellitus. There are many he rbal dietary supplements that are believed to benefit type 2 diabetes mellitus; however, only a few have been proven beneficial through properly designed randomised trials. **Isoflavones** are phytoestrogens with structural or functional similarity to human estrogen and are widely consumed by humans. **Soy isoflavones** are the most studied ones. Consuming isoflavone in high amounts (20-100mg/day) reduces the incidence and mortality rate of type 2 diabetes, heart disease, osteoporosis, and certain cancers.

Omega-3 fatty acids reduce glucose tolerance in patients prone to diabetes. Insulin is required for synthesising long chain n -3 fatty acids; thus, the heart should be susceptible to their depletion in diabetes. **Ethyl esters of n -3 fatty acids** are also potentially beneficial in diabetes.

Docosahexaenoic acid controls insulin resistance and is helpful in neurovascular development. It is very important in women with gestational diabetes mellitus as such a condition demands essential fatty acids during pregnancy.

Lipoic acid is an antioxidant and is used in diabetic neuropathy. It may be more effective as a long term dietary supplement that aims at prophylactic protection of diabetic patients.

Dietary fibres from psyllium have been used as pharmacological supplement s and as food ingredients in processed food to help in weight loss, to control glucose in diabetics, and to reduce lipid levels in hyperlipidaemia.

Magnesium reduces diabetes risk and improves insulin sensitivity; **chromium picolinate**, **calcium** and **vitamin D** promote insulin sensitivity and improve glycaemic control in diabetics; **extracts of bitter melon** and **cinnamon** potentially treat and prevent diabetes.

4.2.3. In CVS Diseases

Worldwide incidences of abundance of chronic di seases, like cardiovascular diseases, cancers, diabetes, and obesity, are rapidly increasing. In 2001, chronic diseases contributed 59% of the 56.5 million total reported deaths in world.

Cardiovascular Diseases (CVD) are a group of disorders of heart and blood vessels, that include hypertension (high blood pressure), coronary heart disease (heart attack), cerebrovascular disease (stroke), heart failure, peripheral vascular disease, etc. In 1999, CVD contributed to 1/3 rd of global deaths and by 2010 it was the leading cause of death in developing countries. CVD are mostly preventable and controllable. Evidences suggest that less consumption of fruits and vegetables is associated with a high mortality in CVD.

Nutraceuticals in the form of **antioxidants**, **dietary fibres** , **omega-3 Polyunsaturated Fatty Acids** (n-3 PUFAs), **vitamins**, and **minerals** along with physical exercise helps in preventing and treating CVD. **Polyphenols** found in grapes and wine alter cellular metabolism and signalling, which consequently reduces arterial disease.

Flavonoids are found in onion, endives, cruciferous vegetables, black grapes, red wine, grapefruits, apples, cherries, and berries. In plants, they are available as **flavones** (containing apigenin found in chamomile), **flavanones** (containing hesperidins found in citrus fruits; silybin in milk thistle), and **flavonols** (containing quercetin found in tea; kaempferol and rutin in grapefruit; rutin in buckwheat; ginkgo flavone glycosides in ginkgo), which play a major role in curing CVD.

Flavonoids inhibit angiotensin-converting enzyme (that increases blood pressure) by blocking the suicide enzyme, i.e., cyclooxygenase, that breaks down prostaglandins; thus, preventing platelet aggregation. Flavonoids also protect the vascular system and strengthen the tiny capillaries that deliver oxygen and essential nutrients to all the cells. Flavonoids block the enzymes that produce estrogens, thus reduce the risk of cancers induced by estrogens.

4.2.4. In Cancer

Botanicals are in use in cancer treatment since a long time. Many cancer chemotherapeutic drugs are derived from plants, like the alkaloids of Vinca species (vincristine and vinblastine) and *Taxus brevifolia* (taxol). In the ancient cultures, a wide range of techniques were used for treatment and prevention of diseases, and for maintaining health. One subset of these techniques is plant extracts. Often, a number of cultures use similar plants for the same symptoms or diseases; thus, indicating that they are medicinally effective for those ailments.

Besides these medical advances, cancer still is a worldwide health problem, and various plant extracts are used for its treatment and prevention. Evidences suggest that **foods low in simple carbohydrates** and moderate amounts of **high-quality protein**, **fibre**, and **fat** (especially, fats of omega-3 fatty acid series) are beneficial for cancer patients. Nutraceuticals are also helpful in reducing toxicity associated with chemotherapy and radiotherapy, thus lead to better life conditions by reducing cancer cachexia. Phytochemicals have shown different mechanism of actions at different cellular levels. Most of them are versatile source of antioxidants affecting the signalling pathway related to redox-mediated transcription factors. They also directly modulate the endocrine system immunological cascade and enzymes related to inflammation. Some of them show direct effect on DNA repair and cleavage process.

Molecular Targets of Nutraceuticals in Cancer Care

Initial *in vitro* studies stated that phytochemicals help the tumorigenic actions of carcinogens, block their mutagenic activity, and suppress cell proliferation. **Chemoprevention** is the use of natural or synthetic chemicals to reverse, suppress, or prevent carcinogenesis process. In early stage, solid cancers appear as intraepithelial neoplasia or carcinoma *in situ,* corresponding to the promotion and progression stages. Therefore, anti-promotion and anti-progression agents are of particular clinical interest.

Even very low concentrations of dietary bioactive substances have a great impact on regulation of gene expression. On continuing research on the effects of nutraceuticals on gene expression, a better knowledge of prevention mechanism of diseases (such as obesity, diabetes, atherosclerosis, hypertension, and cancer) by dietary manipulations can be obtained.

It was also found that phytochemicals provide protection against lipid peroxidation, and modulate innate and inflammatory responses. These effects of plant extracts and also their lack of toxicity make them potentially effective against cancer. However, the mechanism of action and effectiveness of each compound in a specific type of cancer should be studied so that the correct compound can be used in appropriate clinical situation. The term **nutritional genomics** describes the research at the interface of plant biochemistry, genomics, and human nutrition.

A few studies on the activity of selected nutraceuticals have led to further detailed investigation of these molecules, using various genetic diseased animal models. Besides the active role of nutraceuticals and functional foods in control of cancer, there is also a great need to develop the food supplements as the add-on therapy to provide better quality of life for a cancer patient.

Some cancer patients show cachexia, i.e., significant alterations in carbohydrate, protein and fat metabolism. This leads to bad quality of life, reduces response to therapy, and shortens the survival span. These metabolic alterations in cancer patients can be reversed with nutritional modulation. Nutritional intervention is a powerful tool for controlling malignant diseases and for reducing toxicity related to chemotherapy and radiotherapy. Nutraceuticals can also increase the functioning of Natural Killers (NK) cells and Tumour Necrosis Factor (TXFα) in patients with late stage cancer.

Main Phytochemicals Studied for Cancer Care

Dietary phytochemicals are classified on the basis of their chemical structures, botanical origin, biological properties, biosynthesis, etc.

Polyphenols

Polyphenols are plant secondary metabolites containing one or more hydroxyl groups attached to a benzene ring in their structure. More than 8000 different polyphenols found in food (wine, tea, coffee, cocoa, vegetables, and cereals) are present in human diet.

Polyphenols are classified into different groups depending on the number of phenol rings and structure that links these rings. The groups of phenolic acids, flavonoids, stilbenes, and curcuminoids are very important for their ability to block initiation of carcinogenic process and to suppress cancer progression.

Epigallocatechin-3-Gallate (EGCG)

EGCG is the major catechin found in green tea (*Camellia sinensis*). Frequent consumption of green tea in Asian countries was found to be related to several health benefits and is recognised as the most effective cancer-preventive beverage. Its antitumor properties have been identified on multiple cancer cell lines, including less common tumours such as anaplastic thyroid carcinoma and malignant mesothelioma.

Studies determining the anticancer drug properties of EGCG are mostly preclinical; so, for better understanding of specific effects, clinical trials should be carefully designed to evaluate EGCG effectiveness. Clinical applications of green tea have the limitation of low bioavailability and conversion into inactive methylated metabolites. Biotransformation of green tea polyphenols is different in humans than in rats and mouse; this explains that inter-species difference exists in anti-carcinogenic properties.

Genetic polymorphisms in gene responsible for EGCG biotransformation, such as Catechol-O-Methyltransferase (COMT), should be considered while designing efficacy studies for green tea.

However, the numerous antitumor effects exerted by EGCG suggest that it is a potential tool for cancer prevention and therapy, both alone and together with antitumor drugs or other phytochemicals.

Resveratrol

Resveratrol is the most important stilbene related to cancer. It exhibits a natural anti-proliferative activity due to its role as a phytoalexin (plant antibiotic). It also has anti-cancer, anti-carcinogenesis and anti-inflammatory bioactivities. The mechanisms by which resveratrol produce these effects are not clear, but the main molecular mechanism is believed to be the activation of sirtuin proteins.

There is a considerable interest in developing resveratrol for cancer prevention and treatment. Plasma pharmacokinetics of resveratrol in humans is now well-defined, and studies show that its repeated daily doses are safe and well-tolerated.

However, pharmacokinetic studies of resveratrol show poor bioavailability (only 1%) due to extensive glucuronidation and sulfation, and metabolism by gut bacterial enzymes.

Quercetin

Quercetin (a representative member of flavonoid class) is a compound derived from various fruits and vegetables that can reach levels in human diet as high as 16-25mg/day.

Effects of quercetin are related to induction of cell apoptosis through multiple mechanisms. *In vivo* studies of the anticancer effects of quercetin indicate that its oral administration can prevent induced carcinogenesis in the colon, inhibit melanoma growth, invasion, and metastatic potential. However, just like resveratrol, quercetin also faces the problem of low bioavailability.

Vitamins and Minerals in Cancer Management
In several independent studies, vitamins (A, C, and E) and trace elements (selenium) were found to prevent cancer. Supplementation with micronutrients as adjuvant in cancer patients may pro ve to be helpful. Vitamin C (ascorbate) is an essential nutrient in human diet, but is also a widely used medicinal product, and has long been held as a remedy for various diseases.

Studies on mechanism of ascorbate toxicity reported induction of apoptosi s through cell cycle arrest, activation of apoptosis factors, and interference with iron uptake in cells. However, ascorbate acts as an electron donor in redox reactions, and evidences suggest that oxidative stress plays a major role in the mechanism of ascorbate toxicity in tumor cells. Other *in vitro* and *in vivo* studies include evaluating the real potentialities of ascorbate, by combining it with chemotherapeutic drugs.

4.2.5. In Irritable Bowel Syndrome

Ulcerative Colitis (UC) and Crohn's Disease (CD) are together known as Inflammatory Bowel Disease (IBD). Etiology of these conditions is not completely understood; however, the hypotheses for causation of these conditions include genetic susceptibility, e nvironmental risk factors, inappropriate and chronic immune responses to members of intestinal microflora, and failed immune regulatory mechanisms.

Pathophysiology of IBD involves continued intestinal inflammation, presence of pro-inflammatory cytokines, inc reased Reactive Oxygen Species (ROS), and tissue injury triggered by luminal bacteria. Natural product therapy in IBD includes modulation of mediators involved in inflammatory process alter ing luminal bacteria, modification of the immune response, and rej uvenation of intestinal healing.

5-Aminosalicylic Acid (5-ASA) is a well -established therapeutic agent in the management of UC; but, its involvement in CD is unclear. The NF-κβ pathway is an important target. In IBD, presence of pro-inflammatory cytokines such as TNF-α causes phosphorylation of iκ-β and results in activation of NF-κβ, thus initiating the synthesis of more pro-inflammatory cytokines. 5-ASA inhibits TNF-α-induced stimulation of iκ-β phosphorylation, thus disrupts a signal transduction pathway involved in the onset and progression of chronic inflammation.

Aloe vera gel (an extract of *Aloe barbadensis*) is used in the treatment of IBD. In a Randomised Controlled Trial (RCT), in which aloe vera gel was administered for four weeks to patients with active UC, the results showed that they had greater symptom alleviation than placebo.

Andrographis paniculata shows a significant reduction in transcriptional activity of NF-κβ and reduces secretions of pro-inflammatory cytokines, including TNF-α and IL-6, both of which are elevated in IBD patients. In a RCT (n = 224), greater clinical response was encountered in UC patients receiving *A. paniculata* treatment than placebo. Similar results were obtained in a clinical trial in which the efficacy of *A. paniculata* was compared to conventional mesalazine therapy.

In animal studies, **boswellic acid** (active component of *Boswellia serrate*) caused leukocyte recruitment, and hence, protected the intestinal mucosa from inappropriate immune reaction in IBD. On administering capsules of ***B. serrata* Extract** (BSE) in 400mg dose and comparing with placebo in patients with IBD, a statistical difference was found in remission rates between BSE and placebo groups in patients with collagenous colitis. However, in a 52 week trial, the remission rates did not show statistical significance between control and treatment groups (p = 0.85). BSE treatment was well-tolerated and offered long-term safety, as **Holtmeier *et al.*** (2011) suggested that those treated with BSE experienced less adverse effects than those treated with placebo (p = 0.087),

Curcuma longa is predominantly present in the diet in Asian countries and improves colonic morphology by counter-acting the generation of damaging ROS produced by inflamed colon cells. **Curcumin** also inhibits the secretion of inflammatory cytokines by modulating the activation of NF-κβ in IBD patients. It suppresses NF-κβ activation by blocking the phosphorylation of inhibitory factory, i κβ kinase. This down-regulates the expression of downstream pro-inflammatory eicosanoids. Curcumin also blocks the action of pro-inflammatory, TNF-α, by inhibiting the production of TNF transcription factors, thus causing transcriptional repression.

In a pilot study of 5 patients with UC and 5 with CD, it was observed that their symptoms improved during the 2-month period of curcumin administration. In a multicentre RCT study, patients were given curcumin along with 5-ASA, and their symptoms showed significant improvement than the placebo given with 5-ASA. Curcumin-treated patients also showed a lower relapse rate, 6 months after study. In a prospective phase 1 study in adults, a higher dose of curcumin was used to treat cancer (8gm/day), and no toxic effects occurred, thus confirming the safety of the dosage used to treat IBD.

In a double-blind RCT study, 23 patients with active distal UC were administered with oral wheatgrass juice or placebo for 4 weeks. Patients treated with wheatgrass juice showed greater reductions in a composite clinical disease activity index, severity of rectal bleeding, and the doctor's global assessment than those in the placebo group. No side effects were encountered.

Some studies suggested the efficacy in UC of a **Germinated Barley Food (GBF) product** consisting of dietary fibre and glutamine-rich protein that act as a prebiotic. 11 patients given GBF for 4 weeks as an adjunctive treatment showed greater reduction in clinical disease activity than the 9 patients given conventional therapy alone. In a follow-up study of 21 patients, GBF administered along with 5-ASA and

steroid therapy for 24 weeks reduced rectal bleeding and nocturnal diarrhoea. On administering adjunctive GBF for 12 months to 22 patients with UC in remission, a lower relapse rate was observed than on conventional therapy given to 37 patients. GBF was found to be well-tolerated and safe in all the reports.

Polyphenols are present in food substances produced from plants that play a biologically active role and are potentially immunomodula ting. For IBD, polyphenols down -regulate the inflammatory mediators and NF -κβ. Several polyphenols have been identified, of which five (i.e., resveratrol, epigallocatechin, curcumin, quercetin, and *B. serrate*) have shown to benefit animals and humans with IBD.

Supplementation with **omega-3 fatty acids** proved to be beneficial in t reating or preventing relapse of chronic inflammatory diseases. For IBD, *in vitro* and *in vivo* animal studies showed that omega-3 fatty acids effectively prevent and treat mice models of colitis. It was earlier reported that by using an enteric -coated formulation for CD, a lower relapse rate for the fish oil group was observed than the control group (28% compared with 69%; $p<0.001$). However, the available data are not sufficient to make conclusions about the effects of omega -3 fatty acids on clinical, endoscopic, or histologic scores or induced remission rates.

Patients with IBD, even when in remission, commonly suffer from vitamin D deficiency. Vitamin D Receptor (VDR) is a physiologic regulator of intestinal inflammation in IBD. Vitamin D deficiency occurs in both forms of IBD.

Microbial environment is important in IBD establishment; therefore, targeting the microbiota presents an option for therapeutic intervention. Probiotics are live microorganisms that on consumption in adequate quantities provide hea lth benefits to the host. They have been used in the treatment of many inflammatory conditions, including UC and CD.

Based on the results from the treatment of experimental colitis with VSL#3, *Lactobacillus* GG, and other strains, several clinical trials have been executed for both CD and UC. Although mixed results were obtained for benefiting CD as either an induction or maintenance adjunct to standard medical therapy, probiotics have demonstrated benefits in UC for both induction and continued remission of disease.

4.2.6. In Various Gastrointestinal Diseases

Nutraceuticals in Gastritis

Gastritis, i.e., inflammation of stomach lining, is the most common disorder of stomach that occurs due to infection caused by *Helicobacter pylori* and/or the effect of NSAIDs. It can also be caused by irritation due to excessive alcohol, smoking, cocaine, severe illness, autoimmune problems, radiation therapy, and Crohn's disease. Gastritis can be diagnosed in its acute phase, when the patients experience nausea, pain and discomfort in the upper abdomen due to superficial inflammation of the stomach. In the developed stage, gastritis is termed **chronic gastritis**, which causes pain in the upper abdomen, feeling of fullness, and loss of appetite. Gastritis

caused by duodenogastric bile reflux and NSAIDS is termed **reactive** or **chemical gastritis**. It causes oedema, vasodilatation, congestion of gastric lamina propria, and a paucity of inflammatory cells. **Proton Pump Inhibitors** (PPIs) such as omeprazole (OPZ) and its derivatives are commonly used in gastritis. OPZs give rise to side effects and drug interactions, and are also associated with gastric gland toxicity, which although can be reversed by vitamin C.

Antiulcer drugs are used as co-medications to prevent the damage of gastric mucosa from NSAIDs. This is useful during long-term pain and anti-inflammatory therapies. **PPIs**, **histamine type 2 receptor antagonists**, **sucralfate**, or **acid neutralisers** are used for neutralising gastric acidity. **Triple eradication therapy** (consisting of clarithromycin, amoxicillin, and omeprazole) provides 80% protection, however its efficacy has declined due to *H. pylori*. This therapy also involves too many pills, which may give rise to severe side effects. Recognition of *H. pylori* as the main causative agent of chronic gastritis has allowed the researchers to focus on natural products, including phytochemicals, microorganisms, and plants. The compounds of natural origin modulate at various levels by affecting immune mucosal response, H^+/K^+ pump, histamine release from mast cells, and mucus wall structure, or by regulating Prostaglandin (PG), Myeloperoxidase (MPO), and Nitric Oxide (NO). The results obtained from published preclinical *in vivo* studies may also be extrapolated to human subjects.

Phenolic Compounds

Phenolic compounds (or flavonoids) are found in various drinks and edible plants such as strawberry, apple, tea, red wine, beer, etc. They exhibit biological properties, such as antiviral, anti-inflammatory, antihistaminic, antioxidant, and free-radical scavenging abilities. The gastroprotective effect of flavonoids may be attributed to its effectiveness in increasing the endogenous PG, reduction in histamine secretion, scavenging oxygen-derived free radicals, and gastric mucous stimulation. These properties restore the gastric mucosal integrity by dynamic balance and homeostasis between epithelial cell renewal and cellular apoptosis.

Plant-origin flavonoid substances like Solon (Sophoradin extract), Amaranth seed extract, Grapefruit Seed Extract (GSE), and capsaicin (chilli pepper extract) provide protection against gastritis by increasing gastric microcirculation to enhance the expression of constitutive NOS and release NO and neuropeptides. Flavonoid-rich extract of *Syngonanthus bisulcatus* shows gastroprotective effects through mucus and prostaglandins, which are integral parts of gastrointestinal mucosa's cytoprotective mechanisms against aggressive factors.

Quercetin is a flavonoid found in various vegetables, fruits, and beverages such as tea and red wines. It is known to prevent gastric injuries in rats. It prevents gastric damage from the harmful effects of activated neutrophil infiltration by inhibiting the MPO activity. It also increases the activity of superoxide dismutase (SOP) to reduce lipid peroxidation and of protein carbonyl compounds to protect gastric mucosa against inflammation. **Ethanol** consumption increases erythrocyte and tissue malondialdehyde (MDA) and serum NO concentration and decreases antioxidant enzyme activities of SOD, glutathione peroxidase (GSHPx) and

catalase (CAT). Treatment with quercetin decreases the ele vated MDA and NO, and increases the reduced antioxidant enzyme activities. Therefore, quercetin provides protection against ethanol-induced gastric ulcer by decreasing oxidative stress and increasing antioxidant enzyme activity.

Wogonin is a strong anti -inflammatory compound that targets arachidonic acid metabolism and inhibits activation of 5-Lipoxygenase (LOX) and COX-2. It was found to be as effective as **rebamipide** (a well-known drug prescribed clinically for the treatment of gastritis and gastric ulcer) in the prevention of alcohol stomach injury.

Curcumin is the most active constituent of the perennial herb *Curcuma longa*. Curcumin-based therapy was found to be associated with clinical amelioration and a statistically significant decrease of gastric inflammation. It also inhibits the growth of *H. pylori* by inhibiting the shikimate pathway, which is e ssential for synthesising aromatic amino acids in bacteria.

Nutraceuticals in Peptic Ulcer

Peptic ulcer is a common disease in which the gastric mucosa gets damaged and perforations lead to bleeding. There are many causative factors of gastric ulcer, but 70-80% is caused by *H. pylori*, and 25% occurs due to the use of NSAIDs.

Nutraceutical-Based Treatment Options for Peptic Ulcers

Anthocyanosides, from *Vaccinium myrtillus*, showed significant preventive and curative antiulcer activity. They stimulate the biosynthesis of mucopolysaccharides, and thus improve the efficiency of mucus barrier at the gastric level.

An **ethanolic extract of celery**, i.e., *Apium graveolens*, was also used against gastric ulcer in rats. At 250 and 500mg/kg body weight of dose, it showed anti-gastric ulcer activity against indomethacin, cytodestructive agents (80% ethanol, 0.2M NaOH, and 25% NaCl), and cold-restraint stress-induced ulceration in rats. Its antioxidant property provides protection to the gas tric mucosa and suppresses the basal gastric secretion.

Bilberry was found to reduce the occurrence and severity of experimentally -induced ulcers in animals. Roots of ***Bupleurum falcatum*** (species of flowering plant of Apiaceae family) showed weak anti -ulcerogenic activity in pylo rus ligated ulcer model. The polysaccharide fraction of *B. falcatum* was found to possess potent antiulcer activity against HCl/ethanol-induced lesions in mice.

Curcumin (a yellow pigment and an active constituent of *Curcuma longa*) showed anti -inflammatory properties by suppressing PG synthesis. **Turmeric root extract** was found to relieve pain from biliary dyskinesia during a double -blinded study and improved endoscopic healing of peptic ulcers and also symptoms of non -ulcer dyspepsia. The prophylactic actio ns of **triterpene saponins (** derived from tea seeds) against ethanol -induced gastric mucosal lesions and of **black tea extract** against various ulcerogens have been studied in rat models. **Theaflavin** (TF, an active constituent of black tea) healed indomethacin-induced gastric ulcer through its antioxidative properties, synthesis of PGE2, and enhancement of mucin secretion.

Compounds obtained from **liquorice** (root of *Glycyrrhiza glabra*) increase the prostaglandin level and promote mucus secretion from stomach, w hich further elevates the life span of surface cells of stomach and present an antipepsin activity that heals the ulcer. Liquorice extracts due to their antioxidant effect have the ability to accelerate healing of gastric ulceration (in stomach and oesoph agus). **Carbenoxolone** (a succinate derivative of glycerrhetinic acid) is an antiulcer drug that has become the preferred form of liquorice to promote healing of ulcers.

Saponins derived from the fruits of *Kochia scoparia* showed gastroprotective properties by activating mucous membrane protective factors.

Lagenaria vulgaris showed antiulcer activity through an anti -oxidative pathway by modulating glutathione level. Roots of ***Panax ginseng*** has been used clinically for treating gastrointestinal disorders.

Phyllanthus emblica *L*. or ***Emblica officinalis*** is a strongest rejuvenative among Indian medicinal plants due to its anticancer, anti -inflammatory and antioxidant properties. In a clinical study, its significant healing effect on gastric syndrome has been rep orted. Previous reports state that ethanolic extract of fruits of *P. emblica* show antiulcer activity in a dose -dependent manner through its anti - oxidative properties by modulation of IL -10 level. The active component of the ethanolic extract of fruits of *P. emblica* also showed antiulcer activity by modulating COX or NOS pathway.

Picrorhiza kurroa (a small hairy perennial herb) forms a major ingredient of many medicinal preparations that were traditionally used for dyspepsia, bilious fever, and chronic dys entery. **Iridoid glycosides**, **picroside I**, **II** and **III**, and **kutkoside** are the most important active constituents of roots and rhizomes of *P. kurroa*. Picroside I and kutkosi de were found to possess potent gastroprotective properties due to their antioxidative activity.

The **leaf oil of *Piper betle*** was found to exhibit anti -ulcerogenic activity. One of its active components, **allylpyrocatechol**, demonstrated the best antiulcer activity by modulating arginase metabolism and shift of cytokine balance.

The resinous exudate from ***Pistacia lentiscus*** was used by traditional healers for relieving upper abdominal discomfort, gastralgia, dyspepsia, and peptic ulcer. Various experiments showed a significant reduction in the intensity of gastric mucosal damage induced by py loric ligation, aspirin, phenylbutazone, reserpine, and restraint cold stress.

Clinical trials of ***Pteleopsis suberosa*** presented a protective action against ethanol-induced and indomethacin -induced ga stric mucosa damage by stimulating PG synthesis.

Shilajit has been used traditionally in the treatment of bronchial asthma, diabetes, genitourinary infections, wound healing, and stomach ulcer. Shilajit - derived **4-Methoxy-6-Carbomethoxy Biphenyl** (MCB) caused changes in the mucosa and provided resistance again st the effect of ulcerogens and against shedding of mucosal cells.

Silymarin (a flavonolignan complex present in milk thistle, *Silybum marianum*) has been found to be effective in some experimentally -induced gastric ulcers. Its anti-ulcerogenic effect can be related to its inhibitory mechanism on lipoxygenase pathway, thus avoiding leukotriene synthesis. **Flavonoids** derived from sophoradin, isolated from roots of *Sophora subprostrata* , exhibit gastroprotective and ulcer healing properties.

Spinach was found to provide better protection from hydrochloric acid secreted in gastric juice and reduce the risk of ulcers in rats by forming a thicker layer of mucous lining of gastric wall.

Parts of ***Tectona grandis*** tree affected the protein content of gastric juice, a nd reversed aspirin-induced changes in peptic activity, protein, and sialic acid.

Sanyal *et al.* studied the activity of ***Plantain banana*** against ulcers induced by phenylbutazone, prednisolone, and restraint stress. **Best *et al*.** and **Elliott** and **Heward** described the antiulcer activity of various preparations of dried unripe *P. banana* against aspirin-induced ulcers in rats.

Further studies indicated that banana increased the mucosal defence by promoting mucus secretion; thus, increased mucoprotein content of mucosa, decreased shedding of cells and leakage of protein in gastric secretion in response to ulcerogenic agents, and pro moted healing by increasing thymidine uptake by gastric mucosal cells and causing a concen tration-dependent increase in eicosanoid stimulation in incubates of human gastric and colonic mucosa. It was observed endoscopically that 70% of duodenal ulcers healed after 12 weeks of treatment with banana powder as compared to approximately 16% with placebo.

Mowrey and **Clayson** discovered that ***Zingiber officinale*** is effective in motion sickness, reduces gastric distress in humans, and also has marked antiulcer activity.

Nutraceuticals in Chronic or Prolonged Inflammation, like Appendicitis
Anti-inflammatory nutraceuticals were found to be ef fective in various conditions arising from chronic or prolonged inflammation, like rheumatoid or osteoarthritis, psoriasis, gastritis, menin gitis, ulcerative colitis, and appendicitis. These nutraceuticals include omega -3 poly -unsaturated fatty acids, soy isoflavonoids, plants, spices, and chitosan that act against pro -inflammatory agents.

Nutraceuticals in other GI Conditions
Tea polyphenols were found to counteract bacterial peritonitis and other infective conditions.

A pilot study was performed to eva luate the effect of oral **curcumin with piperine** on pain and the mark ers of oxidative stress in patients with Tropical Pancreatitis (TP). This therapy reversed lipid peroxidation in patients with tropical pancreatitis, although did not improved the pain.

4.3. DIFFERENT HERBS AS HEALTH FOOD

4.3.1. Introduction

Nowadays, scientists and scholars are giving great attention to discover the relation between dietary nutrients and disease prevention. Most of the herbs which were in use since ages have proved to be useful in the treatment and prevention of various diseases. A plant-based diet contains many non-nutritive phytoconstituents, along with macro- and micro-nutrients such as proteins, fats, carbohydrates, vitamins or minerals necessary for normal metabolism. These constituents together play an essential role in keeping human body healthy and disease-resistant.

Table 4.15: Common Herbs, their Constituents and Health Benefits

Common Names	Biological Names	Constituents	Health Benefits
Garlic	Dried bulbs of *Allium sativum* (Liliaceae).	Alliin and allicin	Anti-inflammatory, antibacterial, antigout, and nervine tonic.
Maiden Hair Tree	Leaves of *Ginkgo biloba* (Ginkgoaceae).	Ginkgolide and bilobalide	PAF antagonist, memory enhancer, and antioxidant.
Ginger	Rhizomes of *Zingiber officinale* (Zingiberaceae.)	Zingiberene and gingerols	Stimulant, ch ronic bronchitis, hyperglycaemic, and used in throat ache.
Echinacea	Dried herb of *Echinacea purpurea* (Asteraceae)	Alkylamide and echinacoside	Anti-inflammatory, immunomodulator, and antiviral.
Ginseng	Dried root of *Panax ginseng* (*Araliaceae*)	Ginsenosides and panaxosides.	Stimulating immune and nervous system , and adaptogenic properties.
Liquorice	Dried root of *Glycyrrhiza glabra* (Leguminosae).	Glycyrrhizin and liquirtin	Anti-inflammatory, anti-allergic, and expectorant.
St. John's Wort	Dried aerial part of *Hypericum perforatum* (Hypericaceae).	Hypericin and hyperforin	Antidepressant, and used against HIV and hepatitis-C virus.
Turmeric	Rhizome of *Curcuma longa* (Zingiberaceae).	Curcumin	Anti-inflammatory, antiarthritic, anticancer , and antiseptic.
Onion	Dried bulb of *Allium cepa Linn.* (Liliaceae).	Allicin and alliin	Hypoglycaemic activity, antibiotic, and anti - atherosclerosis.
Valeriana	Direct ro ot of *Valeriana officinalis Linn.* (Valerianaceae).	Valerenic acid and valerate	Tranquilliser, used to cure migraine and menstrual pain, intestinal cramps, and bronchial spasm.
Aloes	Dried juice of leaves *Aloe barbadensis Mill*. (Liliaceae).	Aloins and aloesin	Dilates capillaries, anti - inflammatory, emollient, and wound healing properties.

Goldenseal	Dried root of *Hydrastis c anadensis*. (Ranunculaceae).	Hydrastine and berberine	Antimicrobial, astringent, antihaemorrhagic, and used in the treatment o f mucosal inflammation.
Senna	Dried leaves of *Cassia angustifolia* (*Leguminosae*).	Sennosides	Purgative.
Asafoetida	Oleo gum resin of *Ferula asafoetida L.* (Umbelliferae).	Ferulic acid and umbellic acid	Stimulant, carminative, and expectorant.
Bael	Unripe fruits of *Aegle marmelos Corr. (*Rutaceae*)*	Marmelosin	Digestive, appetiser, and used in the treatment of diarrhoea and dysentery.
Brahmi	Herbs of *Centella asiatica* (Umbelliferae).	Asiaticoside and madecassoside	Nervine tonic, spasmolytic, and anti-anxiety.

4.3.2. Alfalfa

Alfalfa (*Medicago sativa and* belongs to the family Fabaceae) is also named as Buffalo Herb, Lucerne, Purple Medick, Purple Medical, and Purple Medic. It is a perennial plant and its dried leaf is sold as an herbal tea, tincture, tablet, or powder. It is also used as animal feed. Its leaves, sprouts, and seeds are used for treating various health disorders. Alfalfa is native of South and Central Asia , but is now grown all around the world for commercial purposes.

Different parts of the alfalfa plant have different uses and show different effects. Fresh juice of alfalfa was used to treat kidney stones, and its root was used in treating fevers and jaundice in traditional Chinese medicine system.

Following are some other **medicinal effects** of alfalfa plant:

1) **Kidney, Bladder, and Prostate Conditions:** It is believed that alfalfa acts as a diuretic, and therefore is used for treating disorders of kidney, bladder, and prostate.
2) **Lowering Cholesterol:** Alfalfa is a highly fibrous plant and also contains saponins. Alfalfa reduces serum (blood) cholesterol levels due to the presence of saponin which binds cholesterol with bile salts in the body.
3) **Neuroprotective Effects:** *In vitro* studies performed in mice showed that supplementation with alfalfa exert neuroprotective effects.
4) **Osteoarthritis and Rheumatoid Arthritis:** It is believed that alfalfa cures arthritis by reducing inflammation and helping the body to maintain a healthy pH.
5) **Diabetes:** Alfalfa grass is highly fibrous, therefore it is believed to control blood sugar levels. Fibre is the indigestible part of carbohydrate, thus it is slowly released in the blood circulation and slowly increases the blood sugar.
6) **Promotes Menstruation and Lactation:** Alkaloids found in alfalfa seeds can promote menstruation and lactation. Alfalfa is considered to be a galactagogue (a food that increases milk supply), however, not much data is available to support this claim.

4.3.3. Chicory

Chicory (*Cichorium intybus* and belongs to mono-generic family Asteraceae) is a herbaceous plant and is also known as **kasni**. It exhibits many medicinal properties. It is grown all over the world, but Pakistan is the largest producer. Generally, it is grown along with some other plants like lucerne (*Medicago falcate*) and berseem (*Trifolium alexandrinum*).

Major components of chicory are **aliphatic compounds** and their derivatives, while terpenoids are the minor constituents. **Chicoric acid** is the main chemical compound obtained from methanolic extracts of chicory. Its flowers contain **saccharides**, **methoxycoumarin cichorine**, **flavonoids**, and **essential oils**. The blue colour of the perianth is due to the presence of **anthocyanins**. Major volatile compounds of chicory are octane, n-nonadecane, pentadecanone, and hexadecane.

Chicory possesses many therapeutic properties such as hepatoprotective, anti-inflammatory, antioxidant, sedative, immunological, reproductive, cardiovascular, hypolipidemic, anticancer, anti-protozoal, gastro-protective, anti-diabetic, analgesic, anthelmintic, antimicrobial, wound healing, and bitter tonic.

4.3.4. Ginger

The generic name of ginger is *Zingiber*, which has been derived from the Greek word ***Zingiberis*** which in turn has been derived from ***Singabera*** (Sanskrit name of ginger). It is in use since ancient times in India as well as in China, and by the 1st century traders had transported ginger to the Mediterranean region. Ginger is the rhizomes of *Zingiber officinale* Roscoe (and belongs to family Zingiberaceae), scrapped to remove the outer skin and dried in the sun. It is known as **Jamaica ginger** in the market.

Ginger has its origin in South East Asia; although it is cultivated in Caribbean islands, Africa, Australia, Mauritius, Jamaica, Taiwan, and India. More than 35% of the world's production of ginger is from India.

Ginger contains **volatile oil** (1-4%), **starch** (40-60%), **fat** (10%), **fibre** (5%), inorganic material (6%), residual moisture (10%), and acrid resinous matter (5-8%). Ginger oil is made up of **monoterpene hydrocarbons**, **sesquiterpene hydrocarbons**, **oxygenated mono** and **sesquiterpenes**, and **phenyl propanoids**.

The content of sesquiterpene hydrocarbons in all types of ginger oil is the same and includes **α-zingiberene**, **β-bisabolene**, **α-farnesene**, **β-sesquiphellandrene**, and **α-curcumene**.

Ginger obtains its aroma from the fragrant principles of volatile oil, and its flavour, pungency and pharmacological action is inherited from the phenolic ketones of oleo-resin (**gingerols** like shogaols, zingerone, paradols, gingediols hexahydrocurcumin, and *o*-methyl ethers of these compounds). Some components of volatile oil (isometric terpenic aldehydes like geranial and citral) give the delicate and lemony aroma to ginger. Some of the sesquiterpene oil hydrocarbons impart a spicy touch to ginger.

Ginger has the following **therapeutic uses**:

1) It is used as a stomachic, aromatic, carminative, stimulant, and flavouring agent
2) Its powder is effective in motion sickness.
3) Due to its adsorbent, aromatic, and carminative properties on GIT, it enable s adsorption of toxins and acid -enhanced gastric motility; thus blocking the effects of gastrointestinal reactions and nausea.
4) A methanolic extract of ginger has molluscicidal effects, and can also control parasitic infections.

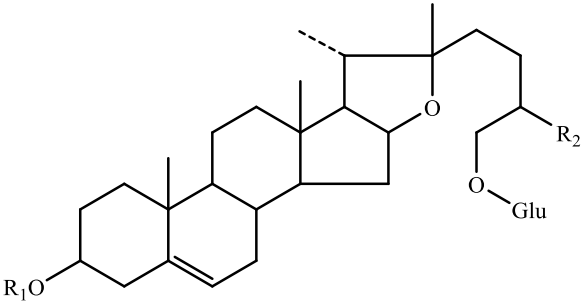
4.3.5. Fenugreek

Fenugreek is an essential part of Indian spices and is used in food as taste enhancer and also for various health benefits. It is a 30 -60cm tall annual herb. Fenugreek is dried seeds of *Trigonella foenum-graecum* Linn. (and belongs to family Fabaceae). Fenugreek has been grown in various parts of the world like India, Europe, Africa, and United States.

Chief c hemical constituents of f enugreek seed s are **steroidal saponins** . Trigofoenoside A, B, C, D, E, F, and G , trigonelloside C, yamogenin tetro xide B and C, tenug rin B, trigogenin, neotigogenin, yemogenin, diosgenin, and gitogenin are the other saponins found in fenugreek.

Fenugreek seeds also contain **glycosides of diosgenin** , i.e., graecunins A, B, C, H, I, J, K, L, M, and N. **Flavonoid compounds** , such as quercet in, luteolin, vitexin, isovitexin, saponaretin, homoerietin, vicenin -1, and vicenin -2 are also present. Fenugreek seeds are rich in **4-hydroxyisoleucine**.

Coumarin derivatives , such as trigocoumarin, trigoforin, 4 -methyl-7-acetoxycoumarin, and *p*-coumaric acid, are also found in fenugreek seeds.



	R_1	R_2
Trigofoenoside A	Glu - Rha	$-CH_3$
Trigofoenoside B	Glu - Rha	α-Me
Trigofoenoside C	Glu - Rha - Rha	β-Me
Trigofoenoside D	Glu - Rha - Glu	$-CH_3$
Trigofoenoside E	Glu - Rha - Xyl	$-CH_3$
Trigofoenoside F	Glu - Glu - Rha	$-CH_3$
Trigofoenoside G	Glu - Glu - Rha - Xyl	$-CH_3$

Fenugreek has the following **therapeutic uses**:

1) Seeds and leaves of fenugreek show anticholesterolemic, anti -inflammatory, antitumour, carminative, demulcent, emollient, and expectorant properties.

2) Along with these properties, the leaves and seeds are also used as febrifuge, galactogogue, hypoglycaemic, laxative, parasiticide, restorative, and uterine tonic.
3) From the fenugreek seeds a strong mucilaginous substance is obtained, which is used for curing inflammation and ulcers of stomach and intestines.
4) An alkaloid **trigonelline**, found in fenugreek seeds, have shown anticancerous properties.
5) A saponin, **diosgenin**, found in fenugreek seeds, is used in the synthesis of oral contraceptives and sex hormones.

4.3.6. Garlic

Garlic is being used medicinally in Egypt since ancient times. Earlier, it was used in the treatment of leprosy, but later it was started to be used in the treatment of scurvy, ear aches, flatulence, etc. Garlic is the fresh compound bulb of *Allium sativum* Linn. (and belongs to family Liliaceae). It is cultivated in India, Russia, USA, Italy, and Southern Europe. Plentiful of minerals, vitamins, carbohydrates, amino acids, volatile oils, and other trace elements are found in garlic bulbs. Garlic has the maximum sulphur content amongst all the members of Allium species. The **sulphur compounds** found in garlic include diallyldisulphide, diallyltrisulphide, methylallyltrisulphide, allyl propyl disulphide, alliin, ajoene, etc.

Concentration of volatile oils in garlic is about 0.1 -0.5%. On crushing the garlic clove, the enzyme **alliinase** catalyses the conversion of **alliin (S-allyl-l-cysteine sulfoxide)** into **2-propene-2-sulfenic acid**, which further undergoes dimerisation and forms **allicin (diallylthiosulfinate)**. This compound imparts the pungent odour and also some of the pharmacological activities to garlic.

Other sulphur compounds of garlic, such as alliin, allicin, diallyldisulphide, etc., are also responsible for its pharmacological activities. Minerals like phosphorus, calcium, magnesium, potassium, iron, selenium, germanium, etc. are also present in garlic, along with some vitamins like B_1, A, C, etc.

Garlic has the following **therapeutic uses**:
1) It exhibits various therapeutic properties like analgesic, carminative, gastric stimulant, anticonvulsant, antibacterial, aphrodisiac, and diuretic.
2) It aids in digestion and absorption of food.
3) It is used in the treatment of malignant tumors, hypertension, atherosclerosis, tuberculosis, whooping cough, piles, duodenal ulcer, epilepsy, diabetes, chronic bronchitis, and bronchial asthma.
4) It also prevents blood clotting, lowers cholesterol and blood sugar levels, and boosts immunity.
5) Oil of garlic is used as an insecticide.

4.3.7. Honey

Honey is a highly nutritious product which is also used in traditional medicine and as an alternative remedy for clinical conditions, including wound healing and cancer treatment.

Honey is a sweet and viscid secretion of honey bee, which is formed by various species of bees such as *Apis dorsata*, *Apis florea*, *Apis indica*, *Apis mellifica* (and belongs the natural order *Hymenoptera* and family *Apideae*) and is stored in the honey comb. Honey is available in Africa, India, Jamaica, Australia, California, Chile, Great Britain, and New Zealand.

Honey bees reside in colonies in honey comb and form honey and beeswax. In a honey comb, there is one **queen** or **mother bee**, under whose command a large number of **employees** are present, which are mostly sterile female bees and some male bees. The main work of these employees is to collect nectar from sweet smelling flowers from far and nearby places. The nectar mostly contains aqueous solution of sucrose (around 25% sucrose and 75% water) and pollens. Invertase enzyme, found in the saliva of bees, converts the nectar into invert sugar. Some part of this invert sugar is consumed by the bee for its survival and the remaining part is stored into the honey comb.

As time passes, the water in nectar gets evaporated, thereby producing honey (i.e., around 80% invert sugar and 20% water). When the cell of the comb fills up completely, the bees seal it using wax. Thus, bees preserve honey for using it in off-season.

Honey is collected by the removal of wax-seal using a sterilised sharp knife. The pure honey is obtained by centrifugation and filtering through a moistened cheese-cloth. The professional honey collectors smoke away the bees at night, drain-out honey, and warm the separated combs to recover the beeswax.

Honey contains **moisture** (14-24%), **dextrose** (23-36%), **levulose** (fructose) (30-47%), **sucrose** (0.4-6%), **dextrin** and **gums** (0-7%), and **ash** (0.1-0.8%). Small amounts of essential oil, beeswax, pollen grains, formic acid, acetic acid, succinic acid, maltose, dextrin, colouring pigments, vitamins, and an admixture of enzymes (**e.g.,** diastase, invertase, and inulase) are also found in honey.

However, the sugar concentration in honey differs from one country to another as it depends on the source of nectar (i.e., availability of fragment flowers in the particular region) and on the enzymatic activity that controls the conversion of nectar into honey.

Honey has the following **uses**:

1) It is used as a sweetening agent in confectionaries.
2) Due to its demulcent properties, it relieves dryness, and is therefore, used in coughs, colds, sore-throats, and constipation.
3) It is a good source of nutrient for infants, elderly persons, and convalescing patients.

4.3.8. Amla

This plant is mainly known for its fruit which is edible and has the same name. In India, amla is considered a sacred tree. Its fruit is very nourishing but it has a sour taste. The fruits possess health benefits in both dried and fresh forms.

Amla consists of dried and fresh fruits of *Emblica officinalis* Gaertn (*Phyllanthus emblica* Linn.) (and belongs to family Euphorbiaceae). Amla grows indigenously in tropical Southeast Asia, particularly in Central and Southern India. It is also grown in Sri Lanka, Malaysia, and China. It is commonly found in the dec iduous forests of India, growing up to 1350mt. above mean sea level on the hills. On a commercial scale , it is cultivated in northern states like Uttar Pradesh and Himachal Pradesh.

The fruits of amla are a rich natural source of **vitamin C** , **fat** (about 0. 5%), **phyllemblin,** and **tannin** (5%). They also contain mineral matters like phosphorus, iron, and calcium. **Pectin** is also found to be present significantly. Around 75% moisture is present in fresh fruits. But the fruits are dehydrated which do not affect the vitamin content of dried fruits due to the retardation of vitamin C oxidation by the tannins present.

Amla has the following **therapeutic uses**:

1) It is very helpful in skin diseases.
2) It is required for glowing skin and it delays wrinkles and skin loosening.
3) It facilitates hair growth by stimulating the hair follicles and it also improves hair texture.
4) It prevents premature greying of hair and occurrence of dandruff.
5) It acts as a natural hair conditioner that provides good nourishment and also normalises blood supply to hair.
6) It is used to effectively and naturally treat indigestion, acidity, constipation, gastric troubles, and flatulence.
7) It improves the functioning of liver.
8) It lowers cholesterol and blood sugar level.
9) It also proves beneficial in chronic cough, childhood and allergic asthma, and tuberculosis.
10) It nourishes the nerves, thus, is helpful in paralytic conditions.
11) It is also a brain tonic, thus, helps in alertness of memory.
12) It improves the quality of sperms due to its madhur (sweet) vipaka property.
13) It also acts as an anti-inflammatory agent, thus, suppresses swelling and pain.
14) It improves eyesight.
15) It also modulates the i mmune system, therefore, helps the human body to fight diseases.
16) Its fruit has acrid, cooling, refrigerant, diuretic and laxative properties.
17) Dried fruit is used in haemorrhage, diarrhoea, diabetes, and dysentery.
18) It is used to treat anaemia, jaundice and dyspepsia when combined with iron.
19) Fermented liquor obtained from the fruits is helpful in jaundice, dys pepsia, and cough.
20) It also acts as an antibacterial, antifungal and antiviral agent.

4.3.9. Ginseng

The term **ginseng** is derived from the Chinese term **rénshēn** (Ren = person; shen = plant root). It is a type of herb, consisting of fork -shaped root, resembling the legs of a person.

Ginseng (belongs to family Araliaceae) consists of dried roots of various *Panax* species, such as:
1) *Panax ginseng* (Korean ginseng),
2) *P. japonica* (Japanese ginseng),
3) *P. notoginseng* (Chinese ginseng) and,
4) *P. quinquefolium* (American ginseng).

Ginseng herbs are found in the forests of northern China and North Korea. *P. quinquefolium* (American ginseng) is grown in the woodlands of the eastern United States. This species requires humus soil and shade which are the best soil condition favouring their growth.

Mixture of several **saponin glycosides** (belonging to **triterpenoid** group) are found in ginseng which are grouped as follows:
1) Ginsenosides,
2) Panaxosides, and
3) Chikusetsu saponin.

Ginseng has the following **therapeutic uses**:
1) It acts as an immunomodulator.
2) It is employed to enhance natural resistance (non-specific resistance) and the power to fight the situation of illness or tiredness.
3) It is enriched in stimulant and sedative properties.
4) The extracts of ginseng are an aphrodisiac.
5) The extracts are also used externally in cosmetics.

4.3.10. Ashwagandha

The name Ashwagandha has been derived from the Sanskrit language and is a combination of the word ***ashva*** meaning **horse** and ***gandha*** meaning **smell**. Thus, the roots have a strong horse-like odour.

Ashwagandha is the dried roots and rhizomes of *Withania somnifera* (and belongs to *family* Solanaceae). The genus *Withania* is found to have 23 species, of which *Withania somnifera* (L.) Dunal. is medicinally essential. *Withania somnifera* is grown in the drier parts and sub-tropical regions. The plant grows wildly in India, Pakistan, Afghanistan, Philistine, Egypt, Jordan, Morocco, Sri Lanka, Spain, Canary Island, Eastern Africa, Congo, Madagascar, and South Africa.

Ashwagandha comprises of the following **constituents**:
1) **Alkaloids:** Ashwagandhine, Withanine, Isopelietierine, and Anaferine.
2) **Steroidal Lactones:** Withanolides and Withaferins.
3) **Phytosterols:** Sitoindosides and B-sitosterol.

Ashwagandha has the following **therapeutic properties**:
1) It is a sedative and hypnotic.
2) It is hypotensive, and shows respiratory stimulant actions along with bradycardia.

3) It is an immunomodulatory agent.
4) Sitoindosides (VII) and (VIII) possess anti-stress activity.
5) Conventionally, it has been used in rheumatism, gout, hypertension, nervine, and skin diseases.
6) It prevents bony degenerative changes in arthritic conditions.
7) It has been used as a sex stimulant and rejuvenator.
8) It provides strength and energy, especially to elderly.
9) Its leaf extracts are found to be active against *Staphylococcus aureus* and Ranikhet virus.

4.3.11. Spirulina

Spirulina (or blue-green algae) is a cyanobacterium, which is a large and diverse group of simple, plant-like organisms found in salt water and some large fresh water lakes. Spirulina can be consumed by humans and other animals. Spirulina is a blue green algae, *Spirulina platensis* or *Spirulina maxima* (and belongs to family Oscillatoriaceae). Current world production of spirulina for human consumption is more than 1 thousand metric tonnes, and commercially it is cultivated in United States of America. It is also cultivated in countries like Thailand, Mexico, India, and China.

Net Protein Utilisation (NPU) of spirulina is upto 62%. Spirulina contains 50-70% of **proteins**, 11.36% of **proteinous nitrogen**, and 13.35% of **total organic** nitrogen (1.9% nitrogen from nucleic acids).

Around 5-6% of **lipid content** is found in spirulina that mainly includes essential fatty acids (vitamin F), composed of oleic, linoleic, γ-linoleic, palmitic, palmitoleic and heptadecanoic acids. Around 40% of the fats have glycolipids including sulpholipids (2-5%) which have significant anti-HIV activity. Spirulina provides 8-14% of Recommended Daily Allowance (RDA) of fats.

In spirulina, **carbohydrates** are mainly found in the form of glycogen and rhamnose which are easily digestible and require less insulin.

Vitamin content of spirulina mainly includes natural β-carotene with 9-*cis*-carotenoid isomer having more anti-oxidant capacity. Other vitamins present in the spirulina are B_1, B_2, B_3, B_6, B_{12} and E_3.

Around 3-6% of spirulina is the **mineral content** in which iron is the major element. Iron present in spirulina can be absorbed easily than other natural iron because of its soluble complexes with phycocyanin, (phycobiliprotein), which is an algal protein having linear tetrapyrrole, i.e., phycocyanobilin, and resembles haemoglobin. A blue-green pigment, **phycocyanin**, boosts the general immunity and used in lymphocytic activity against cancer.

In spirulina, **enzymes** are present in the form of Super Oxide Dismutase (SOD). This enzyme gives free radical scavenging effects and plays an essential role in pathophysiological conditions such as atherosclerosis, arthritis, cataract, and diabetes. SOD enzyme is also used to relieve emotional stress and to slow down ageing process. Around 0.8% of **crude fibres** and 6% of **ash** are also found in spirulina.

Following are some of the findings regarding the **therapeutic use** of spirulina:

1) It show s immunostimulant activities as it stimulates the production and activity of bone marrow stem cells, macrophages , and T -cells. It also enhances the functioning of spleen and thymus gland.
2) *In vitro* studies on spirulina have shown that it increases cell nucleus enzyme activity and DNA repair, and therefore shows anti-cancer properties.
3) Water extract of spirulina inhibits HIV-1 replication in human derived T-cell lines and in human peripheral blood mononuclear cells. Calcium salt of spirulina, i.e., **calcium spirulan**, inhibits *in vitro* replication of various virus strains (**e.g.,** HIV-1, Herpes simplex, Human cytomegalovirus, Influenza virus, Mumps and Measles virus).
4) γ-Linolenic acid of spirulina reduce s cholesterol levels and also shows appetite suppressing activity.

4.4. SUMMARY

The details given in the chapter can be summarised as follows:

1) **Nutraceutical** is a substance considered as a food or its part, which apart from its normal nutritional value provides health benefits, preven ts diseases, or promotes health.
2) The term **nutraceuticals** was coined from **nutrition** and **pharmaceutical** by **Stephen Defelice** in **1989**. He defined nutraceutical as "**a substance that is food or a part of food and provides medical or health benefits, including the prevention and treatment of diseases**".
3) **Herbals** are herbs or botanical products used as concentrated extracts.
4) **Dietary s upplements** are derived from other sources (**e.g.,** pyruvate, chondroitin sulphate, and steroid hormone precursors) that serve specific functions, **e.g.,** sports nutrition, weight loss supplements, and other dietary replacement.
5) **Traditional nutraceuticals** are natural substances with no changes to the food.
6) **Nutrients**, **e.g.,** vitamins, minerals, amino acids, and fatty acids, have established nutritional functions.
7) **Phytochemicals** are classified on the basis of the chemical name given to them as per their phytochemical properties.
8) **Probiotics** mean for life and are live microorganisms, which on consuming in adequate amounts confer a healthy effect on the host.
9) **Non-traditional nutraceuticals** are artificial foods prepared with the help of biotechnology.
10) **Fortified nutraceuticals** include fortified food from agricultura l breeding or added nutrients and/or ingredients.
11) **Recombinant nutraceuticals** include energy-providing foods, such as bread, alcohol, fermented starch, yogurt, cheese, vinegar, etc.
12) **Alfalfa** (*Medicago sativa and* belongs to the family Fabaceae) is also named as Buffalo Herb, Lucerne, Purple Medick, Purple Medical, and Purple Medic.

13) **Chicory** (*Cichorium intybus* and belongs to mono-generic family Asteraceae) is a herbaceous plant and is also known as kasni.
14) The generic name of **ginger** is *Zingiber*, which has been derived from the Greek word ***Zingiberis*** which in turn has been derived from ***Singabera*** (Sanskrit name of ginger).
15) **Ginger** is the rhizomes of *Zingiber officinale* Roscoe (and belongs to family Zingiberaceae), scrapped to remove the outer skin and dried in the sun.
16) **Fenugreek** is dried seeds of *Trigonella foenum-graecum* Linn. (and belongs to family Fabaceae).
17) **Garlic** is the fresh compound bulb of *Allium sativum* Linn. (and belongs to family Liliaceae).
18) **Honey** is a sweet and viscid secretion of honey bee, which is formed by various species of bees such as *Apis dorsata*, *Apis florea*, *Apis indica*, *Apis mellifica* (and belongs the natural order *Hymenoptera* and family *Apideae*) and is stored in the honey comb.
19) **Amla** consists of dried and fresh fruits of *Emblica officinalis* Gaertn (*Phyllanthus emblica* Linn.) (and belongs to family Euphorbiaceae).
20) The term **ginseng** is derived from the Chinese term **rénshēn** (Ren = person; shen = plant root).
21) The name **Ashwagandha** has been derived from the Sanskrit language and is a combination of the word ***ashva*** meaning **horse** and ***gandha*** meaning **smell**.
22) **Ashwagandha** is the dried roots and rhizomes of *Withania somnifera* (and belongs to *family* Solanaceae).
23) **Spirulina** is a blue green algae, *Spirulina platensis* or *Spirulina maxima* (and belongs to family Oscillatoriaceae).

4.5. EXERCISE

4.5.1. True or False

1) Herbals are herbs or botanical products used as concentrated extracts.
2) Traditional nutraceuticals are natural substances with no changes to the food.
3) Non-traditional nutraceuticals include energy-providing foods, such as bread, alcohol, fermented starch, yogurt, cheese, vinegar, etc.
4) Fenugreek is dried seeds of *Trigonella foenum-graecum* Linn.
5) Amla consists of dried and fresh fruits of *Emblica officinalis* Gaertn.

4.5.2. Fill in the Blanks

6) The term nutraceuticals was coined from nutrition and pharmaceutical by _____ in 1989.
7) _____ are classified on the basis of the chemical name given to them as per their phytochemical properties.
8) _____ are artificial foods prepared with the help of biotechnology.
9) The name Ashwagandha is a combination of the word _____ meaning horse and _____ meaning smell.
10) Spirulina is a blue green algae, _____ or _____ .

Answers

1) True 2) True 3) False
4) True 5) True 6) Stephen Defelice
7) Phytochemicals 8) Non-traditional nutraceuticals
9) *ashva* and *gandha* 10) *Spirulina platensis* and *Spirulina maxima*

4.5.3. Very Short Answer Type Questions

1) Define nutraceuticals.
2) Classify nutraceuticals based on the foods available in the market.
3) What are traditional nutraceuticals?
4) Enlist the examples of recombinant nutraceuticals.
5) Which nutraceuticals are helpful in curing skin and bone health?
6) What is the source of alfalfa and chicory?
7) Give the uses of ginger.

4.5.4. Short Answer Type Questions

1) Classify nutraceuticals according to their chemical nature.
2) Write about the different types of nutraceuticals available in the market.
3) Discuss the different non-traditional nutraceuticals.
4) Give the role of nutraceuticals in diabetes.
5) Write about the role of nutraceuticals in cardiovascular diseases.
6) Give the uses of fenugreek and garlic.

4.5.5. Long Answer Type Questions

1) Discuss briefly about classification of nutraceuticals.
2) Briefly discuss about the market, growth and scope of nutraceutical products available in the market.
3) Write an exhaustive note on the role of nutraceuticals in cancer.
4) Write about the role of nutraceuticals in irritable bowel syndrome.
5) Write about honey, amla and ginseng used as health food.

CHAPTER 5

Herb-Drug and Herb-Food Interaction

5.1. HERB-DRUG AND HERB-FOOD INTERACTIONS

5.1.1. Introduction

Herb-drug interactions occur between herbal medicines and conventional drugs. These interactions are more common than drug-drug interactions because herbal medicines contain multiple pharmacologically active ingredients, while conventional drugs contain a single ingredient. Some of these interactions are significant, although most herbal remedies are not associated with drug interactions and cause serious consequences.

Most herb-drug interactions cause moderate severity. Warfarin, insulin, aspirin, digoxin, and ticlopidine due to their narrow indices are the most commonly involved conventional drugs in herb-drug interactions. The most commonly implicated herbs involved in such interactions are those containing St. John's Wort, magnesium, calcium, iron, or ginkgo. Some **examples** of herb-drug interactions are:

1) St. John's wort (*Hypericum perforatum*) affects the clearance of many drugs, like cyclosporine, SSRI antidepressants, digoxin, indinavir, phenprocoumon, anti-cancer drugs, irinotecan, and imatinib.
2) *Salvia miltiorrhiza* enhance anticoagulation and bleeding in people taking warfarin.
3) Concomitant ephedra and caffeine cause fatalities in rare cases.
4) *Ginkgo biloba* along with warfarin or aspirin cause bleeding.

5.1.2. Classification

The herb-drug interactions are categorised into the following:

1) **Herb-Herb Interaction:** *Piper betel* is contraindicated if the individual is taking *Garcinia morella, Basella alba,* and *Sesamum indicum.*
2) **Herb-Food Interaction:** Payasa (milk preparation) along with Mantha (gruel) is contraindicated wine with steamed grains and radish with milk.
3) **Herb-Animal Origin Drug Interaction:** Kapotamamsa (meat of pigeon) is contraindicated with Sarshapataila (*Brassica alba*). Pork is contraindicated with Narikelataila (oil of *Coccus nucifera*). Equal quantity of Madhu (honey) is contraindicated with Grutha (ghee), and this combination produces toxic efficacy.
4) **Disease-Related Interaction:** Haritaki (*Terminalia chebula*) is contraindicated in pregnancy.

5.1.3. Study of Following Drugs and their Possible Side Effects and Interactions

The following herbal drugs and their possible side effects and in teractions are studied below:

1) Hypercium, 2) Kava-kava, 3) *Ginkgo biloba*, 4) Ginseng,
5) Garlic, 6) Pepper, and 7) Ephedra.

5.1.3.1. Hypercium

St. John's wort (hypercium) is a 50 -100cm tall plant with yellow, star -shaped flowers and five petals. It grows in Euro pe, North and South America, Australia, New Zealand, and Eastern Asia in sunny, well -drained areas. It is most commonly used for depression and symptoms related to mood like nervousness, tiredness, poor appetite, and trouble sleeping. It has been scientifi cally proved to be effective for mild to moderate depression. It is also used for relieving menopause symptoms like hot flashes and mood swings.

Possible Side Effects

Hypercium is safe when taken orally for 12 weeks. As per some evidences, it can be safel y used for a year. It can cause some side effects such as trouble in sleeping, vivid dreams, difficulty in sitting still, nervousness, irritability, stomach upset, tiredness, dry mouth, dizziness, headache, skin rash, diarrhoea, and skin tingling.

Hypercium is however regarded unsafe when taken orally in large doses as it might cause severe skin reactions to sun exposure. Women are at risk of severe skin reactions even at usual doses.

Possible Interactions

1) **Alprazolam with Hypercium:** Alprazolam is used fo r anxiety. Hypercium can increase the excretion of this drug from the body. Therefore, taking hypercium with alprazolam reduces the effectiveness of drug.
2) **Aminolevulinic Acid with Hypercium:** Aminolevulinic acid can make the skin sensitive to sunlight, and hypercium increases this sensitivity. Therefore, taking hypercium with aminolevulinic acid can increase the chances of sunburn, blistering or rashes on skin areas exposed to sunlight.
3) **Amitriptyline with Hypercium:** Amitriptyline is broken down by the body. Hypercium can increase the excretion of this drug from the body. Therefore, taking hypercium with amitriptyline reduces the effectiveness of drug.
4) **Birth Control Pills (Contraceptive Drugs) with Hypercium:** Estrogen present in some birth control pills is br oken down by the body, and hypercium can increase this breakdown process. Therefore, taking hypercium with birth control pills reduces their effectiveness.
5) **Cyclosporine with Hypercium:** Cyclosporine is broken down by the body, and hypercium can increase th is breakdown process. Therefore, taking hypercium with cyclosporine reduces the effectiveness of drug.

6) **Digoxin with Hypercium:** Digoxin improves the heart functioning, and hypercium on the other hand can decrease the amount of digoxin absorbed by the body. Therefore, taking hypercium with digoxin reduces the effectiveness of drug.

7) **Fenfluramine with Hypercium:** Fenfluramine increases the brain chemical, serotonin, and hypercium also increases this chemical. Therefore, taking hypercium with fenfluramine leads to too much serotonin that can cause serious side effects like heart problems, shivering, nausea, headache, and anxiety.

8) **Imatinib with Hypercium:** Imatinib is broken down by the body, and hypercium increases this breakdown process. Therefore, taking hyperc ium with imatinib reduces the effectiveness of drug.

9) **Irinotecan with Hypercium:** Irinotecan is used to treat cancer, and is broken down by the body. Hypercium increases this breakdown process. Therefore, taking hypercium with irinotecan reduces the effecti veness of drug.

10) **Medications Changed by the Liver [Cytochrome P -450 3A4 (CYP3A4) Substrates] with Hypercium:** Some drugs, **e.g.,** lovastatin, ketoconazole, itraconazole, fexofenadine, triazolam, etc., are changed and broken down by the liver. Hypercium can inc rease how fast liver breaks down these drugs. Therefore, taking hypercium with such drugs reduces their effectiveness.

11) **Antidepressant Drugs with Hypercium:** Some antidepressants, **e.g.,** fluoxetine, paroxetine, sertraline, amitriptyline, clomipramine, imipram ine, etc., increase the brain chemical, serotonin, and hypercium also increases this chemical. Therefore, taking hypercium with these medications increases serotonin level and causes serious side effects like heart problems, shivering, and anxiety.

12) **Medications for HIV/AIDS [Non -Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)] with Hypercium:** Some medications used for HIV/AIDS, **e.g.,** nevirapine, delavirdine, and efavirenz, are broken down by the body, and hypercium can increase this breakdown process. Therefore, taking hypercium with these medications reduces their effectiveness.

13) **Medications for HIV/AIDS (Protease Inhibitors) with Hypercium:** Some medications used for HIV/AIDS, **e.g.,** amprenavir, nelfinavir, ritonavir, and saquinavir, are broken down by the body, and hypercium can increase this breakdown process. Therefore, taking hypercium with these medications reduces their effectiveness.

14) **Medications for Pain (Narcotic Drugs) with Hypercium:** Some medications for pain, **e.g.,** meperidine, hydrocodone, mor phine, OxyContin, etc., are broken down by the body, and hypercium can decrease this breakdown process. Therefore, taking hypercium with these medications increases their effects and side effects.

15) **Medications Moved by Pumps in Cells (P -Glycoprotein Substr ates) with Hypercium:** Some medications , **e.g.,** etoposide, paclitaxel,

vinblastine, vincristine, vindesine, ketoconazole, itraconazole, amprenavir, indinavir, nelfinavir, saquinavir, cimetidine, ranitidine, diltiazem, verapamil, corticosteroids, erythromycin , cisapride, fexofenadine, cyclosporine, loperamide, quinidine, etc. , a re moved into the cells by pumps. Hypercium can make these pumps more active and decrease the absorption of these medications by the body. Therefore, taking hypercium with these medicat ions reduces their effectiveness.

16) **Medications that Increase Sensitivity to Sunlight (Photosensitizing Drugs) with Hypercium:** Some medications , **e.g.,** amitriptyline, ciprofloxacin, norfloxacin, lomefloxacin, ofloxacin, levofloxacin, sparfloxacin, gatifloxac in, moxifloxacin, trimethoprim/sulfamethoxazole, tetracycline, methoxsalen, and trioxsalen, can increase sensitivity to sunlight. Hypercium can also increase sensitivity to sunlight. Therefore, taking hypercium with these medications increases the chances of sunburn, blistering or rashes on areas of skin exposed to sunlight.

17) **Meperidine with Hypercium:** Meperidine increases serotonin level in the brain, and hypercium can also increase serotonin. Therefore, taking hypercium with meperidine leads to too much serotonin that can cause serious side effects like heart problems, shivering, nausea, headache, and anxiety.

18) **Nefazodone with Hypercium:** Nefazodone increases serotonin level in the brain, and hypercium can also increase serotonin. Therefore, taking hypercium with nefazodone leads to too much serotonin that can cause serious side effects like heart problems, shivering, nausea, headache, and anxiety.

19) **Nortriptyline with Hypercium:** Nortriptyline is broken down by the body. Hypercium can increase this breakdown pro cess. Therefore, taking hypercium with nortriptyline reduces the effectiveness of drug.

20) **Paroxetine with Hypercium:** Paroxetine increases serotonin level in the brain, and hypercium can also increase serotonin. Therefore, taking hypercium with paroxetine leads to too much serotonin that can cause serious side effects like heart problems, shivering, nausea, headache, and anxiety.

21) **Pentazocine with Hypercium:** Pentazocine increases serotonin level in the brain, and hypercium can also increase serotonin. Therefore, taking hypercium with pentazocine leads to too much serotonin that can cause serious side effects like heart problems, shivering, nausea, headache, and anxiety.

22) **Phenobarbital with Hypercium:** Phenobarbital is broken down by the body. Hypercium can increas e this breakdown process. Therefore, taking hypercium with phenobarbital reduces the effectiveness of drug.

23) **Phenprocoumon with Hypercium:** Phenprocoumon is broken down by the body. Hypercium can increase this breakdown process. Therefore, taking hypercium with phenprocoumon reduces the effectiveness of drug.

24) **Phenytoin with Hypercium:** Phenytoin is broken down by the body. Hypercium can increase this breakdown process. Therefore, taking hypercium with phenytoin reduces the effectiveness of drug.

25) **Reserpine with Hypercium:** Hypercium can reduce the effectiveness of reserpine.

26) **Sedative Medications (Barbiturates) with Hypercium:** Sedatives cause sleepiness and drowsiness, and hypercium can reduce their effectiveness.

27) **Sertraline with Hypercium:** Sertraline increases serotonin level in the brain, and hypercium can also increase serotonin. Therefore, taking hypercium with sertraline leads to too much serotonin that can cause serious side effects like heart problems, shivering, nausea, headache, and anxiety.

28) **Tacrolimus with Hypercium:** Tacrolimus is broken down by the body. Hypercium can increase this breakdown process. Therefore, taking hypercium with tacrolimus reduces the effectiveness of drug.

29) **Tramadol with Hypercium:** Tramadol increases serotonin level in the brain, an d hypercium can also increase serotonin. Therefore, taking hypercium with tramadol leads to too much serotonin that can cause serious side effects like heart problems, shivering, nausea, headache, and anxiety.

30) **Warfarin with Hypercium:** Warfarin slows down b lood clotting. It is broken down by the body, and hypercium can also increase this breakdown. Therefore, taking hypercium with warfarin reduces the effectiveness of drug, which might increase the risk of clotting.

5.1.3.2. Kava-Kava

Kava-kava is prepared from the rhizome and roots of *Piper methysticum* (of Piperaceae family). It is used for treating anxiety. Some people take kava -kava orally to calm anxiety, stress, restlessness, and insomnia. It is also used in Attention Deficit -Hyperactivity Dis order (ADHD), epilepsy, psychosis, depression, migraines, other headaches, Chronic Fatigue Syndrome (CFS), common cold, respiratory tract infections, tuberculosis, muscle pain, to relieve withdrawal symptoms of benzodiazepines, and for cancer prevention.

Possible Side Effects

Kava-kava is safe when taken orally for a short -term. Its extracts have been safely used under medical supervision for up to 6 months. However, after taking kava one cannot drive or operate machinery safely. It can cause liver damage. Using kava for 1 -3 months may urge the need for liver transplants and even cause death. Early symptoms of liver damage include jaundice, fatigue, and dark urine.

However, these cases are rare as most patients using kava do not experience liver toxicity. Some experts believe that liver toxicity in such cases cannot be directly linked to kava, and other factors may have contributed to these toxic effects.

Possible Interactions

1) **Alprazolam with Kava:** Alprazolam can cause drowsiness, and kava can also cause drowsiness. Therefore, taking kava with alprazolam may cause too much drowsiness.

2) **Sedatives (CNS Depressants) with Kava:** Sedatives, **e.g.,** clonazepam, lorazepam (Ativan), phenobarbital, zolpidem, etc., cause sleepiness and drowsiness, and kava also cause sleepiness. Therefore, taking kava with sedatives cause too much sleepiness.

3) **Levodopa with Kava:** Levodopa affects the brain by increasing dopamine level. Kava can decrease dopamine level in brain. Therefore, taking kava with levodopa reduces the effectiveness of drug.

4) **Medications Changed by the Liver [Cytochrome P-450 1A2 (CYP1A2) Substrates] with Kava:** Some medications are changed and broken down by the liver, **e.g.,** clozapine, cyclobenzaprine, fluvoxamine, haloperidol, imipramine, mexiletine, olanzapine, pentazocine, propranolol, tacrine, theophylline, zileuton, zolmitriptan, etc. Kava can decrease how fast liver breaks down these medications. Therefore, taking kava with these drugs increase their effects and side effects.

5) **Medications Changed by the Liver [Cytochrome P-450 2C19 (CYP2C19) Substrates] with Kava:** Some medications are changed and broken down by the liver, **e.g.,** amitriptyline, clomipramine, cyclophosphamide, diazepam, lansoprazole, omeprazole, lansoprazole, phenytoin, phenobarbital, progesterone, etc. Kava can decrease how fast liver breaks down these medications. Therefore, taking kava with these drugs increase their effects and side effects.

6) **Medications Changed by the Liver [Cytochrome P-450 2C9 (CYP2C9) Substrates] with Kava:** Some medications are changed and broken down by the liver, **e.g.,** amitriptyline, diazepam, zileuton, celecoxib, diclofenac, fluvastatin, glipizide, ibuprofen, irbesartan, losartan, phenytoin, piroxicam, tamoxifen, tolbutamide, torsemide, warfarin, etc. Kava can decrease how fast liver breaks down these medications. Therefore, taking kava with these drugs increase their effects and side effects.

7) **Medications Changed by the Liver [Cytochrome P-450 2D6 (CYP2D6) Substrates] with Kava:** Some medications are changed and broken down by the liver, **e.g.,** amitriptyline, clozapine, codeine, desipramine, donepezil, fentanyl, flecainide, fluoxetine, meperidine, methadone, metoprolol, olanzapine, ondansetron, tramadol, trazodone, etc. Kava can decrease how fast liver breaks down these medi cations. Therefore, taking kava with these drugs increase their effects and side effects.

8) **Medications Changed by the Liver [Cytochrome P-450 2E1 (CYP2E1) Substrates] with Kava:** Some medications are changed and broken down by the liver, **e.g.,** acetaminophen,chlorzoxazone, ethanol, theophylline, and anaesthetics used during surgery such as enflurane, halothane, isoflurane, and methoxyflurane. Kava can decrease how fast liver breaks down these medications. Therefore, taking kava with these drugs increase their effects and side effects.

9) **Medications Changed by the Liver [Cytochrome P-450 3A4 (CYP3A4) Substrates] with Kava:** Some medications are changed and broken down by the liver, **e.g.,** lovastatin, ketoconazole, itraconazole, fexofenadine, triazolam, etc. Kava ca n decrease how fast liver breaks down these medications. Therefore, taking kava with these drugs increase their effects and side effects.

10) **Medications Moved by Pumps in Cells (P -Glycoprotein Substrates) with Kava:** Some medications are moved into the cells by pumps, **e.g.,** etoposide, paclitaxel, vinblastine, vincristine, vindesine, ketoconazole, itraconazole, amprenavir, indinavir, nelfinavir, saquinavir, cimetidine, ranitidine, diltiazem, verapamil, corticosteroids, erythromycin, cisapride, fexofenadine, cyclosporine, loperamide, quinidine, etc. Kava can reduce the activity of these pumps and increase the absorption of these medications by the body, thus increasing their amount in the body, which leads to side effects.

11) **Medications that can Harm the Liver (He patotoxic Drugs) with Kava:** Some medications can harm the liver, **e.g.,** acetaminophen, amiodarone, carbamazepine, isoniazid, methotrexate, methyldopa, fluconazole, itraconazole, erythromycin, phenytoin, lovastatin, pravastatin, simvastatin, etc. Kava can al so harm the liver. Therefore, taking kava with these drugs can increase the risk of liver damage.

5.1.3.3. Ginkgo biloba

Ginkgo (*Ginkgo biloba* of Ginkgoaceae family) is a large tree with fan -shaped leaves. Extracts from the leaves of ginkgo tree are used for the treatment of cognitive impairments, dementia, intermittent claudication, and tinnitus. Ginkgo leaf is taken orally for treating memory disorders like Alzheimer's disease. It is also used for conditions that occur due to reduced blood flow in brain (especially in older people), such as memory loss, dizziness, difficulty in concentrating, and mood disturbances. Ginkgo is also used for relieving leg pain when walking related to poor blood flow (claudication).

Possible Side Effects

Ginkgo leaf extract is mostly safe when taken orally in appropriate doses. It can cause some minor side effects like stomach upset, headache, dizziness, constipation, forceful heartbeat, and allergic skin reactions. Ginkgo leaf extract can increase the risk of l iver and thyroid cancers. However, this has only occurred in animals given high doses of ginkgo. No information has been provided to know if it could happen in humans. Ginkgo leaf extract can increase the risk of bruising and bleeding as it reduces the blo od viscosity and decreases its ability to form clots. In some people, ginkgo has caused bleeding in eyes, brain, and lungs and excessive bleeding after a surgery.

Ginkgo leaf extract is considered safe when taken intravenously for a short -term (up to 10 days).

Ginkgo fruit and pulp can cause severe allergic skin reactions and irritation of mucous membranes in individuals who are allergic to poison ivy, poison oak, poison sumac, mango rind, or cashew shell oil.

The **fresh seeds** are unsafe when taken oral ly as they are poisonous and considered dangerous. They can cause seizures and death. **Roasted seeds** or **crude ginkgo plant** is unsafe when taken orally. Eating more than 10 roasted seeds in a single day can cause difficulty in breathing, weak pulse, seizures , loss of consciousness, and shock.

Possible Interactions

1) **Ibuprofen with Ginkgo:** Ginkgo can slow blood clotting, and ibuprofen can also slow blood clotting. Therefore, taking ginkgo with ibuprofen slows down blood clotting too much and increases the risk of bruising and bleeding.

2) **Anticoagulant/Antiplatelet Drugs with Ginkgo:**Some medications can slow blood clotting, **e.g.,** aspirin, clopidogrel, diclofenac, ibuprofen, naproxen, dalteparin, enoxaparin, heparin, warfarin, etc. Ginkgo can also slow blood clotting. Therefore, taking ginkgo with these medications slows down blood clotting too much and increases the risk of bruising and bleeding.

3) **Warfarin with Ginkgo:** Warfarin slows blood clotting, and ginkgo can also slow blood clotting. Therefore, taking ginkgo wi th warfarin slows down blood clotting too much and increases the risk of bruising and bleeding.

4) **Alprazolam with Ginkgo:** Taking ginkgo with alprazolam can reduce the effectiveness of drug.

5) **Buspirone with Ginkgo:** Buspirone affects the brain, and gingko also affects the brain. Therefore, taking ginkgo with buspirone can either make the individuals hyper- or overexcited. However, it is unclear if this interaction was caused by ginkgo or the other medications.

6) **Efavirenz with Ginkgo:** Efavirenz is used to treat HIV infection. Therefore, taking ginkgo with efavirenz can reduce the effectiveness of drug.

7) **Fluoxetine with Ginkgo:** Taking ginkgo with fluoxetine can give rise to hypomania symptoms, i.e., irritation, nervousness, jittery, and excitement. However, it is not known if this interaction was caused by taking ginkgo with fluoxetine.

8) **Medications Changed by the Liver [Cytochrome P-450 1A2 (CYP1A2) substrates] with Ginkgo:** Some medications are changed and broken down by the liver, **e.g.,** clozapine, cyclobenzaprine, f luvoxamine, haloperidol, imipramine, mexiletine, olanzapine, pentazocine, propranolol (Inderal), tacrine, theophylline, zileuton, zolmitriptan, etc. Ginkgo can reduce how fast the liver breaks down these medications. Therefore, taking ginkgo with such medications can increase their effects and side effects

9) **Medications Changed by the Liver [Cytochrome P-450 2C19 (CYP2C19) Substrates] with Ginkgo:** Some medications are changed and broken down by the liver, **e.g.,** amitriptyline, carisoprodol, citalopram, diazep am, lansoprazole, omeprazole, phenytoin, warfarin, etc. Ginkgo can reduce how fast the liver breaks down these medications. Therefore, taking ginkgo with such medications can reduce their effectiveness.

10) **Medications Changed by the Liver [Cytochrome P-450 2C9 (CYP2C9) Substrates] with Ginkgo:** Some medications are changed and broken down by the liver, **e.g.,** amitriptyline, diazepam, zileuton, celecoxib, diclofenac, fluvastatin, glipizide, ibuprofen, irbesartan, losartan, phenytoin, piroxicam, tamoxifen, tolbutamide, torsemide, and warfarin. Ginkgo can reduce how fast the liver breaks down these medications. Therefore, taking ginkgo with such medications can increase their effects and side effects.

11) **Medications Changed by the Liver [Cytochrome P-450 2D6 (CYP2D 6) Substrates] with Ginkgo:** Some medications are changed and broken down by the liver, **e.g.,** amitriptyline, clozapine, codeine, desipramine, donepezil, fentanyl, flecainide, fluoxetine, meperidine, methadone, metoprolol, olanzapine, ondansetron, tramadol, trazodone, etc. Ginkgo can reduce how fast the liver breaks down these medications. Therefore, taking ginkgo with such medications can increase their effects and side effects.

12) **Medications Changed by the Liver [Cytochrome P-450 3A4 (CYP3A4) Substrates] with Ginkgo:** Some medications are changed and broken down by the liver, **e.g.,** lovastatin, clarithromycin, cyclosporine, diltiazem, estrogens, indinavir, triazolam, etc. Ginkgo can affect how fast the liver breaks down these medications. Therefore, taking gin kgo with such medications give rise to various unwanted effects and side effects.

13) **Anti-Diabetes Drugs with Ginkgo:** Some medications are used for diabetes (i.e., for lowering blood sugar), **e.g.,** glimepiride, glyburide, insulin, pioglitazone, rosiglitazone, chlorpropamide, glipizide, tolbutamide, etc. Ginkgo can increase or decrease insulin and blood sugar in type 2 diabetes patients. Therefore, taking ginkgo with diabetes medications can reduce their effectiveness.

14) **Medications that Increase the Chance of ha ving a Seizure (Seizure Threshold Lowering Drugs) with Ginkgo:** Some medications increase the chance of having a seizure, **e.g.,** anaesthesia (propofol), anti -arrhythmics (mexiletine), antibiotics (amphotericin, penicillin, cephalosporins, imipenem), antidepr essants (bupropion, others), antihistamines (cyproheptadine, others), immunosuppressants (cyclosporine), narcotics (fentanyl, others), stimulants (methylphenidate), theophylline, etc. Ginkgo can cause seizures in some individuals. Therefore, taking ginkgo with such medications can increase the risk of having a seizure.

15) **Anticonvulsants with Ginkgo:** Anticonvulsants are used to prevent seizures and affect the chemicals in brain, **e.g.,** phenobarbital, primidone, valproic acid, gabapentin, carbamazepine, phenyto in, etc. Ginkgo can also affect the chemicals in brain. Therefore, taking ginkgo with such medications can reduce their effectiveness.

16) **Trazodone with Ginkgo:** Trazodone affects the chemicals in brain, and ginkgo can also affect the chemicals in brain. Ther efore, taking ginkgo with trazodone can cause serious side effects in brain.

5.1.3.4. Ginseng

Panax ginseng is taken orally to improve thinking, concentration, memory, Alzheimer's disease, work efficiency, physical stamina, and to prevent muscle damage from exercise and athletic endurance. It is also used for depression, anxiety, general fatigue, Chronic Fatigue Syndrome (CFS), multiple sclerosis, for boosting immune system, and for fighting particular infections in cystic fibrosis (a lung disease caused by *Pseudomonas*). *Panax ginseng* is safe when applied to the skin as part of a multi-ingredient product in the short-term.

Possible Side Effects

Panax ginseng is unsafe when taken orally for a long-term (more than 6 months). The most common side effect of ginseng is insomnia. The less common side effects include menstrual problems, breast pain, increased heart rate, high or low blood pressure, headache, loss of appetite, diarrhoea, itching, rash, dizziness, mood changes, and vaginal bleeding. The uncommon side effects include severe rash called Stevens-Johnson syndrome, liver damage, and severe allergic reactions.

Possible Interactions

1) **Alcohol with Ginseng:** The body breaks down alcohol to get rid of it. Taking *Panax ginseng* with alcohol can increase this breakdown process.

2) **Caffeine with Ginseng:** Caffeine can speed up the nervous system, make the individual feel jittery, and speed up the heartbeat. *Panax ginseng* can also speed up the nervous system. Therefore, taking ginseng with caffeine can cause serious problems, like increased heart rate and high blood pressure.

3) **Furosemide with Ginseng:** Taking ginseng with furosemide can reduce the effectiveness of drug. However, there is not enough information available on this interaction.

4) **Insulin with Ginseng:** Insulin is used to decrease blood sugar, and *Panax ginseng* can also reduce blood sugar. Therefore, taking ginseng with insulin can reduce blood sugar too much.

5) **Medications Changed by the Liver [Cytochrome P-450 2D6 (CYP2D6) Substrates] with Ginseng:** Some medications are changed and broken down by the liver, **e.g.,** amitriptyline, clozapine, codeine, desipramine, donepezil, fentanyl, flecainide, fluoxetine, meperidine, methadone, metoprolol, olanzapine, ondansetron, tramadol, trazodone, etc. *Panax ginseng* can decrease how fast the liver breaks down these medications. Therefore, taking ginseng with such medications can increase their effects and side effects

6) **Medications for Depression (MAOIs) with Ginseng:** Some medications are used for depression and can stimulate the body, **e.g.,** phenelzine, tranylcypromine, etc. *Panax ginseng* can also stimulate the body. Therefore, taking ginseng with such medications can cause too much stimulation, and give rise to effects like anxiousness, headache, restlessness, and insomnia.

7) **Anti-Diabetes Drugs with Ginseng:** Anti-diabetes medications, **e.g.,** glimepiride, glyburide, insulin, pioglitazone, rosiglitazone, chlorpropamide, glipizide, tolbutamide, etc., are used to lower blood sugar. *Panax ginseng* can also reduce blood sugar. Therefore, taking ginseng with such medications can reduce the blood sugar too much.

8) **Immunosuppressants with Ginseng:** Immunosuppressants, **e.g.,** azathioprine, basiliximab, cyclosporine, daclizumab, muromonab-CD3, mycophenolate, tacrolimus, sirolimus, prednisone, corticosteroids (glucocorticoids), etc., decrease the immune system. But, *Panax ginseng* increases the immune system. Therefore, taking ginseng with such medications reduce their effectiveness

9) **Anticoagulant/Antiplatelet Drugs with Ginseng:** Some medications slow down blood clotting, **e.g.,** aspirin, clopidogrel, diclofenac, ibuprofen, naproxen, dalteparin, enoxaparin, heparin, warfarin, etc. *Panax ginseng* can also slow down blood clotting. Therefore, taking ginseng with such medications increase the chances of bruising and bleeding.

10) **Stimulant Drugs with Ginseng:** Stimulant drugs, **e.g.,** diethylpropion, epinephrine, phentermine, pseudoephedrine, etc., speed up the nervous system, and make individuals feel jittery and speed up their heartbeat. *Panax ginseng* can also speed up the nervous system. Therefore, taking ginseng with such medications can cause serious problems, like increased heart rate and high blood pressure.

11) **Warfarin with Ginseng:** Warfarin is used to slow down blood clotting. *Panax ginseng* can reduce the effectiveness of warfarin. But it is not clear if this interaction is of major concern.

5.1.3.5. Garlic

Modern phytotherapy utilises garlic (*Allium sativum* L., belonging to family Alliaceae) for treating hypercholesterolaemia and preventing arteriosclerosis. However, no convincing clinical proofs are available. **Standardised garlic powder** containing 1.3% allin and 0.6% allicin, **garlic aged extract** containing high amounts of water-soluble phytochemicals (diallyl sulphides), and **garlic oil** (an essential oil obtained from the distillation of garlic cloves) are some of the useful garlic preparations.

Possible Side Effects

Oral intake of garlic is usually safe. Garlic has been researched for up to 7 years and proved to be safe. Upon oral consumption, garlic causes bad breath, a burning sensation in the mouth or stomach, heartburn, gas, nausea, vomiting, body odour, and diarrhoea. Raw garlic worsens these side effects. Garlic can also raise the risk of bleeding. Reports suggest cases of bleeding after surgery upon ingestion of garlic. Asthma problem and some other allergic reactions are seen in people working with garlic.

Garlic skin products, like gels, pastes, and mouthwashes containing garlic, are safe and can be used for up to 3 months; but, sometimes might cause skin damage like a burn. Raw garlic application to the skin should be avoided as it may cause severe skin irritation.

Possible Interactions

1) **Isoniazid with Garlic:** Garlic decreases the absorbed levels of isoniazid in body. Therefore, taking garlic with isoniazid reduces the effectiveness of drug.

2) **Medications used for HIV/AIDS [Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)] with Garlic:** Some medications used for HIV/AIDS, **e.g.,** nevirapine, delavirdine, and efavirenz, are broken down by the body. Garlic increases this breakdown process. Therefore, taking garlic with these medications reduces their effectiveness.

3) **Saquinavir with Garlic:** Saquinavir is broken down by the body. Garlic potentiates this breakdown process. Therefore, ta king garlic with saquinavir decreases the effectiveness of drug.

4) **Birth Control Pills (Contraceptive Drugs) with Garlic:** Some estrogen-containing birth control pills, **e.g.,** ethinyl estradiol and levonorgestrel, ethinyl estradiol and norethindrone, etc., are broken down by the body. Garlic can increase this breakdown process. Therefore, taking garlic with such medications reduce their effectiveness.

5) **Cyclosporine with Garlic:** Cyclosporine is broken down by the body. Garlic can potentiate this breakdown proces s. Therefore, taking garlic with cyclosporine decreases the effectiveness of drug.

6) **Medications Changed by the Liver [Cytochrome P-450 2E1 (CYP2E1) Substrates] with Garlic:** Certain drugs are converted and broken down by the liver, **e.g.,** acetaminophen, chlor zoxazone, ethanol, theophylline, and anaesthetic drugs during surgery like enflurane, halothane, isoflurane, and methoxyflurane. Garlic oil can decrease how fast the liver breaks down these medications. It also affects the metabolism of the medications tha t are converted by the liver. Therefore, taking garlic oil with such medications either potentiates their action or elevates their side effects.

7) **Medications Changed by the Liver [Cytochrome P-450 3A4 (CYP3A4) Substrates] with Garlic:** Certain drugs are con verted and broken down by the liver, **e.g.,** lovastatin, ketoconazole, itraconazole, fexofenadine, triazolam, etc. Garlic can increase how fast the liver breaks down these medications. Therefore, taking garlic with such medications reduces their effectiveness.

8) **Medications that Slow Blood Clotting (Anticoagulant/Antiplatelet Drugs) with Garlic:** Some medications delay blood clotting, **e.g.,** aspirin, clopidogrel, diclofenac, ibuprofen, naproxen, dalteparin, enoxaparin, heparin, warfarin, etc. Garlic also delays blood clotting. Therefore, taking garlic with such medications can increase the chances of bruising and bleeding.

9) **Warfarin with Garlic:** Warfarin slows down blood clotting process. Garlic can potentiate the effectiveness of warfarin. Therefore, taking garl ic with warfarin can increase the chances of bruising and bleeding due to slow clotting.

5.1.3.6. Pepper

Pepper (*Piper nigrum* of family Piperaceae) is found in India and other tropical Asian countries. It is the most commonly used spice around the world. Black pepper and white pepper belong to same plant species, but their preparation method is different. Black pepper is obtained by cooking the dried unripe fruit, while the white pepper is obtained by cooking and drying the ripe seeds.

Black pepper contains piperine which is pharmacologically active. It kills bacteria, fungi, and parasites. Piperine also aids in absorption of some medications and is effective against cancer.

Possible Side Effects

Black pepper is considered safe if orally ingested in amounts found in foods. There is no evidence to prove that oral consumption of black pepper as a medicine is safe. Black pepper oil is applied to skin and inhaled through nose or mouth and is said to be safe.

Black pepper gives a burning aftertaste and causes stomach disturbance. Its exposure to eyes must be avoided or else it causes a burning sensation. Cough may occur if black pepper oil is inhaled through nose or mouth. Some individuals may get allergic to black pepper. On oral consumption of black p epper in large amounts, it can accidentally reach the lungs and cause death; this incident mostly occurs in children.

Possible Interactions

1) **Carbamazepine with Black and White Pepper:** Black and white pepper can elevate the amounts of carbamazepine absorbed by the body. They also slow the breakdown of carbamazepine in the body. Therefore, taking pepper with carbamazepine can raise the amount of drug in the body and increase the chances of side effects.

2) **Lithium with Black and White Pepper:** Black pepper and w hite pepper produce diuretic-like effects. They reduce the breakdown and excretion of lithium from the body. Therefore, taking pepper with lithium increases the level of drug in body and produces serious side effects.

3) **Medications Changed by the Liver [Cytochrome P-450 3A4 (CYP3A4) substrates] with Black and White Pepper:** Some medications, **e.g.,** lovastatin, ketoconazole, itraconazole, fexofenadine, triazolam, etc., are biotransformed by liver. Black and white pepper slows this transformation process (breakdown) by the liver. Therefore, taking pepper with such medications can increase the chances of side effects.

4) **Medications Moved by Pumps in Cells (P -Glycoprotein Substrates) with Black Pepper and White Pepper:** Some medications are moved into the cells by pum ps, **e.g.,** etoposide, paclitaxel, vinblastine, vincristine, vindesine, ketoconazole, itraconazole, amprenavir, indinavir, nelfinavir, saquinavir, cimetidine, ranitidine, diltiazem, verapamil, corticosteroids, erythromycin, cisapride, fexofenadine, cyclospor ine, loperamide, quinidine, digoxin, etc. Therefore, taking pepper with such medications can lower the activity of these pumps, increase the absorption of such medications, and cause side effects.

5) **Phenytoin with Black and White Pepper:** Black and white pepper can elevate the absorption of phenytoin, and thus its concentration in the body. Therefore, taking pepper with phenytoin increases the effects and side effects of drug.

6) **Propranolol with Black and White Pepper:** Black and white pepper can enhance the absorption of propranolol, and thus its concentration in the body. Therefore, taking pepper with propranolol increases the effects and side effects of drug.

7) **Rifampin with Black and White Pepper:** Black and white pepper can enhance the absorption of rifampin, and thus its concentration in the body. Therefore, taking pepper with rifampin increases the effects and side effects of drug.

8) **Theophylline with Black and White Pepper:** Black and white pepper can enhance the absorption of theophylline, and thus its concentration in the body. Therefore, taking pepper with theophylline increases the effects and side effects of drug.

5.1.3.7. Ephedra

Ephedra obtained from *Ephedra sinica* of family Ephedraceae, is an alkaloid that provides relief in breathlessness, chest tightness, and wheezing due to bronchial asthma. It falls into the category of over-the-counter formulations for the temporary relief of bronchial asthma.

Possible Side Effects

Consumption of ephedra or its active ingredients should be avoided as it is unsafe for children as well as adults. It is a very harmful drug or can put individual in disabling conditions. Ephedra can cause high blood pressure, heart attacks, muscle disorders, seizures, strokes, irregular heartbeat, loss of consciousness, and even death. These side effects worsen if ephedra is taken in high doses or for long-term. Doses greater than 32mg/day may increase the risk of haemorrhagic stroke up to three times. The serious side effects are of greater concern than any potential benefit.

Some minor serious side effects of ephedra are dizziness, restlessness, anxiety, irritability, heart pounding, headache, loss of appetite, nausea, and vomiting.

Possible Interactions

1) **Medications that can Cause Irregular Heartbeat (QT Interval-Prolonging Drugs) with Ephedra:** Some medications cause irregular heartbeat, **e.g.,** amiodarone, disopyramide, dofetilide, ibutilide, procainamide, sotalol, thioridazine, quinidine, etc. Ephedra can also increase heartbeat. Therefore, taking ephedra with such medications can cause serious side effects like heart attack.

2) **Methylxanthines with Ephedra:** Methylxanthines, **e.g.,** aminophylline, caffeine, and theophylline, stimulate the body. Ephedra can potentiate the effects of methylxanthines. Therefore, taking ephedra with methylxanthines can produce side effects like jitteriness, nervousness, fast heartbeat, high blood pressure, and anxiety.

3) **Stimulant Drugs with Ephedra:** Stimulant drugs, **e.g.,** diethylpropion, epinephrine, phentermine, pseudoephedrine, etc., exaggerate the nervous system and cause feeling of jitteriness and elevated heartbeat. Ephedra also stimulates the nervous system. Therefore, taking ephedra with stimulant drugs can give rise to serious problems, like greater heart rate and high blood pressure.

4) **Dexamethasone with Ephedra:** Dexamethasone is broken down by the body for its removal. Ephedra can increase this breakdown process. Therefore, taking ephedra with dexamethasone can decrease the effectiveness of drug.

5) **Ergot Derivatives with Ephedra:** Ergot derivatives, **e.g.,** bromocriptine, dihydroergotamine, ergotamine, and pergolide, are known to increase blood pressure. Ephedra can also raise blood pressure. Therefore, taking ephedra with ergot derivatives can increase blood pressure to lethal state.

6) **Medications for Depression (MAOIs) with Ephedra:** Ephedra bear chemical agents that act as body stimulants. Some anti-depressants, **e.g.,** phenelzine, tranylcypromine, etc., increase these chemicals. Therefore, taking ephedra with anti-depressants can cause serious side effects like fast heartbeat, high blood pressure, seizures, and nervousness.

7) **Anti-Diabetes Drugs with Ephedra:** Medications for diabetes, **e.g.,** glimepiride, glyburide, insulin, pioglitazone, rosiglitazone, chlorpropamide, glipizide, tolbutamide, etc., lower blood sugar level. Ephedra on the contrary raises blood sugar concentration. Therefore, taking ephedra with anti-diabetics can decrease their effectiveness.

8) **Anticonvulsants with Ephedra:** Medications used to prevent convulsions, **e.g.,** phenobarbital, primidone, valproic acid, gabapentin, carbamazepine, phenytoin, etc., affect the chemicals in brain. Ephedra can also affect these chemicals. Therefore, taking ephedra with anticonvulsants can decrease their effectiveness.

5.2. SUMMARY

The details given in the chapter can be summarised as follows:

1) **Hypericum** can increase the excretion of **alprazolam** from the body. Therefore, taking hypericum with alprazolam reduces the effectiveness of drug.
2) Hypericum can increase the excretion of **amitriptyline** from the body. Therefore, taking hypericum with amitriptyline reduces the effectiveness of drug.
3) Hypericum can increase the breakdown of **birth control pills**. Therefore, taking hypericum with birth control pills reduces their effectiveness.
4) Hypericum can increase the breakdown of **cyclosporine**. Therefore, taking hypericum with cyclosporine reduces the effectiveness of drug.
5) Hypericum can decrease the amount of **digoxin** absorbed by the body. Therefore, taking hypericum with digoxin reduces the effectiveness of drug.
6) Hypericum can increase the breakdown of **imatinib**. Therefore, taking hypericum with imatinib reduces the effectiveness of drug.
7) Hypericum can increase the breakdown of **phenytoin**. Therefore, taking hypericum with phenytoin reduces the effectiveness of drug.
8) Hypericum can reduce the effectiveness of **reserpine**.
9) **Kava** can decrease dopamine level in brain. Therefore, taking kava with **levodopa** reduces the effectiveness of drug.

10) Taking ginkgo with ibuprofen slows down blood clotting too much and increases the risk of bruising and bleeding.
11) Taking ginkgo with **efavirenz** can reduce the effectiveness of drug.
12) The body breaks down alcohol to get rid of it. Taking *Panax ginseng* with **alcohol** can increase this breakdown process.
13) ***Panax ginseng*** can reduce blood sugar. Therefore, taking ginseng with **insulin** can reduce blood sugar too much.
14) **Garlic** decreases the absorbed levels of **isoniazid** in body. Therefore, taking garlic with isoniazid reduces the effectiveness of drug.
15) Garlic potentiates the breakdown of **saquinavir**. Therefore, taking garlic with saquinavir decreases the effectiveness of drug.
16) **Black and white pepper** can enhance the absorption of **propranolol**, and thus its concentration in the body. Therefore, taking pepper with propranolol increases the effects and side effects of drug.
17) Black and white pepper can enhance the absorption of **rifampin**, and thus its concentration in the body. Therefore, taking pepper with rifampin increases the effects and side effects of drug.
18) Black and white pepper can enhance the absorption of **theophylline**, and thus its concentration in the body. Therefore, taking pepper with theophylline increases the effects and side effects of drug.
19) **Ephedra** can increase the breakdown of dexamethasone.. Therefore, taking ephedra with dexamethasone can decrease the effectiveness of drug.
20) Ephedra can raise blood pressure. Therefore, taking ephedra with **ergot derivatives** can increase blood pressure to lethal state.

5.3. EXERCISE

5.3.1. Very Short Answer Type Questions

1) Give some examples of herb-drug interactions.
2) Classify herb-drug interactions.
3) Give two interactions undergone by hypercium.
4) Enlist two interactions undergone by garlic.
5) Give any four interactions undergone by ephedra.

5.3.2. Short Answer Type Questions

1) Write about the interactions undergone by kava-kava.
2) Discuss the interactions that ginseng undergoes.
3) Give the interactions that ephedra undergoes.

5.3.3. Long Answer Type Questions

1) Discuss briefly about herb-drug interactions.
2) Write an exhaustive on the interactions undergone by pepper and garlic.

CHAPTER 6

Herbal Cosmetics

6.1. HERBAL COSMETICS

6.1.1. Introduction

The **products having desirable physiological properties** like healing, enhancement of appearance, and conditioning properties **due to the herbal ingredients present in them** are called herbal cosmetics. Owing to the deteriorating effects of processed foods and over-medication, the importance of herbs has increased in the modern time, and therefore herbs are used in cosmetics, foodstuffs, and alternate medicines on a large scale. The changes in modern life-style have resulted in the maximum use of herbs in daily life because individuals believe that herbs can be used as potent remedial medicines.

In herbal cosmetics, herbs are used either in crude form or as extracts. Herbal cosmetics used in skin care have been formulated using the principles from the ancient texts of Rig Veda, Yajur Veda, and Ayurveda, Unani and Homeopathic systems of medicines.

Safe, elegant and effective cosmetic products are formulated nowadays by combining the knowledge as well as experience of herbs and modern cosmetic technology, which is widely accepted. In true means, herbal cosmetics should be the result of merging nature with modern technology.

The adverse effects of herbs are least or negligible, and this increases consumer compliance. In India, herbal cosmetics make up 10% of the total cosmetic industry that is estimated to be around 200 crores. The current growth rate of Indian cosmetic industry is 20-25% per year, of which herbal cosmetics alone make up for 60%.

6.1.2. Skin Care Products

Formulation of some herbal skin care products is described below:

1) **Herbal Creams:** The key ingredients in the formulation of herbal creams are plant derivatives. Following are the important types of herbal creams:
   i) **Cold Creams: Galen** formulated the first herbal cold cream using beeswax, water, olive oil (as emollient), and rose petal (as fragrant). **For example,** Nyle cold cream with red apple extract.

      Cold creams are water-in-oil emulsion (w/o), and the bases used in their preparation are:
      a) Almond oil and white bees wax, and
      b) Borax (as emulsifier) and rose water.

Borax is added and dissolved in heated rose water. The lipoid constituents are heated in a water bath at 70 °C temperature. The aqueous and the lipid phases are homogeneously mixed with constant stirring at a maintained temperature, and mixing is continued for around 30 minutes. The resultant mixture is allowed to cool slowly up to 45 -50°C temperature. Lastly, perfuming agents are added after cooling the mixture so that evaporation does not occur.

ii) **Vanishing Creams:** These are oil -in-water emulsion (o/w), and are hardly visible when applied to skin. They impart moisturising as well as emollient effect. **For example,** jojoba vanishing cream.

The common ingredients of vanishing cream are glycerine, stearic acid, triethanolamine, lanolin, natural jojoba extract, water, preservative, and perfume. The waxy materials (stearic acid and lanolin) are melted together. The resultant mixture is added with water, jojoba extract, triethanolamine, and glycerine. Lastly, preservatives and perfumes are added to the mixture and stirred constantly so that a uniform mass can be obtained.

iii) **Nourishing Creams:** These creams are non -greasy, and provide nourishment as well as protection to the skin. **For example,** nourishing skin cream (Himalaya).

Following ingredients are present in nourishing creams:

a) Aloe vera to nourish and moisturise the skin,
b) Indian kino tree and ashwagandha to protect the skin from pollution and dry weather, and
c) Gotu Kola to increase collagen production.

Along with the above mentioned ingredients, nourishing creams also include liquid paraffin, glycerine, BHT, sodium EDTA, phenoxyethanol, methylparaben, etc., which act as formulation base.

iv) **Night Creams:** These creams are applied during night. They consist of revitalisers, moisturisers, and skin-rejuvenating nutrients. Night creams prevent evaporation and moisturise the skin. **For example,** revitalising night cream (Himalaya).

For nourishment of skin, the following herbal agents are added in the night creams:

a) ***Pyrus malus*** **(Crab Apple)** for cooling, soothing and keratolytic effect.
b) ***Triticum sativum*** **(Wheat)** for preventing black heads.
c) ***Citrus limon*** **(Lemon)** for protecting the skin from oxidative damage.
d) ***Lilium polyphyllum*** **(White Lily)** for astringent effect.
e) ***Solanum lycopersicum*** **(Tomato)** for its antioxidant effect.

v) **Moisturiser Creams:** These creams are applied on dry skin as they heal and repair dry skin, and maintain the softness of skin. They maintain skin hydration by reduction evaporation. **For example,** aloe moisturising cream.

Herbal moisturiser creams contain aloe vera gel, tocopherol (v itamin E), chamomile extract, beeswax, and coconut oil. Coconut oil is added to and melted with the heated beeswax. This molten mixture is stirred continuously and allowed to cool slowly. Aloe vera gel is added drop wise during the stirring process. When the mixture become s uniformly thick, stirring is stopped Lastly, chamomile extract and vitamin oilare added.

vi) **Anti-Acne Creams:** These creams are ap plied on the skin surface, and mainly act on hair follicles and sebaceous glands. **For example,** Himalaya acne and pimple cream.

Following ingredients are present in anti-acne creams:
a) ***Lens culinaris* (Lentil)** for reducing inflammation,
b) **Silk cotton tree** that acts as an astringent and emollient, and
c) ***Vitex negundo*** that exhibits anti-inflammatory action.

vii) **Sunscreen Creams:** These creams are used topically to protect the skin from harmful effects of sunrays. They act either by scattering the sunlight or by absorbin g the erythematous rays of sun. **For example,** Ayur sunscreen.

Herbal sunscreen includes the following ingredients:
a) Aloe vera,
b) Fat-soluble walnut extract,
c) Bees wax, and
d) Hydrogenated ricinus oil.

viii) **Anti-Wrinkle Cream s:** These creams are used for delaying wrin kles and reducing the already present fine lines. On using regularly , these creams prevent oxidative damage of skin. **For example,** Divya Tejas anti-wrinkle cream.

The main ingredients present in an anti-wrinkle cream are:
a) ***Aloe vera*** as antifungal and antibacterial,
b) ***Papaver rhoeas*** as an emollient,
c) ***Vitis vinifera*** to nourish the skin,
d) ***Solarium lycopersicum*** as an antioxidant, and
e) ***Santalum album*** to reduce itching and inflammation.

ix) **Fairness Cream s:** These creams reduce melanin formation as well as skin pigmentation. **For example,** Himalaya fairness cream.

The main ingredients of fairness creams are:
a) ***Rosa centifolia*** to improve complexion,
b) ***Citrus reticulata*** as a blemish remover, and
c) ***Aloe vera*** as a moisturiser and emollient.

2) **Herbal Powders:** A range of powders are avai lable in the market such as dusting powder, talcum powder, body powder, after-bath powder, after-shave powder, and baby powder. A minor difference exists among the formulation of talcum powder, dusting powder, after -shave powder , and baby powder. Therefore, these powders are considered same to some extent . Powders are

dispensed through flat, oval, round or angular plastic or metal cans , or sometimes a puff is used so that powder can be applied easily. Generally powders have the following ingredients:

i) **Talcum Powders**
   a) Talc (71%),
   b) Potato starch (30%),
   c) Zinc stearate (3%),
   d) Boric acid (5%), and
   e) Perfume (1%).

ii) **Body Powders**
   a) Talc (50%),
   b) Boric acid (2%),
   c) Precipitated chalk (17%), and
   d) Perfume (1%).

iii) **After-Shave Powders**
   a) Talc (71%),
   b) Titanium dioxide (3%),
   c) Potato starch (4%),
   d) Precipitated chalk (20%),
   e) Golden ochre (0.5%), and
   f) Perfume (1%)/

iv) **Baby Powders**
   a) Talc (63.63%),
   b) Barley (20%),
   c) Zinc stearate (5%),
   d) Precipitated chalk (5%),
   e) Boric acid (6%),
   f) Oxyquinoline benzoate (0.12%), and
   g) Perfume (0.25%).

3) **Herbal Face Washes:** These are used to remove dirt, dust and other debris adhered to the facial skin. These preparations also have antiseptic as well as antimicrobial properties. Depending on the need and skin type of consumers, different types of face washes are formulated:
   i) **Gentle Face Washes:** These are used for mild cleansing and are applied very gently on the face. Daily use of these face washes protects the skin against dust, dirt, and pollutants.
   ii) **All Skin Type Face Washes:** These are formulated without any soap , and thus can be used on daily basis for almost all skin types.

4) **Herbal Face Packs:** These formulations are applied on face to stimulate blood circulation in facial region, provide muscle toning, make the facial skin supple and elastic, and clean clogged skin pores by removing impurities. **For example,** neem face pack (Himalaya).

Following are the ingredients commonly used in the formulation of herbal face packs:

Composition	Actions
Azadirachta indica	Antibacterial and controls acne and pimples
Fuller's earth	Anti-inflammatory
Curcuma longa	Antiseptic

5) **Herbal Lip Balms:** These are used on lips to prevent them from cracking, chapping and drying. Edible ingredients should be used in the formulation of lip balms. They also contain ingredients that act as natural filter to UV rays and vitamin E to provide nourishment and softness.

Following are the ingredients commonly used in the formulation of lip balms:

Composition	Actions
Ricinus communis	Relieves various inflammatory conditions of the skin and mucous membrane
Cocos nucifera	Emollient for softening the lips
Triticum sativum	Prevents loss of moisture from the skin
Wrightia tinctoria	Antibacterial and astringent
Daucus carota	Sunscreen and fragrance

6) **Herbal Soaps:** These are used for cleansing the body. Soaps are generally made up of a mixture of fatty acids sequestered by alkali metals. The basic fatty acids used in the formulation of soaps are triglycerides such as tallow, coconut oil, or palm oil.

Quality and properties of the soap depends on the proportions of fats and their combination used for their preparation. Soaps made up of tallow are harder than the soaps made up of coconut oil; while potassium soaps are softer than sodium soaps, but are rarely used. The properties of soaps can be enhanced by adding other ingredients, like opacifiers, emollients, and chelating agents.

6.1.3. Hair Care Products

The following herbal cosmetics are used as hair care products:

1) **Hair Gels:** These are used for hair styling as they make hair manageable, easy to handle, and reduce their tendency to fly. **For examples**,
   i) **Bay-Rum Hair Gel Preparations:** These are prepared by macerating bay leaves in rum. The resultant mixture is kept undisturbed for two weeks and then the mixture is filtered. A measured quantity of the water is added to it, and the finished preparation is transferred to an airtight bottle and refrigerated. This finished preparation is used as required.

   Following are the ingredients commonly used in the formulation of bay-rum hair gel preparations:

Formula

a)	Bay leaves	500gm
b)	Rum	500ml
c)	Water	500ml

ii) **Clove Hair Gel Preparation s:** These are prepared by heating benzoate lard. The remaining ingredients are mixed with this molten lard to form a cream with a pleasant fragrance and ability to set hair.

Following are the ingredients commonly used in the formulation of clove hair gel preparations:

Formula

a)	Almond oil	1 cup
b)	Palm oil	2 tsp
c)	Benzoate lard	500gm
d)	Lemon juice	2 tsp
e)	Oil of cloves	1 tsp

2) **Herbal Shampoo s:** These are used for cleaning hair. Various herbal shampoos, containing a unique blend of natural ingredients, are available in the market as per the requirement of consumer s and type of hair. **For examples**,

i) **Lime Shampoo s:** These are prepared by boiling a mla, shikakai, char, charilla, and khus in water till half of the volume of water evaporates. The resultant mixture is filtered and the remaining ingredients are added to it. The resulting mixture is stirred to mix all the ingredient s properly. The finished product is stored in an air tight container and dispensed. Lime s hampoos are applied properly for 2 -3 minutes on wet hair and then washed with lukewarm water. Following are the ingredients commonly used in the formulation of lime shampoos:

Formula

Amla	100gm
Shikakai	200gm
Char	100gm
Charilla	100gm
Khus	100gm
Reetha	200gm
Water	2 ½ litres
Glycerine	8 tsp
Lime juice	4 tsp
Sodium benzoate	1½tsp

ii) **Methi-Shikakai Shampoo s:** These are powder -based shampoo s as all the ingredients present are crushed, pulverised, and powder ed. Two hours before using, this shampoo should be soaked in half cup of water. Following are the ingredients commonly used in the formulation of methi-shikakai shampoos:

Formula

Methi	250gm
Shikakai	1kg
Orange/lemon peels	Handful

3) **Herbal Hair Colour s:** These are used to cover-up grey hair or as a style statement. Herbal hair colours are prepared by boiling the leaves of desirable herb in water. The resultant mixture is left undisturbed for a few hours, and then strained to remove the leaves. Lastly, alcohol and perfume are added.

Pyrogallol and metallic salts are added to produce a range of colours with henna. But they may produce toxic effects if used on broken skin.

Formula

Henna leaves (coarsely ground)	10.00gm
Alcohol	44.00 gm
Water	45.75gm
Perfume	0.25gm

4) **Herbal Hair Conditio ners:** These pre parations are used to condition the hair by moisturis ing them properly. If water is directly applied on hair for moisturising, no effect is observed as the water evaporates. This problem can be overcome by using w/o emulsion as its aqueous component moisturises the hair and the lipid component locks the moisture and prevents evaporation.

The formula given below is used to formulate several types of herbal hair conditioners:

i) **Avocado Hair Conditioner s:** These conditioners are prepared by mixing avocado paste with beaten egg to obtain a smooth mixture, which is applied for 30 minutes and then washed with lukewarm water.

Formula

Avocado paste	1 cup
Egg yolk	2 eggs

ii) **Wheat Hair Conditioner s:** These conditioners are prepared by mixing all the ingredients with the beaten egg. The resultant mixture is massaged on scalp, and washed after sometime with lukewarm water mixed with lemon juice (a tablespoon). Following are the ingredients commonly used in the formulation of wheat hair conditioners:

Formula

Wheat germ oil	1 tsp
Milk	1 tbsp
Egg yolk	1 egg
Water	1 cup
Lemon juice	1 tsp
Glycerine	1 tbsp

5) **Herbal Hair Oils:** These preparations provide nourishment to the scalp and hair roots, as well as impart a lustrous texture to hair . Herbal hair oils are prepared by the following procedure:

i) **Collection and Authentication of Plant:** Leaves of bhringraj (*Eclipta alba*), flowers of China rose (*Hibiscus rosa sinensis*), and rhizomes of jatamansi (*Nardostachys jatamansi*) are collected and dried in shade. These dr ied parts are pulverised, mixed , and filtered through sieve number 80. The pharmacognostic parameter of each drug should also be studied.

ii) **Preparation of Herbal Hair Oil:** To prepare herbal hair oil, 10%w/v of *Eclipta alba* and *Hibiscus rosa sinensis* and 5% w/v of *Nardostachys jatamansi* are boiled in one litre of coconut oil till the crude vegetable drug gets charred and attains black colour. The so obtained oil is filtered and stored in an airtight bottle.

6.1.4. Oral Hygiene Products

Oral care products are either mechanical devices or chemical formulations. They include the products designed to be used with prostheses, like denture. Artificial dentures can also be affected by plaque and stain , just like natural dentures. Oral care produ cts based on their functions are categorised into cosmetic or therapeutic. It depends on the product, whether or not it offers any health benefit.

1) **Toothpastes:** These serve dual purpose; firstly, they remove stains from the teeth, and secondly, they fres hen up breath and mouth. These objectives are fulfilled as toothpastes have mild abrasives and some specific flavours in them. Apart from these basic and vital functions of toothpastes, some additional functions can also be incorporated in them.

   Various t oothpastes are available with different physical characters and dispensers. They are present as viscous liquids and pastes that can be extruded from inflatable tubes, as pastes that can be extruded from pumps, and as clear products (called gels) for enhancing their external appearance. Sparkles or soft plastic particles of various colours are also added in many types of toothpaste. Two or three different coloured toothpastes can also be used.

   Traditional toothpastes are used for removing deposits (such as stains, plaque, etc.) from the teeth surface as they make the teeth appear dull. It is known by the regulatory authority as well as by the consumers that toothpastes cannot improve the colour tone of the teeth as dentine imparts colour to the teeth and enamel plays a very minor role in it.

   Researchers have developed a formulation using peroxides; this formulation makes teeth whiter by bleaching them. However, whether or not their prolonged and repeated use is safe is a matter of doubt. Recently, the American Dental Association (ADA) has approved two peroxide -containing products as safe and effective; one is used in dental surgery and the other can be used on daily basis. Both the agents have been evaluated on safety grounds by ADA. Still many researchers ar e formulating OTC toothpastes containing peroxides.

2) **Tooth Powders:** These are considered to be forerunner of toothpaste s; however, they are now losing popularity. Tooth powders are mixtures of dental abrasives, flavouring agents, sweetening agents, and foam ing agents. They are packed in containers having an orifice on top for sprinkling. The major **disadvantage** of toothpowders is that a calculated amount is difficult to obtain.

3) **Mouthwashes:** These are flavoured liquids used for rinsing the oral cavity after b rushing and flossing. Mouthwashes are used orally for maintaining dental hygiene. They mainly clean teeth, prevent tooth decay and gum diseases, and also freshen up the breath. An **ideal mouthwash** should have the following **properties**:
   i) It should be quick in action and potent enough to show its intended action at specific dilution.
   ii) It should have a strong flavour to mask the foul smell of mouth.
   iii) It should have an acceptable taste.

iv) Its production cost should be low.
v) It should not irritate the oral cavity or mucous membrane.
vi) It should be non-toxic.

4) **Gargles:** These are medicated aqueous preparations used for treating pharyngitis, laryngitis, and any other throat infections. Gargles are diluted before use. They should never be swallowed but should be spitted out after rinsing the oral cavity. Gargles are formulated using the following ingredients:
   i) **Flavouring agents** (eucalyptol, menthol, etc.) impart a distinct taste and flavour.
   ii) **Preservatives** (sodium benzoate) inhibit and prevent microbial growth.
   iii) **Sweetening agents** (sodium saccharin and sucralose) provide acceptable taste.
   iv) **Water** helps in liquefaction of all the ingredients.
   v) **Colouring agents** enhance the organoleptic property and increase the aesthetic value.
   vi) **Fluoride** is added in a limited amount to strengthen the teeth and prevent mottling of teeth.
   vii) **Detergents** provide cleansing action as they remove plaque and food particles adhered to the teeth.
   viii) **Calcium** strengthens the teeth, and prevents tooth decay and mottling.

6.2. SOURCES AND DESCRIPTION OF RAW MATERIALS OF HERBAL ORIGIN USED IN HERBAL COSMETICS

6.2.1. Introduction

Sources and description of the following raw materials of herbal origin used in formulating herbal cosmetics are discussed below:

1) Fixed oils,	2) Waxes,	3) Colours,
4) Perfumes,	5) Protective agents,	6) Bleaching agents,
7) Antioxidants,	8) Surfactants, and	9) Preservatives.

6.2.2. Fixed Oils

Oils are derived from vegetable and mineral sources, and are used in cosmetics. **Examples** of vegetable oils are almond oil, arachis oil, castor oil, olive oil, and coconut oil. **Examples** of mineral oils are light and heavy paraffin.

1) **Almond Oil:** It is a fixed oil obtained by expressing the seeds of *Prunus amygdalus* (family Rosaceae). It is pale yellow in colour and has a characteristic odour. The active principles of almond oil are the mixture of glycoside with oleic acid, linoleic acid, myristic acid, and palmitic acid. Due to its emollient action, it is used in the preparation of creams and lotions.

2) **Arachis Oil:** It is a fixed oil obtained from the seeds of *Arachis hypogea* (family Leguminosae). It is pale yellow in colour and has a faint nutty odour. Refined arachis oil is colourless, and its active principles include oleic acid,

linoleic acid, and a small amount of other acids. At 3°C, it turns cloudy, and at a lower temperature, it solidifies. Arachis oil is used in the preparation of hair oils and brilliantines.

3) **Castor Oil:** It is obtained from the seeds of *Ricinus communis* (family Euphorbiaceae). It is either yellow in colour or colourless and has a slight odour. Castor oil consists of a mixture of glycosides, in which 80% of ricinoleic acid is the major constituent. At 0°C, it forms a clear liquid. Due to its emollient action, it is used in the preparation of lipsticks, hair oils, creams, and lotions.

4) **Olive Oil:** It is obtained from the fruits of *Olea europea* (family Oleaceae). It is either pale yellow or greenish yellow in colour, and has a slight odour. Olive oil consists of glycerides of oleic, palmitic, linoleic, stearic and myristic acids. At low temperature, it gets solidified or partially solidified. Due to its emollient action and soothing properties, it is used in the preparation of creams, lotions, and bath oils.

5) **Coconut Oil:** It is obtained from the dried solid part of the endosperm of coconut, i.e., *Cocos nucifera* (family Palmae). It exists as a white or pearl-white unctuous mass in winter and colourless in summer.

6) **Light Liquid Paraffin:** It consists of a mixture of hydrocarbons and appears as a colourless and odourless oily liquid. Its viscosity and weight per ml (0.83-0.87gm) are low. Due to its better spreadability, it is used in the preparation of bath oils, hair oils, brilliantines, lotions, and creams.

7) **Heavy Liquid Paraffin:** It is obtained from petroleum. It is a mixture of hydrocarbons, and appears as a colourless and odourless oily liquid. Due to its soothing effect on the skin, it is used in the preparation of creams, lotions, brilliantines, hair oils, and bath oils.

6.2.3. Waxes

Waxes are the esters formed by the condensation of high molecular weight straight chain fatty acids with high molecular weight straight chain monohydric alcohol of methanol series. They are used as a base in cosmetics, along with oils and fats. Some commonly used waxes are:

1) **Beeswax:** It is a purified wax separated from the honeycomb of bees, *Apis mellifera* (family Apidae). It is composed of 70% myricyl palmitate ester. It is a yellowish brown coloured solid with honey-like odour. Under cold conditions, it turns brittle; and on bleaching, it becomes a yellowish-white solid with faint characteristic odour. Its melting point is 62-65°C. Beeswax helps in water incorporation to form an emulsion.

2) **Carnauba Wax:** It is obtained from the leaves of the Brazilian wax palm, *Copernica cerifera* (family Palmae). It is available in various grades, with the highest grade existing as light-brown to pale-yellow in colour. It occurs as moderately coarse powder or flakes with a characteristic bland odour. Its melting point ranges from 81-86°C. Carnauba wax is hard and is used in the manufacture of candles, wax varnishes, and leather and furniture polishes.

3) **Paraffin Wax:** It is obtained by the distillation of petroleum. It is a mixture of solid hydrocarbons, mainly containing n-paraffins, and their isomers to

some extent. Thus, it is also called **hard paraffin wax**. It is colourless, odourless, or a white, translucent, wax-like solid, and is slightly greasy to touch. Its melting point ranges from 50-57°C.

4) **Spermaceti:** It is a solid wax obtained from the head, blubber and ear case of the sperm whale, *Physeter catodon* (family Physeteridae). It consists of cetyl palmitate and cetyl myristate spermaceti in a solid wax, which is a translucent crystalline, pearly-white, unctuous mass with a slight odour and taste. It melts at a specific gravity of about 0.94. Spermaceti is also available synthetically and consists of a mixture of esters of saturated fatty alcohols and saturated fatty acids. Synthetic spermaceti occurs as white to off-white translucent flakes with a crystalline structure and a pearly lustre. Its melting point ranges from 43-47°C.

6.2.4. Colours

Humans are using colours in cosmetics since ancient times. The desire to buy a cosmetic product is controlled by three senses, i.e., sight, touch, and smell. Thus, colour is an important ingredient of cosmetic formulations. Some commonly used natural colours in cosmetics are:

1) **Cochineal:** It is a red dyestuff obtained from the dried female insect, *Dactylopius coccus* (family Coccidae). The main colouring constituent in cochineal is carminic acid, which forms red needles on crystallisation; these needles darken at 130°C and carbonise at 250°C. Cochineal is extracted with water, and alum is added to this solution to precipitate carmine lake (the red aluminium salt).

2) **Saffron:** It is the stigmas and tops of the styles of the plant, *Crocus sativus* (family Iridaceae). It is a perennial plant grown in Jammu and Kashmir. Saffron powder is yellowish and easily soluble in water, thus is used as flavouring and colouring agent in food preparations. It consists of a few carotenoids, of which crocin is an important natural saffron carotenoid. Picrocrocin is a colourless bitter glycoside that imparts a characteristic odour to saffron.

3) **Chlorophyll:** It is the natural green pigment abundantly found in nature. It is responsible for photosynthesis.

6.2.5. Perfumes

Some commonly used perfuming agents in cosmetics are:

1) **Rose:** It is obtained by steam distillation of the flower petals of *Rosmarinus officinalis* (family Labiatae). For obtaining rose oil, the blossoms (before they open) are collected a little before sunrise.

2) **Jasmine Essential Oil:** It is obtained from the flowers of *Jasminum grandiflorum* (family Oleaceae). For obtaining jasmine oil, solvent extraction method is used. It is used in perfumery industries.

3) **Lavender Oil:** It is obtained from the flowers and stalk of *Lavandula officinalis* (family Labiatae).

4) **Tuberose Oil:** It is obtained from *Epimedium acuminatum* (also known as mistress of the night). Its oil is a brown, viscous liquid with a sweet, heavy and sensuous scent.

5) **Geranium Oil:** It is obtained by distillation of the flowers, leaves and stalks of *Pelargonium graveolens* (family Geraniaceae).

6) **Champa Oil:** It is obtained from the flowers of *Michelia champaca*.

7) **Cinnamon Oil:** It is obtained from the different parts of cinnamon tree, i.e., its leaves, barks, and roots of *Cinnamon zeylanicum* (family Lauraceae). The oil obtained from the bark is of utmost value, and has a warm, spicy and sweet character.

8) **Neroli Oil:** It is an essential oil obtained by distillation of the flowers of bitter orange tree. It can be stored in amber-coloured bottles under refrigeration.

6.2.6. Protective Agents

Silicones are added as protective agents in the formulation of creams. Silicones combined with other barrier agents, like petroleum jelly beeswax, paraffin, etc., can formulate excellent barrier creams.

6.2.7. Bleaching Agents

The most commonly used bleaching agents are:

1) **Mercury Compounds:** Mercuric chloride (HgCl), red mercuric oxide (HgO), and ammoniated mercury are mercury compounds possessing skin bleaching properties. However, at the current time, use of mercury compounds in cosmetics is prohibited.

2) **Hydroquinones:** They are used as bleaching agents at 1.5-2% concentration for temporarily lighting the skin. In 5% concentration, they may cause redness and burning of skin. Reverse action of hydroquinones occurs on exposure to sunlight. If cosmetics containing hydroquinone are discontinued, a similar effect can be observed.

3) **Catechol and its Derivatives:** They exhibit skin lightening effects. 4-Isopropyl catechol is the most potent de-pigmenting agent. Catechol derivatives can cause irritation and sensitisation reaction at 3% or more concentrations.

4) **Ascorbic Acid and its Derivatives:** They are not very effective as a de-pigmenting agent, but can be used safely. Ascorbic acid is mostly used in skin bleaching creams, containing hydroquinone as a stabiliser (antioxidant). Ascorbyl oleate is used at 3% and 5% concentrations in skin bleaching cream for bleaching freckles in human skin.

6.2.8. Antioxidants

Natural antioxidants (like tocopherols), present in fats and oils, are destroyed during the refining process. Hence, antioxidants should be essentially added in cosmetics to avoid the rancidity of fats and oils due to oxidative deterioration. Some commonly used antioxidants used in cosmetics are:

1) **Tamarind:** *Tamarindus indica* (family Fabaceae) is widely grown in tropical regions. Tamarind seeds exhibit radical scavenging, anti-microbial and lipid peroxidation reducing activities. Due to its antioxidant activity, tamarind is added in anti-wrinkle cosmetics.

2) **Vitamin C:** It prevents free r adical damage by donating free radicals. It boosts up the immune system. Carrots, peaches, sweet potatoes, oranges, broccoli, etc. are the major sources of vitamin C.

3) **Vitamin E:** It is known as scavenger of free radicals. It is beneficial against certain ty pes of cancer and cardiac problems. Almonds, nuts, whole cereal grains, vegetable oils, etc. are the major sources of vitamin E.

4) **Pomegranate:** The extract of pomegranate plant, *Punica granatum*, exhibit antioxidant and antiviral properties, and enhance the e ffectiveness of topical sunscreens. Pomegranate seed oil exhibit chemopreventive activity against skin cancer. Pomegranate peel extracts foster dermal regeneration. Pomegranate seed oil fractions facilitate epidermal regeneration.

5) **Resveratrol:** It is a po lyphenolic phytoalexin compound, present in the skin and seeds of grapes, berries, peanuts, and other foods. It is a potent antioxidant, anti-inflammatory, and anti-proliferative agent. It has been found to prevent skin cancer and other conditions generated by the sun.

6) **Ferulic Acid:** It is a potent antioxidant that provides photoprotection to skin, and is thus added in sunscreens, cosmetic lotions, and other skin products. It is also believed to act synergistically with vitamins C and E and β-carotene.

7) **Liquorice:** *Glycyrrhiza glabra* extract is used to treat skin irritation, dermatitis, eczema, pruritus, and cysts. Glycyrrhizin is an important constituent of liquorice, and has a chemopreventive action.

6.2.9. Surfactants

Surfactants (or surface active agents) reduce the boundary tension in one or more than one interface in the system. They also stabilise one or more interface by forming absorbed layers. Due to these properties, surfactants are incorporated in cosmetics. Surfactants are used in the preparation of cosmetics due to the following five uses:

1) Detergency, 2) Wetting, 3) Foaming,
4) Emulsification, and 5) Solubilisation.

All the surfactants are amphipathic molecules having two distinct parts, namely, a hydrophobic part and a hyd rophilic part. The hydrophobic part consists of hydrocarbons, chain rings, or a mixture of both; while the hydrophilic part consists of a polar group, such as a carboxylic, sulphate or sulphonated group. Non -ionic surfactants contain a number of hydroxyl o r ether groups; due to which, they absorb at interfaces.The commonly used surfactants in cosmetics are:

1) **Anionic Surfactants:** They contain anionic groups directly connected to the hydrophobic unit. Fatty acid soaps [$R - COO^-$] are an **example** of anionic surfactant.

2) **Cationic Surfactants:** They contain cationic group separated from the hydrophobic group. Quaternised amides of ethylene diamine [$RCONH–CH_2–CH_2 N^+ [CH_3]_3 X^-$] are an **example** of cationic surfactant.

3) **Non-Ionic Surfactants:** They contain multiple unchar ged polar groups. Fatty acid alkanolamide s [$RCONH–CH_2–CH_2–OH$] are an **example** of non-ionic surfactant.

4) **Clove Oil:** It is obtained from the buds of *Eugenia caryophyllus* (family Myrtaceae). It can also be used in perfume industries in small doses.

5) **Ambrette Oil:** It is obtained by expressing the seeds of *Abelmoschus moschatus* (family Malvaceae). The oil is rich, sweet, floral and musky in nature. It can be used as an anti-ageing agent.

6) **Sandalwood Oil:** It is obtained by steam distillation of the hard wood of *Santalum album* (family Sundalaceae). It is used as a fixative agent in most of the perfumes.

6.2.10. Preservatives

Preservatives are used to prevent spoilage of cosmetic products and also the growth of microorganisms. They are t he products of oxidation of oils and fats. Most cosmetic preparations, especially those containing water are prone to deterioration if not added with preservatives.

An **ideal preservative** should possess the following **characteristics**:
1) It should be compatible with the formulation.
2) It should be soluble to the extent needed to achieve an effective concentration.
3) It should be stable enough to provide a sustained antimicrobial effect.
4) It should be colourless and odourless.
5) It should be non-irritant and non-allergic in the concentrations used.

Examples
1) Organic acids, like Benzoic acid and Formic acid.
2) Alcohols, like Ethyl alcohol and Isopropyl alcohol.
3) Aldehydes, like Formaldehyde and Cinnamic aldehyde.
4) Phenolics, like Cresol and Phenol.
5) Esters, like Methyl-*p*-hydroxy benzoate and Ethyl-*p*-hydroxy benzoate.
6) Mercurials, like Thiomersol and Nitromersol.
7) Surfactants, like Benzalkonium chloride and Cetyl pyridinium chloride.
8) Miscellaneous compounds, like Ethyl vanillin and Vanillin.

6.3. SUMMARY

The details given in the chapter can be summarised as follows:
1) **Galen** formulated the first herbal cold cream using beeswax, water, olive oil (as emollient), and rose petal (as fragrant).
2) **Vanishing creams** are oil-in-water emulsion (o/w), and are hardly visible when applied to skin.
3) **Nourishing creams** are non-greasy, and provide nourishment as well as protection to the skin.
4) **Moisturiser creams** are applied on dry skin as they heal and repair dry skin, and maintain the softness of skin.
5) **Anti-acne creams** are applied on the skin surface, and mainly act on hair follicles and sebaceous glands.

6) **Fairness creams** reduce melanin formation as well as skin pigmentation.
7) **Herbal face washes** are used to remove dirt, dust and other debris adhered to the facial skin.
8) **Gentle face-washes** are used for mi ld cleansing and are applied very gently on the face.
9) **All skin type face-washes** are formulated without any soap, and thus can be used on daily basis for almost all skin types.
10) **Herbal face packs** are applied on face to stimulate blood circulation in facial region, provide muscle toning, make the facial skin supple and elastic, and clean clogged skin pores by removing impurities.
11) **Hair g els** are used for hair styling as they make hair manageable, easy to handle, and reduce their tendency to fly.
12) **Lime s hampoos** are prepared by boiling amla, shikakai, char, charilla, and khus in water till half of the volume of water evaporates.
13) **Herbal hair oils** provide nourishment to the scalp and hair roots, as well as impart a lustrous texture to hair.
14) **Mouthwashes** are flavour ed liquids used for rinsing the oral cavity after brushing and flossing.
15) **Gargles** are medicated aqueous preparations used for treating pharyngitis, laryngitis, and any other throat infections.
16) **Almond oil** is a fixed oil obtained by expressing the seeds of *Prunus amygdalus* (family Rosaceae).
17) **Arachis oil** is a fixed oil obtained from the seeds of *Arachis hypogea* (family Leguminosae).
18) **Castor oil** is obtained from the seeds of *Ricinus communis* (family Euphorbiaceae).
19) **Olive oil** is obtained from the fruits of *Olea europea* (family Oleaceae).
20) **Coconut oil** is obtained from the dried solid part of the endosperm of coconut, i.e., *Cocos nucifera* (family Palmae).
21) **Beeswax** is a purified wax separated from the honeycomb of bees, *Apis mellifera* (family Apidae).
22) **Carnauba wax** is obtained from the leaves of the Brazilian wax palm, *Copernica cerifera* (family Palmae).
23) **Spermaceti** is a solid wax obtained from the head, blubber and ear case of the sperm whale, *Physeter catodon* (family Physeteridae).
24) **Cochineal** is a red dyestuff obt ained from the dried female insect, *Dactylopius coccus* (family Coccidae).
25) **Saffron** is the stigmas and tops of the styles of the plant, *Crocus sativus* (family Iridaceae).
26) **Rose** is obtained by steam distillation of the flower petals of *Rosmarinus officinalis* (family Labiatae).
27) **Jasmine essential oil** is obtained from the flowers of *Jasminum grandiflorum* (family Oleaceae).

28) **Lavender oil** is obtained from the flowers and stalk of *Lavandula officinalis* (family Labiatae).
29) **Tuberose oil** is obtained from *Epimedium acuminatum* (also known as mistress of the night).
30) **Geranium oil** is obtained by distillation of the flowers, leaves and stalks of *Pelargonium graveolens* (family Geraniaceae).
31) **Champa oil** is obtained from the flowers of *Michelia champaca.*
32) **Cinnamon oil** is obtained from the different parts of cinnamon tree, i.e., its leaves, barks, and roots of *Cinnamon zeylanicum* (family Lauraceae).
33) **Hydroquinones** are used as bleaching agents for temporarily lighting skin at 1.5-2% concentration.
34) **Vitamin C** prevents free radical damage by donating free radicals.
35) **Vitamin E** is known as scavenger of free radicals.
36) The extract of **pomegranate** plant, *Punica granatum*, exhibit antioxidant and antiviral properties, and enhance the effectiveness of topical sunscreens.
37) **Resveratrol** is a polyphenolic phytoalexin compound, present in the skin and seeds of grapes, berries, peanuts, and other foods.
38) **Ferulic acid** is a potent antioxidant that provides photoprotection to skin, and is thus added in sunscreens, cosmetic lotions, and other skin products.
39) ***Glycyrrhiza glabra*** extract is used to treat skin irritation, dermatitis, eczema, pruritus, and cysts.
40) **Cationic surfactants** contain cationic group separated from the hydrophobic group.
41) **Anionic surfactants** contain anionic groups directly connected to the hydrophobic unit.
42) **Non-ionic surfactants** contain multiple uncharged polar groups.
43) **Clove oil** is obtained from the buds of *Eugenia caryophyllus* (Myrtaceae family).
44) **Ambrette oil** is obtained by expressing the seeds of *Abelmoschus moschatus* (family Malvaceae).
45) **Sandalwood oil** is obtained by steam distillation of the hard wood of *Santalum album* (family Sundalaceae).

6.4. EXERCISE

6.4.1. True or False

1) Night creams are applied on the skin surface, and mainly act on hair follicles and sebaceous glands.
2) Nourishing creams are applied on dry skin as they heal and repair dry skin, and maintain the softness of skin.
3) Herbal face washes are used to remove dirt, dust and other debris adhered to the facial skin.
4) Herbal gels provide nourishment to the scalp and hair roots, as well as impart a lustrous texture to hair.
5) Gargles are flavoured liquids used for rinsing the oral cavity after brushing and flossing.

6) Arachis oil is a fixed oil obtained from the seeds of *Arachis hypogea*.
7) Beeswax is a purified wax separated from the honeycomb of bees, *Apis mellifera*.
8) Rose oil is obtained from *Epimedium acuminatum*.
9) Champa oil is obtained from the flowers of *Michelia champaca*.
10) Vitamin C is known as scavenger of free radicals.

6.4.1. Fill in the Blanks

11) _____ formulated the first herbal c old cream using beeswax, water, olive oil, and rose petal.
12) Olive oil is obtained from the fruits of _____.
13) _____ is a red dyestuff obtained from the dried female insect, *Dactylopius coccus*.
14) Rose is obtained by steam distillation of the flower petals of _____.
15) _____ are used as bleaching agents for temporarily lighting skin at 1.5 -2% concentration.
16) _____ prevents free radical damage by donating free radicals.
17) _____ is a potent antioxidant that provides photoprotection to skin, and is thus added in sunscreens, cosmetic lotions, and other skin products.
18) _____ contain anionic groups directly connected to the hydrophobic unit.
19) Ambrette oil is obtained by expressing the seeds of _____.
20) _____ contain cationic group separated from the hydrophobic group.

Answers

1) False 2) False 3) True
4) False 5) False 6) True
7) True 8) False 9) True
10) False 11) Galen 12) *Olea europea*
13) Cochineal 14) *Rosmarinus officinalis* 15) Hydroquinones
16) Vitamin C 17) Ferulic acid 18) Anionic surfactants
19) *Abelmoschus moschatus* 20) Cationic surfactants

6.4.1. Very Short Answer Type Questions

1) Give any two herbal skin care products.
2) Give the formulation of herbal night creams.
3) Give one example of herbal hair gel.
4) Enlist the ingredients of gargles.
5) Give two examples each of natural colours and perfumes used in cosmetics.
6) State the examples of bleaching agents used in herbal cosmetics.

6.4.2. Short Answer Type Questions

1) Write about herbal creams.
2) Discuss about herbal shampoo and conditioners.
3) Write a short note on oral hygiene products.
4) Discuss about the different fixed oils and waxes of herbal origin.
5) Write about the surfactants and antioxidants used in herbal cosmetics.

6.4.3. Long Answer Type Questions

1) Discuss briefly about herbal skin care products.
2) Briefly discuss about sources and description of raw materials of herbal origin used in herbal cosmetics.

CHAPTER 7

Herbal Excipients

7.1. HERBAL EXCIPIENTS

7.1.1. Introduction

Substances used as a **medium for delivering a medicament** are termed **excipients**. In pharmaceutical formulations, natural polysaccharide polymers are used to aid in the processing of drug delivery system during its manufacture, to protect, and to enhance stability, bioavailability or patient acceptability. Natural polysaccharides also assist in product identification, or enhance other attributes of the overall safety, effectiveness or delivery of the drug during storage or use. **Examples** of natural pharmaceutical excipients of plant origin are starch, agar, alginates, carrageenan, guar gum, xanthan gum, gelatin, pectin, acacia, tragacanth, and cellulose. These natural excipients are used in pharmaceutical industries as binding agents, disintegrates, sustaining agents, protectives, colloids, thickening agents, gelling agents, bases in suppositories, stabilisers, and coating materials. Some common herbal excipients, along with their sources and uses are mentioned in **table 7.1**:

Table 7.1: Various Herbal Excipients with their Sources and Uses

Excipients	Sources	Uses
Agar	*Gelidium amansii* (Gelidiaceae)	Laxative, suspending agent, emulsifying agent, gelling agent in suppositories, surgical lubricant, table disintegrates, and medium for bacterial culture.
Gum Ghatti	*Anogeissus latifolia* (Combretaceae)	Binder, emulsifier, and suspending agent.
Tragacanth	*Astragalus gummifer* (Leguminosae)	Thickening agent, demulcent, suspending agent, emulsifying agent, emollient in cosmetics, and sustained release agent.
Albizia gum	*Albizia zygia* (Leguminosae)	Binding agent.
Aloe mucilage	*Aloe species* (Liliaceae)	Gelling agent and sustained release agent.
Bavchi mucilage	*Ocimum canum* (Gigarginaceae)	Suspending agent and emulsifying agent.
Senna Tora	*Cassia tora Linn* (Leguminosae)	Binding agent.
Gum acacia	*Acacia arabica* (Combretaceae)	Suspending agent, emulsifying agent, binder in tablets, demulcent and emollient in cosmetics.
Khaya gum	*Khaya grandifoliola* (Labiatae)	Binding agent.
Shatavari mucilage	*Asparagus racemosus* (Apocynaceae)	Binding agent and sustaining agent in tablet.
Tamarind seed	*Tamarindus indica* (Leguminosae)	Binding agent and emulsifier.
Gellan gum	*Pseudomonas elodea* (Leguminosae)	Disintegrating agent.

7.1.2. Advantages

Following are the advantages of herbal excipients:

1) **Biodegradable:** Polymers obtained from natural sources are produced by living organisms; therefore, they do not produce any adverse effects on the environment or humans.
2) **Biocompatible and Non -Toxic:** Natural polymers are non -toxic because these plant products are chemically carbohydrates and are formed by repeated monosaccharide units.
3) **Economic:** These naturally obtained polymers are cheaper and their production cost is less than that of the synthetic materials.
4) **Safe and Devoid of Side Effects:** They are obtained from natural sources, and therefore are safe and do not produce any side effects.
5) **Easy Availability:** In many countries, these products are easily obtainable due to their application in many industries.

7.1.3. Disadvantages

Following are the disadvantages of herbal excipients:

1) **Microbial Contamination:** They are prone to microbial contamination as they are exposed to external environment during production.
2) **Variation:** A standard or controlled procedure with fixed quantities of ingredients is followed for the synthesis of synthetic excipients; whereas, production of natural polymers depends on environmental and physical factors.
3) **Uncontrolled Rate of Hydration:** The percentage of chemical constituents of herbal excipients varies because there are differences in the collection of natural materials at different times, as well as differences in region, species, and climatic conditions.
4) **Slow Process:** Rate of production of natural subs tances is very slow and cannot be changed becaus e the production rate depends on the unavoidable environmental and many other factors.
5) **Heavy Metal Contamination:** The main concern regarding the use of herbal excipients is that the chances of h eavy metal co ntamination are often associated with them.

7.2. SIGNIFICANCE OF SUBSTANCES OF NATURAL ORIGIN AS EXCIPIENTS

7.2.1. Introduction

The following excipients of natural origin and their significance are discussed below:

1) Colourants, 2) Sweeteners, 3) Binders, 4) Diluents,
5) Viscosity builders, 6) Disintegrants, 7) Flavours, and 8) Perfumes.

7.2.2. Colourants

Many natural coloured substances are found in plants and animals. The difference between a dye and a pigment is that the former gets absorbed by the material when applied to fibresand imparta permanent colourthat is resistant to theaction of light,

water or soap; while, the latter is only applied to the surface. The coloured compounds are called **chromogen**, and has a chromophore group and/or auxochrome, which appear as coloured substance by absorbing light in the near UV regions.

Ideal Properties of a Colourant

1) It should be non-toxic.
2) It should be physiologically inactive.
3) It should be free from harmful impurities.
4) It should have a defined chemical composition to make its colouring power reliable, and its assay practicable and easier.
5) It should have a high tinctorial (colouring) power so that only small quantities are required.
6) It should be stable on storage, and resistant to light, tropical temperatures, hydrolysis and microorganisms.
7) It should remain unaffected by oxidising or reducing agents and pH changes.
8) It should be compatible with medicaments.
9) It should be readily soluble in water; however, oil-soluble and spirit-soluble colours are also required.
10) It should not interfere in the tests and assays which the preparations containing it undergo.
11) It should not get adsorbed on to the suspended matter.
12) It should not have unacceptable taste and odour.
13) It should be easily available and economical.

Some common herbal colourants, along with their sources and colour shades are mentioned in **table 7.2**:

Table 7.2: Various Herbal Colorants with their Sources, Compounds, and Shades

Sources	Compounds	Colour Shades
1) **Anthraquinones**		
i) *Dactylopius coccus* (Cochineal)	Carminic acid	Red
ii) *Rubia tinctorum* (Madder)	Alizarin	Red
iii) *Coccus lacca E* (Lac)	Laccaic acid	Red
iv) *Kermes ilicis* (Shield louse)	Kermisic acid	Scarlet
2) **Naphthoquinones**		
i) *Lawsonia inermis* (Henna) & *Lawsonia alba*	Lawsone	Orange
ii) *Juglans regia* (Walnut) and *Juglans nigra*	Juglone	Brown
iii) *Lithospermum erythrorhizon* (Shikone)	Shikonin	Violet
3) **Carotenoids**		
i) *Capsicum annum* (Capsicum)	Capsanthin	Orange-red
ii) *Crocus sativus* (Saffron)	Crocin	Yellow-orange
iii) *Tagetes erecta* (Marigold)	Lutein	Yellow
iv) *Bixa orellana* (Annatto)	Bixin	Yellow-orange
4) **Indole Derivatives**		
i) *Murex brandaris* (Mollusk)	Bromo-indigotin	Tyrian purple
ii) *Indigo tinctoria* (Indigo)	Indigotin	Blue
5) **Oxyindole Glycoside**		
Beta vulgaris (Beet root)	Betanin	Red
6) **Diaryl Heptanoid**		
Curcuma longa (Turmeric)	Curcumin	Yellow
7) **Benzopyrone**		
Haematoxylon (Longwood)	Haematin	Black

Turmeric

Turmeric is a spice which provides yellow colour to the curry. In India, it is in use for thousands of years as a spice as well as a medicinal herb. Curcuma is the dried and fresh rhizomes of *Curcuma longa* Linn. (*C. domestica*) (and belongs to family Zingiberaceae). *C. amada*, *C. angustifolia*, *C. aromatica*, *C. caesia*, *C. zedoaria*, and *C. longa* are some other varieties of curcuma. Curcuma is a genus having around 70 species of rhizomatous herbs. It is found to be growing widely distributed in South -East Asia, especially in India, China, Thailand, Italy, Malaysia, Archipelago, and N. Australia.

India cultivates around 90% of the total output of turmeric in the world. Around 70% of total output is cultivated in **Tamil Nadu** and **Andhra Pradesh**. **Kerala** also produces turmeric of superior quality in large amounts which is exported on a large scale.

Turmeric has the following **morphological properties**:

1) **Colour:** Yellowish-brown.
2) **Odour:** Characteristic.
3) **Taste:** Slightly bitter.
4) **Shape:** Round rhizomes are oblong, while long varieties are cylindrical and short branched.
5) **Surface:** Root scars and annulations are present.
6) **Fracture:** Horny and internal surface is orange.

Curcuma consists of volatile oil (1 -6.5%), resin, numerous zingiberaceous starch grains, and **curcuminoids** (yellow coloured substances). **Curcumin** (50-60%) is the major constituent of curcuminoids. Curcumin and other related curcuminoids impart the yellow colour in some species. Volatile oil contains mono- and sesquiterpenes (like α- and β-pinene, α-phellandrene, camphor, camphene, zingiberene, and α-, β-curcumenes. *C. angustifolia* and *C. caulina* species have high content of starch.

Turmeric has the following **uses**:

1) It is used as a colouring agent for ointments and creams.
2) It is used for the detection of boric acid.
3) It is used as an anti-inflammatory.
4) In China, *C. wenyjuin* (*C. aromatica*) is used for cervical cancer.
5) It is used as an anti-arthritic agent, which has been isolated from *C. aromatic* species.

Annatto

Seeds of achiote tree yield an orange-red coloured pigment, called annatto, which is used as a colouring agent in food and condiments. It is used in food for imparting yellow or orange coloration, but can also be used as a flavouring agent that gives a slightly nutty, sweet and pepper-like flavour.

Annatto consists of the dried seeds of the plant *Bixa orellana* L. (and belongs to family Bixaceae). The plant is cultivated in **Peru**, **Jamaica**, **Mexico**, **Kenya**, **India**, and **Brazil**.

Annatto has the following **morphological properties**:

1) **Fruits:** Spherical or broadly elongated, 2-4.5cm, flattened, 2 valved, densely covered with long bristles, and green, greenish-brown or red when mature.
2) **Capsules:** Sub-globose or ovoid, 2-4.5cm, slightly laterally compressed, densely purple-brown spiny, and rarely smooth.
3) **Spines:** 1-2 cm long.
4) **Seeds:** Numerous, bright orange-red fleshy coats, obovoid-angular, 4-5 mm, and smooth.

The seeds of annatto contain **bixin dye** and are covered with aril. The content of seeds includes 12% of annatto oleoresin. 50% of this resin is water-soluble. 4-5% of pigment and 0.3-0.8% of volatile oil are also present. Bixin is the monomethyl ester derivative of a dicarboxylic acid, **norbixin**. During extraction, it gets hydrolysed into dicarboxylic acid by an alkali. The extracts of annatto yield potassium salts of norbixin. Bixin is much stable in tinctorial strength than β-carotene, but on storage the tinctorial strength gets diminished. Annatto has optimum stability at pH 8 but heat and light also have an adverse effect on its tinctorial value.

Bixin has the following **uses**:

1) Bixin possesses antioxidant properties.
2) It acts as a filter for UV radiation.
3) It has hepatoprotective properties.
4) Annatto is mainly used as colouring agent in foods, cosmetics, alcoholic and non-alcoholic beverages, dairy desserts, fats and oils and in margarine.

7.2.3. Sweeteners

Sweeteners are agents which either impart a sweet taste or increase the perception of sweet taste. On the basis of synthesis, sweetening agents are of **two types**:

1) Natural sweeteners of plant origin, and
2) Chemically synthesised artificial or synthetic sweeteners.

Due to the adverse effects of synthetic sweeteners, the natural sweetening agents are preferred. **Examples** of plant-based natural sweeteners are stevioside, glycyrrhizin, neohesperidin, thaumatin, monellins, and sucralose.

Natural sweetening agents are non-saccharides. They are of low calories, still excessively sweet (100-10,000 times sweeter than sugar), non-toxic, and can overcome the problems of sucrose and synthetic sweeteners. These are also used as sugar substitutes for diabetic patients. In plants, the active sweet principles are stored as terpenoids, steroidal saponins, dihydroisocoumarins, dihydrochalcones, proteins, polyols, volatile oils, etc. Sweeteners may also be classified as:

1) **Nutritive sweeteners** (**e.g.,** sorbitol, mannitol, xylitol, lactitol, mixture of glucosylsorbitol and glucosylmannitol, and fructose).
2) **Non-nutritive sweeteners** (**e.g.,** aspartame, saccharin, cyclamate, acesulfame-k, and alitame).

Some common herbal sweeteners, along with their sources are mentioned in **table 7.3**:

Table 7.3: Various Herbal Sweeteners with their Sources and Compounds

Sources	Compounds
Stevia rebaudiana (Compositae) - Leaf	Stevioside and Rebaudioside (160 -170 times sweeter than sucrose)
Glycyrrhiza glabra (Leguminosae)- Liquoriceroot	Glycyrrhizin (50-100 times)
Citrus aurantium (Rutaceae) - Bitter orange	Neohesperidin dihydrochalcone (330 times sweeter than sucrose)
Thaumatococcus daniellii (Marantaceae) - Fruit aril	Thaumatin (3500 times sweeter than sucrose)
Dioscoreophyllum cumminssi (Meninsperamaceae) - Fruit	Monellins (2000 times sweeter than sucrose)
Semi-synthetic	Sucralose (600 times sweeter than sucrose)

Stevia

Stevia rebaudiana is a shrub of up to 30 cm height. It has composite wrapped flowers with 3-4 cm long sessile leaves. Stevia is found in **Paraguay** where it is known by the names of **sweetleaf** or **sugarleaf**. The Stevia plant is intensely sweet and its active ingredients are **diterpene glucosides**, particularly stevioside (4-10%), rebaudioside (2-4%). Other chemical constituents of stevia are volatile oils (**e.g.,** nerolidol and caryophyllene); and flavonoids (**e.g.,** quercetin, apigenin, austroinulin). *Stevia rebaudiana* has a high sweetening index as stevioside is 200-300 times sweeter than sucrose.

Stevia has the following **uses**:

1) It is used as a mild osmotic laxative.
2) It is slightly hypoglycaemic.
3) It is used as a hypotensive and antibacterial.
4) It is used for treating constipation.
5) It is a sugar substitute for diabetics.

Neohesperidin Dihydrochalcone

It is a flavonoid present in bitter orange , *Citrus aurantium* variety Amara. (and belongs to family Rutaceae). Neohesperidin dihydrochalcone is obtained by hydration of neohesperidin under alkaline conditions. It can also be obtained from flavonoid **naringin**, present in peels of various other Citrus spp.

The stability of neohesperidin dihydrochalcone is acceptable under food processing and storage conditions, even though it s glycosidic bond can easily undergo hydrolytic cleavage. It is 330 times sweeter than sucrose. The main characteristic feature of neohesperidin dihydrochalcone is that it produces methanol-like after-taste, and therefore it has a very limited use in food and pharmaceutical industry.

It acts synergistically with other sweeteners, **e.g.,** acesulfame and aspartame, and very small quantity of it is blended with these sweeteners.

Neohesperidin dihydrochalcone has the following **uses**:

1) It is used in confectionery products, chewing gum s, beverages , and dairy products.
2) It is also used to enhance flavour in various foods and other products.

7.2.4. Binders

Binders are agents used to impart cohesiveness to the granules so that the tablet s remain intact after compression. They are added to tablet formulation to impart plasticity, and increase the inter -particulate bonding strength within the tablet s. Binders are used to hold various powders together during tablet formation. Fillers do not have good binding capacity; therefore, binder is either added in dry mix or mixed in granulating liquid. Binder and filler toget her form matrix with the drug embedded in it. After drying, the solid binder forms glue which holds the particles together. The wet binder is the most important ingredient in wet granulation. Binders are generally hydrophilic and soluble in water.

Examples of naturally obtained binders are plant starch, pre -gelatinised starch, gelatin, and plant gums (acacia and tragacanth).

Advantages

1) They are less toxic, biodegradable, easily available, and economic.
2) They c an affect the relea se of drug, thereby, influe nce the absorption and bioavailability of the incorporated drug.
3) They improve the stability, precision and accuracy of dosage form.
4) They enhance the organoleptic properties of the drugs to increase patient compliance.

Disadvantages

1) Sometimes, they cause tablet hardening and consequently decrease the dissolution performance.
2) If polymer binders are used, strong disintegrants (such as super disintegrants) need to be added, which are costly and also exert a negative effect on product stability as well as film coating appearance of the finished products.

Acacia

According to the USP, acacia is the dried gummy exudation obtained from the stems and branches of *Acacia senegal* (L.) Willd. or other African species of Acacia. It is also found in the stems and branche s of *Acacia arabica*, Willd. (and belongs to family Leguminosae). Acacia is a genus of plant including different types of plants, such as trees and shrubs. Some forms of acacia contain toxic chemicals that can potentially cause hair loss, affect GIT's abili ty to take in nutrients, and stunt growth.

A. senegal is found in the drier parts of **Anglo-Egyptian Sudan** and the northern Sahara. It is also found throughout the vast area from Senegal to the Red sea and to eastern India. It extends southwards to norther n Nigeria, Uganda, Kenya, Tanzania, and southern Africa. In **India**, *A. arabica* (babul tree) grows wildly in Punjab, Rajasthan and on Western Ghats. The tree is found in the dry monsoon forests of India and Sri Lanka.

Acacia has the following **morphological properties**:

1) **Colour:** Tears are white, pale yellow or beige to red coloured; powder is off-white, pale yellow, or light brown coloured.

2) **Odour:** Odourless.
3) **Taste:** Bland and mucilaginous.
4) **Shape:** Tears are mostly spheroidal or ovoidal.
5) **Size:** Tears have a diameter of about 2.5-3.0cm.
6) **Solubility:** Soluble in water resulting in a viscous and acidic solution; insoluble in alcohol.
7) **Appearance:** Tears are invariably opaque either due to the presence of cracks or fissures produced on the outer surface during ripening; th e exposed surface is glossy.
8) **Fracture:** Usually very brittle.

Arabin, a complex mixture of calcium, magnesium and potassium salts of Arabic acid, is the chief constituent of acacia. Arabic acid hydrolyses into L -arabinose, L -rhamnose, D -galactose, and D -glucuronic acid. It also contains oxidase and peroxidase enzymes. Since it contains diastase, it readily converts into powdered guaiacum resin. On drying at 100°C, its moisture content decreases by about 12-14% and it yields 2.7-4.0% of ash.

Acacia has the following **uses**:
1) Its mucilage is a demulcent.
2) It is an essential pharmaceutical aid for emulsification and to be used as a thickening agent.
3) It is used as a binding agent in tablet formulations.
4) It is used in the granulation process of tablet manufacturing due to its compatibility with other plant hydrocolloids, starches, carbohydrates, and proteins.
5) It is combined with gelatin to form coacervates for drug microencapsulation.
6) It is a colloidal stabiliser.
7) It is used in making candies and other food products.
8) It is used in manufacturing spray -dried fixed flavours which are powdered flavours used in packaging of dry-mix products (puddings, desserts, and cake mixes).

Gelatin
Gelatin is a product obtained by partial hydrolysis of collagen, derived from the skin, white connective tissue, tendons, ligament and bones of ox (*Bos ta urus* Linn.), sheep (*Ovis aries* Linn), etc. (and belongs to family Bovidae).

Gelatin has the following **properties**:
1) It is colourless or slightly yellow coloured.
2) It is transparent, brittle, and available in the form of sheets, flakes, or course granular powder.
3) It is practically odourless and tasteless.
4) When kept in water it swells and absorbs 5 -10 times its weight of water and forms a gel in solutions below 35-40°C.
5) It is soluble in hot wat er, glycerol, and acetic acid; and insoluble in cold water and organic solvents.

6) It is amphoteric in nature.
7) It remains stable under dry conditions, but is attacked by bacteria when moist or in solution.
8) Its gelatinising property is reduced if boiled for a long time.
9) Its quality is determined on th e basis of its jelly strength (bloom strength) using a bloom gelometer.
10) Commercially gelatin is available in two types, i.e., **gelatin A** and **B**.
11) The isoelectric point for type A lies between pH 7 and 9.
12) Type A is i ncompatible with anionic compounds (such as acacia, agar , and tragacanth).
13) The isoelectric point for type B lies between 4.7 and 5.
14) Type B is used with anionic mixtures.

Gelatin consists of **glutin** protein which hydrolyses into a mixture of amino acids. The amino acid mixture contains glycine (25.5%), alanine (8.7%), valine (2.5%), leucine (3.2%), isoleucine (1.4%), cystine and cysteine (0.1%), methionine (1.0%), tyrosine (0.5%), aspartic acid (6.6%), glutamic acid (11.4%), arginine (8.1%), lysine (4.1%), and histidine (0.8%).

From nut ritional point of view, gelatin is an incomplete protein as it lacks tryptophan. The gelatinising compound is known as **chondrin** and the adhesive nature of gelatin is due to the presence of glutin.

Gelatin has the following **uses**:
1) It is used in the preparation of pastilles, pastes, suppositories, capsules, pill - coatings, and gelatin sponge.
2) It is used as a suspending agent, tablet binder, coating agent, a stabiliser, thickener and texturiser in food.
3) It inhibits crystallisation in bacteriology for preparing cultures and as a nutrient.
4) It is used as a substitute for blood plasma.
5) It is also used for microencapsulating drugs in which the drug is sealed within a micro -sized capsule or beadlet, which may then be handled as a powder.
6) It forms glycerinated gelatin with glycerine and then is used as a vehicle and for manufacturing suppositories.
7) It forms zinc gelatin with zinc and then used as a topical protectant.
8) It is commonly used as a gelling agent in food, pharmaceutical drugs, vitamin capsules, photography, and cosmetic manufacturing.
9) It is used in the manufacturing of rubber substitutes, adhesives, cement , lithographic and printing inks, plastic compounds, artificial silk, photographic plates and films, light filters for mercury l amps, clarifying agent, in hectographic matters, sizing paper, and textiles.

7.2.5. Diluents

Diluents are used in tablet formulation to provide properties which make the tablets better like:
1) To improve cohesion,

2) To allow direct compression manufacturing,
3) To increase flow, and
4) To adjust weight of tablet as per the capacity.

Ideal Characteristics of a Diluent

1) It should neither support microbiological growth nor contribute to microbiological load in the dosage form.
2) It should neither adversely affect the product dissolution nor interfere with the bioavailability of active therapeutic ingredient.
3) It should be colourless.
4) It should be inert and not react with the drug substance.
5) It should not have any effect on the other excipients and their functions.
6) It should not exhibit its own physiological or pharmacological activity.
7) It should have constant physical and chemical properties.
8) It should neither initiate nor contribute to segregation of granules or powder blend to which they are added.
9) It should be able to be milled (to reduce its size) if required to match the particle size distribution of the active therapeutic ingredient.

Lactose

Lactose is a natural disaccharide containing galactose and glucose. It is obtained from the milk of most mammals. It is a white or almost white crystalline powder having no odour and a faintly sweet taste. It is stable in air but readily absorbs odours. Lactose is available in several varieties, such as anhydrous α-lactose, α-lactose monohydrate, and anhydrous β-lactose.

Lactose is available in various grades, but fine grades of lactose are generally used in the preparation of tablet by the process of wet granulation. The compressibility of direct compression grades of lactoseis more, and these grades of lactose include spray-dried lactose, containing pure α-lactose monohydrate and amorphous lactose (in a small amount). Other specially produced direct compression grades of lactose contain glassy areas (andnot amorphous material) to improve compressibility.

Tablet lubricant (**e.g.,** 0.5%w/w magnesium stearate) is required for direct compression grades of lactose combined with microcrystalline cellulose or starch.

Lactose has the following **uses**:

1) It is used as a filler or diluent in tablets and capsules.
2) It is also used in infant feed formulae and in dry powder inhalations.
3) It is used with sucrose to prepare sugar coating solutions.

Mannitol

Mannitol is a hexahydric alcohol isolated from manna or seaweeds. It can also be chemically synthesised by mannose reduction.

Mannitol has the following **properties**:

1) It is a white, odourless, non-hygroscopic, and crystalline powder with a sweet taste.

2) Its crystals are orthorhombic prisms.
3) Its melting point is 166-168°C.
4) It is freely soluble in water and insoluble in alcohol.
5) Its specific gravity is 1.52.
6) It is optically inactive or slightly laevorotatory.

Mannitol has the following **uses**:
1) It is used as an excipient for tablets.
2) In liquid preparations, it is used as a diluent.
3) It is used as stabiliser, thickener, and nutritive sweetener.
4) It is also used as a texturising agent, nutrient and diagnostic agent.
5) Mannitol does not get absorbed from GIT. If injected, it does not metabolise and gets eliminated by glomerular filtration, therefore it is used as a diagnostic aid and as an osmotic diuretic.

7.2.6. Viscosity Builders

Viscosity builders are added to mixture to increase the viscosity without modifying other properties like taste, odour, etc. These agents also increase the stability of the preparation. They are also added to provide or improve palatability or pourability to the dosage form.

Ideal Characteristics of a Viscosity Builder
1) It should provide a structured vehicle.
2) It should be highly viscous at negligible shear during storage and less viscous at high shearing rates during pouring.
3) It should exhibit yield stress.
4) It should be compatible with other excipients.
5) It should be non-toxic.
6) It should impart viscosity that should not get affected by temperature or ageing.

Advantages
High viscosity of a pharmaceutical preparation:
1) Inhibits crystal growth,
2) Enhances the physical stability, and
3) Prevents the transformation of metastable crystal to a stable crystal.

Disadvantages
High viscosity of a pharmaceutical preparation:
1) Hinders the re-dispersibility of the sediments,
2) Reduces the absorption of drug, and
3) Creates problems in handling of material during manufacturing.

Carrageenan
Chemically, carrageenan is a sulphated polysaccharide, and is obtained from the seaweed (or Irish moss), the red algae *Chondrus crispus* Linn. (and belongs to family Gigartinaceae and class Rhodophyceae).

France, Denmark, and the United States are the major producers of carrageenan in the world market.

Carrageenan has the following **morphological properties**:

1) **Colour:** Before bleaching the drug is purplish -red to purplish -brown in colour; and after bleaching the drug is yellowish white, translucent and horny.
2) **Odour:** Slight odour.
3) **Taste:** Mucilaginous or saline.
4) **Shape:** Strips, flakes, or coarse powder.
5) **Solubility:** Swells in cold water and above 75% dissolves in hot water.

The major constituent of Irish moss is **galactans** (or **carrageenan**). On the basis of 3, 6-anhydro-D-galactose and the position of ester sulphate groups, carrageenan is classified into **three major types**:

1) Kappa-carrageenans,
2) Iota-carrageenans, and
3) Lamda- carrageenans.

Hydrolysis of polysaccharides yield galactose, glucose, fructose, arabinose , and calcium salt of acid esters of sulphuric acid. Carrageenan has the following **uses**:

1) In various pharmaceutical and nutraceutical preparations, it is used as an emulsifier, stabiliser, solubiliser, and viscosity builder.
2) It is u sed in the preparation of tooth pastes, creams, lotions , and other cosmetic products.
3) In food indu stry, it is used in milk products, ice creams, and gels (in 0.5-1% concentration).
4) It is used as a phlogistic agent for inducing inflammation in rat paw oedema model to study its anti-inflammatory activity.

Xanthan Gum

Xanthan gum is a polysaccharide gum produced by the bacterium , *Xanthomonas campestris* on some specific carbohydrates.

Xanthan gum has the following **properties**:

1) It is a yellowish-white, odourless, and free-flowing powder.
2) It gets swiftly dissolved in water on shaking and turns into a highly viscous solution at relatively low concentrations.
3) Its aqueous solutions are extremely pseudoplastic.
4) On evaporation of its aqueous solutions, it forms a strong film.
5) It is fairly stable and resistant to thermal degradation.
6) Its viscosity does not depend on temperature ranging between 10-70^{o}C.
7) It is compatible with various salts.

The chief chemical constituents of xanthan gum are **D-glucosyl, D -mannosyl** and **D-glucosyluronic acid residues** , and variant quantum of O -acetyl and pyruvic acid acetal. The pri mary structure of these chemical compounds comprises of a cellulose backbone with trisaccharide side chains and the repeating moiety being a pentasaccharide.

Xanthan gum has the following **uses**:
1) It is used to enhance oil recovery.
2) Due to the pseudoplastic property of its aqueous solutions, it is used in toothpastes and ointments to enable them to hold their shape and also to spread readily.
3) Due to its excellent suspending and emulsifying nature, it is used in pharmaceutical preparations.

7.2.7. Disintegrants

The agents added to tablets, capsules, and some encapsulated formulations to promote their breakdown into smaller fragments in an aqueous environment are termed disintegrants. Thus, disintegrants increase the available surface area and promote rapid release of drug particles. Swelling, porosity and capillary action, and deformation are the three mechanisms and factors affecting tablet disintegration.

Ideal Characteristics of a Disintegrant
1) It should strongly interact with water to exert its disintegrating action.
2) It should act via combining of swelling and/or wicking and/or deformation mechanisms.
3) Super disintegrants give significant improvements over starch.
4) Sometimes hygroscopicity is the major problem in some formulations.

Advantages
1) They are effective even in low concentrations.
2) They impart a less effect on compressibility and flow ability of the granules or powder.
3) They are more effective in intra-granular form.

Disadvantages
1) They are more hygroscopic, therefore cannot be used with moisture-sensitive drugs.
2) Some of them are anionic, therefore can slightly bind to cationic drugs *in-vitro* (not a problem *in-vivo*.)

Guar Gum

Guar gum is the powder of the endosperm of the seeds of *Cyamopsis tetragonolobus* Linn. (and belongs to family Leguminosae). Guar gum powder is obtained from the Guar seed undergoing multiple industrial processes. Guar gum attains uniformity and very high viscosity at low concentrations by getting rapidly hydrated in cold water. Being colloidal in nature, it provides excellent thickening to the solution.

The plant from which guar gum is obtained is an annual shrub either growing wildly or cultivated in dry climate. In **India**, it is cultivated in Maharashtra, Gujarat, Karnataka, and Rajasthan. The plant is also grown in **Pakistan**.

Guar gum has the following **morphological properties**:
1) **Colour:** Colourless or pale yellowish-white.

2) **Odour:** Characteristic.
3) **Taste:** Mucilaginous.
4) **Solubility:** Completely soluble in cold and hot water; insoluble in alcoh ol; practically insoluble in oils, greases, hydrocarbons, ketones, and esters.
5) **Extra Features:** Solutions of guar gum in water are tasteless, odourless, non-toxic, neutral, heat stable, and possess 5 -8 times thickening power than starch. In water, guar gum forms a thick colloidal solution and swells rapidly.

Galactomannan (guaran) is the major constituent of guar gum. This substance hydrolyses to yield **galactose** and **mannose**. The water -soluble content of guar gum is **guaran** which consists of linear chains of (1→4) –β-D mannopyranosyl units with α–D-galactopyranosyl units attached by (1→6) linkages. However, the ratio of D -galactose to D -mannose is 1:2. The gum also contains 5 -7% of proteins.

Guar gum has the following **uses**:
1) It is used as a bulk laxative.
2) It is used as a protective colloid.
3) Since its thickening power is 5 -8 times more than starch, it is used as a thickener.
4) It is used in treating peptic ulcer.
5) It is an appetite depressant.
6) It is used as a binding and disintegrating agent in tablet manufacturing.
7) It is used in paper sizing.
8) It is widely used as film -forming agent for cheese, salad dressing, ice -cream and soups.
9) It is used pharmaceutically to produce jelly.
10) It is used in suspensions, emulsions, lotions, creams, and toothpastes.
11) It is used as flocculants and filtering agents in mining industry.
12) It is also used in water treatment plants as a coagulant aid.

Starch
Starch is a polysaccharide granule obtained from the grains of maize (*Zea mays* Linn.); rice (*Oryza sativa* Linn.); wheat (*Triticum aestivum* Linn.); or potato tubers (*Solanum tuberosum* Linn.). Maize, rice and wheat belong to **Gramineae** family and potato belongs to family **Solanaceae**.

Starch is a white, colourless, solid carbohydrate ($C_6H_{10}O_5$) which occurs in the form of minute granules in seeds, tubers, and other plant parts. They are an important constituent of rice, corn, wheat, beans, potatoes, and many other vegetables.

Amylose (β-amylose) and **amylopectin** (α-amylose) are the two different polysaccharides present in starch in 1:2 ratio. The fo rmer is water-soluble, while the latter is water -insoluble, but swells in water and is responsible for gelling property of starch. With iodine, amylose produces blue colour, wh ile amylopectin produces bluish-black colour.

Starch has the following **uses**:
1) It is used as an absorbent and demulcent.
2) Its protective and absorbent property makes it a suitable ingredient in dusting powder.
3) It is used as a disintegrator and binder in tablets and pills.
4) It is also used as a diluent (or filler) and lubricant in capsules and tablets.
5) It is used as a diagnostic aid for proper identification of crude drugs.
6) It is used as an indicator in iodimetric analysis.
7) It is used as an antidote in iodine poisoning.
8) **Glycerine of starch** is used as an emollient and a base for suppositories.
9) It is used as the starting material for producing liquid glucose, glucose syrup, dextrose and dextrin on a large scale.
10) It is applied topically in itching.
11) It is used industrially for sizing of paper and textile.
12) It is used in laundry starching.

7.2.8. Flavours

Flavours or flavouring agents are the excipients added to enhance the palatability of pharmaceutical preparations. Some of the commonly used natural flavours are fruit, nut seafood, spice blends, vegetables , and wine. Flavouring agents mainly include flavour substances, flavour extracts , or flavour preparations, which impart flavouring properties (i.e., taste or odour or both) to food.

Flavours or flavouring agents are of the following **three types**:
1) **Natural Flavour s or Natural Flavouring Agents:** These agents are acceptable for human consumption. They are obtained by physical processing of natural resources like vegetables, fruits, etc.
2) **Nature-Identical Flavouring Agents:** These agents are either chemically obtained from aromatic raw materials or synthetically obtained. Their chemical composition is similar to substances present in natural products meant for human consumption, either processed or not.
3) **Artificial Flavouring Agents:** These agents are synthesised chemica lly and have not been intended for human consumption either processed or not.

Cardamom Oil

Cardamom is the dried ripe fruits of *Elettaria cardamomum* (and belongs to family Zingiberaceae). Cardamom grows wildly in **Sri Lanka** , **Myanmar**, **Malaysia**, and **Malabar hills**. In **India** it is grown in Karnataka, Tamil Nadu, and Kerala. Guatemala is the largest producer of cardamom in the world.

Cardamom has the following **morphological properties**:
1) **Cardamom Fruit (Capsule)**
   i) **Colour:** Pale green or cream.
   ii) **Odour:** Characteristic and aromatic.
   iii) **Taste:** Characteristic and aromatic.
   iv) **Size:** Length 1-2cm.
   v) **Shape:** Ovoid or oblong.

vi) **Nature:** Fruit developed from an inferior ovary (i.e., the inferior fruit); and inferior ovary is the one in which gynoecium is present below androecium.

vii) **Extra Features:** The apex of capsule is curved and has the remains of calyx; while the base is round and has the remains of stalk. Capsules of different grades and varieties are of different sizes, shapes, and surfaces. The capsule contains three alveoli, containing three placentas having two rows of tightly joined seeds.

2) **Cardamom Seed**
   i) **Colour:** Ripe seeds are dark red-brown; unripe seeds are pale red.
   ii) **Odour:** Strongly aromatic.
   iii) **Taste:** Pleasantly aromatic with a sensation of pungency.
   iv) **Size:** Length 4mm and width 3mm.
   v) **Shape:** Angular.
   vi) **Extra Features:** Seed is covered with transversely wrinkled testa (a seed coat); and the testa is covered with a membranous aril. The seeds have groove at one end which marks the position of the raphe, and a depression at the other end.

3) **Cardamom Oil**
   i) **Colour:** Pale yellow liquid.
   ii) **Odour:** Balsamic.
   iii) **Taste:** Sweet and aromatic.
   iv) **Viscosity:** Watery.

The chemical constituents of cardamom fruits are **volatile oil** (2.8-6.2%), **starch** (50%), **fixed oil** (1-10%), and **calcium oxalate**. The principal constituents of oil are α-pinene, β-pinene, limonene, α-terpineol, geraniol, methyl eugenol, myrcene, sabinene, α-phellandrene, ρ-cymene, terpinolene, linalool, linalyl acetate, α-terpineol acetate, citronellol, and *trans*-nerolidol.

Cardamom has the following **uses**:
1) It is a stimulant and carminative.
2) It is used for treating indigestion, constipation, and flatulence.
3) In India, green cardamom (*A. subulatum*) is used for treating teeth and gum infections.
4) It is used for preventing and treating throat troubles, congestion of lungs, and pulmonary tuberculosis.
5) It is used in inflammation of eyelids.
6) It is used as an antidote for snake as well as scorpion venom.
7) It is regarded as a cure for obesity.
8) It is used as a breath-freshener.
9) It is used in nausea (even the nausea related to pregnancy) and heartburn.
10) Its oil is used as an antiseptic, antispasmodic, carminative, digestive, stomachic and tonic, diuretic, expectorant, and stimulant.

Cinnamon Oil

Cinnamon consists of the dried inner bark of the shoots of coppiced trees of *Cinnamomum zeylanicum* Nees., (syn. *Cinnamomum verum*) (and belongs to family Lauraceae).

Originally, the spice cinnamon was found near **Sri Lanka** and **Malabar Coast of India**. Jamaica and Brazil are also the sites of cinnamon. But mostly the demand of cinnamon is fulfilled by Sri Lanka, therefore, a true cinnamon is referred to as **Sri Lanka cinnamon**.

Cinnamon has the following **morphological properties**:

1) **Colour:** Outer surface is dull yellowish-brown; inner surface is dark yellowish-brown.
2) **Odour:** Fragrant.
3) **Shape:** Found in the form of compound quills.
4) **Size:** Length of bark is 1m, diameter is 1cm, and thickness is 0.5mm.
5) **Taste:** Aromatic and sweet followed by warm sensation.
6) **Fracture:** Splintery.
7) **Surface:** On the outer surface of bark wavy longitudinal striations with small holes of scars left by the branches are present, while on the inner surface longitudinal striations are found.

The crude drug contains many essential constituents such as **volatile oil** (0.5-1.0%) and **phlobatannins** (1.2%). Other constituents found in cinna mon bark are mucilage, calcium oxalate, starch grains, and mannitol. Among these, volatile oil is considered to be the active constituent which on distillation appears light yellow in colour. However, it changes its colour during storage and becomes red. Cinnamon bark yields approximately14-16% of 90.0% alcohol-soluble extractive.

Cinnamon oil (yellow to red in colour) is composed of a variety of constituents such as **cinnamaldehyde** (60-70%), **eugenol** (5-10%), **benzaldehyde**, **cuminaldehyde**, and **terpenes** (phellandrene, pinene, cymene, caryophyllene, etc.).

Cinnamon has the following **uses**:

1) It is highly enriched in carminative, stomachic, and mild astringent properties.
2) It may be employed as a flavouring agent, stimulant, an aromatic, and an antiseptic.
3) On a commercial scale, cinnamon bark is commonly employed as a spice and condiment.
4) The oil is also used in candies, dentifrices, and perfume preparations.

7.2.9. Perfumes

Perfumes are used to enhance the odour of the formulation. G enerally, perfumes include an active ingredient or enhancer and one or more adjuvants (such as extenders, antioxidants, fixatives, etc.). The aroma or odour is imparted by the active ingredient that enhances or augments the aroma of an existing perfume composition.

Other ingredients of the perfumes are fixatives and extenders. The fixative agents are used to slow down the evaporation rate of perfume by reducing the volatility, whereas an extender is added to enhance the volume of the perfume composition without diluting or reducing the aroma.

Sandalwood Oil

Sandalwood oil is an essential oil steam-distilled from the chips and billets cut from the heartwoods of many species of sandalwood trees. Sandalwood oil is distilled from the heartwood of the plant *Santalum album* Linn. (and belongs to family Santalaceae). Sandalwood tree is an evergreen plant of **India** and **Malaysia** It is about 10-12m in height and is grown largely in the parts of India. Such plants are cultivated exclusively in the forests of Karnataka, Tamil Nadu, and Kerala. It covers 30°N to 40 °S of Indonesia (in the east) to Juan Fernandez Islands (Chile) (in the west) and from Hawaiian Archipelago (in the north) to New Zealand (in the south).

Sandalwood has the following **morphological properties**

1) **Colour:** The oil is pale yellow to colourless, while the wood is yellow or pale red in colour.
2) **Odour:** Characteristic and persistent.
3) **Taste:** Unpleasant.
4) **Solubility:** Soluble in water (very slightly), alcohol, and chloroform.
5) **Texture:** Darker and higher zones.

Sandalwood oil contains 95% of two isomeric sesqui -terpene alcohols, i.e., **α-santalol** and **β-santalol**. The other constituents are **aldehyde santalol** ($C_{16}H_{22}O$), **santene**, **santenone**, **teresantol**, **santalone**, and **santalene**. The oil is only present in the woody part of the plant, and not in the secretory cells or glands

Sandalwood has the following **uses**:

1) It is used as a perfumery in cosmetics and incense sticks preparations.
2) The sandalwood paste has been used since ancient times to comfort headache and reduce fever.
3) The paste also acts as a medicament for prickly heat, and controls extreme sweating during unfavourable environmental situations. Sweating can also be controlled by applying a mixture of dry sandalwood powder and rose water over the affected area.
4) The paste is also used to cure skin inflammation.
5) Since ancient times, the wood and its oil act as an expectorant, diuretic, and diaphoretic. It also guards against harmful infect ions caused by pathogenic microorganisms, i.e., *Eberthella typhosa* and *Escherichia coli.*

Lavender Oil

Lavender oil (volatile or essential oil) is extracted from the flower spikes of certain species of lavender by distillation. Mainly **two forms of lavender oil** are known:

1) **Lavender Flower Oil:** It is colourless oil with density of 0.885 gm/ml and is insoluble in water.
2) **Lavender Spike Oil:** It is a distillate with density of 0.905g m/ml and is obtained from the herb of *Lavandula latifolia.*

Lavender oil is a volatile oil extracted by steam distillation from the fresh flowering tops of the plant *Lavandula officinalis* Chaix (L. Vera D.C.). (and belongs to family Labiatae). This plant, also known as **true** or **common lavender**, is the most popular variety of lavender. The other species of lavender is *Lavandula stoechas* (marketed by the name of **French lavender)** is used for isolating oil

Lavender is grown towards the east all over the **Mediterranean region** and **Portugal**. It is also grown in some parts of India. It was originally found in mountainous or hilly areas of **Europe**.

Lavender has the following **morphological properties**:

1) **Colour:** Colourless or yellow liquid.
2) **Odour:** Characteristic, pleasant, and aromatic.
3) **Solubility:** Slightly soluble in water, soluble in 4 volumes of 70% alcohol, and carbon disulphide.

The vital constituents of the steam -distilled products prepared via gas chromatography are indicated in **table 7.4**. To set the internat ional standards, density and other physical properties should be measured. In most of the essential oil products, the final quality test is to check the organoleptic properties (taste or smell) by the flavourist.

Table 7.4: Vital Constituents Present in the Three Oil Groups of Lavender

Characters	Lavender	Lavandin	Spike Lavender
Density	0.876-0.892	0.885-0.897	0.895-0.917
Camphor (%)	0.51-1.00	04-11	10-20
Caryophyllene (%)	03-12		
Cineole (%)	01-02	05-10	20-30
Linalool (%)	30-49	30-40	40-50
Linalyl acetate (%)	30-45	20-30	1
Ocimene (%)	2.5-6.0		
Pinene (%)			01-03

Lavender is employed as:

1) A flavouring agent in perfumes and cosmetics, and
2) An aromatic and carminative.

7.3. SUMMARY

The details given in the chapter can be summarised as follows:

1) Substances used as a medium for delivering a medicament are termed **excipients**
2) The coloured compounds are called **chromogen**, and has a chromophore group and/or **auxochrome**, which appear as coloured substance by absorbing light in the near UV regions.
3) **Curcuma** is th e dried and fresh rhizomes of *Curcuma longa* Linn. (*C. domestica*) (and belongs to family Zingiberaceae).
4) **Annatto** consists of the dried seeds of the plant *Bixa orellana* L. (and belongs to family Bixaceae).
5) **Neohesperidin dihydrochalcon e** is a flavonoid present in bitter orange, *Citrus aurantium* variety Amara (and belongs to family Rutaceae).

6) **Binders** are agents used to impart cohesiveness to the granules so that the tablets remain intact after compression.
7) **Acacia** is found in the stems a nd branches of *Acacia arabica*, Willd. (and belongs to family Leguminosae).
8) **Gelatin** is a product obtained by partial hydrolysis of collagen, derived from the skin, white connective tissue, tendons, ligament and bones of ox (*Bos taurus* Linn.), sheep (*Ovis aries* Linn), etc. (and belongs to family Bovidae).
9) **Lactose** is a natural disaccharide containing galactose and glucose.
10) **Mannitol** is a hexahydric alcohol isolated from manna or seaweeds.
11) **Viscosity builders** are added to mixture to increase the viscosity witho ut modifying other properties like taste, odour, etc.
12) Chemically, **carrageenan** is a sulphated polysaccharide, and is obtained from the seaweed (or Irish moss), the red algae *Chondrus crispus* Linn. (and belongs to family Gigartinaceae and class Rhodophyceae).
13) **Xanthan gum** is a polysaccharide gum produced by the bacterium, *Xanthomonas campestris* on some specific carbohydrates.
14) The agents added to tablets, capsules, and some encapsulated formulations to promote their breakdown into smaller fragments in an aqueo us environment are termed **disintegrants**.
15) **Guar gum** is the powder of the endosperm of the seeds of *Cyamopsis tetragonolobus* Linn. (and belongs to family Leguminosae).
16) **Starch** is a polysaccharide granule obtained from the grains of maize (*Zea mays* Linn.); ri ce (*Oryza sativa* Linn.); wheat (*Triticum aestivum* Linn.); or potato tubers (*Solanum tuberosum* Linn.). Maize, rice and wheat belong to Gramineae family and potato belongs to family Solanaceae.
17) **Amylose** (β-amylose) and **amylopectin** (α-amylose) are the two diff erent polysaccharides present in starch in 1:2 ratio.
18) **Flavours** are the excipients added to enhance the palatability of pharmaceutical preparations.
19) **Natural flavours** are acceptable for human consumption.
20) **Nature-identical flavouring agents** are either chem ically obtained from aromatic raw materials or synthetically obtained.
21) **Artificial flavouring agents** are synthesised chemically and have not been intended for human consumption either processed or not.
22) **Cardamom** is the dried ripe fruits of *Elettaria cardamomum* (and belongs to family Zingiberaceae).
23) **Cinnamon** consists of the dried inner bark of the shoots of coppiced trees of *Cinnamomum zeylanicum* Nees., (syn. *Cinnamomum verum*) (and belongs to family Lauraceae).
24) **Perfumes** are used to enhance the odour of the formulation.
25) **Sandalwood oil** is distilled from the heartwood of the plant *Santalum album* Linn. (and belongs to family Santalaceae).
26) **Lavender flower oil** is colourless oil with density of 0.885 g/ml and is insoluble in water.
27) **Lavender spike oil** is a distillat e with density of 0.905 g/ml and is obtained from the herb of *Lavandula latifolia.*

7.4. EXERCISE

7.4.1. True or False

1) Annatto consists of the dried seeds of the plant *Bixa orellana* L.
2) Starch is the powder of the endosperm of the seeds of *Cyamopsis tetragonolobus* Linn.
3) Natural flavouring agents are either chemically obtained from aromatic raw materials or synthetically obtained.
4) Sandalwood oil is colourless oil with density of 0.885 g/ml and is insoluble in water.
5) Sandalwood oil is distilled from the heartwood of the plant *Santalum album* Linn.

7.4.2. Fill in the Blanks

6) _____ is a flavonoid present in bitter orange, *Citrus aurantium* variety Amara.
7) _____ is a hexahydric alcohol isolated from manna or seaweeds.
8) _____ and _____ are the two different polysaccharides present in starch in 1:2 ratio.
9) Cardamom is the dried ripe fruits of _____.
10) _____ is a distillate with density of 0.905 g/ml and is obtained from the herb of *Lavandula latifolia*.

Answers

1) True
2) False
3) False
4) False
5) True
6) Neohesperidin dihydrochalcone
7) Mannitol
8) Amylose and amylopectin
9) *Elettaria cardamomum*
10) Lavender spike oil

7.4.1. Very Short Answer Type Questions

1) What are herbal excipients?
2) Give a few examples of herbal excipients.
3) Give the advantages of herbal excipients.
4) Enlist the ideal properties of colourants used as herbal excipients.
5) Give two examples of binders and diluents used as herbal excipients.
6) Mention the advantages and disadva ntages of viscosity builders used as herbal excipients.

7.4.2. Short Answer Type Questions

1) Write about herbal excipients.
2) Discuss about any two colourants used as herbal excipients.
3) Write a short note on sweeteners used as herbal excipients.
4) Discuss about a binder and a diluent used as herbal excipients.
5) Write a short note on disintegrants as herbal excipients.

7.4.3. Long Answer Type Questions

1) Briefly discuss about the significance of substances of natural origin as excipients.
2) Give a brief review on flavours and perfumes as herbal excipients.

CHAPTER 8

Herbal Formulations

8.1. CONVENTIONAL HERBAL FORMULATIONS

8.1.1. Introduction

Herbal formulations are dosage forms that consist of one or more herbs or processed herbs in specified quantities to provide specific nutritional and cosmetic benefits meant to be utilised for diagnosing, treating, mitigating diseases of human beings or animals, and for altering the structure or physiology of humans or animals. An active substance or herbal substance, or a herbal preparation or herbal substance, along with one or more herbal preparations are present in herbal formulations.

Herbal formulations can be obtained by subjecting herbal substances to extraction, distillation, expression, fractionation, purification, concentration, or fermentation. Comminuted or powdered, whole, fragmented or cut plants, plant parts, algae, fungi, or unprocessed lichens (usually dried but sometimes fresh) were used for preparing herbal formulations. Herbal substances are defined by the plant part used and the botanical name as per the binomial system (genus, species, variety, and author).

Tinctures, extracts, essential oils, expressed juices, and processed exudates are the different herbal formulations.

8.1.2. Syrups

A saturated solution of sucrose formed in purified water with the concentration of 66% w/w sugar is known as **simple syrup**. These preparations are viscous and sweet in taste. Due to the following reasons the syrups are frequently used:

1) They get hydrolysed partially in reducing sugars, like laevulose and dextrose, thus, retards oxidation.
2) Bacterial growth, fungal growth, and growth of molds are the main reasons of decomposition of vegetable material in solution form. Such contaminations are prevented by syrups due to their high osmotic pressure, which prevents decomposition of many vegetable substances.
3) It is advantageous to incorporate syrups in nauseous preparations as the sweetness of sugar makes the preparation palatable.

Syrups are sweet, viscous, concentrated aqueous solutions of sucrose or other sugars. Syrups containing therapeutic or medicinal agents are **medicated syrups**, while syrups with flavours but no medicinal agents are **flavouring** or **flavoured** or **non-medicated syrups**.

8.1.2.1. Classification

Syrups can be classified into the following three classes:

1) **Simple Syrups:** These syrups are made up of simple solutions or are admixture of solutions. **Examples** of simple syrup include syrups I.P., ginger syrup, orange syrup, and lemon syrup. The formulae for syrup I.P. is given below:

Syrup I.P.

Sucrose	667gm
Purified water, q.s. to produce	1000gm

Preparation: Sucrose is added to purified water and heated with occasional stirring until it gets dissolved. The solution is then cooled and sufficient purified water is added to make up the desired weight.

2) **Medicated Syrups:** These syrups include therapeutic agents. **Examples** of medicated syrups are chlorpheniramine maleate syrup, ephedrine sulphate syrup, etc.

3) **Flavoured Syrups:** These syrups comprise of different flavoured or aromatic substances, which impart a pleasant smell and taste. These are usually added to the preparation for providing a flavour, as a preservative, or as a vehicle. These syrups do not have any pharmacological activity. **Examples** of flavoured syrups are cherry syrups, Tolu balsam syrup, etc. The formulae for Tolu syrup I.P. is given below:

Tolu Syrup I.P.

Tolu balsam	12.5gm
Sucrose	660.0gm
Purified water, q.s. to produce	1000.0gm

Preparation: Tolu balsam is mixed with purified water in a tarred vessel and boiled for about half an hour with frequent stirring. The vessel is left half covered with a lid. The boiled solution is cooled, mixed with purified water to make up the desired volume, and then filtered. Further, sucrose is added to the filtered solution and again heated on a water bath to facilitate its dissolution. Finally, purified water is added to make up the desired volume of the solution.

8.1.2.2. Preparation

The preparative methods for syrups are:

1) **Hot Process:** This method is not suitable for heat-labile or volatile ingredients. In this method, firstly, sucrose is weighed accurately in a tarred dish and then dissolved in purified water. The solution is further heated on a water bath to completely dissolve the sucrose in water. The obtained product is strained completely and added with the desired quantity of boiling purified water to make up the required volume of the product. During the formulation of syrup, precautions should be taken while heating. This is because overheating can cause sucrose inversion. An instrument known as **saccharometer** is used for determining the specific gravity of the syrup. Syrups prepared by this method include syrup I.P., acacia syrup NF, cocoa syrup NF, and Tolu syrup I.P.

2) **Percolation (Cold Process):** For preparing U.S.P. syrup, this method is used. In this process, sucrose is placed in a percolator and an aqueous solution or

purified water is allowed to pass slowly through the sucrose. Loosely compressed cotton is placed and packed in the percolator neck. The dissolution rate of sucrose is dependent on the percolation rate. To dissolve the sucrose completely, percolate should be returned back to the percolator. With the aid of water, the percolator should be washed from within and cotton plug should also be washed. Then the final volume of the preparation is made up as needed.

3) **Addition of Medicating or Flavouring Liquid to Syrup:** This method is used for preparing syrups containing fluid extracts, tinctures, or other liquids. These liquids contain alcohol to facilitate the dissolution of resinous and oleo resinous substances; but when added to the syrup, these liquids may precipitate the substances soluble in alcohol as they get diluted with water. This alcohol also functions as a preservative in these syrups.

4) **Agitation without Heat:** This preparative method is used when the active constituent is heat-labile. In this method, sucrose and other required ingredients are solubilised in purified water in a bottle having the volume twice than that required for the syrup in order to facilitate thorough shaking. The bottle is closed by the stopper to avoid contamination and water loss through evaporation. When not being agitated, the bottle is rested on its side. For the formulation of syrups by this method on a large scale, glass-lined tanks fitted with mechanical agitators are used. An **example** of syrup prepared by this method includes ferrous sulphate syrup U.S.P.

8.1.3. Mixtures

Mixtures are liquid dosage forms meant for oral administration. In these preparations, any solid or liquid medicament is dispensed in a suitable vehicle either by dissolving or suspending the medicament in it. Normally, liquids contain more than one dose, and are therefore dispensed in large bottles. When the mixture dispensed in a bottle contains only single dose, it is known as a **draught**. Usually these are meant for the treatment of acute conditions, like constipation, cough, indigestion, diarrhoea, etc.

8.1.3.1. Classification

Mixtures are classified as follows:

1) Depending on composition and uniformity:
   i) **Homogeneous Mixtures:** These mixtures consist of uniformly spread particles and possess certain consistent and specific properties, **e.g.,** mixtures present in any amount possess the same properties and composition. **Example** of a homogeneous mixture includes solution in which a uniform mixture of one or more solutes is dissolved in the solvent.

   ii) **Heterogeneous Mixtures:** These mixtures do not have uniformity and consistency in their composition. The two phases of the mixtures can be separated from each other mechanically. The **examples** of heterogeneous mixtures are:
      a) **Suspensions:** These heterogeneous mixtures consist of two components in which the size of the particle of at least one component must be larger than the colloidal particles, i.e., greater

than 1000nm (1μm), in at least one direction. Since the particle size of suspensions is larger than that of colloids, they settle down in liquids after a particular period of time and also disperse light when suspended in air, i.e., they exhibit Tyndall effect. **Example** of suspension includes sand in water.

b) **Colloidal Dispersions:** These are a mixture of components present in one or more phases. In these mixtures, the size of the particles of the components is smaller than those in a suspension, but larger than those in a solution, and at least one dimension of the particles of the components must be in range of 0.001 -1μm. A colloidal dispersion when left for standing does not settle down as in suspensions. When light passes through the colloidal dispersion, it shows Tyndall effect. **Examples** of colloidal dispersions include jelly, milk, blood, paint, fog, and glue.

2) Depending on miscibility:
   i) **Positive Mixtures:** These mixtures are irreversible in nature. In positive mixtures, water-soluble solid is dissolved or two or more miscible liquids are mixed with each other in such a way that they do not create any hindrance during mixing.
   ii) **Negative Mixtures:** These mixtures form reversible mixtures. Formation of immiscible liquids takes place when the insoluble solid substances are mixed with water or two immiscible liquids are mixed with each other. Since negative mixtures involve immiscible or insoluble liquids and solids respectively, they require a high degree of mixing of materials.
   iii) **Neutral Mixtures:** In these mixtures, the substances are not instantly miscible with each other but when mixed, they form stable and irreversible mixtures.

3) Depending on the basic concepts and different viewpoints on mixtures:
   i) **Perfect Mixtures:** In these mixtures, two types of particles sampled randomly from any mixture contain same proportion of each particle as the proportions of the sampled particles found in the mixture taken as a whole.
   ii) **Random or Stochastic Mixtures:** When two immiscible components possessing same properties (size, shape, elasticity, etc.) are mixed with each other in an ideal mixer, the mixing quality reaches an asymptotic limit due to random mixing of the components.
   iii) **Ordered Mixtures:** When two compatible components are mixed together, a specific order or a structure is formed in the mixture during the mixing process. Formation of such an ordered unit results due to the cohesion or agglomeration of two components with other or a mixture of two components. In order to obtain a mixture containing perfectly ordered structures, following **conditions** should be fulfilled:
      a) The agglomerate of the minor component (cohesive fraction) formed can be broken down into smaller fractions by applying sufficient energy so that they can be evenly distributed on the available sites of

the carrier particles. The se particles should provide sufficient sites for holding the minor components (cohesive fractions); else these components re-agglomerate to form lumps.

b) Complete randomisation of carrier particles should also be ensured.

iv) **Partially Ordered Random Mixture s:** After all the available sites of the carrier particles are occupied by the cohesive fraction, the left over components agglomerate and randomly mix with the ordered units, resulting in the formation of the partially ordered random mixtures.

8.1.3.2. Formulation

Formulation of mixtures includes the following basic substances:

1) **Vehicles:** The commonly used vehicles in the preparation of mixtures are:
   i) **Water:** Mixtures should always be prepared in purified water (rather than in potable water as it contains both volatile and non-volatile impurities which might cause unwanted changes in the dissolved active pharmaceutical ingredients). In case of special preparations, either cooled or freshly boiled purified water free from vegetative bacteria is used.
   ii) **Aromatic Water:** It is used in the preparation of mixtures due to their flavouring properties . It also possess es carminative and preservativ e properties. Aromatic water is the saturated solution of volatile substances and oil in purified water. It is employed in the preparation of mixtures to enhance their flavour, palatability, and preservation.
   iii) **Medicated Vehicle s:** These possess a specific therapeutic activity and are used occasionally. **For example,** infusion of senega (expectorant), compound gentian infusion (a bitter that stimul ates appetite), and orange peel infusion (bitter and carminative) are employed as medicated vehicles in the preparation of mixtures. These infusions can be prepared by diluting one volume of concentrated infusion with seven volumes of purified water.

2) **Adjuncts:** In order to enhance the stability, colour and flavour of the mixtures, the following adjuncts are used:
   i) **Chemical Stabilisers:** These c hemicals possess antioxidant or reducing properties and are employed in the preparation of mixtures to enhance their chemical stability. **Examples** of chemical stabilisers include:
      a) Sodium metabisulphite (0.1%) is added in mixtures containing sodium salicylate to avoid the darkening of mixtures caused by the atmospheric oxidation.
      b) Ascorbic acid (0.1%) is included in the mixt ures of ferrous sulphate to avoid oxidation of ferrous ions into ferric ions because these ions are relatively ineffective in the formation of haemoglobin.
   ii) **Colouring Agents:** Several mixtures contain coloured active constituents which impart colour to the whole preparation.
   iii) **Flavouring Agents:** The c ommonly used flavouring agents in the mixtures are:
      a) Aromatic water, **e.g.,** anise water.

b) In order to mask the astringent and metallic taste of iron salts in the mixtures meant for paediatric purposes, orange syrup and compound orange spirit are added to it.
c) In order to mask the saline taste of certain mixtures, liquid extract of liquorice is used.
d) Syrup and glycerol are added to the preparations of paediatrics for providing the sweet taste.
e) To mask the alkaline taste of citrates, spirit lemon is added to the mixtures.

iv) **Preservatives:** Chloroform (0.25%v/v) and benzoic acid (0.1%w/v) are used as preservatives in the mixtures to prevent the growth of microorganisms (including bacteria and fungi) due to the presence of diluted vegetable extract and flavouring agent.

8.1.3.3. Formulation Methods

Different methods are used for the pr eparation of different mixtures, thus indicating that the formulation methods of mixtures depend on the types of mixtures:

1) **Simple Mixtures Containing So luble Substances:** These mixtures consist of only those ingredients which are soluble in it.

Simple mixtures containing soluble substances can be prepared as follows:
i) The solid material is dissolved in 3/4th of the vehicle.
ii) The solution is observed against light to detect the presence of any foreign particle so that it can be strained out by a cotton wool.
iii) The other liquid ingredients are added to the above mixture.
iv) The final volume is made up by adding more of the liquid to the formed mixture.
v) The mixture is transferred into a bottle and stoppered.
vi) The finger prints are removed from the bottle by polishing it thoroughly.
vii) The label is attached to the bottle, wrapped and then dispensed.

2) **Mixtures Containing Diffusible Solids:** The solid material, which does not get dissolved in water , mixes with it when shaken so that the powder drug gets evenly distributed in each dose by diffusing properly throughout the liquid for a sufficient time. **Examples:** bismuth sub -nitrate, bismuth carbonate, quinine sulphate, light kao lin, magnesium carbonate (heavy or light), magnesium oxide (heavy or light), etc.

Mixtures containing diffusible solids can be prepared as follows:
i) The diffusible solid is triturated in a mortar to form po wder containing fine particles.
ii) Any soluble drug is added and mixed properly.
iii) A smooth cream is formed with 3/4 th volume of the vehicle and the leftover amount of vehicle is added to the mixture.
iv) The contents in the mortar are transferred to a measuring cylinder.
v) If some of the content still remains in the mortar, it is rinsed with a small quantity of vehicle and again transferred to the measuring cylinder.

vi) If any liquid ingredient is present, it is added to the mixture formed above.

vii) The final volume of the mixture is made up by adding sufficient amount of vehicle.

viii) The mixture is transferred to a dispensing bottle and stoppered.

ix) The label along with additional secondary label mentioning "Shake well before use" is attached to the bottle and then dispensed.

3) **Mixtures Containing Indiffusible Solids:** In these mixtures, a suspending agent is used for uniformly distributing the drug substance throughout the preparation as the indiffusible solids do not get solubilised in water and thus do not remain distributed uniformly for longer time in the vehicle of the mixture.

The commonly used **suspending agents** in the mixtures comprising of indiffusible solids are:

i) **Compound Tragacanth Powder:** It is used in the proportion of 10 grains/ounce (2gm/100ml) of the mixture preparations. It is employed in the preparations in which the vehicle used includes all types of waters except for normal water and chloroform water.

ii) **Tragacanth Mucilage:** It is used in the proportion of $1/4^{th}$ of the total volume of the mixture in which the vehicle used is either chloroform water or simply water.

Mixtures containing indiffusible solids can be prepared as follows:

i) The size of indiffusible solids is reduced to fine particles, and then the diffusible solids or any soluble substance are added along with compound tragacanth powder.

ii) The above ingredients are mixed properly to form a uniform mixture.

iii) About $3/4^{th}$ volume of the vehicle is added to the above mixture to form a smooth cream by triturating it in a mortar.

iv) The remaining amount of vehicle is added to the cream formed.

v) The mixture formed is observed to detect the presence of any foreign particle so that it can be strained out by passing through muslin cloth.

vi) The mortar is rinsed with a small amount of vehicle.

vii) Any liquid ingredient (if present) is added to the above mixture and then transferred to the measuring cylinder.

viii) Final volume of the mixture is made up by adding sufficient amount of vehicle and is then transferred to a bottle.

ix) The bottle is cleaned properly, the label mentioning "Shake well before use" is attached, and then dispensed.

4) **Mixtures Containing Precipitate-Forming Liquids:** Some liquid mixtures contain resinous substances, which when mixed with water get precipitated out, form a clotted precipitate or stick to the sides of the bottle, and does not get re-dissolved even on shaking. To prevent such precipitation, tragacanth mucilage or compound tragacanth powder is added to the mixtures.

Mixtures containing precipitate-forming liquids are prepared as follows:

i) The size of diffusible and indiffusible solids is reduced to a fine powder in mortar and mixed with compound tragacanth powder.

ii) About 3/4th volume of the vehicle is added to the above formed mixture to form a smooth paste.
iii) Remaining amount of vehicle is added to the paste, and the amount of precipitate formed in the liquid kept in the dry is measured.
iv) This liquid is added in the centre of the cream in a slow stream with vigorous stirring.
v) If any soluble ingredient is present, it is dissolved in required amount of vehicle and slowly added to the cream with regular stirring to prevent the formation of local high concentrations which might neutralise the effect of suspending agent.
vi) The mixture formed is observed to detect the presence of any foreign particle so that it can be strained out by passing through muslin cloth.
vii) The mortar is rinsed with a small amount of vehicle.
viii) Any liquid ingredient (if present) is added to the above mixture and then transferred to a measuring cylinder.
ix) Final volume of the mixture is made up by adding sufficient amount of vehicle and then transferred to a bottle.
x) The bottle is cleaned properly, the label mentioning "Shake well before use" is attached, and then dispensed.

5) **Mixtures Containing Slightly Soluble Liquid:** These mixtures are added with a suspending agent to dissolve and diffuse the insoluble part of the slightly soluble liquids. Tragacanth mucilage and compound tragacanth powder are used as the suspending agents in the same proportion as stated in the preparation of mixtures containing indiffusible solids.

Mixtures containing slightly soluble liquids are prepared as follows:
i) Paraldehyde and tragacanth mucilage are taken in a bottle and thoroughly shaken.
ii) In a specific amount of water, the liquid extract of glycyrrhiza and syrup are dissolved and slowly added to a bottle containing the mixture formed above.
iii) The contents of the bottle are transferred to a measuring cylinder.
iv) Sufficient amount of water is added to make up the desired volume.
v) The mixture obtained is transferred to a fresh bottle, stoppered, a ttached with a label and dispensed.

8.1.4. Tablets

Tablets are **solid unit dosage form of medicaments** with or without suitable diluents and **prepared** either by **moulding** or **compression**. They are solid, flat, or biconvex discs in shape. They vary greatly in shape, si ze, and weight which depend on the amount of medicament used and mode of administration. They also vary in hardness, thickness, disintegration and dissolution characteristics, and in other aspects depending on their intended use and manufacturing method.

According to the **Indian Pharmacopoeia**, pharmaceutical tablets are **solid, flat, or biconvex discs, unit dosage form, prepared by compressing drugs or a mixture of drugs, with or without diluents** . It is the most popular dosage form

and 70% of the total medi cines are dispensed in the form of a tablet. All medicaments are available in the tablet form except where it is difficult to formulate or administer. The **ideal properties** of a tablet are:

1) It should be attractive having its own identity and free from defec ts such as cracks, chips, contamination, discolouration, etc.
2) It should have chemical and physical stability to maintain its physical integrity over time.
3) It should prevent any alteration in chemical and physical properties of medicinal agent(s).
4) It should withstand the rigors of mechanical shocks encountered during its production, packaging, shipping, and dispensing.
5) It should release the medicament(s) in the body in a predictable and reproducible manner.

8.1.4.1. Merits

Tablets have the following merits:

1) They are unit dosage forms that provide an accurate, stable dose with greatest precision and least content variability.
2) They are easy to use, handle, and carry by the patient.
3) They are attractive and pleasing in appearance.
4) They are the most stable dosage form wit h respect to their physical, chemical, and microbiological attributes.
5) Their manufacturing cost is low as compared to other dosage forms and their manufacturing speed is also quite high.
6) Their packaging and shipping are comparatively easy and cheap.
7) They can be coated to mask the unpleasant taste and odour of medicament(s) incorporated.
8) They suffer from fewer incompatibilities of medicament(s) and their deterioration due to environmental factors.
9) Whenever a fractional dose is required, they are divided into halves and quarters by drawing lines during manufacturing to facilitate breakage.
10) They are more suitable for large scale production.
11) They provide administration of even minute drug doses in accurate amount.
12) Their identification is easy because of variety of shapes and colours.
13) They are formulated with certain special release profile products, such as enteric or delayed release products.
14) They are economical as their cost is lowest than other oral dosage forms.

8.1.4.2. Demerits

Tablets have the following demerits:

1) Drugs which are amorphous in nature or have low density character are difficult to compress into a tablet.
2) Hygroscopic drugs are not suitable candidates for compressed tablets.
3) Drugs having poor wetting properties, slow dissolution profile, and high optimal gastrointestinal absorption are difficult to formulate as a tablet.

4) Drugs having a bitter taste and objectionable odour require special treatment, like coating or encapsulation, which may increase their production cost.
5) Drugs sensitive to oxygen may require certain treatment, like special coating as well as packaging, which may increase the overall manufacturing cost.
6) High dose drugs are difficult to formulate as tablets.
7) Some drugs which get absorbed from the upper GIT may cause bioavailability problems in tablets.
8) Liquid drugs are difficult to formulate as a tablet.
9) Children and critically ill patients face difficulty in swallowing tablets.

8.1.4.3. Classification

The tablets are classified into various types as shown in **figure 8.1**:

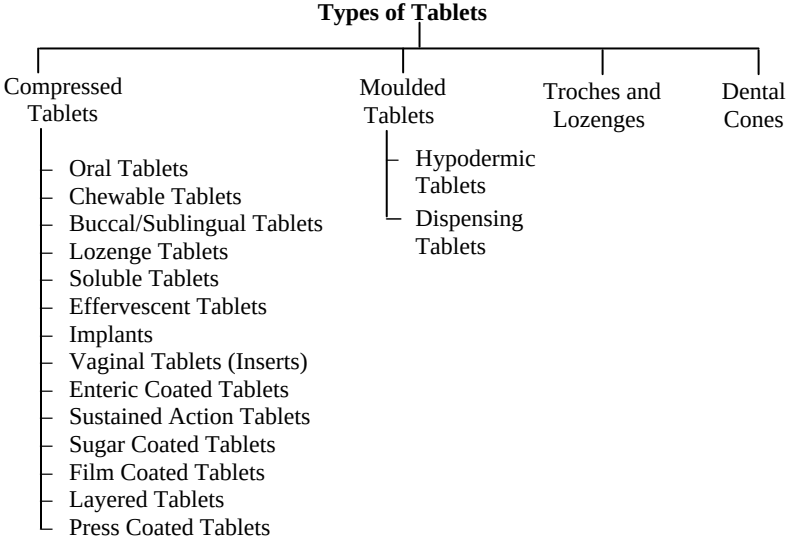


Figure 8.1: Types of Tablets

8.1.4.4. Preparation

Tablets can be prepared as follows:

1) **Dispensing:** All the ingredients to be used for manufacturing tablets are accurately weighed and dispensed according to their dose. This step being highly critical should be directed by the concerned technicians.
2) **Sizing:** The ingredients are finely divided by size reduction process for better flowability and ease of mixing.
3) **Powder Blending:** The powdered drug substance and ingredients are mixed in a blender by geometric dilution to yield a uniform and homogeneous powdered mix.
4) **Granulation:** Small powder particles are gathered into layers, and converted into permanent aggregates so that they can flow freely.
5) **Drying and Dry Screening:** The screened wet granules are dried in a tray dryer or fluid bed dryer for a specific time period at 55 °C temperature to obtain dried granules, which are screened through a suitable mesh screen.

6) **Tablet Compression:** The dried granules are compressed into flat, convex, round, oblong, or unique shaped tablets that are engraved with an identifying symbol and/or code number using tablet press.

7) **Coating:** The compressed tablets are coated to mask the unpleasant taste/odour of some drugs, to enhance the appearance of uncoated tablets, or to control the release of drugs from the tablets by enclosing the c ore tablet with coating solutions.

8.2. NOVEL DOSAGE FORMS

8.2.1. Introduction

In the past few decades, the researchers have focused on the development of novel drug delivery system for herbal drugs. Herbal drugs are becoming popular in t he modern world due to their application to cure diseases with better therapeutic effects and less toxic effects. Novel herbal drug carriers cure a disease by targeting the affected area in a patient's body and delivering the drug to that area. Novel drug delivery system delivers the herbal drugs at predetermined rate and at the site of action, thereby reducing the toxic effects and increasing the bioavailability of drugs.

In novel drug delivery technology, drug distribution can be controlled by incorporating the drug in carrier system or by changing the drug structure at molecular level. Incorporation of herbal drugs in delivery system also increases solubility, enhances stability, provides protection from toxicity, enhances pharmacological activity, impro ves tissue macrophage distribution, sustains delivery, and prevents physical and chemical degradation.

For example , liposomes act as potential carriers for anti -cancer agents by increasing the amount of drug in tumor area and decreasing the exposure or accumulation of drug in normal cells/tissues, thus preventing tissue toxicity effects. Phytosomal carriers have been studied for effective delivery of herbal extracts of ginseng (*Ginkgo biloba*), etc.

8.2.2. Importance of Novel Drug Delivery Systems in Herbal Medicines

Novel drug delivery system is a novel approach of delivering drug that addresses the limitations of the traditional drug delivery systems. India has a vast knowledge of Ayurveda whose potential is being realised in the recent years. However, the drug delivery system for administering herbal medicines to patients is traditional and out-dated, resulting in reduced drug efficacy.

If novel drug delivery technology is applied in herbal medicine, it increases the efficacy and reduces the side effects of va rious herbal compounds and herbs. This is the basic idea behind incorporating novel method of drug delivery in herbal medicines. Thus, novel drug delivery system and Indian Ayurvedic medicines should be integrated to combat more serious diseases.

Herbal medicines for a long time were not considered as novel formulations for development due to lack of scientific justification and processing difficulties, such as standardisation, extraction and identification of individual drug components in complex poly herbal systems. However, modern phytopharmaceutical research can solve the scientific needs (such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required, etc.) of herbal medicines to be incorporated in novel drug delvery system, such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles, etc. Various drug delivery and drug targeting systems are being developed to reduce drug degradation and loss, to prevent harmful side effects, and to increase drug bioavailability and fraction of drug accumulated in the required zone.

8.2.3. Advantages of Novel Drug Delivery Systems

Novel drug delivery systems in herbal medicines have the following advantages:

1) They enhance drug solubility.
2) They improve drug bioavailability.
3) They provide protection against toxicity.
4) They enhance the pharmacological activity of drugs.
5) They enhance drug stability.
6) They improve tissue macrophages distribution.
7) They provide sustained drug delivery.
8) They provide protection from physical and chemical degradation.

8.2.4. Types of Novel Herbal Drug Delivery Systems

The different types of formulations in novel herbal drug delivery system include phytosomes, liposomes, niosomes, transferosomes, ethosomes, dendrimers, etc.

8.2.4.1. Phytosomes

Phytosome is a novel technology that emerged in **1989**. The term **phyto** means **plant/herb** and **some** means **cell-like structure**. Phytosome is a technology used as controlled and sustained release delivery syste m that consists of phospholipid complex system of herbal extract or phytoconstituents in nano size range [<100nm] of particles. Phytosomes are produced by the reaction of a stoichiometric amount [1:1 or 1:3] of phospholipid [phosphatidylcholine] with the s tandardised extract or phytoconstituents in a non -polar solvent. It is a patented technology to encapsulate standardised extracts or phytoconstituents into phospholipids to fabricate molecular complexes for enhancing their permeation and bioavailability. P hytosomes are most suitable for drugs having poor aqueous solubility and strong tendency to self-aggregate.

Properties

1) They can accommodate the active principle anchored to the polar head of phospholipids, thus becoming an integral part of the membrane. **For example**, in catechindistearoyl phospholipid complex, H -bonds form between the phenolic hydroxyls of flavones moiety and the phosphate ion on phospholipid complex side.
2) They are advanced forms of herbal products that are better absorbed, utilised, and thus, produce better results than conventional botanical he rbal extracts.

Increased bioavailability of phytosomes over the non -complexed botanical derivatives has been demonstrated by pharmacokinetic studies or by pharmacodynamic tests in experimental animals and in human subjects.

3) They are lipophilic substances with a definite melting point, free solubility in non-polar solvents, and moderate solubility in fats.
4) On treatment with water, they assume a micellar shape and form structures that resemble liposomes with fundamental differences.

Advantages

1) They increase bioavailability due to phospholipid complex, thus improves therapeutic effect.
2) They are required in fewer doses due to high bioavailability.
3) They improve gastrointestinal absorption.
4) They show high stability.
5) Due to their h igh lipophilicity, they cause high penetrability, hence used in cosmetics over liposomes.
6) They have greater clinical benefits.

Method of Preparation

Phosphatidylcholine and cholesterol are accurately weighed, dissolved in 10ml of chloroform in a round bottom flask, and sonicated f or 10 minutes in a bath sonicator. The organic solvent is removed by using rotary evaporator (at 45 - 50°C). After complete removal of solvent, a thin layer of phospholipid mixture is formed which is hydrated with methanolic extract of plant in rotary evapor ator (at 37-40°C for 1 hour). After hydration, the mixture of lipid and plant extract is sonicated for 20 minutes in ice bath for heat dissipation. The obtained phytosomes are filled in amber-coloured bottle and stored in freezer (at 2-8°C).

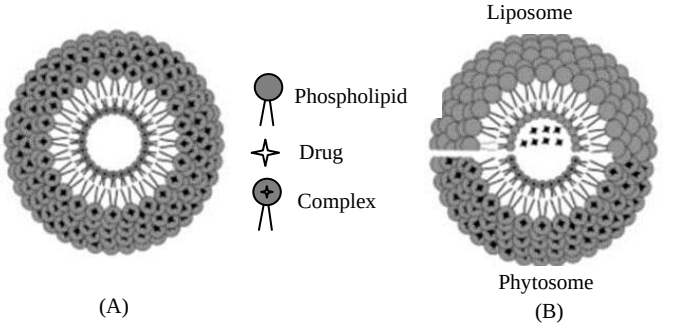


Figure 8.2: Schematic Representation of the Structure of Phytosome (A) and Major Difference between Liposome and Phytosome (B)

Table 8.1: Phytosomal Herbal Formulations

Biological Sources	Chemical Classification	Advantages	Uses	Active Ingredients
Sibelium marianum	Flavonoids	Increases absorption	Hepatoprotective and antioxidant	Silybin
Vitis vinifera	Proanthocyanodins	Increases antioxidant property	Antioxidant and anticancer	Catechin and epicatechin

Curcuma longa	Polyphenols	Increases bioavailability	Antioxidant, anti - inflammatory, and anticancer	Curcumin, demethoxycurcumin, and bisdemethoxycurcumin
Thea sinensis	Polyphenols and flavon-3-ol	Increases bioavailability	Antioxidant, neuro-protective, and anticancer	Epigllocatechin-3-gallate, epigallocatechin, epicatechin, and epicatechin-3-gallate
Panax ginseng	Saponin glycosides	Inhibits lipid peroxidation	Immunomodulator	Ginseng
Ginko biloba	Terpenoids	Improves bioavailability	In cerebral insufficiency	Ginkoflavoneglucoside, ginkgolides, ginkgoic acids, and bilobalide

8.2.4.2. Liposomes

Liposomes are bilayer vesic ular carrier systems of phospholipids or cholesterol. Their size ranges from 25 -2.5nm. Liposomes are advantageous due to their ability to encapsulate various materials and their structural versatility. They can encapsulate drugs having varying solubility o r lipophilicity. They encapsulate a fraction of the solvent, in which they freely diffuse into their interior.

Properties

1) They can have one, several, or multiple concentric membranes. They are made up of polar lipids having a lipophilic and hydrophilic gr oup on the same molecules.
2) The polar lipids on interaction with water self -assemble and form self - organised colloidal particles.
3) Liposome cross-section (**figure 8.3**) shows that the hydrophilic heads of the amphiphile orient towards the water compartment an d the lipophilic tails orient away from the water compartment towards the centre of the vesicle, thus forming a bilayer. As a result, water - soluble compounds get entrapped in the water compartment and lipid -soluble compounds aggregate in the lipid section.

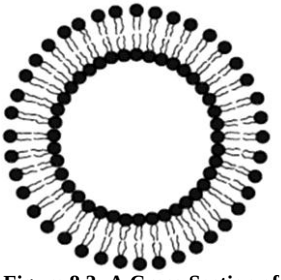


Figure 8.3: A Cross-Section of Liposome

4) They can encapsulate hydrophilic as well as lipophilic materials.
5) They can enhance product performance by increasing ingredient solubility, improving ingredient bioavailability, enhancing intracellular uptake, and altering pharmacokinetics and bio-distribution.
6) Liposomes made up of natural lipids are biodegradable, biologically inactive, non-immunogenic, and exhibit limited intrinsic toxicity.
7) Liposomes made up of phospholipids can be used to change the pharmacokinetic profiles of drugs, herbs, vitamins, and enzymes.

Advantages

1) They provide selective passive targeting to tumor tissues.
2) They increase the efficacy and therapeutic index.

3) They increase drug stability by encapsulation.
4) They decrease the toxicity of encapsulated drugs.
5) They improve pharmacokinetic effects (reduce elimination and increase circulation life times).
6) They provide flexibility to couple with site-specific ligands to achieve active targeting.
7) They are biodegradable and flexible.
8) They can incorporate micro and macro molecules.
9) They can carry water- as well as lipid-soluble drugs.

Methods of Preparation

Various methods have been used for manufacturing liposomes, like mechanical methods including film method and ultrasonic method; methods involving replacement of organic solvent; methods involving fusion of prepared vesicles or transformation of size by Freeze Thaw Extrusion (FTE) method; and Dehydration-Rehydration (DR) method.

The **mechanical method of liposomal preparation** includes the simplest film method in which an organic solvent is used to hydrate the thin lipid film. After complete hydration of the lipid film, the organic solvent is completely removed by deposition process. Then, an aqueous buffer is used to hydrate the solid lipid mixture. As a result, the lipid gets swelled and hydrated, thus forming liposomes.

Another mechanical method of liposomal preparation includes **ultrasonic method**, in which ultrasonication process is employed for forming liposomes. Two types of sonicators have been used for ultrasonication of an aqueous dispersion of phospholipids, namely, probe sonicator (used for small volume) and bath sonicator (used for large volume).

Liposomes can also be prepared by **replacement of organic solvent**. In this method, the lipid is co-solvated by using an organic solution, which is later dispersed into aqueous phase containing the material to be entrapped in the liposome. This method is further differentiated as **reverse phase evaporation**, in which the solvent is removed from the lipid mixture taken in a round bottom flask using a rotary evaporator.

Nitrogen is introduced into the system followed by re-dissolvation of lipids in the organic phase. This results in the formation of semi-solid gel due to the evaporation of solvent under reduced pressure. The non-encapsulated material is removed and forms liposomes.

Another method of replacement of organic solvent includes **ether vaporisation method**, which is further differentiated as **ethanol injection method** and **ether injection method** on the basis of the solvent used. In the former method, the lipid is rapidly injected with a fine needle into an excess of saline or other aqueous medium; while in the latter method, lipid is slowly injected with a fine needle into an excess of saline or other aqueous medium.

Another method of liposomal preparation involves the **fusion of pre-formed vesicles** or **transformation of size**, which can be further categorised as **FTE method** and **DR method**. In FTE method, the liposomes formed by film method and the solute to be entrapped are together whirled continuously until the entire film gets suspended. The obtained MLVs (Multi-Lamellar Vesicles) are frozen in lukewarm water and whirled again. The sample is extruded three times after performing two cycles of freeze thaw and whirling, along with six cycles of freeze thaw and eight extrusions of sample. This results in the rupture and diffusion of SUVs (Small Unilamellar Vesicles). The solute under this condition attains equilibrium between inside and outside and results in the fusion of liposomes. Thus, they grow in size and form **Large Unilamellar Vesicles by Extrusion Technique (LUVET)**. This method is also used for encapsulating proteins.

In DR method, SUVs are incorporated in an empty buffer. An aqueous fluid containing the material to be entrapped is used for rehydration of empty buffer containing SUVs. After rehydration, the SUVs are dried, resulting in solid lipids dispersing in a finely subdivided form. Rehydration of vesicles leads to the formation of large sized liposomes. Oligolamellar vesicles are also prepared by this technique.

Table 8.2: Liposomal Herbal Formulations

Formulations	Active Ingredients	Applications	Biological Activities	Preparation Methods	Administration Routes
Quercetin liposomes	Quercetin	Reduces dose and enhances penetration in BBB	Antioxidant and anticancer	Reverse evaporation	Intranasal
Liposome encapsulated silymarin	Silymarin	Improves bioavailability	Hepatoprotective	Reverse evaporation	Buccal
Liposoma artemisia arboresence	Artemisia arboresence essential oil	Enhances penetration in cytoplasmic barrier	Antiviral	Film method and sonication	*In vitro*
Ampelopsin liposome	Ampelopsin	Increases efficiency	Anticancer	Film-ultrasound	*In vitro*
Paclitaxel liposome	Paclitaxel	High entrapment efficiency and pH sensitive	Anticancer	Thin film hydration	*In vitro*
Curcumin liposome	Curcumin	Long circulating and high entrapment efficiency	Anticancer	Ethanol injection	*In vitro*
Garlicin liposomes	Garlicin	Increases efficiency	Antioxidant for lungs	Reverse phase evaporation	–
Flavonoids liposomes	Quercetin and rutin	Enhances binding of flavonoids with Hb	Antioxidant for Hb	Solvent evaporation	*In vitro*

Usnea acid liposomes	Usnea acid	Increases solubility and localisation	Antimicrobial	Hydration of a thin lipid film with sonication	*In vitro*
Wogonin liposomes	Wogonin	Sustained release effect	Anticancer	Film dispersion	*In vivo*
Colchicine liposomes	Colchicine	Enhances skin accumulation and prolong release	Anti-gout	Rotary evaporation sonication	Topical
Catechins liposomes	Catechnins	Increases permeation through skin	Antioxidant and chemoprotective	Rotary evaporation sonication	Transdermal
Breviscapine liposomes	Breviscapine	Sustained delivery	CVDs	Double emulsification	Intramuscular

8.2.4.3. Niosomes

Niosomes (**figure 8.4**) are microscopic lamellar structures formed by admixture of a non -ionic surfactant, cholesterol and a charge -inducing agent with subsequent hydration in aqueo us media. They are made up of both hydrophobic and hydrophilic moieties, and thus can accommodate drug molecules with a wide range of solubility. Niosomes have been evaluated in many pharmaceutical and therapeutic applications due to their ability to reduc e systemic toxicity by encapsulation of treatment agents and minimise clearance of such agents from the body by slow drug release.

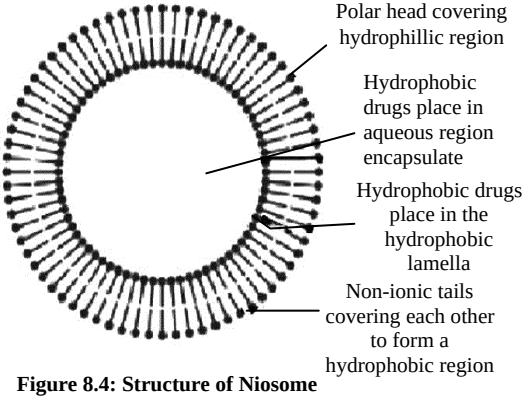


Figure 8.4: Structure of Niosome

Advantages

1) They are biodegradable, biocompatible, non-toxic, and non-immunogenic.
2) They can encapsulate large amount of materials in a small volume of vesicles.
3) They provide better patient adherence and satisfaction and better effectiveness than conventional oily formulations.
4) They can entrap wide range of hydrophilic, lipophilic and amphiphilic drugs due to their unique structure.
5) Their shape, fluidity and size can be easily controlled by changing their structural composition and production method.
6) They can be administered via oral, parenteral, topical, etc. routes in different dosage forms such as semi-solids, powders, suspensions, etc.
7) Their storage is easy due to chemical stability of structural composition.

Methods of Preparation

Niosomes are prepared by hydration of a surfactant and lipid mixture at elevated temperatures, followed by niosome size reduction to obtain a colloidal suspension. Some well -studied standard methods for preparation of niosomes

include ether injection, hand shaking, sonication and microfluidisation methods. Subsequently, the non -entrapped drug is separated from the entrapped drug by centrifugation, gel filtration, or dialysis. Some common preparative methods of niosomes are discussed below:

1) **Passive Trapping Techniques:** These include most of the techniques used for preparing niosomes in which drug is incorporated:
   i) In **ether injection method**, the surfactant is dissolved in diethyl ether. The resultant solution is injected through a 14 -gauge needle into an aqueous solution of drug maintained at 60°C. This results in the evaporation of ether and subsequent formation of single -layered vesicles with 50-1000nm diameters. However, a small amount of residual ether often remains in the niosomal suspension.
   ii) In **hand-shaking** or **thin-film hydration method**, surfactant and cholesterol are dissolved in a volatile organic solvent and transferred to a rotary evapora tor. After evaporation, a thin layer of solid mixture gets deposited on the walls of the flask. This dried layer is hydrated with an aqueous phase containing the drug to be entrapped. This process is carried out at room temperature with gentle agitation.
   iii) In **sonication method**, a mixture of surfactant, cholesterol, and aqueous phase containing the drug are sonicated at 60°C for 3 minutes. As a result, small and uniformly sized vesicles are produced.
   iv) In **microfluidisation method**, two fluidised streams move forw ard through a precisely defined micro -channel, and interact with each other at an ultra-high velocity to form uniformly sized niosomes.
   v) In **reverse phase evaporation technique** , cholesterol and surfactant (in 1:1 ratio) are dissolved in a mixture of ether an d chloroform. On adding aqueous drug solution to this, water-in-oil emulsion is formed. Then, two phases are sonicated at 4 -5ºC and the emulsion is dried in a rotary evaporator at 40 °C to form a semi -solid gel of large vesicles. Phosphate Buffered Saline (PBS) is added in small amounts to the clear gel and sonicated again. The organic phase is removed at 40ºC under reduced pressure. Viscous niosomal suspension is diluted with phosphate buffered saline, and heated on a water bath at 60ºC for 10 minutes to form niosomes.
   vi) In **multiple membrane extrusion method** , a mixture of surfactant, cholesterol and dicetyl phosphate in chloroform forms a thin film by rotary evaporator. This film is hydrated with aqueous drug polycarbonate membranes. Solution and the resultant suspension are extruded through polycarbonate membrane and placed in a series for up to 8 passages.
2) **Active Trapping Techniques:** These include loading of the drug after the formation of niosomes. Niosomes are prepared and the drug is loaded under maintained pH gradient or ion gradients to facilitate uptake its drug into the niosomes. Noisomes formed by this method offers advantages of 100% entrapment, high drug-lipid ratios, absence of leakage, cost effectiveness, and suitability for labile drugs.

3) **Trans-Membrane pH Gradient Drug Uptake Process**

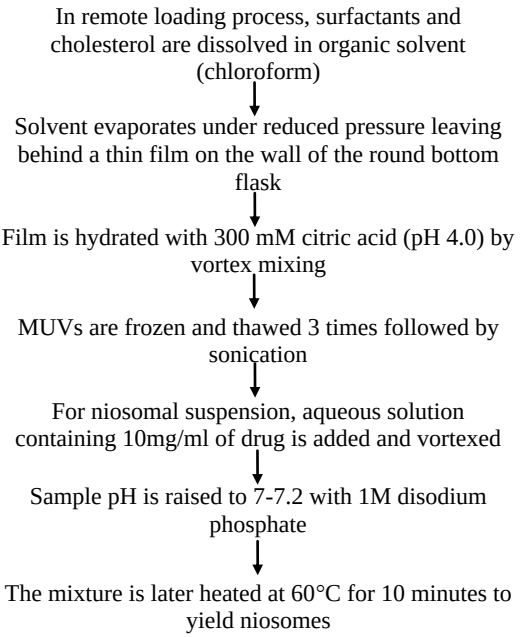


Figure 8.5: Trans-Membrane pH Gradient Drug Uptake Process of Preparing Niosomes

4) **Miscellaneous Methods:** These include the following methods:

i) **Emulsion Method:** In this simple method, oil -in-water emulsion is prepared from an organic solution of surfactant, cholesterol, and a n aqueous solution of drug. Then, the organic solvent is evaporated and niosomes are dispersed in the aqueous phase.

ii) **Heating Method:** In this one -step, scalable, and non -toxic method, suitable aqueous medium (buffer distilled water, etc.) is added with mixtures of non -ionic surfactants, cholesterol and/or charge -inducing molecules in the presence of a polyol (glycerol). The resultant mixture is heated (at low shear forces) until the vesicles are formed.

iii) **Formation of Niosomes from Proniosomes:** Proniosomes are dry formulations in which each water -soluble particle is covered with a thin film of dry surfactant. Niosomes are recognised by adding aqueous phase with brief agitation when T > Tm; where, T is temperature and Tm is the mean phase transition temperature.

iv) **Lipid Injection Method:** In this method, a mixture of lipids and surfactant is melted and then injected into a highly agitated heated aqueous phase containing the dissolved drug. Drug dissolves in molten lipid and the mixture is injected into agitate, heat aqueous phase containing surfactant.

Table 8.3: Applications of Niosomal Herbal Formulations

Drugs	Applications of Herbal Niosomes	Biological Activities
Colchicine	Prolongs release profile	Rheumatic complaints
Silymarin	Increases drug bioavailability	Liver and gallbladder disorders

8.2.4.4. Transferosomes

The term **transferosome** means **carrying body**, and is derived from the Latin term ***transferre*** meaning **to carry across** , and from the Greek term ***soma*** meaning **body**. Transferosomes are artificial vesicles resembling the natural cell vesicle, thus are suitable for targeted and controlled drug delivery. Transferosomes are vesicular system made up of phospholipids as the main ingredient with 10 -25% surfactant (such as so dium cholate) and 3 -10% ethanol. The surfactants work as edge activators and impart ultra-deformability to transferosomes, to help them to squeeze through the pores in stratum corneum.

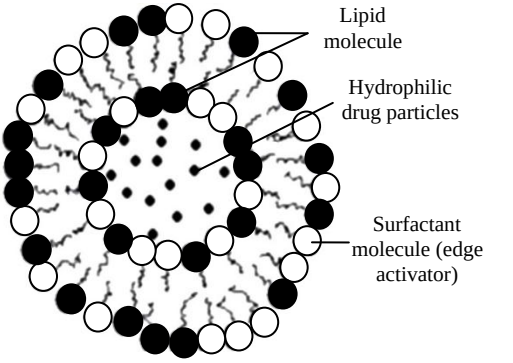


Figure 8.6: Structural Representation of a Transferosome

Advantages

1) They can deform and pass through the narrow constriction (from 5-10 times less than their own diameter) without measurable loss.
2) They have high entrapment efficiency, in case of lipophilic drug near to 90%.
3) Their high deformability allows better penetration of intact vesicles.
4) They can act as a carrier for low and high molecular weighed drugs, **e.g.,** analgesics, anaesthetics, corticosteroids, sex hormones, anti -cancers, insulin, gap junction proteins, and albumin.
5) They are made up of hydrophobic and hydrophilic moieties, thus can accommodate drug molecules with a wide range of solubility.
6) They act as depot and release their contents at a slow and steady rate.
7) They can be used for systemic as well as topical drug delivery.
8) They are biocompatible and biodegradable as they consist of natural phospholipids.
9) They protect the encapsulated drug from metabolic degradation.
10) They are easy to scale up, as the procedure is simple and short, and avoid the unnecessary use of pharmaceutically unacceptable additives.

Methods of Preparation

1) Thin film hydration method,
2) Modified hand shaking method, and
3) Lipid film hydration technique.

Table 8.4: Transferosomes Herbal Formulations

Biological Sources	Categories	Applications	Uses	Active Ingredients
Capsicum annum	Resin	Increases skin penetration	Treatment of rheumatism	Capsaicin
Curcuma longa	Resin	Increases skin permeability	Anti-inflammatory	Curcumin
Catharanthus roseus	Indole alkaloid	Increases permeability	Anticancer	Vincristine
Colchicum automnale	Amino alkaloid	Reduces GIT effects	Treatment of gout	Colchicine

8.2.4.5. Ethosomes

Ethosomes (**figure 8.7**) are slightly modified version of well -established drug-carrier liposome. They are soft lipid vesicles made up of phospholipids, alcohol (ethanol and isopropyl alcohol in relatively high concentration), and water. Their size range may vary from tens of na nometers (nm) to microns (μ). Ethosomes rapidly permeate through the skin layers and possess higher transdermal flux.

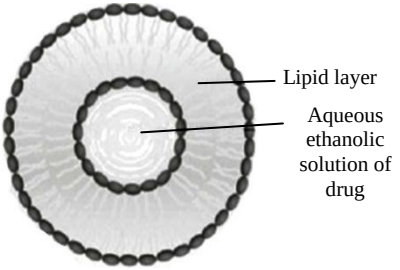


Figure 8.7: Structural Representation of an Ethosome

Advantages

1) They are used for delivering large molecules (peptides and proteins).
2) They contain non-toxic raw materials.
3) They enhance drug permeation through skin for transdermal drug delivery.
4) They can be widely used in pharmaceutical, veterinary, and cosmetic fields.
5) They provide high patient compliance when administrated in semi-solid form (gel or cream).
6) They are passive, noninvasive, and available for immediate commercialisation.

Methods of Preparation

1) Cold method,
2) Hot method, and
3) Classic mechanical dispersion method.

Table 8.5: Ethosomal Herbal Formulations

Biological Sources	Categories	Applications	Uses	Active Ingredients
Glycyrrhiza glabra	Triterpenoid saponins glycoside	Improved anti - inflammatory activity and sustained release action	Treatment of dermatitis, eczema and psoriasis	Ammonium glycyrrhizinate
Cannabis sativa	Renin	Improved patient compliance and increased skin permeation	Treatment of rheumatoid arthritis	Tetrahydrocanna bi-diol (THC)
Tripterygium wilfordii	Diterpene oxide	Increased percutaneous permeability	Anti-inflammatory and anti-tumour	Triptolide
Sophora alopecuroides	Quinazoline alkaloid	Increased permeability	Anticancer and anti-endotoxic	Matrine, oxymatrine, sophoridine, and sophocarpine (alkaloid extract)
Curcuma longa	Resins	Improved bioavailability	Anti-inflammatory	Curcumin

8.3. SUMMARY

The details given in the chapter can be summarised as follows:

1) **Herbal formulations** are dosage forms that consist of one or more herbs or processed herbs in specified quantities to provide specific nutritional and cosmetic benefits meant to be utilised for diagnosing , treating, mitigating diseases of human beings or animals, and for altering the structure or physiology of humans or animals.
2) Tinctures, extracts, essential oils, expressed juices, and processed exudates are the different herbal formulations.
3) A saturate d solution of sucrose formed in purified water with the concentration of 66% w/w sugar is known as **simple syrup**.
4) Syrups are sweet, viscous, concentrated aqueous solutions of sucrose or other sugars.
5) Syrups containing therapeutic or medicinal agents are **medicated syrups**, while syrups with flavours but no medicinal agents are **flavouring** or **flavoured** or **non-medicated syrups**.
6) **Simple syrups** are made up of simple solutions or are admixture of solutions.
7) **Medicated syrups** include therapeutic agents.
8) **Flavoured sy rups** comprise of different flavoured or aromatic substances, which impart a pleasant smell and taste.
9) **Hot process** method is not suitable for heat-labile or volatile ingredients.
10) An instrument known as **saccharometer** is used for determining the specific gravity of the syrup.
11) **Percolation method** is used for preparing U.S.P. syrup.
12) The method of **addition of medicating or flavouring liquid to syrup** is used for preparing syrups containing fluid extracts, tinctures, or other liquids.
13) The method of **agitation without heat** is used when the active constituent is heat-labile.
14) **Mixtures** are liquid dosage forms meant for oral administration.
15) **Homogeneous mixtures** consist of uniformly spread particles and possess certain consistent and specific properties.
16) **Heterogeneous mixtures** do not have uniformity and consistency in their composition.
17) **Suspensions** consist of two components in which the size of the particle of at least one component must be larger than the colloidal particles, i.e., greater than 1000nm (1μm), in at least one direction.
18) **Colloidal dispersions** are a mixture of components present in one or more phases.
19) **Positive mixtures** are irreversible in nature.
20) **Negative mixtures** form reversible mixtures.
21) In **neutral mixtures** , the substances are not instantly miscibl e with each other but when mixed, they form stable and irreversible mixtures.
22) In **perfect mixtures** , two types of particles sampled randomly from any mixture contain same proportion of each particle as the proportions of the sampled particles found in the mixture taken as a whole.

23) **Chemical stabilisers** possess antioxidant or reducing properties and are employed in the preparation of mixtures to enhance their chemical stability.
24) Chloroform (0.25%v/v) and benzoic acid (0.1%w/v) are used as preservatives in the mixtures to prevent the growth of microorganisms.
25) **Simple mixtures containing soluble substances** consist of only those ingredients which are soluble in it.
26) In **mixtures containing indiffusible solids** , a suspending agent is used for uniformly distributing the drug substance throughout the preparation as the indiffusible solids do not get solubilised in water and thus do not remain distributed uniformly for longer time in the vehicle of the mixture.
27) **Mixtures containing slightly soluble liquid** are added wit h a suspending agent to dissolve and diffuse the insoluble part of the slightly soluble liquids.
28) Tablets are **solid unit dosage form of medicaments** with or without suitable diluents and **prepared** either by **moulding** or **compression**.
29) According to the **Indian Pharmacopoeia**, pharmaceutical **tablets** are solid, flat, or biconvex discs, unit dosage form, prepared by compressing drugs or a mixture of drugs, with or without diluents.
30) **Phytosome** is a novel technology that emerged in **1989**. The term **phyto** means **plant/herb** and **some** means **cell-like structure**.
31) **Liposomes**are bilayer vesicular carrier systems of phospholipids or cholesterol.
32) The **mechanical method of liposomal preparation** includes the simplest film method in which an organic solvent is used to hydrate the thin lipid film.
33) Another mechanical method of liposomal preparation includes **ultrasonic method**, in which ultrasonication process is employed for forming liposomes.
34) In **replacement of organic solvent** method, the lipid is co-solvated by using an organic solutio n, which is later dispersed into aqueous phase containing the material to be entrapped in the liposome.
35) **Ether vaporisation method** is further differentiated as **ethanol injection method** and **ether injection method** on the basis of the solvent used.
36) Another method of liposomal preparation involves the **fusion of pre-formed vesicles** or **transformation of size**, which can be further categorised as **FTE method** and **DR method**.
37) **Niosomes** are microscopic lamellar structures formed by admixture of a non-ionic surfactant, cholesterol and a charge -inducing agent with subsequent hydration in aqueous media.
38) In **microfluidisation method**, two fluidised streams move forward through a precisely defined micro-channel, and interact with each other at an ultrahigh velocity to form uniformly sized niosomes.
39) The term **transferosome** means **carrying body** , and is derived from the Latin term ***transferre*** meaning **to carry across** , and from the Greek term ***soma*** meaning **body**.
40) **Transferosomes** are artificial vesicles resembling the natural cell vesicl e, thus are suitable for targeted and controlled drug delivery.
41) **Ethosomes** are slightly modified version of well -established drug -carrier liposome.

8.4. EXERCISE

8.4.1. True or False

1) Hot process method is used for preparing U.S.P. syrup.
2) Homogeneous mixtures do not have uniformity and consistency in their composition.
3) Negative mixtures form irreversible mixtures.
4) In neutral mixtures , the substances are not instantly miscible with each other but when mixed, they form stable and irreversible mixtures.
5) Ether vapori sation method is further differentiated as ethanol injection method and ether injection method on the basis of the solvent used.
6) Niosomes are slightly modified version of well-established drug-carrier liposome.

8.4.2. Fill in the Blanks

7) _____ are made up of simple solutions or are admixture of solutions.
8) _____ is used for determining the specific gravity of the syrup.
9) _____ are liquid dosage forms meant for oral administration.
10) _____ are a mixture of components present in one or more phases.
11) The term _____ means plant/herb and some means cell-like structure.
12) The term transferosome is derived from the Latin term _____ and from the Greek term _____ .

Answers

1) False	2) False	3) False
4) True	5) True	6) False
7) Simple syrups	8) Saccharometer	9) Mixtures
10) Colloidal dispersions	11) Phyto	12) *transferre and soma*

8.4.1. Very Short Answer Type Questions

1) Define herbal formulations.
2) What are syrups?
3) Classify mixtures depending on miscibility.
4) Classify tablets.
5) Give the ideal properties of tablets.
6) Enlist a few examples of phytosomal herbal formulations.
7) Draw a well-labelled structure of niosomes.
8) Mention two examples each of transferosomes and ethosomes.

8.4.2. Short Answer Type Questions

1) Write about preparation of syrups.
2) Discuss the formulation methods of mixtures.
3) Give the advantages and disadvantages of tablets.
4) Discuss the importance of novel drug delivery systems in herbal medicines and their advantages.
5) Discuss the preparation of liposomes.
6) Discuss all the preparative methods of niosomes.

8.4.3. Long Answer Type Questions

1) Briefly discuss about mixtures used as herbal formulations.
2) Give a brief review on any two types of novel herbal drug delivery system.

CHAPTER 9

Evaluation of Drugs

9.1. EVALUATION OF DRUGS

9.1.1. Introduction

A drug is evaluated for identifying it, determining its quality and purity, and detecting the adulteration type. Crude drug evaluation is required for studying the:

1) Biochemical variation a drug undergoes,
2) Deterioration while being treated and during storage, and
3) Substitution and adulteration due to carelessness, ignorance, or fraud.

A drug can be evaluated by the following **6 methods**:

1) Organoleptic evaluation,
2) Microscopic evaluation,
3) Physical evaluation,
4) Chemical evaluation, and
5) Biological evaluation.

9.1.2. Organoleptic Evaluation

Organoleptic evaluation of a drug involves determining its colour, odour, taste, size, shape, touch, texture, etc. It is a qu alitative evaluation type in which the morphological and sensory characters of drugs are studied. Study of a drug's macroscopy involves its visual appearance to the naked eye. This study depends on the plant part from which the drug is derived. A specific systematic examination is performed for specific morphological group.

The organised drugs of the following morphological groups are classified as:

1) **Barks:** The woody stem tissues present on the outer surface of inter - fascicular cambium form the bark drugs, **e.g.,** cinnamon, cinchona, quillaia, ashoka, kurchi bark, etc. Barks are collected as narrow strips by strip ping them from the trunk or branches of the desired trees. After collection, the barks are dried during which they attain different shapes (**figure 9.1**) by undergoing unequal contractions.

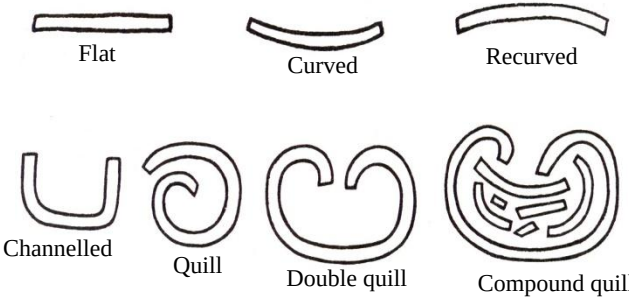


Figure 9.1: Different Shapes of Bark Drugs

2) **Underground Structures:** These structures are of different forms and are used by the plants for storing food. The underground plant parts are mostly swollen, thus are cut into either thin slices or small pieces to ease their drying. The dark coloured cork in some drugs is removed in order to obtain a light coloured product. Some **examples** of underground plant parts are roots, rhizomes, and stolons.

Roots do not have buds, scale leaves, or leaf scars, but a central core of woody xylem tissue is present (as in podophyllum, liquorice, jatamansi, and rauwolfia). On the other hand, rhizomes and stolons are underground stems in which buds, scale leaves, and leaf scars are present, along with central pith (as in ginger, turmeric, and dioscorea). Underground roots and rhizomes of various shapes are shown in **figure 9.2**:

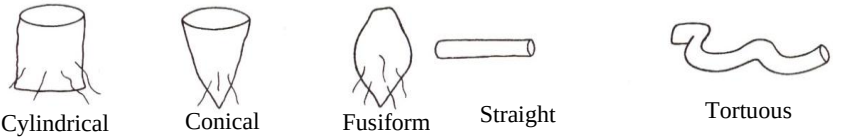


Figure 9.2: Different Shapes of Underground Drugs

3) **Leaves:** These are of different shapes and sizes. A **simple leaf** contains all the photosynthetic organs originating from a node on a stem; whil e a **compound leaf** has many leaflets (**figure 9.3**).

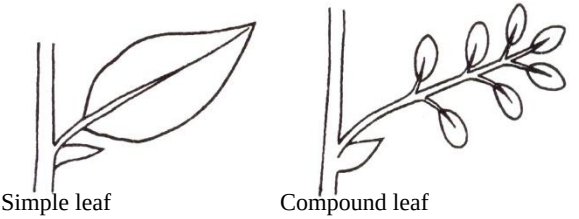
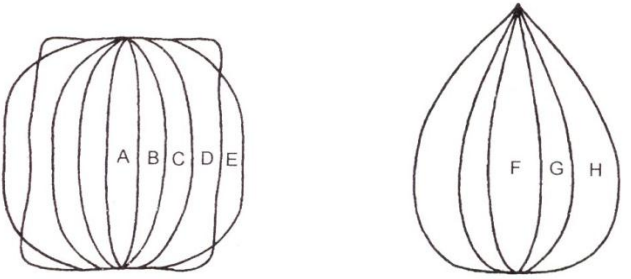


Figure 9.3: Types of Leaf

Leaves of various shapes, their margin, base, apex, and venation are given in **figure 9.4**. These characteristics aid in drug identification.



A: Acicular; B: Elliptical; C: Oval; D: Oblong Round; E: Round

F: Linear; G: Lanceolate; H: Ovate

Figure 9.4: Different Shapes of Leaves

4) **Flowers:** These are the reproductive plant pa rts found in a variety of forms and also grow on the plant in different manners. The 4 parts of a flower are **calyx**, **corolla**, **androecium**, and **gynoecium**. Some plants consisting of flowering structures further consist of individual flowers, thus forming an **inflorescence**.

5) **Fruits:** These globular -, oblong -, or ellipsoidal -shaped plant parts having seeds are often specialised to help in seed dispersal. Fruits mainly develop from the ovary and sometimes from other flower parts. Some **examples** of fruits are cardamom, colocynth, bael, etc. Fruits are of the following **types**:
   i) **Simple Fruits:** These fruits develop from a single carpel or from syncarpous gynoecium. Simple fruits are categorised into **dry** and **fleshy fruits** based on whether the mesocarp is dry or fleshy. Dry fruits are further sub-categorised into **dehiscent** and **indehiscent fruits**.
   ii) **Aggregate Fruits:** These fruits develop from more than one carpels or apocarpous gynoecium.
   iii) **Compound Fruits:** These fruits develop from numerous flowers combined together.

6) **Seeds:** These plant parts develop from the ovules present in the carpels of flowers. Seeds are characterised by a scar left by the funicle (called **hilum**), by a small hole in the ovule marking the entrance point of the pollen tube during fertilisation (called **micropyl)**, or by a vascular tissue ridge connecting the hilum and chalaza (called **raphe**). Some **examples** of seeds are ispaghula, linseed, nux -vomica, psoralea, etc. Seeds of different shapes and types are given in **figure 9.5**:

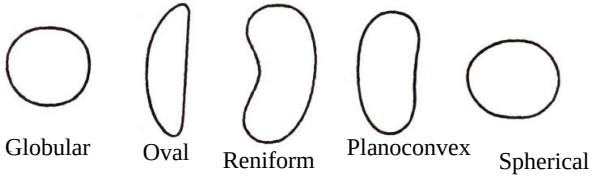


Figure 9.5: Different Shapes of Seeds

7) **Herbs:** A herb should be fully des cribed with a systematic description of stems, leaves, flowers, and fruits present in it.

8) **Sensory Characters:** These include colour, smell, taste, and texture of the drug being evaluated. Drugs containing volatile oil (**e.g.,** cardamom, clove, or cinnamon) h ave a characteristic **odour** which will not be present if the drugs lose their volatile oil content. The **taste** of drugs may be pungent (**e.g.,** capsicum and ginger), bitter (**e.g.,** gentian and chirata), and sweet (**e.g.,** glycyrrhiza). A drug's **texture** is observed by breaking a piece of it. A drug's **fracture** depends on the nature of tissues and the method of drying it; **for example**, the fracture of glycyrrhiza is hard and fibrous as they have woody and fibrous tissues; the fracture of aconite dried at high tempera ture is horny as the starch present in it undergoes gelatinisation.

9.1.3. Microscopic Evaluation

Microscopic evaluation of a drug allows detailed examination so that the organised crude drugs (either in entire or powdered forms) c an be identified by their known histological features. It is a qualitative evaluation type involving identification of organised drugs by cutting them in Transverse Section (T.S.), Longitudinal Section (L.S.), Radial Longitudinal Section (R.L.S.), or Tange ntial Longitudinal Section (T.L.S.).

Due to its magnification property, a microscope enlarges the minute structure being studied and also confirms the structural details of drugs obtained from plants. Effective results can be obtained by distinguishing the cellular structure using various reagents or stains. Microscopic evaluation also involves studying constituents by applying chemical tests to small quantities of powdered drugs or to histological sections of drugs. Histological studies are conducted with very thin sections of drugs. Detailed study of the characteristics of cell wall, cell contents, trichomes, fibres, vessels, etc. can be obtained by microscopic evaluation. Microscopic evaluation also involves microscopic linear measurement and quantitative microscopy.

9.1.3.1. Leaf Constants

Given below are some of the leaf constants:

1) **Palisade Ratio:** It is the average number of palisade cells present below each epidermal cell. It is determined using powdered drugs.
2) **Vein-Islet Number:** It is the number of vein -islets present in per sq. mm of the leaf surface midway between the midrib and margin.
3) **Vein-Termination Number:** It is the number of veinlet terminations present in per sq. mm of the leaf surface midway between the midrib and margin.
4) **Stomatal Number:** It is the average number of stomata present in per sq. mm of leaf epidermis.
5) **Stomatal Index:** It is the percentage which the number of stomata forms to the total number of epidermal cells; each stoma being counted as one cell. It is calculated by:

$$S.I. = \frac{S}{E + S} \times 100$$

Where, S.I. = Stomatal Index.
S = Number of stomata per unit area.
E = Number of epidermal cells in the same unit area.

The leaf constants are determined for microscopic evaluation of some leaf dru gs, **e.g.,** senna, datura, digitalis, buchu, coca, belladonna, etc.

9.1.3.2. Stomata

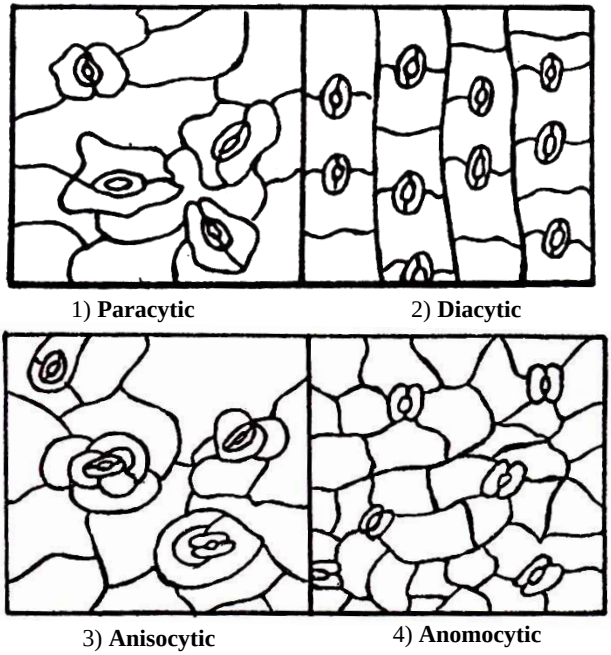
A stoma is a **minute epidermal opening** having a **central pore**, and two kidney-shaped **guard cells** containing chloroplasts; the guard cells are covered by a variable number of subsidiary (epidermal) cells. All the plants do not necessarily have stomata; **for example**, the leaves of bryophytes and submerged leaves of aquatic parts lack stomata.

Stomata are basically present in leaves (green plant p arts), most abundantly in dicot leaves. In some plants, they are present on the upper surface of leaves, in some on the lower surface of leaves (**e.g.,** coca and cherry), while in others on both the surfaces (**e.g.,** senna, belladonna, datura, etc.). The stoma ta distribution between upper and lower epidermis in dicot leaves presents great variation. Stomata may also be present in stems (ephedra), flowers (clove), and fruits (fennel). They are absent in roots.

Functions of Stomata: Its primary function is **gaseous exchange** and secondary function is **transpiration**.

Types of Stomata: Stomata are divided into **four types** based on the **type of guard cells** and **arrangement of subsidiary cells** . The fourth type of stomata shows diagnostic significance. The stomata types are:

1) Moss type,
2) Gymnospermous type,
3) Gramineous type, and
4) Dicotyledonous type.



1) **Paracytic** 2) **Diacytic**

3) **Anisocytic** 4) **Anomocytic**

Figure 9.6: Types of Dicotyledonous Stomata

Dicotyledonous Stomata: These stomata based on the form and arrangement of subsidiary cells, are divided into:

1) **Paracytic or Rubiaceous or Parallel -Celled Stomata:** These stomata have two guard cells covered with two subsidiary cells, whose long axes are arranged parallelly to that of the stoma, **e.g.**, coca and senna leaves.
2) **Diacytic or Caryophyllaceous or Cross -Celled Stomata:** These stomata have two guard cel ls covered with two subsidiary cells arranged at right angle to the stoma, **e.g.**, peppermint, spearmint, and vasaka.
3) **Anisocytic or Cruciferous or Unequal -Celled Stomata:** These stomata have two guard cells covered with three subsidiary cells (one is smaller than the other two), **e.g.**, belladonna, datura and stramonium.
4) **Anomocytic or Ranunculaceous or Irregular -Celled Stomata:** These stomata are surrounded by a variable number of subsidiary cells (similar to other epidermal cells), **e.g.**, buchu, digitalis, and lobelia.

9.1.3.3. Trichomes

Trichomes are also important diagnostic feature used for identifying drugs and detecting adulterants. Trichomes (or **plant hair**) are outgrowths of the epidermal cell either **tubular**, or **elongated**, or **glandular** in shape.

The two parts of trichomes are **root** (inside the epidermis) and **body** (outside the epidermis). Although trichomes are functionless, sometimes they perform secretory functions; they excrete water and volatile oil (**e.g.,** in peppermint). Trichomes are found in leaves (**e.g.,** senna and digitalis), seeds (**e.g.,** nux-vomica and strophanthus), fruits (**e.g.,** *Helicteres isora* and lady finger), etc. Thus, they are present only in the aerial parts of plant, and not in roots. They are absent in coc a, sevin, and hemlock; and sometimes present in buchu and henna.

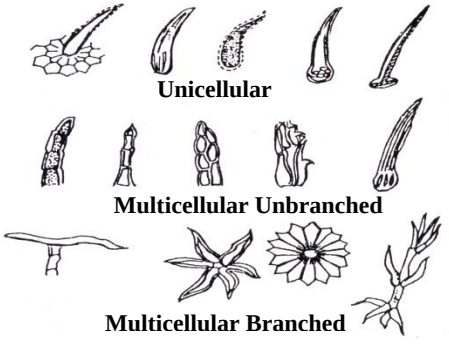


Figure 9.7: Types of Covering Trichomes

Trichomes are classified as follows based on the structure and number of cells present in them (**figure 9.7**):

1) **Covering Trichomes**
   i) **Unicellular**
      a) Lignified trichomes (**e.g.**, nux-vomica and strophanthus).
      b) Short, sharply pointed, curved trichomes (**e.g.**, cannabis).
      c) Large, conical, strongly shrunken trichomes (**e.g.**, lobelia).
      d) Short, conical, unicellular trichomes (**e.g.**, tea and buchu).
      e) Strongly waved, thick-walled trichomes (**e.g.**, *Yerba santa*).

   ii) **Multicellular – Unbranched Trichomes**
      a) **Uniseriate**
         - Bi-cellular, conical trichomes (**e.g.**, datura).
         - Three-celled long trichomes (**e.g.**, stramonium).
         - Three- to four-celled long trichomes (**e.g.**, digitalis).
         - Four- to five-celled long trichomes (**e.g.**, belladonna).

      b) **Biseriate: e.g.**, *Calendula officinali*s.

      c) **Multiseriate: e.g.**, Male fern.

   iii) **Multicellular - Branched Trichomes**
      a) **Stellate: e.g.**, Hamamelis and *Helicteres isora*.
      b) **Peltate: e.g.**, Humulus.
      c) **Candelabra: e.g.**, *Verbascum thapsus.*
      d) **T-shaped Trichomes: e.g.**, Artemisia and pyrethrum.

2) **Glandular Trichomes:** At the top of t hese trichomes, glandular (spherical) cells are present. These trichomes are further classified into:
   i) **Unicellular Glandular Trichomes:** In these trichomes, the stalk is absent, **e.g.**, piper, betel, and vasaka.

   ii) **Multicellular Glandular Trichomes:** These trichomes are further divided into:
      a) Trichomes with unicellular head and stalk, **e.g.**, *Digitalis purpurea.*

b) Trichomes with unicellular head and uniseriate multicellular stalk, **e.g.**, *Digitalis thapsi*, belladonna, etc.
c) Trichomes with multicellular head, and multicellular, biseriate stalk, **e.g.**, Santonica and plants of Compositae, such as sunflower, etc.
d) Trichomes with unicellular stalk and biseriate head, **e.g.**, *Digitalis purpurea.*
e) Trichomes with short stalk with secreting head formed of rosette or club-shaped cells, **e.g.**, mentha species.
f) Trichomes with multicellular, multiseriate, cylindrical stalk and a rosette of secretory cells, **e.g.**, *Cannabis sativa.*
g) Trichomes with multicellular, multis eriate head and multicellular, uniseriate stalk, **e.g.**, Indian hemp and tobacco.

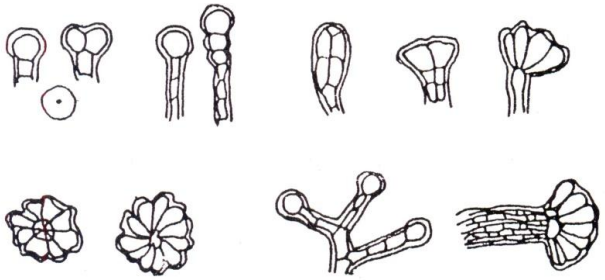


Figure 9.8: Types of Glandular Trichomes

3) **Hydathode:** These are water absorption or secretion organs developed in some particular plants, **e.g.**, *Piper betle*, London pride, etc.

9.1.3.4. Quantitative Microscopy

It involves different parameters like:

1) **Palisade Ratio:** It is the average number of palisade cells underneath each epidermal cell. **For example,** *Atropa belladonna* and *Digitalis lanata.*

2) **Stomatal Number:** It is the average number of stomata per squar e millimetre area of epidermis. **For example,** *Atropa belladonna*: 6.0 to 14 - 37.5 (upper surface), 62.5 to 93-174 (lower surface).
   i) **Stomatal Index:** It is the percentage which the number of stomata forms to the total number of epidermal cells; each stoma being counted as one cell. It is calculated by:

$$S.I. = \frac{S \times 100}{(E + S)}$$

Where, S.I. = Stomatal index.
S = Number of stomata per unit area.
E = Number of epidermal cells in the same unit area.

For example, *Atropa belladonna*: 2.3-3.9 to 10.5 (upper surface) and 20.2 to 21.7 -23.0 (lower surf ace); *Digitalis purpurea* : 1.6 -2.7 to 4.0 (Upper surface) to 19.2-25.2 (lower surface).

   ii) **Vein Islet Number:** It is the average number of vein islet per square millimeter of the leaf surface midway between midrib and the margi n. **For example,** *Digitalis lanata*: 2.0-8.0; *Digitalis purpurea*: 2.0-5.5.

iii) **Vein Termination Number:** It is the average numbers of vein terminations per square millimetre of the leaf surface midway between midrib and the margin. **For example,** *Atropa belladonna* : 6.3 -10.3; *Atropa acuminate*: 1.4-3.5.

9.1.4. Physical Evaluation

Physical evaluation of crude drugs is a necessity. The physical parameters remain constant in rare cases, but they help in evaluating the following in different solvent

1) **Moisture Content:** The active chemical constituents in crude drugs are expressed in percentage on air -dried basis. Thus, a drug's moisture content should be determined by heating it at 105°C in an oven up to a constant weight (**Table 9.1**).

Table 9.1: Crude Drugs with Moisture Content Limit

Drugs	Moisture Content Limits (%)
Aloes	Not more than 10
Digitalis	Not more than 5
Ergot	Not more than 8
Acacia	Not more than 15
Starch	Not more than 15

2) **Viscosity:** A liquid drug's viscosity at a given temperatur e is constant and is an index of its composition; thus, is used for its standardisation. **Table 9.2** shows some **examples**:

Table 9.2: Crude Drugs with Viscosity Limit

Drugs	Viscosity Limits
Liquid paraffin	Kinematic viscosity not less than 64 centistokes at 37.8°C.
Pyroxylin	Kinematic viscosity, 1100 - 2450 centistokes.

3) **Melting Point:** A crude drug's purity can be determined by its melting point. Pure chemicals or phytochemicals have very sharp and constant melting points. **Table 9.3** mentions the range of m elting points which is determined for establishing the purity of the given crude drugs:

Table 9.3: Melting Point Range for a Few Crude Drugs

Drugs	Melting Points (°C)
Colophony	75 - 85
Kokum butter	39 - 42
Cocoa butter	30 - 33
Beeswax	62 - 65
Wool fat	34 - 44

4) **Solubility:** An adulterant can be detected in a crude drug by solubility studies. Alkaloidal bases are soluble in chloroform, while alkaloidal salts are soluble in polar solvents. Glycosides can be extracted with alcohol and water, while their aglycone moieties are soluble in non-polar solvents (**e.g.,** benzene or solvent ether).

5) **Optical Rotation:** Some optically active substances either in pure form or in solution form can rotate the plane of polarised light; this property is called **optical rotation**. The plane of polarised light can be rotated either towards right (dextrorotatory) or towards left (levorotatory). Optical rotation is determined using sodium lamp (light source) at 25°C.

Optical rotations of some crude drugs are mentioned in **table 9.4**:

Table 9.4: Optical Rotation Values for a Few Crude Drugs

Drugs	Angles of Optical Rotation
Caraway oil	+75° to +80°
Castor oil	3.5° to +6.0°
Clove oil	0° to −1.5°
Honey	+3° to −15°
Eucalyptus oil	0° to +10°
Chenopodium oil	−30° to −8°

6) **Refractive Index:** A light ray bends from its original path on passing from one medium to another of different density. Thus, the ratio of light velocity in a vacuum to its velocity in substance is called **refractive index of the second medium**. This property is constant for a liquid based on purity, and can be used for its standardisation. A substance's refractive index changes with the incident light wavelength, temperature, and pressure. Refractive indices of some substances determined using sodium light at 25°C are given in **table 9.5**:

Table 9.5: Refractive Indices of Some Phytoconstituents

Drugs	Refractive Indices
Arachis oil	1.4678 - 1.470
Caraway oil	1.4838 - 1.4858
Castor oil	1.4758 - 1.527
Clove oil	1.527 - 1.535

7) **Ash Values/Content and Extractives**

i) **Ash Content:** It is the residue left behind after incineration of the drug. Ash content of drug represents inorganic salts occurring naturally in it or adhering to it or added to it purposely, as an adulterant. Total ash of the drug includes both **physiological** and **non-physiological ash**. The former is obtained from plant tissues, while latter is the residue of extraneous matter (sand, soil, etc.) found adhered to the herb. Ash content of a drug can be determined by incinerating it in powdered form so that its organic matter burns completely. Ash value of a crude drug is a standard for identifying it or determining its purity. Total ash comprises of carbonates, oxides, phosphates, silicates, and silica. **Table 9.6** enlists the total ash values of some crude drugs:

Table 9.6: Crude Drugs with their Ash Contents

Drugs	Total Ash (% w/w)	Acid Insoluble Ash (%w/w)
Agar	–	1.00
Aloe	05.0	–
Ashoka	11.0	
Bael	03.5	–
Belladonna	–	3.00
Black catechu	06.0	–
Cannabis	15.0	5.00
Cardamom	06.0	3.50
Clove	07.0	0.75
Gelatin	03.6	–
Ginger	06.0	1.7 (water-soluble ash)
Valerian	12.0	–

ii) **Extractives:** When crude drugs are exhausted they leave behind extracts which represent the estimated measures of their chemical constituents. The following types of extractives can be determined by using various solvents selected by considering the variability in chemical nature and properties of contents of drugs:

a) **Water-Soluble Extractives:** These extractives contain water-soluble active constituents of crude drugs (**e.g.,** tannins, sugars, plant acids, mucilage, glycosides, etc.), given in **table 9.7**:

Table 9.7: Water-Soluble Extractive Values of Some Crude Drugs

Drugs	Water-Soluble Extractive Values (% w/w)
Aloe	Not less than 25.0
Glycyrrhiza	Not less than 20.0
Linseed	Not less than 15.0
Senna leaves	Not less than 30.0
Senna pods	Not less than 28.0
Ginger	Not less than 10.0

b) **Alcohol-Soluble Extractives:** Various chemicals like tannins, resins, etc. are extracted using alcohol as an ideal solvent. Thus, an estimate of the resin content of drug can be determined by this method. For determining alcohol-soluble extractive, around 95% ethyl alcohol is used. Diluted alcohol is also used in some cases; however, it depends on the solubility of constituents of crude drugs. **Table 9.8** mentions the limits for alcohol-soluble extractive values for some drugs:

Table 9.8: Alcohol-Soluble Extractive Values of Some Crude Drugs

Alcohol-Soluble Extractive Values		
Drugs	**(% w/w)**	
Aloe	Not less than	10.0
Benzoin	Not less than	90.0 (Siam benzoin) 75.0 (Sumatra benzoin)
Asafoetida (90% alcohol)	Not less than	50.0
Ginger (90% alcohol)	Not less than	04.5
Valerian (60% alcohol)	Not less than	30.0
Alcohol-Insoluble Extractive Values		
Myrrh	Not less than	70.0
Benzoin	Not less than	24.0

c) **Ether-Soluble Extractives:** Volatile and non-volatile types of ether-soluble extractives are determined for crude drug evaluation. **Table 9.9** mentions the limits for non-volatile ether-soluble extractive values for some drugs:

Table 9.9: Non-Volatile Ether-Soluble Extractive Values of Some Drugs

Drugs	Limits for Non-Volatile Ether Soluble Extractives (% w/w)
Capsicum	Not less than 12.0
Male fern	Not less than 01.5
Linseed	Not less than 25.0
Nutmeg	Not less than 25.0

8) **Volatile Oil Content:** The aromatic crude drugs are pharmaceuti cally vital owing to their volatile oil content. Therefore, such drugs are standardised based on their volatile oil content . The **examples** of some drugs are given in **table 9.10**:

Table 9.10: Volatile Oil Content of Some Crude Drugs

Drugs	Volatile Oil Content (% w/w)
Caraway	Not less than 2.5
Fresh lemon peel	Not less than 2.5
Clove	Note less than 15.0
Fennel	Not less than 1.4
Dill	Not less than 2.5
Cardamom seed	Not less than 4.0

9) **Foreign Organic Matter:** The monograph of crude drugs has the maxim um limit for foreign organic matter. If the matter exceeds the mentioned limits, the drug quality declines. The limit for foreign organic matter is mentioned in the respective monographs particularly for natural drugs of vegetable origin.

The physical, as well as physicochemical parameters, are used for determining the quality profile of a crude drug, thus form an important part of qualitative evaluation.

9.1.5. Chemical Evaluation

Chemical evaluation of crude drugs involves different chemical tests and assays. It also involves isolation, purification, and identification of active constituents of drugs. Preliminary phytochemical screening forms a part of chemical evaluation. The qualitative type of chemical tests is used for detecting the adulteration type.

Chemical assay comprises of the conventional titrimetric techniques as used for determining alkaloids from crude drugs, ester and aldehyde contents of volatile oils, gravimetric methods, etc. Chemical evaluation is defined as the **chemical process of determining the active constituents in a drug**.

Acid value, iodine value, saponification value, ester value, etc. are some quantitative physicochemical constants used for evaluation of fixed oils and fats.

9.1.5.1. Phytochemical Investigations

Plant materials' investigation for their phytochemical behaviour involves the following **stages**:

1) Procurement of raw material and quality control,
2) Extraction, purification, and characterisation of the pharmaceutically active constituents,
3) In process quality control,
4) Investigations of biosynthetic pathways to particular compounds, and
5) Quantitative evaluation.

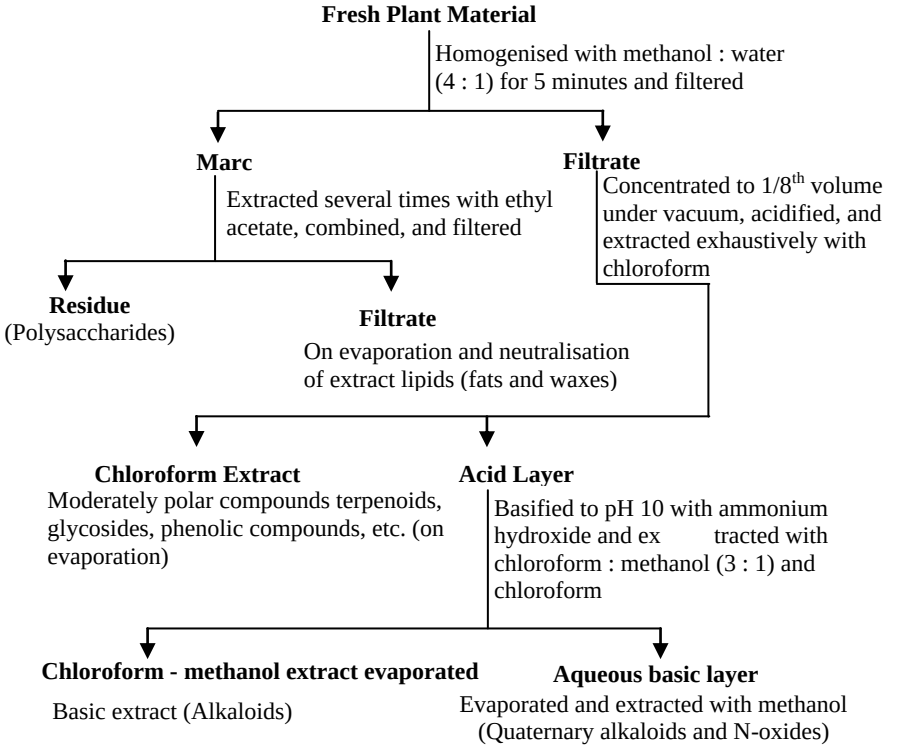


Figure 9.9: Extraction of Constituents from Plant Material

9.1.5.2. Qualitative Chemical Examination

The obtained extracts are subjected to qualitative tests for identifying the following plant constituents:

1) **Detection of Alkaloids:** Separate and small amounts of solvent -free chloroform, alcoholic and water extracts are stirred with a few drops of dilute hydrochloric acid and filtered. The filtrate obtained is tested with Mayer's, Dragendorff's, Hager's and Wagner's reagents and the presence of alkaloids is confirmed if the filtrate gives a precipitate of cream, orange, brown, yellow, and reddish-brown colour on treating with respective reagents.

2) **Detection of Carbohydrates and Glycosides:** These constituents can be detected by the following methods:
   i) 200mg of separate alcoholic and aqueous extracts are dissolved in 5ml distilled water and filtered. The obtained filtrate is then treated with Molisch's test for detecting carbohydrates.
   ii) One more small quantity of extract is hydrolysed for few hours using dilute hydrochloric acid in water bath and then treated with Liebermann - Burchard's, Legal's and Borntrager's tests for detecting different glycosides.
   iii) A small quantity of extract is dissolved in water and then treated with Fehling's, Barfoed'sand Benedict's reagents for detecting different sugars.

3) **Detection of Phytosterols:** Petroleum ether, acetone, and alcoholic extracts are separately refluxed using alcoholic solution of potassium hydroxide until they are completely saponified. The obtained mixture is subjected to dilution

with distilled water and extraction with ether. The obtained ethereal extract is evaporated and the residue (unsaponifiable matter) is treated with Liebermann's and Burchard's tests.

4) **Detection of Fixed Oils and Fats:** Petroleum ether and benzene extracts in small quantities are separately pressed between two filter papers. The presence of fixed oil is confirmed if oil stains are left on the paper. To the petroleum ether or benzene extract, a few drops of 0.5N alcoholic potassium hydroxide and one drop of phenolphthalein are added and mixed.

   The presence of fixed oils and fats is confirmed if on heating this mixture for 1-2 hours on water bath, soap is formed or the alkali undergoes partial neutralisation. The presence of volatile oil can also be confirmed by hydro - distillation of 50gm air-dried or fresh plant material.

5) **Detection of Saponins:** 1ml of alcoholic and aqueous extracts are separately diluted with distilled water up to 20ml and sha ken for 15 minutes in a graduated cylinder. The presence of saponins is confirmed if 1cm layer of foam is formed. The test solution may also be subjected to test for haemolysis.

6) **Detection of Phenolic Compounds and Tannins:** Presence of these compounds can b e confirmed by treating s mall quantities of alcoholic and aqueous extracts in water with 5% dilute ferric chloride solution, 1% gelatin solution containing 10% sodium chloride, 10% lead acetate, and aqueous bromine solutions.

7) **Detection of Proteins and Free Amino Acids:** Presence of these compounds can be confirmed by dissolving small quantities of alcoholic and aqueous extracts in a few ml of water and subjecting the resulta nt solution to millon's, biuret and ninhydrin tests.

8) **Detection of Gums and Mucilages:** 10ml of aqueous extract is mixed with 25ml absolute alcohol with constant stirring. The precipitate obtained is air - dried and examined for its swelling properties and for the presence of carbohydrates.

9) **Detection of Volatile Oils:** These can be detected by hydro-distillation of 50gm powdered material in a volatile oil estimation apparatus. In the distillate (collected in the graduated tube of the assembly), the aqueous portion automatically separates out from the volatile oil portion (if present in the drug), after which it is returned back to the distillation flask.

9.1.6. Biological Evaluation

Some drugs need to be evaluated by biological means if not successfully assayed by chemical or physical methods of evaluation. Biological eval uation is performed using whole animals, animal preparations, isolated living tissues, or microorganisms.

This assay method is termed **biological assay** or **bioassay** as living organisms are used. The methods of biological evaluation are comparatively less p recise, more time-taking, and expensive.

With the help of a biological assay, the biological activity of a given sample can be determined. In a complete single test, animals of one strain only should be used. Bioassay is the measure of the capability of s ample under test to produce a biological effect in comparison to the standard preparation. Such activity is represented in units known as **International Unit (I.U.)**.

9.1.6.1. Biological Testing of Herbal Drugs

Herbal drugs are standardised by the methods of evaluating their biological efficacy. These methods utilise an animal model suitable for testing and control, experimental methods, and result assessment. The **protocols** for evaluation of the following biological activities are discussed below:

1) **Hepatoprotective Activity:** Male/female albino rats are used for evaluating this activity. Hepatitis is caused by the hepatitis virus, and also by certain chemicals, drugs, industrial pollutants, ethyl alcohol, and immunogenic reactions. Carbon tetrachloride is most commonl y used for liver damage by acute toxicity; alcohol, paracetamol, and rifampicin can also be used for the same purpose as they cause sub-acute or chronic toxicity.

   Liver toxicity can be evaluated by the following **parameters**:
   i) Physiological (hexobarbital hypnosis),
   ii) Biochemical serum estimation of enzymes like SGPT, SGOT, superoxide dismutase, and other factors like blood proteins, cholesterol, triglyceride levels, etc., and
   iii) Histopathological (liver tissue necrosis and fatty degeneration).

2) **Hypoglycaemic Activi ty:** Several plant extracts, **e.g.,** karela (*Momordica charantia*), jambul (*Syzygium cumini*), fenugreek (*Trigonella foenum - graecum*), and gudmar (*Gymnema sylvestre*) have been used for evaluation of their hypoglycaemic activity. These extracts are used for treat ing diabetes mellitus. During the test, diabetes is experimentally induced in animals by a suitable dose of alloxan (derived from urea), which causes selective necrosis of pancreatic β-cells, thus inducing moderate diabetes (having fasting blood sugar level of 180-250mg/ml). Herbal drug extracts are used in such cases for checking their efficacy. Glucose oxidase and *ortho*-toluidine are used for measuring the **blood glucose levels** in all the cases. Radio -Immunoassay (RIA) or Enzyme Linked Immuno Sorbent Assay (ELISA) is carried out for measuring blood insulin levels.

3) **Anti-Fertility Testing:** There are many herbal drugs which have been used for testing their abortifacient or antifertility activity; however only a few have shown scientific evidences, **e.g.,** embelin from *Embelia ribes* have an abortifacient activity or gossypol from *Gossypium* species is a male anti - fertility agent. These activities occur in the following ways:
   i) **In Females**
      a) By destroying zygotes, thus leading to early abortion, and
      b) By preventing ovulation, fertilisation, or implantation.
   ii) **In Males**
      a) By acting as a spermicidal, and
      b) By acting as anti-androgenic.

Abortifacients and contraceptives are anti -fertility drugs. Anti-fertility activity in females is determined by measuring the pregnancy rate, thus including anti-ovulation and anti-implantation drugs. Anti-fertility activity in males is determined by measuring the inhibition rate of spermatogenesis or sperm motility.

4) **Anti-Inflammatory Activity:** Certain plant-derived drugs due to their anti -inflammatory activity are used for treating rheumatoid arthritis, gout, dysmenorrhoea, etc. These drugs can produce their action on many sites in the body. Inflammation can result due to mechanical causes, infections, or autoimmune diseases.

   Evaluation of anti-inflammatory activity is based on the principle of reducing local oedema induced by injecting irritant, inflammatory substances in the rat paw. Carrageenan (a mucopolysaccharide isolated from Irish Sea moss, *Chondrus cripus*) in the dose of 0.1ml, 1%w/v in sal ine is most commonly used as an inducer.

   The antagonist (herbal drug extract) is given either 60 minutes or 30 minutes before the test via oral or intraperitoneal route, respectively; and the agonist (carrageenan) is injected into plantar surface of the right hind -paw. The volume of paw is measured just after the injection and after every hour atleast for 5 times by volume displacement method, **e.g.**, using plethysmometer.

5) **Neuropharmacological Activity:** There are a large number of plants having neurological activity. Such plants, **e.g.,** opium, pilocarpus, brahmi, etc. are used for medicinal or narcotic purposes. The pharmacological spectrum and biological efficacy of these herbal drugs can be established due to the development of various neuropharmacological testing protocols.

9.1.6.2. Microbiological Assays

Drugs either suppressing or influencing the microbial growth (like antibiotics and some vitamins) are analysed by microbial assay methods.

The antibiotics can be analysed by the following microbial assay methods:

1) **Cylinder Plate Method:** In this method, a solid nutrient medium is poured in petri plates and inoculated with a microbial culture. Cylindrical holes of suitable sizes are made in the medium surface and test compound of various dilutions are poured in them.

   After incubation, the diameter of microbial growth inhibition surrounding the cylinders is measured. Inhibition produced by the test compound and that produced by the reference standard of known concentration are compared.

2) **Turbidimetric Method:** In thi s method, microbial growth inhibition indicated by turbidity (transmittance) of microbial suspensions in a fluid medium containing the test compound is measured. Transmittance changes produced by the test compound and those produced by the standard of known concentrations are compared.

9.2. WHO AND ICH GUIDELINES FOR THE ASSESSMENT OF HERBAL DRUGS

9.2.1. Introduction

According to WHO and ICH guidelines, **herbal medicines** are defined as "**finished, labelled medicinal products that contain active ingredients as aerial o r underground parts of plants, or other plant material s, or combinations thereof, whether in the crude state or as plant preparations**".

In **1991**, the **Director-General of WHO** stated the importance of medicinal plants for the health of individuals and commun ities in a report to the 44th World Health Assembly. In **1978**, the 31st World Health Assembly adopted a resolution (WHA31.33) that called on the Director -General to compile and periodically update a therapeutic classification of medicinal plants, related to the therapeutic classification of all drugs.

Thereafter, in **1987**, a resolution WHA40.33 was adopted that insisted the member states to conduct quality control of drugs obtained from traditional plant remedies by using modern techniques and suitable stan dards and good manufacturing practices. In **1989**, another resolution WHA42.43 was adopted that insisted the member states to introduce measures for regulation and control of medicinal plant products and for establishment and maintenance of suitable standards. In **1978**, the International Conference on Primary Health Care was held in Alma -Ata, USSR, and recommended, *inter alia*, the accommodation of proven traditional remedies in national drug policies and regulatory measures.

In developed and developing countr ies, current and authoritative information on the beneficial properties and potential harmful effects of all herbal medicines should be provided to consumers and health care providers.

In **1986**, the **Fourth International Conference of Drug Regulatory Authorities**, held in Tokyo, organised a workshop on the regulation of herbal medicines moving in international commerce. In **1989**, another workshop on the same matter was held in the **Fifth International Conference of Drug Regulatory Authorities** in Paris. Both the workshops put their considerations to the commercial exploitation of traditional medicines through OTC labelled products. In the meeting in Paris, it was concluded that the WHO should prepare model guidelines with basic elements of legislation to help the countries that wish to develop appropriate legislation and registration.

9.2.2. Objectives

The objective of WHO and ICH guidelines is to put forward a basic criteria for evaluating the quality, safety and efficacy of herbal medicines, and to assist national reg ulatory authorities, scientific organisations and manufacturers to evaluate the documentation/submissions/dossiers in respect of such products. As a general rule, traditional experience means that long -term use and medical, historical and ethnological background of those products should be considered.

The definition of long -term use may differ for different countries and should be at least several decades old. Therefore, the evaluation should take into account a description in the medical/pharmaceutical l iterature or similar sources, or a documentation of knowledge on the application of an herbal medicine without a clearly defined time limitation. Marketing authorisations for similar products should be taken into account.

These guidelines aim to provide:
1) Guiding principle for evaluating the quality with respect to the safety of herbal medicines with specific reference to contaminants and residues,
2) Model criteria for using while identifying possible contaminants and residues,
3) Example of methods and techniques, and
4) Example of practical procedures for controlling the quality of finished herbal products.

9.2.3. Assessment of Quality

Pharmaceutical Assessment

This should cover all important aspects of the quality assessment of herbal medicines. It should be suffic ient to make reference to an existing Pharmacopoeial monograph. If there is no available monograph, a monograph should be supplied and set out as in an official Pharmacopoeia. All the procedures should be in accordance with GMPs.

Crude Plant Material

The botanical definition, including genus, species, and authority, should be given to ensure correct plant identification. Definition and description of the plant part from which the medicine is derived (**e.g.,** leaf, flower, root) should be provided, along with an indication of whether fresh, dried , or traditionally processed material is used. The active and characteristic constituents should be specified, and content limits should be defined. Foreign matter, impurities, and microbial content should be defined o r limited. Voucher specimens, representing each batch of plant material processed, should be authenticated by a qualified botanist and stored for 10 years. A batch number should be assigned and put on the product label.

Plant Preparations

Plant preparatio ns include comminuted or powdered plant materials, extracts, tinctures, fatty or essential oils, expressed juices, and preparations manufactured by fractionation, purification, or concentration. The manufacturing procedure should be described in detail. If other substances are added while manufacturing plant preparations to adjust the preparation to a certain level of active or characteristic constituents or for any other purpose, the added substances should also be mentioned along with the manufacturing pr ocedure. The method adopted for identification and assay of the plant preparation should be mentioned. If an active principle cannot be identified, atleast a characteristic substance or mixture of substances should be identified (**e.g.**, chromatographic fing erprint) to ensure consistent quality of the preparation.

Finished Product
The manufacturing procedure and formula, including the amount of excipients, should be described in detail. A finished product specification should be defined. The method adopted for identification and quantification of the plant material in the finished product should also be defined. If an active principle cannot be identified, atleast a characteristic substance or mixture of substances should be identified (**e.g.**, chromatographicfingerprint) to ensure consistent quality of the product.

The finished product should comply with the general requirements for particular dosage forms. The imported finished products, should comply with the regulatory status in the country of origin. The WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce should be applied.

Stability
The physical and chemical stability of the product in the container in which it is to be marketed should be tested under specified storage conditions to establish the shelf-life.

9.2.4. Assessment of Safety

This should cover all relevant aspects of the safety assessment of a medicinal product. A principle that if the product has been traditionally used without demonstrated harm, no specific restrictive regulatory action should be taken unless new evidence demands a revised risk-benefit assessment, should be followed.

A review of the relevant literature should be provided with original articles or references to the original articles. References can be made to the existing official monograph/review results. Long-term use without any evidence of risk may indicate that a medicine is harmless; however, it is uncertain how long one can rely on long-term usage to assure the harmlessness of medicine in the light of concern expressed in recent years over the long-term hazards of some herbal medicines. The reported side effects should be documented according to normal pharmacovigilance practices.

Toxicological Studies
Toxicological studies should be a part of the assessment, and literature should be indicated as above.

Documentation of Safety Based on Experience
Documentation of a long-term drug usage should be considered while evaluating safety, thus indicating that when no detailed toxicological studies are available, documented experience of long-term use without demonstrated safety problems should form the base of risk assessment. However, it may happen that drugs used for a long period give rise to chronic toxicological risks that remain unrecognised. The period of use, the health disorders treated, the number of users, and the experienced countries should be specified. Toxicity data should be submitted if a toxicological risk is known. The assessment of dose-independent or dose-dependent risk should be documented. In case of dose-dependent risk, the dosage should be specified during risk assessment. A detailed explanation of the risks should be given. Potential for misuse, abuse, or dependence should be documented. If long-term traditional use cannot be documented or there are doubts on safety, toxicity datashould be submitted.

9.2.5. Assessment of Efficacy

This should cover all important aspects of efficacy assessment of a medicinal product. A review of the relevant literature should be made, copies of the original articles should be provided, or proper references to the original articles should be made. The existing research studies should be taken into consideration.

Activity

The pharmacological and clinical effects of the active ingredients and their constituents, along with therapeutic activity, should be described.

Evidence Required to Support Indications

The indications on medicine use should be specified. In case of traditional medicines, requirements for proof of efficacy should depend on the kind of indication. For treating minor disorders and for non-specific indications, some relaxation in requirements for proof of efficacy should be justified, considering the extent of traditional use. The same considerations should be applied to prophylactic use. Individual experiences recorded in reports from physicians, traditional health practitioners, or treated patients should be considered. Where traditional use has not been established, appropriate clinical evidence should be required.

Combination Products

The assessment should differentiate between old and new combination products. This is because many herbal remedies consist of a combination of several active ingredients, and as experience of the use of traditional remedies is based on combination products. Identical requirements for the assessment of old and new combination products lead to unsuitable assessment of certain traditional medicines. In case of traditionally used combination products, documentation of traditional use (such as classical texts of Ayurveda, traditional Chinese medicine, Unani, and Siddha) and experience should be considered as evidence.

A new combination of well-known substances, including effective dose ranges and compatibility, should be required along with the documentation of traditional knowledge of each single ingredient. Each active ingredient should contribute to the efficacy of medicine. Clinical studies should justify the efficacy of a new ingredient and its positive effect on the total combination.

9.2.6. Intended Use

Product Information for the Consumer

Product labels and package inserts should be easy to understand by the consumer or patient. The package should contain necessary information regarding the proper use of the product:

1) Product name,
2) Quantitative list of active ingredient(s),
3) Dosage form,
4) Indications:
    i) Dosage (specified for children and elderly),
    ii) Administration mode,

iii) Duration of use,
iv) Major adverse effects,
v) Overdosage information,
vi) Contraindications, warnings, precautions and major drug interactions, and
vii) Use during pregnancy and lactation.
5) Expiry date,
6) Lot number, and
7) Holder of the marketing authorisation.

Identification of the active ingredient(s) by the Latin botanical name, along with the common name in the preferred language of the national regulatory a uthority, is recommended. Sometimes not all information that is required may be available, so drug regulatory authorities should determine their minimal requirements.

Promotion
Advertisements and other promotional material directed to health personnel and the general public should be fully consistent with the approved package information.

9.2.7. Utilisation of these Guidelines

The guidelines for the assessment of herbal medicines facilitate the work of regulatory authorities, scientific bodies, and industries in the development, assessment and registration of such products. The assessment should reflect the scientific knowledge obtained in that field. Such assessment forms the basis for future classification of herbal medicines in different parts of the world. Apart from the herbal products, other types of traditional medicines can be assessed similarly.

Effective regulation and control of herbal medicines moving in international commerce also demands a close link between national institutions that regularly review all aspects of production and use of herbal medicines, and also conduct or sponsor assessment of their efficacy, toxicity, safety, acceptability, cost and relative value compared with other drugs used in modern medicine.

9.3. STABILITY TESTING OF HERBAL DRUGS

9.3.1. Introduction

Herbal drugs are of different types and have different constituents. Stability testing of finished herbal drug products is difficult because they have low concentration of active constituents. Due to this reason, the entire herb or the her bal product is considered as the active matter, irrespective of whether or not the constituents with defined therapeutic activity are known.The most important aspect in the evaluation of stability study of a product is its storage condition. Stability tes ting aims to prove how the quality of herbal products varies with time under the influence of environmental factors such as temperature, light, oxygen, moisture, other ingredients in the dosage form, particle size of drug, microbial contaminat ion, trace metal contamination, and leaching from the container. It also establishes a recommended storage condition and shelf-life of the product. Based on the climatic conditions, only storage conditions can be determined.

Stability studies should be p erformed on three production batches of the herbal products for the proposed shelf-life, which is denoted as long term stability and is performed under natural atmospheric conditions. Modern analytical techniques (like spectrophotometry, HPLC, and HPTLC) a re used and proper guidelines are followed to yield a fitting stability data of herbal products and to predict their shelf-life that will help in improving the global appropriateness of herbal products.

9.3.2. Specific Characteristics of Herbal Medicinal Products

Herbal drugs and preparations are classified like the Active Pharmaceutical Ingredient (API) in the Herbal Medicinal Products (HMPs). From chemical and analytical point of view, herbal drugs, herbal preparations and HMPs are complex in nature due to diff erent chemical classes and analytical behaviours (**e.g.,** flavonoids *versus* essential oils). Sometimes, these constituents have a very low concentration, especially in the finished product.

With respect to the constituents responsible for the pharmacologica l activity of herbal preparations, the European Pharmacopoeia and the Quality Guideline sub-divided them as follows:

1) Standardised extracts,
2) Quantified extracts, and
3) Other extracts.

Standardised extracts have a fixed content of constituents with known therapeutic activity, **e.g.,** silymarines in *Silybum marianum* . Therefore, these extracts are treated in the same way as chemically -defined APIs; **for example**, dissolution testing for oral forms.

Quantified extracts have a defined range of constituents that con tribute to known therapeutic activity; **for example**, hypericin in *Hypericum perforatum.*

Other extracts without known effective constituents are defined by their production process and specifications, i.e., the ratio of herbal substance to genuine herbal preparation (Drug-Extract Ratio, DER).

9.3.3. Choice of Markers

Herbal drugs or preparations are complex mixtures. The quantity of herbal substance or preparation in an HMP can be determined by using single chemically-defined constituents or groups of constituents as markers, also termed **active markers** for quantified extracts and **analytical markers** for other extracts. The choice of marker should be justified by its ability to identify and assay in a selective and robust manner. The following recommendations sho uld be taken into account:

1) Literature research about known constituents,
2) EP monograph or other pharmacopoeias and monograph drafts (Pharmeuropa),
3) Analytical feasibility of the marker in the drug substance and drug product,
4) The marker’s suitability for stability studies, and
5) Reference standards, i.e., availability, quality, and costs.

Monographs are helpful in defining a marker and provide valuable information on a suitable method. However, these monograph methods can be used only for the purpose speci fied in the Pharmacopoeia. These methods are generally not applicable for a finished product containing this drug substance as the resulting concentration is too low, or matrix effects lead to a lack of selectivity. Methods and markers mentioned in Pharmac opoeias are only intended for batch release purposes (and not for stability studies), therefore, they are often not considered for this kind of use. Thus, the authorities should not bind the applicant to the markers mentioned in the monographs, and should allow alternative approaches wherever applicable and if justified.

9.3.4. Role of Markers

Markers are chemically known compounds, which may or may not have therapeutic effect. They are used to determine the quantity of herbal medicinal ingredients in HMPs. The choice of marker has to be justified. Selecting the right analytical marker is essential for stability testing of HMPs. Typical sources for finding markers are:

1) Monographs and drafts (EDQM Pharmeuropa),
2) Experience, transfer from other plants/constituents,
3) Literature research about known constituents, and
4) Scientific research.

9.3.5. Analytical Methods for Herbal Products

Herbal preparations due to their complex composition are analysed by running High Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), or Thin Layer Chromatography (TLC). Quantitative determinations are done by UV-visible spectroscopy or combinations of these. By using HPLC and GC methods, a specific fingerprint chromatogram for identification and purity testing, and detection of single compounds for assay can be done in a single analysis.

But in case of a combined product having multiple active ingredients, a specific determination and quantification of each drug preparation becomes difficult. In such cases, highly sophisticated and expensive methods, **e.g.,** LC and GC mass coupling (LC-MS/GC-M, etc.) have to be used. The guideline on Quality of Combination Herbals Medicinal Products/Traditional Herbal Medicinal Products mentions a method to run the determination jointly **e.g.,** by UV-visible spectroscopy. Although group determination is a useful tool for an assay, all the individual active substances should undergo appropriate fingerprint chromatograms for their identification or for an individual specific constituent, **for example** by TLC. Identification process can be carried out at an earlier production stage, **e.g.,** in the primary bulk extract before blending and mixing. The necessity and appropriateness of the method combination should be demonstrated by the applicant.

Sometimes, herbal medicinal products are combinations of herbal preparations with vitamins and/or minerals. The pharmacological action of the vitamins and minerals should be ancillary and linked to the indication(s) of the herbal preparation. If vitamins and minerals ar e categorised as an API, they should be analyse d with respect to the effective requirements (chemical defined substances, vitamins, etc.).

9.3.6. Stability Studies

Stability is the capacity of a drug substance or product to remain within the established specifications which maintain its identity, strength, quality, and purity throughout the retest or expiration dating period. Stability study aims to determine the shelf-life and the time period of storage at a specified condition within which the drug product meets its established specifications. Stability influences the quality, safety and efficacy of a drug product. A drug product of insufficient stability can change the physical (hardness, dissolution rate, phase separation, etc.) and chemical characteristics (formation of high risk decomposition substances). Stability evaluation of drug substance or product is the key to drug quality as it determines the efficacy of any drug or dosage form. Stability testing proves that the quality of a drug substance or product changes with time under the influence of various environmental conditions such as temperature, relative humidity, light, etc.

Stability study involves a series of tests to obtain an assurance of drug product stability, namely maintenance of the drug product packed in it specified packaging material and stored in the established storage condition within the determined time period.

9.3.7. Stability Protocol

Stability protocol should include information on the following:

1) Batches tested (commercial formula),
2) Unit composition (or cross-reference),
3) Container-closure system (commercial),
4) Literature and/or supporting data,
5) Stability specifications (only for finished pharmaceutical products),
6) Analytical methods, i.e., stability indicating (cross-reference),
7) Stability plan (schedule),
8) Tabulated test results (including specifications),
9) Analysis/discussion of data,
10) Re-test or shelf-life proposal (including storage condition), and
11) Post-approval commitments.

9.4. SUMMARY

The details given in the chapter can be summarised as follows:

1) **Organoleptic evaluation** of a drug involves determining its colour, odour, taste, size, shape, touch, texture, etc.
2) Woody stem tissues present on the outer surface of inter-fascicular cambium form the **bark drugs**.
3) **Underground structures** are of different forms and are used by the plants for storing food.
4) A **simple leaf** contains all the photosynthetic organs originating from a node on a stem; while a **compound leaf** has many leaflets.
5) **Flowers** are the reproductive plant parts found in a variety of forms and also grow on the plant in different manners.

6) **Fruits** are globular-, oblong-, or ellipsoidal-shaped plant parts having seeds are often specialised to help in seed dispersal.
7) **Simple fruits** develop from a single carpel or from syncarpous gynoecium. Simple fruits are categorised into **dry** and **fleshy fruits** based on whether the mesocarp is dry or fleshy. Dry fruits are further sub-categorised into **dehiscent** and **indehiscent fruits**.
8) **Aggregate fruits** develop from more than one carpels or apocarpous gynoecium.
9) **Compound fruits** develop from numerous flowers combined together.
10) **Seeds** develop from the ovules present in the carpels of flowers.
11) **Microscopic evaluation** of a drug allows detailed examination so that the organised crude drugs (either in entire or powdered forms) can be identified by their known histological features.
12) **Palisade ratio** is the average number of palisade cells present below each epidermal cell. It is determined using powdered drugs.
13) **Vein-islet number** is the number of vein-islets present in per sq. mm of the leaf surface midway between the midrib and margin.
14) **Vein-termination number** is the number of veinlet terminations present in per sq. mm of the leaf surface midway between the midrib and margin.
15) **Stomatal number** is the average number of stomata present in per sq. mm of leaf epidermis.
16) **Stomatal index** is the percentage which the number of stomata forms to the total number of epidermal cells; each stoma being counted as one cell.
17) A **stoma** is a minute epidermal opening having a central pore, and two kidney-shaped guard cells containing chloroplasts.
18) The primary function of stomata is gaseous exchange and secondary function is transpiration.
19) **Paracytic or rubiaceous or parallel-celled stomata** have two guard cells covered with two subsidiary cells, whose long axes are arranged parallelly to that of the stoma.
20) **Diacytic or caryophyllaceous or cross-celled stomata** have two guard cells covered with two subsidiary cells arranged at right angle to the stoma.
21) **Anisocytic or cruciferous or unequal-celled stomata** have two guard cells covered with three subsidiary cells (one is smaller than the other two).
22) **Anomocytic or ranunculaceous or irregular-celled stomata** are surrounded by a variable number of subsidiary cells (similar to other epidermal cells).
23) **Trichomes** (or plant hair) are outgrowths of the epidermal cell either tubular, or elongated, or glandular in shape.
24) The ratio of light velocity in a vacuum to its velocity in substance is called **refractive index of the second medium**.
25) **Ash content** is the residue left behind after incineration of the drug.
26) **Chemical evaluation** is defined as the chemical process of determining the active constituents in a drug.
27) According to WHO and ICH guidelines, **herbal medicines** are defined as "finished, labelled medicinal products that contain active ingredients as aerial or underground parts of plants, or other plant materials, or combinations thereof, whether in the crude state or as plant preparations".

9.5. EXERCISE

9.5.1. True or False

1) Fruits are used by the plants for storing food.
2) Aggregate fruits develop from more than one carpels or apocarpous gynoecium.
3) Vein-islet number is the number of veinlet terminations present in per sq. mm of the leaf surface midway between the midrib and margin.
4) Stomatal index is the average number of stomata present in per sq. mm of leaf epidermis.
5) Paracytic stomata have two guard cells covered with two subsidiary cells arranged at right angle to the stoma.

9.5.2. Fill in the Blanks

6) Dry fruits are further sub-categorised into _____ and _____ fruits.
7) _____ fruits develop from numerous flowers combined together.
8) _____ is the average number of palisade cells present below each epidermal cell.
9) _____ is the residue left behind after incineration of the drug.
10) _____ stomata are surrounded by a variable number of subsidiary cells.

Answers

1) False
2) True
3) False
4) False
5) False
6) Dehiscent and indehiscent
7) Compound
8) Palisade ratio
9) Ash content
10) Anomocytic

9.5.3. Very Short Answer Type Questions

1) Enlist the methods of drug evaluation.
2) What is stomatal index?
3) Define vein-islet number and vein-termination number.
4) Write the tests for detection of carbohydrates.
5) How will you define herbal medicines?

9.5.4. Short Answer Type Questions

1) Write organoleptic evaluation.
2) Write about quantitative microscopy.
3) Discuss about a few parameters of physical evaluation.
4) Write a note on biological testing of herbal drugs.

9.5.5. Long Answer Type Questions

1) Briefly discuss about microscopic evaluation.
2) Give a brief review on chemical evaluation.
3) Write an exhaustive note on WHO and ICH guidelines for the assessment of herbal drugs.
4) Give a detailed note on stability testing of herbal drugs.

CHAPTER 10

Patenting and Regulatory Requirements of Natural Products

10.1. PATENTING AND REGULATORY REQUIREMENTS OF NATURAL PRODUCTS

10.1.1. Introduction - IPR

Intellectual Property Rights (IPRs) are rights that allow making, using, and selling a new product or technology that is granted generally for 17-20 years to the inventor or to the corporation that files a claim on behalf of the inventor. IPRs in general reward the innovators, inventors, and researchers. It is a motivation that brings rapid growth and progress in industries. Under IPR law, owners get some exclusive rights to various intangible assets like musical, literary and artistic works, discoveries and inventions, words, phrases, symbols, and designs.

Some common types of intellectual property are **copyrights**, **trademarks**, **patents**, **industrial design rights**, and **trade secrets** under certain jurisdictions. Some IPR patents and trademarks are significant for pharmaceutical industries. Inventions based on existing knowledge do not come under the protection of IPR.

10.1.2. Patent

A patent is a monopoly right granted to a patentee for a definite time period, during which he/she is given the exclusive right to stop anyone else from using his/her invention without approval. It is considered a negative right as it does not allow others to produce or do anything, but stops them from producing or doing something already patented. Patents being a legal institution have grown for years. The scope, length and purpose of protection under patent rights has changed several times and is valuable for understanding the developments with respect to the developments in Southern countries (however, at a much faster rate as a means of mirroring the development).

There is a long history of association of patents and thievery. Columbus carried letters patent from the King and Queen of Spain while travelling to discover a world that was new to him. The patents' granting procedure, the requirements for the same, and the extent of exclusive rights given to the patentee vary as per countries and their national laws and international agreements. A typical patent application should have one or more claims defining the invention that has to be new, inventive, and useful or applicable.In many countries, normal persons as well as corporate entities can apply for a patent. The patent grant and enforcement are done through national laws and international treaties. Pharmaceutical companies employ traditional knowledge of plants and their ingredients to develop new drugs. Tribal information cut down time required in this type of research. Researchers screen plant substances for obtaining newproduct for treating ailments.

10.1.2.1. Procedure for Getting a Patent

An application for an ordinary patent can be filed by the inventor, his legal representative, or his assignee, either alone or with any other person. In case the application for the original patent is pending or patent has been granted by its registered owner, then the applicant alone should file an application. A convention application for a patent (for invention in a convention country) can be filed by the applicant, his assignee or his legal representative.

A prescribed format is given for a **complete specification** document that should include the following details:

1) Complete description of the process, operation and use of the invention,
2) A method of performing the invention for which the claim for protection can be applied, and
3) A statement of claim(s) describing the invention for which patent is to be granted. If an application is submitted with a provisional specification, a complete specification document should be filed within a year from the date on which application was filed.

After receiving the application for a patent along with the complete specification document, the controller should refer to an examiner to generate a report with respect to the following:

1) Fulfilment of the requirements of the Act by the application and specifications,
2) If a reason is available to oppose the grant of patent under the Act,
3) The result of investigations made under section 13, and
4) Other issues mentioned in the application.

The examiner should generate this report within 18 months. If the report contains some points against the applicant or if the report is required to be revised, the Controller should inform the applicant about the grounds for which the application has been opposed and also allow him/her to rectify the issues. Sometimes, the Controller refuses or asks for the amended application. If the generated report favours the applicant and the complete specification document has been accepted, the Controller should inform the applicant. Advertisement in the Official Gazette should be made regarding the acceptance of the specifications and public inspection of the specifications should be allowed.

Starting from the advertisement date of the acceptance of complete specification document till the date of patent sealing, the applicant should be allowed rights as if a patent for the invention had been sealed on the date of advertisement itself. Four months from the date of acceptance of advertisement, the patent can be opposed by any individual for the following reasons:

1) If an invention has been done illegally,
2) If the invention has been published before the priority date of claim:
   i) In any specification, along with a patent application filed in India, either on or after 1st January, 1912, or
   ii) In any other document in India or elsewhere.

3) If the claim of a n invention's complete specification has been published on or after the expiry date of the appli cant's claim and filed along with the patent application in India,
4) If the public knew about the invention and employed in India befo re the expiry date of the claim,
5) If the inventive step is missing in invention,
6) If the subject of any complete specification claim is not an invention or is not patentable as per this Act,
7) If the complete specification lacks overall details of the invention or its preparation method,
8) If the applicant fails to provide detailed information of the invention to the Controller or gives misleading information about the invention, and
9) If convention application has not been filed by the applicant withina year from the date of first application for invention protection in a convention country.

Upon receiving opposition notice, the Controller should inform the applicant and before taking the final decision should give the applicant a chance to rectify the issues. After the acceptance of complete specification and before the grant of a patent, the Controller may come to know that the complete specification of the invention has been before the priority date of the claim:

1) In any specification along with the application for a patent filed in India, either on or after 1st January, 1912, or
2) In any other document in India or other countries.

In such a case, the Controller may not grant patent until th e complete specification is rectified within the given time duration. The Controller may permit to mention the inventor's name in the patent, but this should not violate any rights under the patent. Upon grant of a patent , it should be sealed by the Controller with the seal of the patent office. The date of sealing is also noted in the register by the Controller. The date of filing of complete specification is the date of patent. The Controller can amend the patent if the applicant of the sealed patent dies or if a body corporate does not appear before the patent is sealed.

10.1.2.2. Conditions for Grant of Patent

Following conditions are considered for granting a patent:

1) A machine, apparatus or any article for which the patent is to be granted or a process that has been granted patent, can be imported or made by or used on behalf of the Government for its own use,
2) Any process that has been granted patent can be used by or on behalf of the Government for its own use,
3) Any machine, apparatus or article given patent, or an article produced through a process for which the patent is granted, may be made or employed by any person for its experiment or research work, which incl udes instructions for beginners, and
4) Any medicine or drug under patent imported by the Government for its own use or for distribution in any dispensary, hospital or other institution maintained by or on behalf of the Government; or any other dispensary, hospital or other medical institution established by Central Government for public service.

10.1.2.3. Secrecy of Certain Inventions

If the invention for which the application for a patent is applied is considered relevant to defence purposes by the Controller, he may prohibit the advertisement of such application to any person(s). The Central Government may reconsider the decisions of Controller, within 9 months from the date of issue to not more than 12 months. If the Central Government founds that the advertisement of the invention is not harmful to th e country's defence system, the Controller is informed to cancel the previous orders.

10.1.2.4. Rights of Patentees

The patentees own the following rights:

1) If a patent is granted prior to the initiation of this Act, the patentee gets the right for its invention to be used, exercised, sold or distributed in India, and
2) If a patent is granted after the start of this Act, the patentee has the right to:
   i) Use, exercise, sell or distribute its invented substance s (for which a patent has been granted) in India, or
   ii) Use or exercise a method or process under patent (for which a patent has been granted) in India.

Patent rights are not violated for employing a foreign article, etc., temporarily or by chance in India.

10.1.2.5. Rights of Co-owners of Patents

The co-owners should get same rights on the patent, until an agreement against it is filed. A licence should not be granted under the patent, having two or more registered proprietors. A patent in sharing could not be assigned by one member without the knowledge of the other. The purchaser should deal with the patented article as if it has been sold by a single patentee, even when it is sold by one or more registered proprietors of a patent. The rules for ownership and shift of movable property should be applied to patents, and in case of dead person the mutual rights or responsibilities of its trustees or legal representatives should remain unaffected.

10.1.2.6. Term of Patent

The time period for which a patent is valid is mentioned in **table 4.1**:

Table 4.1: Time Period of the Validity of any Patent

Patent	Time Period of Patent
Any invention, claiming the manufacture method or process of a substance that is intended for use, or can be used as food or medicine or drug.	5 years from the date of sealing or 7 years from the date of patent (whichever is earlier).
Patent of addition	Term equal to that of the pa tent for the main invention or so much thereof as has not been expired.
Any other invention	14 years from the date of patent.

10.1.2.7. Restoration of Lapsed Patents

If the renewal fee for an expired patent has not been paid on time, an application can be filed for restoration of the patent within a year from its expiry date, with the leave of the Controller. If the Controller has any objection, he notifies th e

applicant for his opposition; while if the Controller is satisfied, he directs to advertise the applica tion and the applicant receives a favourable decision. The patent is restored upon the direction of Controller only when full payment of the total amount due has been deposited by the applicant. No suit or other proceedings should be scheduled for a patent infringement between the date of patent expiry and the date of applica tion advertisement for restoration of the patent.

10.1.2.8. Surrender of Patents

A patentee should notify the Controller before surrendering his/her patent. On receiving the notice, the Control ler should advertise the offer of surrender, inform everyone who are interested in the patent, and record their names in a register. If the Controller is satisfied after hearing the patentee and an opponent (if any) who wants to surrender their patent, he may order to cancel the patent.

10.1.2.9. Revocation of Patents

The following reasons may be responsible for the cancellation of a patent by the High Court:

1) If the invention claim ed under complete specification has already been claimed under complete specification for a different patent granted in India,
2) If the patent has been granted to an applicant who is not allowed to apply for a patent,
3) If the patent has been granted illegally against the rights of the petitioner or any other person under or through whom the claim has been made,
4) If the claim of complete specification is made on a subject which:
   i) Is not an invention according to this Act,
   ii) Is not a novel,
   iii) Does not involve any inventive step,
   iv) Is not useful, and
   v) Is not patentable under this Act.
5) If the claim of comp lete specification made is not based on the matter revealed in the specification,
6) If the patent has been obtained on a false suggestion or representation,
7) If the applicant has violated any rule passed under Section 35 or filed an application for the grant of a patent outside India, against the laws of Section 39, or
8) If the patent has been obtained by claiming false complete specification, and thus, needs amendment.

10.1.2.10. Register of Patents

The registers of patents are kept in the patent offices, and include th e following details:

1) The names and addresses of patentees,
2) Notifications of assignments and transmissions of patents, licenses under patents, amendments, extensions, and revocation of patents, and
3) Details of other matter affecting the validity or ownership of patents.

The register is kept under the Controller's supervision. The register can be inspected by the public at any suitable time. Properly sealed certified copies of any specific entry in the register should be handed over to any person after paying the mentioned fee.

10.1.3. Farmer's Right

Farmer's rights are a precondition for the maintenance of crop genetic diversity, which forms the basis of all food and agriculture production in the world. Farmer's rights enable the farmers to maintain and develop crop genetic resources (as they have been doing since the dawn of agriculture) and recognise and reward them for their vital contribution to the global pool of genetic resources.

However, the International Treaty does not define farmer's rights, which is a working definition developed on the basis of the research of the Farmer's Rights Project and can be seen as a lowest common denominator of all stakeholders consulted and all documents and literature surveyed. Farmer's rights include the customary rights of farmers to save, use, exchange and sell farm-saved seeds and propagating materials. They should be recognised, rewarded and supported for their contribution to the global pool of genetic resources, to the development of commercial varieties of plants, and to participate in decision making on issues related to crop genetic resources.

India is one of the first countries to pass a law allowing farmer's rights through Protection of Plant Varieties and Farmer's Rights Act, 2001 (PPVFR). This law of India is exceptional, distinct, and gives immense importance to farmers and breeders as agriculture has a major stake in the overall Indian economy. It not only provides employment but also has a considerable share in the country's GDP.

In the recent years, the suicide rates of farmers have increased. In India, nothing is mentioned about agriculture in intellectual property protection laws. Even a proper legal system does not exist to protect plant breeder rights. The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs), bilateral and multilateral pressure from other countries was put forth on India for establishing IPR in agriculture.

Indian PPVFR, 2001 Act supports the farmers in saving, exchanging and distributing seed materials. It also allows the farmers to claim intellectual property rights over their selected plant varieties. This Act gives protection on new, extant and derived plant varieties.

Under the **PPVFR Act**, the following **nine rights are given to farmers**:

1) **Right to Seed:** The Act provides the farmers the right to save, use, exchange or sell seed. But, the farmers cannot sell the seeds in a packed form labelled with registered name.
2) **Right to Index Own Varieties:** Similar to the commercial breeders, the farmers can get intellectual property right on their own varieties. This right is unique to Indian PPVFR 2001 Act.

3) **Right to Reward and Recognition:** The Act provides for establishment of National Gene Fund through which the work of farmers are recognised and rewarded.

4) **Right to Benefit Sharing:** National Gene Fund authority also facilitates benefit sharing by publishing the registered varieties and inviting claims for benefit sharing. The rewards from the gene fund are only given to a farmer/community who can prove th at they have contributed to the selection and preservation of materials used in the registered variety.

5) **Right to Information and Compensation for Crop Failure:** The breeder should provide information about the expected performance of registered variety. If the material fails to perform as expected, the farmers may claim for compensation under the Act.

6) **Right to Compensation for Private Use of Traditional Varieties:** If the breeder does not wish to disclose the use and source of traditional varieties, compensation can be granted through the Gene Fund.

7) **Right to Sufficient Accessibility of Registered Varieties:** The breeder should supply sufficient seeds to the public at a reasonable price. If after three years of registration, the breeder fails to do so, any other person can apply for the license.

8) **Right to Service Free of Charge:** The PPVFR 2001 Act excludes the farmers from paying any service charges. Thus the services, like registration of varieties, conducting tests on the registered varieties, and renewal of registration, are done without charging any fees. There is also no fee for legal proceedings under this Act.

9) **Protection from Legal Encroachment in Case of Lack of Awareness:** The PPVFR 2001 Act has considered the low literacy levels in India, and provided protection against innocent encroachment by the farmers. Farmers who breach the rights of a breeder unintentionally should not be penalised if he/she can prove that they were not aware of the existence of breeder's rights.

Farmer's rights should be dealt as intellectual property rights, and not as reward mechanism, because the working of the reward mechanism may be *ad hoc* and not transparent. Many Indian farmers feel that they should have some kind of ownership over their varieties because companies take the o riginal material from them and sell them at a higher rate. Sometimes even the middlemen raise the price of fruits/vegetables and sell it at higher prices to consumers, while the farmers receive only a small amount of that price. Farmers should have ownership rights, but producing new varieties is not an easy task; so if farmers are provided with money and opportunity, they can also invent and innovate.

The Indian law on farmer's rights is considered partially successful by many stakeholders. It is for the first time when the rights of farmers received such wide attention and debate both within and outside Parliament. Even more government was forced to initiate as it could not manage to pass the legislation without fulfilling these demands.

10.1.4. Breeder's Right

Plant Breeder's Rights (PBR) or Plant Variety Rights (PVR) are granted to the breeder of a new variety of plant. These rights give the breeder exclusive control over the propagating materials (seeds, cuttings, divisions, and tissue culture) and harvested materials (cut flowers, fruits, and foliage) of a new variety for a number of years.

With these rights, the breeder can become the marketer of an exclusive variety, or can obtain the license for other varieties. A variety should be new, distinct, uniform and stable to qualify for these exclusive rights. A variety is:

1) **New** if it has not been commercialised for more than a year in the country of protection,
2) **Distinct** if it is different from the other known varieties in one or more botanical characteristics, such as height, maturity, colour, etc.,
3) **Uniform** if the plant characteristics are consistent from plant to plant with the variety, and
4) **Stable** if the plant characteristics are genetically fixed and remain the same from generation to generation, or after a reproduction cycle in case of hybrid varieties.

The breeder should also give an acceptable **denomination** to the variety that becomes its generic name and should be used by anyone who markets the variety.

The national offices grant plant variety rights after examination. Seed is submitted to the plant variety office, which grows it for one or more seasons to check that whether or not it is distinct, stable, and uniform. If the variety passes these tests, exclusive rights are granted for a specified period (20 -25 years for trees and 25 -30 years for vines). If a breeder wishes to maintain the rights , he should pay the annual renewal fee.

Breeders can bring suit to enforce their rights and can recover damages for infringement. Plant breed er's rights contain exemptions from infringement not recognised under patent law. Commonly, there is an exemption for farm -saved seed. Farmers may store the products in their own bins for their own use as seed, but this does not extend to brown-bag sales of seed. Sales for propagation cannot be done without written approval of the br eeder. There is also a breeder's exemption (research exemption in the 1991 Act) that allows the breeders to use protected varieties as sources of initial variation to create new varieties of plants (1978 Act) or for other experimental purpose (1991 Act). There is a provision for compulsory licensing to assure public access to protected varieties if the national interest requires it and the breeder fails to meet the demand.

10.1.4.1. International Rights

In **1957** in **France**, negotiations regarding the protection of new varieties took place and resulted in the development of the **International Union for Protection of New Varieties of Plant (UPOV)** and adoption of the first text of the **International Convention for the Protection of New Varieties of Plants**

(UPOV Convention) in **1961**. The purpose of Convention was to ensure that its member states party acknowledge the achievements of breeders of new plant varieties by providing them an exclusive prop erty right on the basis of a set of uniform and clearly defined principles.

This Convention was revised in **Geneva** in **1972**, **1978** and **1991**. The 1978 and 1991 Acts set out a minimum scope of protection and offer the member states the possibility of takin g national circumstances into account in their legislation. Under the **1978 Act**, the minimum scope of the plant breeder's right requires that the holder's prior authorisation is required for the production for purposes of commercial marketing, offering for sale, and marketing of propagating material of the protected variety.

The **1991 Act** gives more detailed provisions defining the Acts regarding the propagating material for which the holder's authorisation is necessary. The UPOV Convention establishes a mu ltilateral system of national treatment, under which citizens of any member state are treated as citizens of all member states for obtaining plant breeder's rights.

This Act also sets -up a multilateral priority filing system, under which an application for protection filed in one member state establishes a filing data for applications filed in other member states within a year of that original filing date. This allows a breeder to file in any one member country within a year period to preserve the novelty of their variety. The novelty of variety will still be recognised when the filing is done in other member countries within a year of the original filing date. However, if the applicant does not wish to use the priority filing, he/she has 4 years to apply i n all other member states (except in the U.S.A.) for all species (except tree and vine species) in which case he/she has 6 years to make application.

The UPOV Convention is not self -executing. Each member state should adopt legislation consistent with the convention requirements and submit that legislation to the UPOV Secretariat for review and approval by the UPOV Council, consisting of all the UPOV member states acting in committee.

In compliance with these treaty obligations, the U.K. enacted the **Plant Variety and Seeds Acts, 1964** . Similar legislation was passed in Netherlands, Denmark, Germany, and New Zealand. In **1970**, the United States followed the lead of 17 Western European nations and passed the **Plant Variety Protection Act, 1970** (U.S.). This legi slation provided protection to developers of nov el, sexually reproduced plants.

However, the U.S. originally agreed to the UPOV Convention based on the Plant Patent Act and did not bring the PVP Act into compliance with UPOV requirements till the time whe n the Commissioner of Plant Variety Protection disseminated the rules to do so in 1984. The U.S. Patent Office has been granting patents on plants since the 1980s; including plant varieties , this provides another way of protecting plant varieties in the U.S.A.

Australia passed the **Plant Variety Protection Act, 1987** and the **Plant Breeder's Rights Act, 1994** . Australian patent law also permits the patenting of plant varieties. Total 65 countries have signed the UPOV Convention and adopted plant breeders' rights legislation consistent with the requirements of convention.

The WTO's Agreement on **Trade-Related Aspects of Intellectual Property Rights (TRIPs)** requires the member states to protect plant varieties by patents, by an effective *sui generis* (standalone) system, or by the combination of two. Most countries meet this requirement through UPOV Convention-compliant legislation. India has adopted a plant breeder's rights law that has been rejected by the UPOV Council as it failed to meet the requirements of the treaty.

The most recent **1991 UPOV Convention** established several restrictions on international plant breeder's rights. While the current legislature of the convention recognises novel varieties of plants as intellectual property. Laws were formed regarding the preservation of seeds for future plantation so that the need to buy seeds to be used in subsequent planting seasons would be significantly reduced and even eliminated. The 1991 convention also concerns the method of initiating plant breeding by implementing pre-existing and patented plant species as contributor of vital genetic information in the creation of a new plant variety.

Constituent countries of the World Trade Organisation (WTO) acknowledge the creation of new varieties of plants and support these creations within full recognition of intellectual property rights laws. A formalised legislature, demonstrating the manner of conferring such intellectual property rights, is exemplified by the 1991 UPOV convention that declares such rights on a breeder.

As a result of debate over the protection of hybrid plants as new varieties, the legal measure of double protection, as expressed within the current iteration of the UPOV, can be taken. Double protection mediates the overlap between plant breeder's rights and patents existing within the intellectual property rights law, by enabling the protections of both to be conferred upon a particular plant variety.

10.1.4.2. Plant Breeding Benefits

Since 30 years, the productivity of major agricultural crops has increased by 50%. Experienced plant breeders have made great scientific progress to improve the crops. Innovation in plant breeding provides higher yielding varieties with better agronomic traits, such as disease resistance and stress tolerance, higher yields with hybrid corn and many vegetable crops. Since 60 years, the efforts of North American corn breeders have been rewarded by a 400% increase in corn yields.

Given below are some of the plant breeding **benefits**:

1) Improved time management and on-farm erosion control with herbicide-tolerant crops.
2) New high-value markets in Japan with specially soybeans.
3) Global competitiveness through better yields and high quality.

4) Plant breeders are working on even more problems that can increase the net farm income:
   i) Fusarium head blight control for wheat growers.
   ii) Canola seeds with increased vigour could reduce crop establishment risk.
   iii) Draught resistance is being developed in canola, corn, and soybeans.

10.1.5. Bioprospecting and Biopiracy

Biodiversity prospecting involves **exploration**, **extraction and screening of biological diversity and indigenous knowledge for commercially valuable genetic and biochemical resources**.

Although biodiversity prospecting does not always use indigenous knowledge, still essential chemical compounds derived from plants, animals and microorganisms can be easily identified and are commercially valuable when collected with indigenous knowledge and/or found in territories traditionally inhabited by indigenous people.

Between 1956 and 1976, the U.S. National Cancer Institute screened 35,000 plants and animals for anti-cancer compounds. But, this program failed to identify a greater number of new anti-cancer agents, and thus was ended in 1981.

A retrospective study conducted determined that the success rate in finding valuable species could have been doubled if medicinal folk knowledge was the only information used to target species. Similarly, in another case, scientists found that 86% of the plants used by Samoan healers showed significant biological activity when tested in the laboratory.

Biopiracy involves **stealing of knowledge from traditional and indigenous communities or individuals**. The term **biopiracy** can also be used to indicate a breach of a contractual agreement on the access and use of traditional knowledge to the detriment of the provider and bioprospecting without the permission of local communities.

The **Action Group on Erosion, Technology and Concentration** [ETC group, Canada (former RAFI)] defined biopiracy as "the appropriation of the knowledge and genetic resources of farming and indigenous communities by individuals or institutions seeking exclusive monopoly control (usually patents or plant breeders' rights) over these resources and knowledge".

Biopiracy and bioprospecting are distinctively different from each other. **Biopiracy** refers to the unauthorised and uncompensated taking and use of biological resources; while, **bioprospecting** refers to the search for valuable active chemical compounds in nature, and accessing natural resources through legal means, securing prior informed consent from the custodians of the relevant natural resources and promoting equitable benefit sharing agreements with appropriate parties. Biopiracy deprives the custodians of biological resources as well as the country concerned.

10.2. PATENTING ASPECTS OF TRADITIONAL KNOWLEDGE AND NATURAL PRODUCTS

10.2.1. Introduction

Traditional knowledge refers to the knowledge, innovations and practices of indigenous and local communities around the world. Developed from the experience gained over centuries and adapted to the local culture and environment, traditional knowledge is orally transmitted from one generation to another. It is collectively owned and takes the form of stories, songs, folklore, proverbs, cultural values, beliefs, rituals, community laws, local language, and agricultural practices, including the development of plant species and animal breeds.

Traditional knowledge is a practical nature, particularly in fields of agriculture, fisheries, health, horticulture, forestry, and environmental management. India has played a significant role in the documentation of traditional knowledge, and thus brings the protection of traditional knowledge at the centre stage of the International Intellectual Property System.

In **2000**, WIPO members established an **Intergovernmental Committee (IGC) on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore**, and in **2009** they developed an **International Legal Instrument (s)** that would provide protection to traditional knowledge, genetic resources and traditional cultural expressions (folklore).

10.2.2. Protection of Traditional Knowledge

After the patenting of turmeric, neem and Basmati rice, India and other developing biodiversity-rich countries took attention towards the danger faced by the traditional knowledge. Two types of **intellectual property protection** are:

1) **Defensive Protection:** It aims to stop people outside the community from acquiring intellectual property rights over traditional knowledge. **For example**, India has collected a searchable database of traditional medicine to be used by patent examiners while assessing patent applications as evidence of prior art.

   This followed a case in which the US Patent and Trademark Office granted a patent (however, later cancelled) for using turmeric to treat wounds (a property well-known to traditional communities in India and documented in ancient Sanskrit texts). Defensive strategies can also be used to protect sacred cultural manifestations, such as sacred symbols or words from being registered as trademarks.

2) **Positive Protection:** It aims to grant rights permitting the communities to promote their traditional knowledge, control its uses, and benefit from its commercial exploitation. Some uses of traditional knowledge can be protected by the existing intellectual property system, and many countries have also developed specific legislation. However, any specific protection afforded under national law may not hold for other countries, this is why many indigenous and local communities and governments emphasise on an international legal instrument.

10.2.3. Alternative Regime for the Protection of Traditional Knowledge

Due to the difficulties in application of intellectual property to traditional knowledge and traditional medicines, the need for establishment of the ***sui generis* (specific, special) systems** for the protection of traditional knowledge has arisen. In pharmaceutical research, traditional knowledge contributes towards the identification, development and appropriate drug dosage. This information is gathered through consistent skill, observation and usage by local and indigenous communities. However, the conventional intellectual property systems do not consider this innovation as valuable. Access to such information is assumed to be free.

This has impelled some countries to protect their traditional knowledge by developing their own *sui generis* systems. However, the parameters and modalities are being worked out. The objectives of *sui generis* systems are determination of protectable subject matter, ownership rights, and procedure for acquiring rights.

Many initiatives have been taken to document traditional knowledge. In most cases, the motive is to preserve or disseminate it, or to use it in environmental management, instead of using it for legal protection. There are doubts that making traditional knowledge widely available to the general public through documentation and by permitting to access it on the internet could lead to its misuse or use in ways that were not intended by the traditional knowledge holders.

But, documentation can also help protecting traditional knowledge by providing a confidential or secret record of it reserved for the relevant community. Some formal documentation and registries of traditional knowledge support *sui generis* protection systems, while traditional knowledge databases, such as India's database on traditional medicine, involve in defensive protection within the existing IP system.

These situations demonstrate the importance of ensuring that documentation of traditional knowledge is linked to an intellectual property strategy and does not take place in a policy or legal vacuum.

10.2.4. Case Study of Curcuma

Turmeric is a tropical herb grown in east India. Turmeric powder is widely used in India as a medicine for treating common cold, as a blood purifier, an anti-parasitic for many skin infections, an essential food ingredient in cooking many Indian dishes, and a dye.

The Patent

In **1995**, the **United States awarded patent on turmeric** to **University of Mississippi Medical Centre** for its wound healing property. The claimed subject matter was the use of turmeric powder and its oral as well as topical administration for wound healing. An exclusive right has been granted to sell and distribute turmeric.

The Opposition

The **Council of Scientific and Industrial Research (CSIR) of India** challenged the patent in **1996**. It claimed that the patent lacked novelty as turmeric is being used for healing wounds since ages in India and thus is a part of prior art. CSIR presented 32 references (some of them were hundred years old) to support this fact. In **1997**, the **United States Patent and Trademark Office (USPTO)** rejected all the six claims of the patent as anticipated by the submissions of CSIR, thus declaring the patent invalid.

The University of Mississippi Medical Centre then decided to abandon the patent and the patent was re-assigned to the inventors who chose to further pursue the case on the grounds that "the powder and paste had different physical properties, i.e., bioavailability and absorbability, and therefore, one of ordinary skill in the art would not expect, with any reasonable degree of certainty, that a powdered material would be useful in the same application as a paste of the same material". The inventors also mentioned that "oral administration was available only with honey, which itself was considered to have wound healing properties."

However, the USPTO rejected this objection and stated that "both paste and powder were equivalent" in relation to the references submitted by CSIR. In **1997**, the claims were again rejected, and in **1998** the re-examination certificate was issued which signified the end of case.

10.2.5. Case Study of Neem

Neem tree contains many potential compounds, of which **azadirachtin** is the most essential chemical found in its seeds. It is used as an astringent in many fields. The barks, leaves, flowers and seeds of neem tree are used for treating various disorders like leprosy, diabetes, skin disorders, ulcers, etc. Since ages neem twigs are used as antiseptic tooth brushes.

The opponents' submitted evidence of ancient Indian Ayurvedic texts mentioning that hydrophobic extracts of neem seeds were well-known and used for centuries in India for curing dermatological diseases in humans and for preventing fungal infections of agricultural plants. The EPO (European Patent Office) identified the lack of novelty and cancelled the patent.

The Patent

The **first U.S. patent** on storage-stable composition for **neem seed extract** was issued in **1985** to the inventor, **Robert O. Larsson**. The patent was improved by **W.R. Grace** who developed a storage stable azadirachtin formulation that increased the shelf-life of the pesticide by two years.

Thus, they were granted two co-dependent U.S. patents in **1991** and **1992**. W.R. Grace partnered with U.S.A. as represented by The Secretary of Agriculture and jointly filed a patent application for the formulation to the EPO, which after proper examination granted the patent in **1994**. The major claim of the patent was, however restricted by the EPO in relation to the patent granted in the U.S.

The Opposition

The patents granted to W.R. Grace in Europe and U.S. made the Indians feel that W.R. Grace had claimed for the knowled ge that belonged to India. Thus, the storage stable azadirachtin formulation in spite of being best lacked novelty and any inventive step. Other problems were that the traditional use of this formulation in India would be seen as patent breach if they were to gain a patent in India, and also W.R. Grace could increase the price of neem seeds.

The **U.S.-based foundation on Economic Trends** filed a **petition for re - examination** with evidences that the invention lacked novelty as it is in use since time immemorial in India. However, the petition was turned down due to the geographical limitation in U.S. patent legislation concerning prior use.

In **1995**, **Magda Aelvoet** (European parliament member and representative of the Greens in the European Parliament) along with two CSOs filed an opposition with the EPO with regard to the patent in cooperation. The opponents filed for revocation of the patent on the grounds that the patent lacked novelty in accordance with Article 54(1) and (2) EPC and also lacked inventive step in accordance with Article 56 EPC. They also claimed that the p atent was contrary to morality [Article 53(a) EPC] and pursuant to Article 100 (b) EPC that there was insufficiency of disclosure.

The opposition division found the requirements for sufficiency of disclosure have been fulfilled and Article 53(a) EPC was not applicable to the present case. However, when the formulation's novelty was questioned, the opposition division ruled in favour of the opponents. The opposition division found that the "when" and "where" of alleged prior use has taken place in 1985/1986 in Pune and Sangli districts of Maharashtra, Western India. The opposition division was based on the affidavit and testimony of **Mr A.D. Phadke** (an Indian agronomist who was a witness on behalf of the opponents), who had developed a commercial neem product in India without claiming patent protection and during this work period had conducted extensive field trials with the help of Indian farmers.

During the oral proceedings, the patentee filed a n auxiliary request to amend the neem formulation of the patent. But, the opposition division dismissed the request as it lacked an inventive step in comparison to the prior art represented by the Indian TK. Consequently, the EPO cancelled the patent.

The patentees appealed against this decision, and on **8th March**, **2005**, the **Boards of Appeal of the EPO** gave its final decision. During this time , the patent ownership was transferred from W.R. Grace to **Thermo Trilogy Corporation** (a U.S. company).

But, the U.S. government remained co-proprietor of the patent. The appeal by the patentees was made on the grounds that Mr Phadke's affidavit and testimony were not sufficient to prove the prior use of neem as their credibility could be put into doubt due to their de pendency on precise testimonies of what took place 10 and 14 years ago.

The Board did not decide this question and in consequence the case on the grounds of prior use, which had been the basis for the decision by the opposition division, instead chose not to handle this issue and relied on a less controversial piece of evidence, i.e., "the appellant's main argument was that the recollection of dates and numerals was uncertain for most people and hence some supporting documents, such as laboratory books or notebooks, were required". However, there is no dispute between the parties regarding the existence of the prior art document (8) as a part of the state of the art within the meaning of Article 54(2) EPC. In the Board's view, document (8) is highly relevant for ruling the present case. Thus, it can be left open even if prior use is not proven as the case can be decided based alone on document (8)."

Document (8), as suggested by the Board, is a scientific article published by **H.B. Singh** and **U.P. Singh** in **Australian Plant Pathology** in **1981**. The title of the article is " **Effect of Volatiles of Some Plant Extracts and their Oils on Conidia of *Erysiphe polygoni* DC**". One of the plant extracts discussed in the article was neem oil. The antifungal effect of neem extract and different concentrations of neem oil used in the study were also discussed in the article.

The Board found that the document mentioned the use of neem oil extract as fungicidal on plants, but not included which solvent was employed. The document also did not mentioned the presence of an emulsifying surfactant in the employed formulations. Therefore, the Board found that the claims of the patent were to be regarded as novel over the contents of the article.

Then the Board reviewed and examined the inventive step, and reached the conclusion that the patent should be cancelled for lacking inventive step. The Board of appeal also failed the auxiliary request because it did not fulfil the requirements of article 123 (2) EPC as the amendments extended beyond the content of the original application. Thus, the patent was finally cancelled.

10.3. SUMMARY

The details given in the chapter can be summarised as follows:

1) **Intellectual Property Rights** (IPRs) are rights that allow making, using, and selling a new product or technology that is granted generally for 17 -20 years to the inventor or to the corporation that files a claim on behalf of the inventor.
2) Some common types of intellectual property are copyrights, trademarks, patents, industrial design rights, and trade secrets under certain jurisdictions.
3) A **patent** is a monopoly right granted to a patentee for a definite time period, during which he/she is given the exclusive right to stop anyone else from using his/her invention without approval.
4) A patentee should notify the Controller before surrendering his/her patent.
5) **Farmer's rights** are a precondition for the maintenance of crop genetic diversity, which forms the basis of all food and agriculture production in the world.

6) **Plant Breeder's Rights** (PBR) or Plant Variety Rights (PVR) are granted to the breeder of a new variety of plant.
7) In 1957 in France, negotiations regarding the protection of new varieties took place and resulted in the development of the International Union for Protection of New Varieties of Plant (UPOV) and adoption of the first text of the International Convention for the Protection of New Varieties of Plants (UPOV Convention) in 1961.
8) **Biodiversity prospecting** involves exploration, extraction and screening of biological diversity and indige nous knowledge for commercially valuable genetic and biochemical resources.
9) **Biopiracy** involves stealing of knowledge from traditional and indigenous communities or individuals.

10.4. EXERCISE

10.4.1. Very Short Answer Type Questions

1) What is IPR?
2) Define patent.
3) Enlist the rights given to a farmer.
4) What rights are given to patentees?
5) How a patent is surrendered?

10.4.2. Short Answer Type Questions

1) Write about the procedure for getting a patent.
2) Discuss about biopiracy and bioprospecting.
3) Discuss the case study of neem.
4) Write a note on case study of curcuma.

10.4.3. Long Answer Type Questions

1) Briefly discuss about farmer's right.
2) Give a brief review on breeder's right.
3) Give a detailed note on patenting aspects of tr aditional knowledge and natural products.

CHAPTER 11

Regulatory Issues

11.1. SCHEDULE Z OF DRUGS AND COSMETICS ACT FOR ASU DRUGS

11.1.1. Introduction

Ayurvedic, Siddha and Unani (ASU) drugs came under the Drugs and Cosmetics Act and Rules in 1964 when the **Udupa Committee** (appointed by the government to look into the manufacturing of Ayurvedic and Unani drugs) observed that these drugs contain important components (like gold, musk, saffron, etc.) with many fake claims. However, for effective implementation of the Act, the government should publish an authorised Ayurvedic and Unani Pharmacopoeia to provide standards for such formulations.

All the medicines manufactured as per the formulae prescribed in the authoritative books of Ayurvedic, Siddha and Unani Tibb medicine systems specified in the First Schedule of the Drugs and Cosmetics Act and Rules are included under the category of Ayurvedic, Siddha or Unani drugs. These drugs are intended for internal or external use for the diagnosis, treatment, mitigation or prevention of diseases or disorders in humans or animals. All the poisonous substances under the Ayurvedic and Unani medicine system are listed in Schedule E_1 of the Drugs and Cosmetics Act and Rules.

11.1.2. Regulation of Manufacture of ASU Drugs

There is a set of standards according to which the ASU drugs are manufactured. If any ASU drug is not manufactured as per these standards, its use is prohibited. License for manufacturing these drugs is granted by the licensing authority appointed by the State Government. A separate license is granted for each manufacturing unit. A loan license can also be issued for manufacturing such drugs.

The license is issued by the licensing authority after consultation with the experts appointed by the State Government for this purpose. Licenses are valid upto 31st December of the year next to the year of issue. Manufacture should be carried out in the premises under hygienic conditions as mentioned in Schedule T, and under the direction and supervision of a competent technical staff including atleast one whole time employee with the following qualifications:

1) Having a degree in Ayurveda or Ayurvedic Pharmacy, Siddha or Unani medicine system from a recognised institution, or
2) Having a diploma in Ayurveda, Siddha or Unani medicine system from a recognised institution, or

3) Graduation in Pharmacy/Pharmaceutical Chemistry/Botany from a recognised university along with atleast 2 years' experience in the manufacture of Ayurvedic, Siddha or Unani drugs, or
4) A Vaidya or Hakim registered in a State Register of Practitioners of indigenous medicine systems and having atleast 4 years' experience in the manufacture of Siddha or Unani drugs, or
5) A pharmacist in Ayurvedic, Siddha or Unani medicine system having atleast 8 years' experience in the manufacture of Ayurvedic or Siddha or Unani drugs.

Technical staff appointed for direction and supervision of manufacturing Ayurvedic drugs should have qualification in Ayurveda medicine system; and the **competent staff** appointed for manufacturing Unani drugs should have qualification in Unani medicine system. Proper records of manufacturing and testing raw materials and finished products should be maintained by the licensee. It is the duty of the licensee to allow an Inspector to enter the manufacturing premises for inspection. The Inspector can take samples of raw materials or finished products, and can also inspect the records maintained by the licensee.

Morphine is an official I.P. preparation, and is not a drug used in accordance with the formulae described in any authoritative Ayurvedic text. The prosecution had imposed allegation that the accused was not licensed to manufacture morphine-containing drug. The accused was unable to provide the manufacturing license issued to him, and thus failed to prove that he had a right to use morphine in his Ayurvedic preparation, Sandanasavam. Therefore, the accused breached the provisions of Section 18(c) and 18(a) (ii) of the Act read with rule17 (e) and 96 of the Rules framed under the Act by using morphine without a valid.

Raw materials used in the formulation of Ayurvedic, Siddha or Unani preparations should be identified and tested for their authenticity as per the prescribed standards. Records should also be maintained for such tests. However, the Ayurvedic, Siddha or Unani drugs manufactured by the Vaidyas and Hakims for the use of their own patients and manufactured in small quantities for the purpose of examination, test or analysis are exempted from these conditions.

Central Government may prohibit the manufacture of any Ayurvedic, Siddha or Unani preparations having hazardous substances. **For example,** the manufacture and sale of all Ayurvedic drugs licensed as toothpastes/toothpowders containing tobacco have been prohibited.

There is a provision of imprisonment upto one year or fine not less than ₹2,000 for first conviction on manufacture of any Ayurvedic, Sidha or Unani drugs without licenses or manufacture of adulterated drugs, whereas imprisonment extending upto two years and minimum fine ₹2,000 for the subsequent conviction.

Manufacturing Ayurvedic, Siddha or Unani drugs without licenses or manufacturing adulterated drugs is punishable with imprisonment for up to one year or fine of not less than ₹2,000 for first conviction and imprisonment for up to two years and fine of ₹2,000 for the next convictions. Manufacturing spurious Ayurvedic, Siddha or Unani drugs is also punishable with imprisonment for 1-3

years and fine of atleast ₹5,000 for first conviction and imprisonment for 3 -6 years and fine of atleast ₹5,000 for the next convictions. However the court may charge lesser penalty for adequate and special reasons. The drugs on which an offence has been committed are liable to confiscation. If valid reasons are found, the licensing authority may cancel or suspend a license. A licensee upset by the decision of the licensing authority can appeal again to the State Government within 3 months of date of suspension or cancellation of his license.

11.1.3. Regulation of Sale of ASU Drugs

A separate license is not required for the sale of Ayurvedic, Siddha or Unani drugs if they are manufactured by a person who has been granted license to manufacture drugs under the Act.

11.1.4. Government Analysts and Drug Inspectors

Government Analysts and Drug Inspectors are appointed by the Central or State Government. These officers perform the assigned duties, follow the procedures, and also enjoy the privileges similar to the individuals appointed for allopathic drugs and cosmetics.

Qualifications of Government Analysts

1) A person should be eligible for being appointed as Government Analyst for allopathic drugs, or
2) A person should have a degree in Ayurveda, Siddha or Unani medicine system and atleast 3 years post-graduate experience in the analysis of drugs in laboratory under the control of:
   i) A government analyst, or
   ii) A chemical examiner, or
   iii) Head of an institution approved for this purpose.

Qualifications of Inspectors

1) A person should be eligible for being appointed as Drug Inspector for allopathic drugs, or
2) A person should have a degree or diploma in Ayurveda, Siddha or Unani medicine system.

11.1.4.1. ASU DTAB

The Central Government constitutes the DTAB (Drug Technical Advisory Board) to advise the Central and State Government on technical matters related to Ayurveda, Siddha or Unani drugs. This board includes the following members:

1) *Ex-officio* members:
   i) The Director General of Health Service,
   ii) The Drugs Controller, India,
   iii) Principal Officer dealing with Indian systems of medicine in the Ministry of Health, and
   iv) Director of the Central Drugs Laboratory, Kolkata.
2) Members nominated by the Central Government:
   i) A government analyst,
   ii) A pharmacognosist,

iii) A phytochemist,
iv) Two persons from the members of the Ayurvedic Pharmacopoeia Committee, one from the members of the Unani Pharmacopoeia Committee and one from the members of the Siddha pharmacopoeia Committee,
v) A teacher in Dravyaguna and Bhaishjya Kalpana,
vi) A teacher in Ilmul-Advia and Taklis-wa-Dawasazi,
vii) A teacher in Gunapadam,
viii) Three persons, one each to represent the Ayurvedic, Siddha and Unani drug industry, and
ix) Three persons, one each from the practitioners of Ayurvedic, Siddha and Unani, and Tibb systems of medicine.

A chairman, a secretary and other clerical staff are appointed by the Central Government. Nominated members hold office for 3 years and can be renominated.

11.1.4.2. ASU DCC

Central Government constitutes the DCC (Drug Consultative Committee) to advise the Central Government, State Government, and the Ayurvedic and Unani DTAB on any matter related to securing uniformity throughout India in the administration of this Act as it relates to Ayurvedic, Siddha or Unani drugs. Two persons nominated by the Central Government and a representative nominated by each State Governments are the members of DCC committee.

11.1.5. Labelling, Packing and Limit of Alcohol in ASU Drugs

Following particulars should be mentioned on the label of the container or package of Ayurvedic or Unani drugs:

1) An authentic list of all the ingredients used for manufacturing such drugs, along with the quantity of each ingredient, and a reference to the preparation method as described in the authoritative books specified in the First Schedule of the Act. If the ingredient list is large, it should be printed separately, enclosed with the packing, and its reference should be made on the label.
2) The words, '**Caution. To be taken under medical supervision**' should be mentioned in English and Hindi on the finished product container intended for internal use for the treatment of human ailments containing a substance specified in Schedule E_1 of the Act.
3) Name of the drug as specified in the literature in the First Schedule of the Act.
4) Net contents of the drug in terms of weight or number expressed in metric system.
5) Name and address of the manufacturer.
6) Manufacturing license number headed by the words '**Manufacturing License Number**', or '**Mfg. Lic. No.**' or '**M.L.**'.
7) Batch number or lot number or other distinguishing prefix.
8) Manufacturing date.
9) The words '**Ayurvedic medicine**' or '**Siddha medicine**' or '**Unani medicine**', as the case may be.
10) If the medicine is intended for external application the words '**For external use only'** should be labelled.
11) If the drug is intended for free distribution to the medical profession, the words '**Physician's sample. Not to be sold**' should be labelled.

If any transparent cover, wrapper case, or other covering is used as outer packing for transport or delivery, labelling is not required. Some Ayurvedic preparations, such as Kapur asava, Ahiphenasava and Mrgamadasava, have high content of alcohol as base, therefore these preparations are available in maximum size of 15ml. Some other preparation s, such as Mrit sanjivani sura and Maha drakshasava, each having maximum alcohol content of 16%, are available in the pack of 30 and 120ml, respectively.

Table 11.1: Regulatory Aspects of Natural Products based on Drugs and Cosmetics Act of India

Sections	Items	Criteria
33E	Misbranded drugs	**ASU Drugs are Considered to be Misbranded:** 1) If colouring, coating or polishing is performed to coat or co nceal damage or drugs are made of better therapeutic value than it really is, 2) If labelling is not done in prescribed manner, or 3) If l abel or container of the drug has any misleading or false claims.
33EE	Adulterated drugs	**ASU Drugs are Considered to be Adulterated:** 1) If it contains any filthy, putrid or decomposed substance, either in whole or in part, 2) If it has been prepared, packed or stored under unhygienic conditions, as a result of which it may have been contaminated with filth or ma y have become injurious to health, 3) If its container is made of any poisonous or deleterious substance, either in whole or in part, that may turn the content injurious to health, 4) If it is coloured with a colour ing agent other than the one prescribed, 5) If it has any harmful or t oxic substance which may turn it injurious to health, or 6) If i t has any substance that may reduce its quality or strength.
33EEA	Spurious drugs	**33EEA ASU Drugs are Considered to be Spurious:** 1) If it is marketed, offered or exhibited for sale under the name of another drug, 2) If it is a simulation of or a substitute for another drug or shows similarity with another drug to deceive, or bears upon it or its label or container the name of another drug, unless it is plainly and conspicuously marked so that the true characters are revealed and its identity is concealed with such other drug, 3) If the label or container is printed with the name of an individual or company claiming to be the drug manufacturer, however the individual or company i s fictitious or does no t exist, 4) If it has been substituted completely or partially by any other drug or substance, or 5) If it claims to be the product of a manufacturer of whom it is not truly a product.

33EEB	Regulation of manufacture for sale of ASU drugs	A person eligible as per the prescribed standards should only manufacture, sale or distribute Ayurvedic, Siddha or Unani drugs.
33EEC	Prohibition of manufacture for sale of certain ASU drugs	1) Manufacture for sale or for distribution of: i) Any misbranded, adulterated or spu rious Ayurvedic, Siddha or Unani drugs, ii) Any patent or proprietary medicine, unless the true list of all the ingredients is displayed in the prescribed manner on the label or container, and iii) Any Ayurvedic, Siddha or Unani drug in contravention of any of the provisions of this Chapter or any rule made thereunder; 2) Marketing, stock or exhibit or offer for sale or distribution of any Ayurvedic, Siddha or Unani drug manufactured in contravention of any of the provisions of this Ac t, or any rule made thereunder, or 3) Manufacture for sale or distribution of any Ayurvedic, Siddha or Unani drugs which do not follow the conditions or standards as prescribed.
33EED	Power of Central Government to prohibit manufacture of ASU drugs in public interest	Central government can ban manufacture of Ayurvedic, Siddha or Unani drugs, if: 1) The drugs have any risk to humans or animals, or 2) The drugs do not possess the claimed therapeutic value.
33F	Government analysts	A person having the prescribed qualification and not having an y financial interest in ASU drug can be appointed by the Central or State Government.
33G	Drug inspectors	A person having the prescribed qualification and not having any financial interest in ASU drug can be appointed by the Central or State Government.
33I	Penalty for manufacture, sale, etc. of Ayurvedic, Siddha or Unani drugs	Manufactures for sale or for distribution of any ASU drugs which may be adulterated or distributed by a person without a valid licence.
33J	Penalty for subsequent offences	Punishment with imprisonment for atleast 2-6 years and fine of atleast 5,000 Indian rupees.
33K	Confiscation	If a person convicted under the Act, the respective stock of ASU drug can be confiscated.
33M	Cognisance of offence	1) No prosecution should be instituted except by an Inspector. 2) No court inferior to that of a Metropolitan Magistrate or of a Judicial Magistrate of the first class should try a punishable offence.
33N	Power of Central Government to make rules	After consultation with or o n the recom mendation of the board and after previous publication by notification in the Official Gazette, the Central Government may make rules as per the provisions of this Chapter.
153	Application for licence to manufacture Ayurvedic (including Siddha) or Unani drugs	To ma nufacture for sale any ASU drug , an application for the grant or renewal of a licence should be made in Form 24 -D to the licensing authority along with a fee of ₹60.

154	Licenced manufacture of Ayurvedic (including Siddha) or Unani drugs	If the conditions prescribed in rule 157 are fulfilled, a licence to ma nufacture for sale of any ASU drug should be granted in Form 25-D.
153-A	Loan licence	To ma nufacture for sale of any ASU drug , an application for the grant or renewal of a licence should be made in Form 25 -E to the licensing authority along with a fee of ₹30.
155-B	Certificate of award of GMP of Ayurveda, Siddha and Unani drugs	A license should be is sued to the applicant who complies with the requirements of GMP of ASU drugs as given under Schedule T.
168	Standards to be complied with manufacture for sale or for distribution of Ayurvedic, Siddha and Unani drugs	The standards for identity, purity and strength of single drugs as mentioned in editions of Ayurvedic Pharmacopoeia of India. The upper limit of alcohol in Asavas and Arishtas as self-generated alcohol is 12% v/v.

11.2. SUMMARY

The details given in the chapter can be summarised as follows:

1) All the poisonous substances under the Ayurvedic and Unani medicine system are listed in Schedule E_1 of the Drugs and Cosmetics Act and Rules.
2) **Technical staff** appointed for direction and supervision of manufacturing Ayurvedic drugs should have qualification in Ayurveda medicine system; and the **competent staff** appointed for manufacturing Unani drugs should have qualification in Unani medicine system.
3) Government analysts and drug inspectors are appointed by the Central or State Government.
4) The Central Government constitutes the DTAB (Drug Tech nical Advisory Board) to advise the Central and State Government on technical matters related to Ayurveda, Siddha or Unani drugs.
5) Central Government constitutes the DCC (Drug Consultative Committee) to advise the Central Government, State Government, and the Ayurvedic and Unani DTAB on any matter related to securing uniformity throughout India in the administration of this Act as it relates to Ayurvedic, Siddha or Unani drugs.

11.3. EXERCISE

11.3.1. Very Short Answer Type Questions

1) What is schedule Z?
2) Enlist the members of DTAB.
3) What is ASU DCC?
4) How ASU drugs are sold?

11.3.2. Short Answer Type Questions

1) Write about the regulation of manufacture of ASU drugs.
2) What particulars should be mentioned on the label of ASU drugs?
3) Write a note on government analysts and drug inspectors.

11.3.3. Long Answer Type Questions

1) Briefly discuss about schedule Z of drugs and cosmetics act for ASU drugs.
2) Give a brief review on labelling, packing and limit of alcohol in ASU drugs.

CHAPTER 12

General Introduction to Herbal Industry

12.1. HERBAL DRUGS INDUSTRY

12.1.1. Introduction

A shift in universal trend from synthetic to herbal medicine has been observed in recent times. Medicinal plants have been known and highly valued worldwide since ages as a rich sou rce of therapeutic agents for preventing diseases. Nature has presented a massive wealth of medicinal plants in **India**, and thus it is often referred to as the **medicinal garden of the world**. Several plant remedies are still being used for various conditions in countries with ancient civilisations, such as China, India, South America, Egypt, etc.

India has a unique position in the world since many recognised indigenous medicine systems, such as Ayurveda, Siddha, Unani, Homeopathy, Yoga, and Naturopathy, are utilised for health care. However, the herbal drugs are being popularly used in the rural and urban communities only.

Natural herbal products are considered safe, and this is the major reason behind their popularity and acceptability. Since the natural p roducts, like plant -based medicines, health products, pharmaceuticals, food supplements, cosmetics, etc. are non-toxic, have less side effects, and are easily available at affordable prices, their demands are increasing in developing as well as in developed countries.

At the present time, the interest towards herbal -based medicine is reviving back due to the increasing health hazards associated with the indiscriminate use of modern medicines. Also, the herbal drug industries are now growing very fast in the international market.

12.1.2. Present Scope

India has world's oldest and the largest tradition of medicine systems. The Indian medicine systems include the systems originated in India as well as those originated outside India but got adopted with time. Ayurve da, Siddha, Unani, Homoeopathy, Yoga, and Naturopathy are the various systems of medicines practiced in India, and have become a vital part of India's culture and traditions. Indian traditional knowledge on herbal medicine and vast plant biodiversity has a great potential in this sector.

About 80% of people in developing countries are estimated to rely for their primary health care on traditional medicines based on species of plants and animals. Herbal medicines are in demand and their popularity is incre asing day-by-day. About 500 medicinally useful plants are mentioned in ancient literature

and around 800 plants have been used in indigenous medicine system. Use of herbal medicine is gaining popularity due to toxicity and side effects resulting from allopathic medicines. In India, around 20,000 medicinal plant species have been recorded, but about 800 plant species are used by more than 500 traditional communities for curing different diseases. Plants are important sources of medicines, and around 25% of p harmaceutical prescriptions in the United States have at least one ingredient that has been derived from plants. Ayurveda is the most ancient system of health care, and India has a rich heritage of more than 1000 years of knowledge in this system.

India has one of the richest plant traditions in the world. There are estimated to be around 25,000 effect ive plant-based formulations used in folk medicine and known to rural communities in India. There are approximately 1.5 million practitioners of traditional medicinal system using medicinal plants in preventive, promotional and curative applications. There are over 7800 medicinal drug manufacturing units in India, which consume about 2000 tons of herbs yearly. During 1950 -1970, nearly 100 plant -based new drugs , including reserpine, rescinnamine, reserpine, vinblastine, and vincristine, were introduced in the USA drug market.

From 1971-1990, new drugs such as etoposide, E -guggulsterone, artemisinin and ginkgolides appeared all over the world. Plant -based drugs contribute to modern therapeutics, **for example**, isolation of serpentine from the roots of *Rauwolfia serpentina* in 1953 was a revolutionary event in the treatment of hypertension and lowering blood pressure; vinblastine, isolated from *Catharanthus roseus*, is used for the treatment of Hodgkin's, choriocarcinoma, non -Hodgkin's lymphomas, leukaemia in children, testicular and neck cancers; vincristine is used for acute lymphocytic leukaemia; and *Podophyllum emodi* is used against testicular small cell lung cancer and lymphomas.

More than 64 plants are significant anti -bacterial and more than 24 plants are anti-diabetic. **For example,** teniposide and etoposide, isolated from podophyllum species, are used for testicular and lung cancers; and taxol, isolated from *Taxus brevifolia*, is used for metastatic ovarian and lung cancers.

Market Value of Herbal Medicines

India's share in the export of herbal medicines is US $ 63 billion, i.e., only 0.2% of the global herbal market. Hence, there is a vast scope for Indian manufacturers to enter the growing worldwide opportunity of business in herbal pharmaceutical field. In many countries , the Indian products can be registered and gain the necessary reliability for their export. The registration guidelines for every country are d ifferent and hence there is a possibility of modifying such requirements before identification of market for our product. Global awareness for quality is high and the quality building of the product should be the main focus. The manufacturing facilities an d infrastructure should comply with the GMP standards. In schedule T of the Drugs and Cosmetics Law and Rules, GMP for traditional medicinal products has been defined. Each and every manufacturer should make efforts to comply with these standards.

Indian Herbal Industry

According to a study commissioned by the Associated Chamber of Commerce and Industry (**ASSOCHAM**), the herbal products have gained popularity at the present time and found more applications in medicinal treatment over the world. India has ar ound 25,000 licensed pharmacies of Indian medicine system. At present, about 1000 single drugs and 3000 compound formulations are registered. Indian herbal industry employs about 8000 medicinal plants. However, pharma industries have still not standardised herbal medicines using active compounds as markers linked with confirmation of bioactivity of herbal drugs in experimental animal models.

In India, out of 8000 drug manufactures, there are only 25 large scale manufactures. The annual turnover of Indian herbal industry was estimated around US $ 300 million in Ayurvedic medicine and about US $ 27.7 million in Unani medicine. The annual turnover of Ayurvedic and herbal products rose to US $ 31.7 million in 1998 -1999 and to US $ 48.9 million in 1999 -2000. Export of herbal drugs in India is around $ 80 million.

Table 12.1: Size and Growth of Market for Indian System of Medicine

Market Size	In Million
Ayurvedic medicines	₹35,000 US $824
Homeopathic medicines	₹6,000 US $824
Siddha medicines	₹50 US $824
Unani medicines	₹1,000 US $824

Standardisation of Herbal Products

The products offered by Indian herbal industries are complex formulations. Since many of them are used as traditional medicines, their standardisation should be the prime focus. The cur rent scenario demands regulatory data and proofs of regulations for each product to be exported. Thus, standardisation of herbal products is highly important for various registration procedures in foreign countries. **PHARMEXCIL** (the pharmaceutical export pr omotion council) is ready to act as a coordinator and fascinator for initiating various efforts. India has many opportunities, like cultivation of medic inal plants and exporting value - added herbal formulations to international markets.

Pharmacovigilance of Herbal Medicines

At present, most of the adverse events related to the use of herbal products and medicines are attributable either to poor product quality or to improper use. Such events are caused due to inadequate regulatory measures, weak quality co ntrol systems, and uncontrolled distribution channels. The knowledge about genuine adverse reactions to herbal medicines can be expanded and wastage of limited resources for identifying and analysing adverse events can be avoided by minimising or eliminating the events resulting from such situations.

The WHO member states e ncourage strengthening national regulation, registration and quality assurance and control of herbal medicines. The national health authorities should focus more on consumer education an d qualified practice in the provision of herbal medicines.

In India on the other hand, herbal drugs are an integral part of the Indian Ayurveda medicine system (an ancient and mainstream system). Indian culture is also rich in herbal drugs, which are sold openly, thus causing a high incidence of self-medication. The people who should not use herbal drugs are also using them frequently. Due to these factors, India has the maximum number of herbal product users in the world. The health care providers have not paid any attention towards this issue. Now, Union Health Ministry is working to include Indian system of medicine into modern medical education.

12.1.3. Future Prospects

Due to the increasing use and fast-growing market of herbal medicines and other herbal healthcare products in developing as well as in developed countries of the world, the policy-makers, health professionals, and public are expressing concerns about the safety, efficacy, quality, availability, preservation, and development problems of these products. Public demand has also grown for evidence on the safety, efficacy and quality of herbal products. These concerns can be alleviated and public demands can be met by undertaking extensive research on herbal medicines for their healthcare value and commercial benefits. Extensive phytochemical and pharmacological researches on medicinal plants and herbal medicines are already in process to isolate and identify their active chemical constituents and to validate the claims of their efficacy and safety. As a result, it has been observed that herbal medicines are not completely without scientific basis and most of them have the significant chemical compounds and exert the claimed activity.

At present, it is obvious that despite the concerns and demands of the policymakers, health professionals and public, they do not stop the increasing trend of using herbal medicines. Thus, herbal medicine-based Traditional Medicine (TM) practices remain widespread in developing countries and that of Complementary and Alternative Medicine (CAM) is increasing rapidly in developed countries. This trend of growing and extensive use of herbal medicines increases further throughout the world with more scientific evidences on their quality, efficacy and safety coming from the researchers.

However, the quality and safety of herbal medicines can be proven only if their production, sale and use are officially and legally controlled by established rules and regulations (as for allopathic medicines). But, in most countries these regulations and registration of herbal medicines are not well-developed, and also the quality of herbal products sold is not guaranteed. Therefore, herbal medicines should be legally controlled in the countries where they are used for medical and therapeutic purposes and public awareness about their risks and benefits should also be enhanced.

If herbal medicinal products of assured quality are used properly, the users will experience beneficial therapeutic effects with reduced associated risks. It should also be noted that herbs and herbal products are not totally free from side effects, and may cause adverse effects. One should stop using adulterated herbal

ingredients and inappropriate formulations as this may result in the production of low-quality and harmful or dangerous herbal medicines. Therefore, rules and regulations of GMP should be followed for the production of herbal medicines.

It may be concluded that herbal medicines hold good future prospects, and they may emerge as good substitutes or alternatives for synthetic chemical-based allopathic drugs or may even replace them.

12.2. PLANT-BASED INDUSTRIES AND INSTITUTIONS INVOLVED IN WORK ON MEDICINAL AND AROMATIC PLANTS IN INDIA

12.2.1. Introduction

Many academic, industrial and government institutes are conducting research on Indian medicinal plants. No systematic review of the massive work that is available from this nation has been presented. Many international databases and websites do not even include the work published in Indian Journals. Hence, a global lack of awareness of the amount and nature of work conducted on diverse aspects, like ethnobotany, phytochemistry, pharmacognosy, pharmacology, clinical trials, safety studies, and formulation-research, occurs. Some eminent institutes which are active in research on medicinal plants and in Ayurveda are enlisted in **table 12.2**:

Table 12.2: Herbal Research Institutes/Centres in India

Names	Cities
CCRAS (Central Council for Research in Ayurveda and Siddha)	New Delhi
RRL (Regional Research Laboratory) (CSIR)	Jammu-Tawi
NBRI (National Botanical Research Institute) (CSIR)	Lucknow
Gujarat Ayurveda University	Jamnagar
Bhavan's SPARC	Mumbai
National Institute of Ayurveda	Jaipur
ACARTS	Mumbai
Arya Vaidya Shala	Kottakal
Interdisciplinary School of Health Sciences	Pune
BHU (Banaras Hindu University)	Varanasi
CIMAP (Central Institute for Medicinal and Aromatic Plants) (CSIR)	Lucknow
ICMR (Indian Council for Medical Research)	New Delhi
National Medicinal Plants Board	New Delhi
Indian Drug Manufactures	Mumbai
Regional Medical Research Centre (ICMR)	Belgaum
PERD Centre (Pharmaceutical Education and Research Developmen	Ahmedabad
CCRUM (Central Council for Research in Unani Medicine)	New Delhi
NISCOM (National Institute of Science Communication)	New Delhi
IMPCOPS (Indian Medical Practitioners Co-Operative Pharmacy and Stores Ltd.)	Chennai
IHMMR (Indian Institute of History of Medicine and Medical Research)	New Delhi
Zandu Foundation	Mumbai

Pharmexcil	Hyderabad
Chemexcil	Mumbai
CDRI (Central Drug Research Institute) (CSIR)	Lucknow
IMPLANT Centre (Inter-university Medicinal Plant Laboratory for Analysis, Nurture and Therapeutics)	Rajkot
NIMHANS (National Institute for Mental Health and Neurosciences	Bangalore
Punjab University	Chandigarh
LM College of Pharmacy	Ahmedabad
NBPGR (National Bureau of Plant Genetic Resources)	New Delhi
NPRC (Nicholas Piramal Research Centre)	Mumbai
NCL (National Chemical Laboratory)	Pune
TBGRI (Tropical Botanical Grande and Research Institute)	Thiruvananthapuram
BHU (Banaras Hindu University)	Varanasi
Podar Hospital	Mumbai
Botanical Survey of India	Kolkata
FRHLT (Foundation for Revitalisation of Local Health Traditions)	Bangalore
IASTAM (International Assoc iation for the Study of Traditional Asian Medicine)	Mumbai
ADMA (Ayurvedic Drug Manufacturing Association)	Mumbai

12.2.2. Classification of Medicinal Plant-Based Industry

Medicinal plant-based drug industry can be classified into six categories:

1) Plant drug s for Indian system of medicine (traditional system) including Ayurveda, Unani and Siddha,
2) Over the counter, non-prescription products consisting of plant parts, extracts and galenicals,
3) Essential oils industry,
4) Phytopharmaceuticals,
5) Natural health products:
   i) Health foods,
   ii) Nutraceuticals, and
   iii) Recombinant proteins.
6) Cosmeceutical industry.

12.2.3. Medicinal Plant-Based Industries in Indigenous System of Medicine

Several traditional health care systems of medicine, like Ayurvedic, Siddha, Unani and Tibbi, are in pr actice in Indian subcontinents. The Ayurvedic system of medicine is practiced in India and Nepal; Unani and Tibbi system of medicine are practiced in Pakistan.

All these alternative systems of medicines were introduced at different stages, and they co -exist with their indigenous systems of medicine in the multi -ethnic states of India.

A number of small manufacturing units use medicinal plants , and numerous Vaidyas prepare their own drugs from various plants. Herbal industry in India uses around 8000 medicinal plants, some of which are enlisted in **table 12.3**.

Table 12.3: Frequently Used Medicinal Plants in Traditional Herbal Formulations

Terminalia chebula, T. bellirica	219
Emblica officinalis (Amla)	346
Glycyrrhiza glabra (Mullethi)	141
Piper longum (Pipali)	135
Adhatoda vasica (Vasaka)	110
Withania somnifera (Ashwagandha)	109
Cyperus rotundus (Mastak)	102
Tinospora cordifolia (Guduchi)	88
Berberis aristata (Daruharidra)	65
Holarrhena antidysenterica (Kutaga)	59
Boerhavia diffusa (Punarnava)	52

Several decades ago in India, the practicing physicians used to prepare medicines used in indigenous medicine systems. However in recent decades, organised indigenous drug industries have been established. It is estimated that around 25,000 licen ced pharmacies of Indian medicine systems and around 700,000 registered practitioners of Ayurveda, Siddha and Unani medicines are available at present.

About 1000 single drugs and 3000 compound formulations are registered at the current time. Similarly , Siddha, Unani and Amchi (local version of Tibetan) medicine systems make use of about 600 -800, 700 -800 or 500 -600 medicinal plants, respectively. However, the exact usage of individual plant materials in the traditional medicine systems cannot be quantified due to the lack of reliable data.

Development in Herbal Medicine Industry

Herbal medicines are the finished, labelled medicinal products containing active ingredients from aerial or underground parts of plant o r other plant materials, or their combination, either in crude state or as plant preparations. Plant materials include juices, gums, fatty oils, essential oils, and other substances of the same nature. Apart from the active ingredients, herbal medicines may also contain excipients. Medicines conta ining plant materials along with the chemically - defined active substances, including the chemically -defined isolated constituents of plants, are not considered herbal medicines.

Unusually, in some countries, herbal medicines may also contain natural or ganic or inorganic active ingredients which are not of plant origin.

The annual turnover of Indian herbal industry was estimated around U S $300 million in 1995. In 1997 -98, the export value of Ayurvedic and Unani medici ne was about US $27.7 million. In 1998-99, the turnover again went up to US $31.7 million. In 1999-2000, the total turnover was US $48.9 million of Ayurvedic and herbal products; the major OTC products contributed about US $25.5 million, the ethical formulations around US $13.8 million, and the classical Ayurvedic formulations contributed to the remaining US $9.6 million.

12.2.4. Non-Prescription Production (OTC) Consisting of Plant Parts, Extracts and Galenicals

Direct utilisation of plant material is a feature of traditional medicines in developing countries as well as in developed countries (like Europe and U.S.A.). Europe has been involved since ages in the research and processing of botanical extracts, and has strict regulations, established quality control procedures, and details of clinical data in the support of products. The European market is well-regulated just like the drug industry and many of the compounds sold in U.S.A as dietary supplements are marketed as drugs in other countries.

Herbal formulations on health food shops (**e.g.,** decoctions, tinctures, galenicals, and total extracts of plants) are mentioned in many Pharmacopoeias. The current trend of medicinal plant-based drug industry includes procurement of standardised extracts of plants as raw materials, for which they are trying to establish their own Research and Development unit as per the WHO-issued guideline.

The guidelines aim to define basic criteria for the evaluation of quality, safety and efficacy of herbal medicines, and to assist national regulatory authorities, scientific organisations and manufacturers to evaluate the documentation/submission/dossiers related to such products. Traditional indicates the products in long-term use.

During evaluation, the medical, historical and ethnological background of these products, and also a description in medical/pharmaceutical literature or similar sources, or a documentation of knowledge on the application of a herbal medicine without a clearly defined time limitation should be taken into consideration.

Herbal and related extracts will experience the strongest growth based on expanding scientific evidence of health benefits and rising popularity of alternative medicines. Widely observed health benefits among consumers increase the demand for herbal and related extracts by 10% annually.

Many Pharmacopoeial Committees for Ayurveda, Siddha, Unani and Homeopathy systems of medicine have been established by the Government of India. The Pharmacopoeial Laboratory for Indian Medicines (PLIM) and the Homeopathy Pharmacopoeial Laboratory (HPL) at Ghaziabad provide technical support to these committees. At the current time, about 178 monographs are ready for publication.

The Pharmacopoeia Committees have also published two volumes of Ayurvedic Formularies of India including 635 formulations. The Siddha Pharmacopoeia Committee has published seven volumes including standards of 910 drugs. The Unani Pharmacopoeia Committee has published a National Formulary including 441 Unani formulations. Till now 45 monographs on single Unani drugs have been published. The Homeopathy Pharmacopoeia Committee has published seven volumes including standards of 910 drugs.

12.2.5. Essential Oil Industry

The essential oil industry was traditionally a cottage industry in India. In the last 55 years after independen ce, a few industrial companies have been established for production of essential oils, oleo -resins and perfumes on a large scale. More than 500 tonnes (that account for 90% of world production) of essential oils from plants are being produced in India.

Ajowain oil, celery oil, citronella, cedarwood, devana oil, eucalyptus, lemongrass, mentha species, geranium, lavender, palmarosa, patchouli, rose oil, orange (cold-pressed), jasmine, vetiver, coriander, sandalwood, and pine trees are the Indian aromatic me dicinal plants utilised for large scale production of essential oils.

India has a well-established industry for the production of turpentine oil and resin from pines, having annual production of about 35,000 -40,000 tonnes. India also has a well -established industry for the production of mentha oil from *Mentha arvensis*, eucalyptus oil from *E. globulus* , and lemon oil from the discarded orange and lemon peel. The world production of limonene is about 75,000 tonnes annually, and Brazil is the biggest global p roducer. Limonene is the by -product of citrus, though turpentine oil and eucalyptus oil also yield limonene.

In 2000 -2001, India exported 3,87 5 tonnes of mint oil valued at 1.26 billion. Lemongrass, citronella, palmarosa, vetiver and rose oils are the ma jor essential oils produced in India. India also produces jasmine concentrate, which is of high value product in perfumery industries.

12.2.6. Phytopharmaceuticals

Before inde pendence, plant -based phytophar maceutical industry in India was confined only to quin ine from cinchona in the three state -owned factories. The first industry was established by the British Government at Mungpoo in Darjeeling. In past 55 years, bulk production of plant -based drug has become the major objective of Indian pharmaceutical indus try. Morphine, codeine, papaverine, thebaine, emetine, reserpine, quinine, quinidine, digoxin, caffeine, hyoscyamine, berberine, colchicine, r utin, vinblastine, vincristine, brucine, strychnine, ergot alkaloid, senna glycosides, diosgenin, plant laxatives, podophyllotoxin resin, and citral are the phytopharmaceuticals produced in India.

Phytopharmaceuticals for which technology has been developed by Govt. Institution for large scale production include L. dopa from *Mucuna beans* , ajmaline and ajmalicine from *Rauwolfia serpentina*, *Catharanthus roseus* roots, and 18-β-acetyl glycyrrhetic acid from *Glycyrrhiza glabra.*

Indian Institute of Chemical Technology (IICT), Hyderabad has developed production methods for etoposide and teniposide. CIPLA is also producing it on a commercial basis. National Chemical Laboratory, Pune developed the production method for vincristine (VCR) and vinblastine (VLB). CIPLA has improved the production techniqu e for the same and is the third -largest manufacturer of VCR and VLB in the world.

12.2.7. Natural Health Products Industry

The interest in herbal medicines, phytodrugs, and natural health products, including health foods, nutraceuticals and personal care products, is increasing nowadays:

1) **Health Foods:** These are food products supplemented with herbal ingredients, vitamins, minerals, nutrients, and ingredients isolated from plants. They have physiological benefits that reduce the risk of chronic diseases.

2) **Nutraceuticals:** The term **nutraceutical** is used for health food, and was first origi nated by **Stephen Deffice** (Founder of the Foundation for Innovation in Medicine of New Jersey, U.S.A.). This word is a combination of the terms **nutrition** and **pharmaceutical**. It can be defined as parts of a food that have medical or health benefits including the prevention and treatment of diseases. The three main constituents, which form nutraceuticals are herbal and related extracts, vitamins, minerals and nutrients.

   Antioxidant and herbal teas also form an important part of the nutraceuticals market. The leading antioxidant phytochemicals in demand are vitamins A, C and E, carotenoids, and flavonoids. The U.S. demand for nutraceuticals increased from US $830 million in 1987 to US $1.7 billion in 1996 and was expected to reach US $4.5 billion in 2005.

   Nutraceuticals are the most progressing sector for health food and pharmaceutical industry based on plants. Many functional foods or nutraceutical companies form part of l arger food or phar maceutical industries. Many large food and phar maceutical companies, such as Abbott Laboratories, Smithkline Beecham, Glaxo, Led erle, Dabur, Himalayas, Zandu pharmaceuticals, Allen laboratories, and Aimil pharmaceuticals also manufacture nutraceuticals. Ranbaxy Pharmaceutical Industry has also started its herbal research and development units.

12.2.8. Herbal Cosmetics and Personal Care Products

Cosmetics and personal care products containing natural products are rapidly growing in the market. Beginning in the early 1990s, manufacturers of cosmetics started using the term **cosmeceuticals** to describe the OTC skincare products. These cosmeceutical products, claiming therapeutics benefits, contain phytoconstituents in the form of extracts or in the purified form such as α-hydroxy acids, vitamins, antioxidants and emollient oils rich in vitamin A and E. Aloe extracts, botanical extracts plant acids/enzymes and essential oils are in more demand in cosmetics and coppicing industry.

Botanical Extracts

Some common b otanical extracts include canola (*Brassica napus*), chamomile (*Matricaria cha momilla*) dry extract, marigold (*Calendula officinalis*) dry extract, echinacea (*Echinacea supp.*), bilberry (*Vaccinium myrtillus*) dry extract, pumpkin seed (*Cucurbita pepo*) lipophilic extract, ivy (*Rhus toxicodendron*) soft extract, peruvian bark (*Cinchona su ccirubra*) fluid extract, ginkgo (*Ginkgo biloba*), leaf extract of centella (*Centella asiatica*), hawthorn (*Crataegus spp.*), and willow herb (*Epilobium ciliatum*).

12.3. SUMMARY

The details given in the chapter can be summarised as follows:

1) India has one of the richest plant traditions in the world.
2) **PHARMEXCIL** (the pharmaceutical export promotion council) is ready to act as a co-coordinator and fascinator for initiating various efforts.
3) A number of small manufacturing units use medicinal plants, and numerous Vaidyas prepare their own drugs from various plants.
4) Many Pharmacopoeial Committees for Ayurveda, Siddha, Unani and Homeopathy systems of medicine have been established by the Government of India.
5) India has a well-established industry for the production of turpentine oil and resin from pines, having annual production of about 35,000-40,000 tonnes.
6) **Health foods** are food products supplemented with herbal ingredients, vitamins, minerals, nutrients, and ingredients isolated from plants.
7) The term **nutraceutical** is used for health food, and was first originated by **Stephen Deffice** (Founder of the Foundation for Innovation in Medicine of New Jersey, U.S.A.).
8) Beginning in the early 1990s, manufacturers of cosmetics started using the term **cosmeceuticals** to describe the OTC skincare products.

12.4. EXERCISE

12.4.1. Very Short Answer Type Questions

1) Enlist some herbal research institutes centered in India.
2) Classify medicinal plant-based industry.
3) What are phytopharmaceuticals?
4) Define nutraceutical.

12.4.2. Short Answer Type Questions

1) Write about the future aspects of herbal drug industry.
2) Discuss about medicinal plant-based industries in indigenous system of medicine.
3) Write a note on non-prescription production consisting of plant parts, extracts and galenicals.

12.4.3. Long Answer Type Questions

1) Briefly discuss about the present scope of herbal drug industry.
2) Give a brief review on plant-based industries and institutions involved in work on medicinal and aromatic plants in India.

CHAPTER 13

Schedule T - Good Manufacturing Practice of Indian Systems of Medicine

13.1. SCHEDULE T – GMP OF INDIAN SYSTEMS OF MEDICINE

13.1.1. Introduction

Quality assurance aspects are an integral part of all the systems of medicines, and therefore it is essential to follow them to the fullest extent . The protocols given below should be followed to ensure the quality of a traditional medicine system:

1) Gazette Notification GSR 561 (E) Dated – 23rd June, 2000.
2) Schedule T under Rule 157 of Drugs and Cosmetics Rule, 1945.
3) Applicable to whole country from 23 rd June, 2000 for New AS U manufacturing units.
4) Units registered before 23rd June, 2000 are give n 2 years' time to comply with individual Vaidyas/Siddhas/Hakimas exempted.
5) A GMP certificate made on plain paper.
6) The GMP certificate will be issued within 3 months after pro per investigation.
7) The GMP certificate will be given in form EL (under Rule 157 -B) for a period of 3 years.

13.1.2. Objectives of GMP (Schedule T)

Following are the objectives of GMP (Schedule T):

1) To describe the manufacturing processes as per the standards.
2) To ensure that the manufacturers use authentic raw materials of prescribed quality.
3) To ensure that the raw materials used should be free from contamination.
4) To adopt adequate quality control measures during processing of drugs.
5) To ensure that the manufactured drug is of prescribed quality before being released for sale.
6) To optimise the efficacy of the product regardless of the manufacturing method.
7) To describe manual of methodology.
8) To maintain d ocumentation of the procedure as a manual for reference an d inspection.

13.1.3. Components of GMP (Schedule T)

The manufacturing plant should have sufficient space for different processes, like manufacturing process areas, quality control section, finished goods store, office for receiving and storing raw material s, an d an office for rejected goods/drugs store.

13.1.3.1. Infrastructural Requirements

Location and Surroundings

The premises should be located and surrounded where there is:

1) No open sewage,
2) No drainage coming from public areas and toilets,
3) No factory fume, and
4) No excessive soot, smoke, and dust.

Buildings

The buildings should be compatible with manufacturing operations and located where:

1) Hygienic conditions are maintained,
2) No cobwebs/insects/rodents are present,
3) Adequate light and ventilation are available,
4) The floor and walls are free from dampness and moisture,
5) The floor and walls are even,
6) Adequate working space is available,
7) The equipment is placed such that the risk of mixing, cross-contamination and risk of omission of a control step can be avoided,
8) The premises are so designed, constructed and maintained that insects/ rodents cannot enter,
9) The interior surface is smooth, and easy to clean and disinfect,
10) Mooring is smooth and even to prevent retention or accumulation of dust or waste products, and
11) The premises for manufacturing, processing, packaging and labelling processes are compatible with the provisions of Factory Act.

Proper Drainage System

The drainage system of the premises should:

1) Have proper sanitary fittings and electrical fixtures for safety,
2) Have furnace and Bhatti section covered with tin roof,
3) Have proper ventilation/chimney in factory,
4) Prevent flies and dust in factory premises, and
5) Have proper fire safety measures/exits installed.

Water Supply

There should be proper water supply within the premises because large amount of water is required for washing the premises and containers used in the manufacturing processes. Water used in the manufacturing process should be pure and drinkable.

Disposal of Waste

The wastewater and other residues obtained as by-products of the manufacturing processes and laboratory operations are harmful to work and public health, and thus should be disposed after proper treatment as described in the guidelines issued by the Pollution Control Board.

Container's Cleaning

There should be an area for cleansing of the containers used in the manufacturing processes. These containers should be washed, cleaned and dried properly.

13.1.3.2. Working Space

The manufacturing area should be spacious enough to provide adequate space for manufacturing and quality control processes, and also for orderly arrangement of the equipment and material used in those processes. Adequate measures should be taken to prevent cross -contamination of one drug by another drug being manufactured, stored or handled in the same premises . Therefore, proper facilities for easy and safe working and for reducing or eliminating mixing up of the drugs should be provided.

Table 13.1: Space Requirement for Manufacturing of ASU Drugs

Category of Medicine	Minimum Space Required
Anjana/Pisti	100 sq. ft.
Churna/Nasya/Manjan/Lepa/Kwatha Churna	200 sq. ft.
Pills/Vati/Gutika/Mathirai	100 sq. ft.
Kupi pakva/Ksara/ Parpati	100 sq. ft.
Kupi Pakva/Ksara/Parpati/Satva	150 sq. ft.
Kajal	100 sq. ft.
Capsules	100 sq. ft.
Ointment/Marham Pasi	100 sq. ft.
Pak/Avaleh/Khand/Modakllakayam	100 sq. ft,
Panaka/Syrup/Pravahi Kwathi Manapaku	150 sq. ft.
Asava/Arishta	200 sq. ft.
Sura	100 sq. ft.
Arka/Tinir	100 sq. ft.
Taila/Ghrita/Ney	100 sq. ft.
Aschyotan/Netra Malham/Panir	100 sq. ft.
Bhatti, furnace, boilers, puta, etc.	200 sq. ft.

13.1.3.3. Storage Area

The storage area should be spacious enough for proper storing of raw materials, packing materials, and finished products. The storage area should have proper ventilation and should be free from dampness.

Raw Material Stores

Appropriate number of containers should be present in the storage area for raw materials to maintain their quality for a long time period and also to prevent them from contamination, rodents, or insect infestation. Cabinets should be provided for storage of raw materials of metallic origin, mineral origin, animal origin, fresh herbs, dry herbs, plant parts, excipients, volatile oils/perfumes and flavours, plants extracts, exudates/resins, etc. All the containers used for storage of raw materials should be properly identified and clearly labelled with the name, source, and status (i.e., under test or approved or rejected) of the raw material. The batch or lot number, and date of receiving the consignment should also be mentioned on the label.

All the raw materials to be used should be sampled and properly analysed either by the in-house quality control technical personnel or by the government laboratories. The raw materials should be used only on approval after verifying. Records should be maintained for the receipt, testing, approval, and rejection of raw materials.

Packing Materials
All the packing materials (**e.g.,** bottles, jars, capsules, etc.) should be properly stored. Before packing the products, the container and closure lids should be properly cleaned and dried.

Finished Goods Stores
The finished products are transferred from the production area to packaging area. The packed products are then stored properly on shelves in a quarantine area. The correctness of finished products (with reference to their packing/labelling) and the quality of finished products (as per the standards established) should be checked by the quality control laboratory and experts. Thereafter, the approved finished products are sent to the stock area, and allowed to be dispatched as per the marketing requirements. The records of distribution should be maintained. Special drugs should be stored as per the specified storage conditions.

13.1.3.4. Machinery and Equipment
Machinery and equipment should be according to the size of operation and nature of manufactured product. Machinery available in the manufacturing unit should be manually operated, semi-automatic, or automatic. Machines or equipment for performing crushing, grinding, powdering, boiling, mashing, burning, roasting, filtering, drying, filling, labelling , packing, etc. should be installed in a manufacturing unit.

Adequate space should be available between two machines or rows of machines for easy and proper movement of workers and orderliness in operations. The equipment should be properly installed and maintained by regular cleaning.

13.1.3.5. Standard Operating Procedures (SOPs)
Proper standard operational procedures should be established for cleaning, maintenance and performance of every machine as per the given standards.

13.1.3.6. Health and Hygiene
All the employees in the factory should be healthy and free from any infectious diseases. Clothing and other apparels of the workers should be clean. They should be dressed in proper uniforms, including cloth or synthetic covering of hands and feet, as per the nature of work and the climate.

For personal cleaning, adequate facilities such as clean towels, soap and scrubbing brushes, should be provided. Separate lavatories should be made for men and women, and should be located in an area separated from the processing rooms. Facilities , such as rooms for changing cloth and to keep personal belongings, should also be provided to the workers.

13.1.3.7. Medical Services
The manufacturer should also provide the following medical facilities:
1) Annual medical check-up of all the workers should be performed by a physician to ensure they are free from infectious diseases.

2) At the time of recruitment, a medical examination of the workers should be performed.
3) All the records regarding the health and check -ups of each worker should be maintained.

13.1.3.8. Documentation and Records

Batch Manufacturing Records

Batch manufacturing record of every manufacturing process should be maintained by the manufacturer. Records should be maintained for the raw materials used, quantity obtained from the store, tests conducted during manufacturing, like taste, colour, physical characteristics, chemical tests, etc. Various in-house or Pharmacopoeial tests are performed by the manufacturer for the raw materials, in-process materials, and for finished products.

Records for transferring the manufactured drug to the finished product store, its storage along with other records of the finished product, packaging , etc., should be maintained. All the manufacturing records should be signed by the production and quality control personn el. It is important to maintain a record of date, manpower, machin e, and equipment used and an in -process record of various Shodhana (purificatory procedures of poisonous drugs) and Bhavana (trituration) in terms of internal use.

Distribution Records

Records should be maintained for sale and distribution of each batch of Ayurveda, Siddha and Unani drugs. These records facilitate quick and complete recall of the batch whenever needed.

Record of Market Complaints

A complain register should be maintained for keeping records of the received market complaints related to the products sold in the market. All the data received on market compla ints should be entered in the register by the manufacturers. The manufacturers should also keep a record of the investigations carried out regarding the complaint, along with the corrective action s taken to prevent the reappearance of such market complaints. It is the responsibility of the manufacturers to submit records of these complaints to the licensing authority once in every six months. The complaint register should also be provided d uring any inspection of the premises.

A separate register should be maintained by the manufacturers for recording any adverse reaction occurring after the use of Ayurvedic, Siddha and Unani drugs. The manufacturers should carry out a n investigation on any adverse reaction to check whether the same occurs due to any defect in the product, whether such reactions are already reported in the literature, or whether it is a new observation.

13.1.3.9. Quality Control

Facilities for quality control should be provided by each licensee either in his/her own premise or in a government testing laboratory. The quality control test should be performed as per the standards of Ayurveda, Siddha and Unani Pharmacopoeia.

The tests should be performed according to the manufacturer's specification or other available information, where the standard tests are not prescribed. The quality control section should verify all the raw materials monitored in process, quality checks and control the quality of finished products being transferred to finished goods store/warehouse. An expert should be appointed for such quality control processes. Following facilities should be provided within the quality control section:

1) The quality control section should be of 150 square feet area.
2) Reference books and samples should be maintained for easy identification of raw drugs.
3) Manufacturing records for various processes should be maintained.
4) Controlled samples of finished products of each batch should be kept for 3 years for verification of the finished products.
5) The conditions under which raw materials, semi-finished and finished products are stored should be controlled and monitored.
6) Records should be maintained for establishment of shelf-life and storage requirements for the drugs.
7) Manufacturers should provide their own specifications and control references with respect to manufacturing Ayurveda, Siddha, and Unani drugs.
8) The record of each method and procedure carried out by the manufacturer for any general or specific preparation, i.e., Bhavana, Mardana and Puta (earthen pits) should be maintained.
9) The standards for identity, purity and strength should comply with the standards given in Pharmacopoeias of Ayurveda, Siddha and Unani medicine systems published by Government of India.
10) Raw materials should be monitored for fungal and bacterial contamination to minimise such contamination.
11) Quality control section should have atleast one person with degree qualification in Ayurveda/Siddha/Unani (ASU) as per Schedule II of Indian Medicine Central Council Act, 1970 (84 of 1970) from a recognised university or board, provided that Bachelor of Pharmacy, Pharmacognosy and Chemistry should be associated with the quality control section.

Requirement of Sterile Product

Manufacturing Areas

A separate, enclosed, and specially designed area should be provided for manufacturing sterile Ayurvedic, Unani and Siddha drugs. These areas should be free from dust, should have airlocks for entry, and should be ventilated with an air supply. Bacteria retaining filters (i.e., HEPA filters) with pressure higher than in the adjacent areas should be fixed in the areas where aseptic manufacturing has to be carried out. Performance of these filters should be checked at the time of installation and after periodic intervals, and related records should also be maintained.

In the sterile manufacturing area, the surfaces should be designed such that they facilitate cleaning and disinfection. Routine microbial counts of all Ayurvedic, Siddha and Unani drugs should be performed during the sterile manufacturing process, the results of such counts should be checked against the established in-house standards, and records should also be maintained.

There should be minimum access to the sterile manufacturing area , and only authorised personnel should be allowed to enter . Specific procedure s should be followed while entering and leaving the sterile manufacturing areas , and that procedure should be displayed at the entrance.

The design of the areas for manufacturing Ayurvedic, Siddha and Unani drugs that can be sterilised in their final containers should be such that the products to be sterilised are prevented from getting m ixed with or taken to be products already sterilised . For terminally sterilised products, the design of the areas should prevent mixing up between the non-sterile and sterile products.

Precaution against Contamination and Mix

Following precautions should be taken to avoid mixing and contamination:

1) The manufacturing operations should be performed in an isolated area of the same building or another building.
2) In the process area , an appropriate pre ssure differential device should be installed.
3) The germicidal efficiency of UV lamps should be checked timely and recorded showing the burning hours or checked using intensity.
4) An adequate exhaust system should be installed within the premises.
5) Laminar flow sterile air systems should be present for sterile products.
6) Each filled container of liquids and ophthalmic solutions should be analysed against black and white background installed with diffused light to ensure they are not contaminated with any foreign suspended matter.
7) An expert technical staff appointed by the Licensing Authority should check and compare the actual yield against theoretical yield before the batch is released for final distribution.
8) All the processes should be carried out as per master formula.
9) All the parameter s including adequate room temperature, relative humidity, volume, filled, leakage and clarity , should be checked and associated results should be recorded.

13.2. SUMMARY

The details given in the chapter can be summarised as follows:

1) Quality assurance aspects are an integral part of all the systems of medicines, and therefore it is essential to follow them to the fullest extent.
2) The manufacturing plant should have sufficient space for different processes, like manufacturing pro cess areas, quality control section, finished goods store, office for receiving and storing raw materials, and an office for rejected goods/drugs store.
3) There should be proper water supply within the premises because large amount of water is required for washing the premises and containers used in the manufacturing processes.
4) There should be an area for cleansing of the containers used in the manufacturing processes.

5) The manufacturing area should be spacious enough to provide adequate space for manufact uring and quality control processes, and also for orderly arrangement of the equipment and material used in those processes.
6) The storage area should be spacious enough for proper storing of raw materials, packing materials, and finished products.
7) The finished products are transferred from the pro duction area to packaging area.
8) Machinery and equipment should be according to the size of operation and nature of manufactured product.
9) Proper standard operational procedures should be established for cleaning, maintenance and performance of every machine as per the given standards.
10) All the employees in the factory should be healthy and free from any infectious diseases.
11) Batch manufacturing record of every manufacturing process should be maintained by the manufacturer.
12) Records should be maintained for sale and distribution of each batch of Ayurveda, Siddha and Unani drugs.
13) A complain register should be maintained for keeping records of the received market complaints related to the products sold in the market.
14) Facilities for quality control should be provided by each licensee either in his/her own premise or in a government testing laboratory.

13.3. EXERCISE

13.3.1. Very Short Answer Type Questions

1) What is schedule T?
2) Enlist four objectives of schedule T.
3) How packing materials should be stored as per schedule T?
4) Give the medical facilities to be provided to the manufacturer as per schedule T.

13.3.2. Short Answer Type Questions

1) Write about the infrastructural requirements as per schedule T.
2) Discuss about quality control as per schedule T.
3) Write a note on documentation and records as per schedule T.

13.3.3. Long Answer Type Questions

1) Give a brief review on Schedule T – GMP of Indian systems of medicine.
2) Briefly discuss about the components of GMP.

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Bibliography

- Evans W. C., Trease G. E., *Trease and Evan's Pharmacognos y,* W.B. Saunders.
- Shah B., Seth A.K., *Textbook of Pharmacognosy & Phytochemistry* , Elsevier.
- Jean Bruneton, Caroline K. Hatton, *Pharmacognosy, Phytochemistry, Medicinal Plants*, Lavoisier.
- Kokate C. K., Gokhale S.B. and Purohit A.P., *Textbook* of *Pharmacognosy*, Nirali Prakashan.
- Mukherjee Pulok K., *Quality Control of Herbal Drugs: An Approach to Evaluation of Botanicals*, Business Horizons.
- Rangari V.D., *Pharmacognosy & Phytochemistry (Vol I)*, Career Pub.
- Rangari V.D., *Pharmacognosy & Phytochemistry (Vol II)*, Career Pub.
- Roy Lester Whistler, James N. BeMiller, *Industrial gums: polysaccharides and their derivatives*, Academic Press.
- Seigler David S., *Plant Secondary Metabolism* , Kluwer Academic Publishers.
- Severian Dumitriu, *Polysaccharides: Structural Diversity and Functional Versatility*, CRC Press.
- Wallis T. E., *Textbook of Pharmacognosy*, CBS Publisher.
- Wink M., *Functions and Biotechnology of Plant Secondary Metabolites* , Blackwell Publishing Ltd.