DEPTH OF BIOLOGY

UNIT-1

- Impurities in pharmaceutical substances: History of Pharmacopoeia, Sources and types of impurities, principle involved in the limit test for Chloride, Sulphate, Iron, Arsenic, Lead and Heavy metals, modified limit test for Chloride and Sulphate

General methods of preparation, assay for the compounds superscripted with asterisk (*), properties and medicinal uses of inorganic compounds belonging to the following classes

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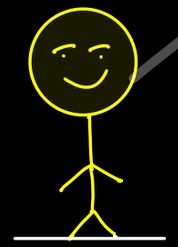
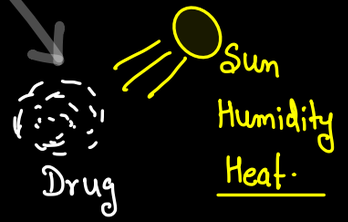
Dosage forms = Drug + Excipients. → filler, Binder, Stabilizer.

Raw Material ← , Heavy Metal, Contaminants.

Dirt, Oil, Hair.



Drug Isolation Or Extraction



(A) Drug + Excipient → Equipment → Sterile, Calibrated.

(B) Drug + Excipient →

Cross Contamination.

GMP.

Drug + Excipient —Chemical Used→ Dosage form.

Chemical residue May found.

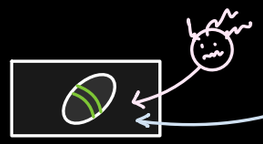
Unreacted Intermediate may found.

Contamination.

↑

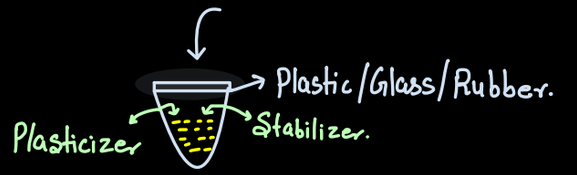
Packaging & Labelling.

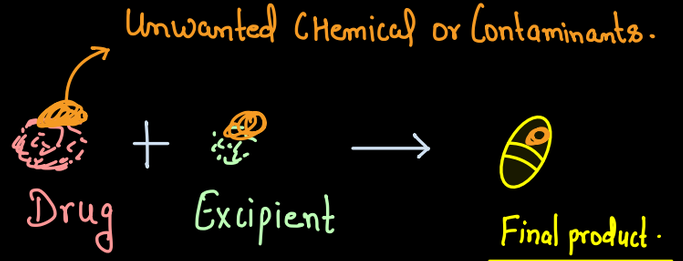
Dosage form (Improper Storage) →



Temp. fluctuation, Humidity

Light, O_2.





Impurities in pharmaceutical substances

Impurities in pharmaceutical substances are unwanted chemicals or contaminants that can be found in drug substances, excipients, or final drug products.

They can originate from various sources during the manufacturing process, storage, or packaging, and may affect the safety, efficacy, and quality of the pharmaceutical product.

Sources of impurities

Impurities in pharmaceutical substances can originate from various sources throughout the lifecycle of the drug product, from raw material procurement to the final formulation and distribution. These impurities can be classified into several categories based on their origin:

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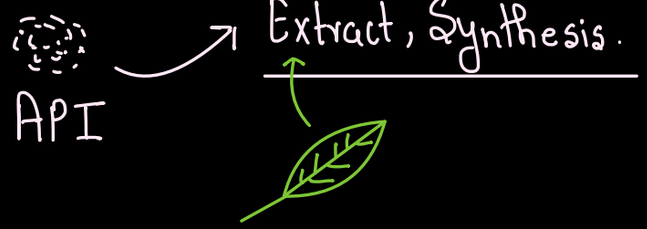
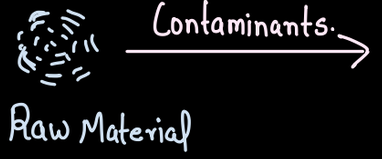


1. Raw Materials

Active Pharmaceutical Ingredients (APIs): Impurities may be introduced during the synthesis or extraction of the API. These can include residual solvents, by-products from the chemical synthesis process, or degradation products from storage.

Excipients: Inactive ingredients like fillers, binders, and stabilizers used in formulations may contain impurities from raw material sources or during their own manufacturing processes.

Contaminants in Raw Materials: Impurities may also come from contaminants in the raw materials, including microbial contamination, heavy metals, or foreign particles.



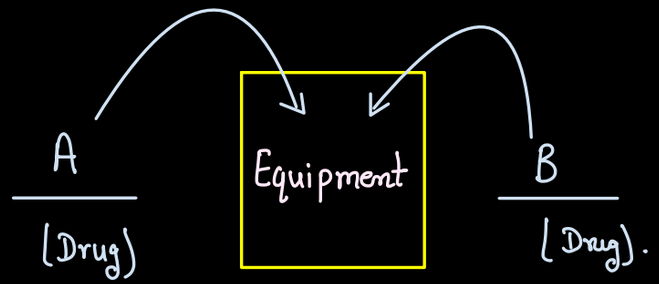
2. Manufacturing Process

Reagents and Solvents: Chemicals used in the synthesis or formulation of the drug may leave residual amounts in the final product. *If not properly removed or purified, solvents, catalysts, and reagents (like acids, bases, or alkylating agents) can remain as impurities.

Intermediate Products: Unreacted intermediates from the chemical synthesis process can become impurities if not fully reacted or removed during purification steps.

**Unreacted Intermediate must be removed in purification Step.

Cross-contamination: In multiproduct manufacturing facilities, impurities may arise from cross-contamination between different drugs produced in the same equipment or facility.



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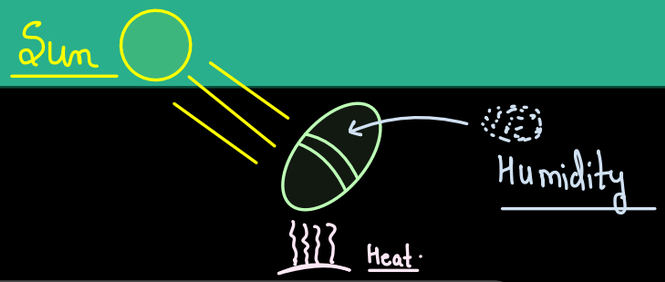
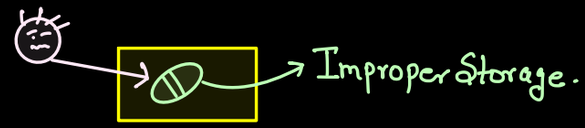


3. Degradation of Active Ingredients

Chemical Degradation: APIs can degrade due to exposure to factors like heat, light, humidity, and oxygen. Common degradation products include oxidation products, hydrolysis products, and photodegradation products.



Microbial Degradation: In some cases, APIs or excipients can be degraded by microorganisms during manufacturing or storage, leading to the production of new impurities.

4. Packaging Materials

Leachables and Extractables: Impurities can leach from packaging materials (such as plastics, rubber, or glass) into the drug product. These leachables may include plasticizers, stabilizers, or other chemical components that are part of the packaging material.

Contamination from Handling: Packaging and labeling processes may introduce impurities such as dust, oils, or residues from human contact or machinery.

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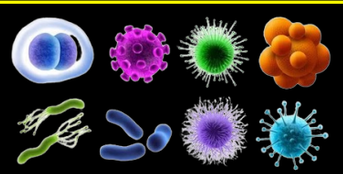
5. Storage Conditions

Temp. fluctuation.
Humidity, Light
Or Oxygen.

Environmental Factors: Exposure to temperature fluctuations, humidity, light, or oxygen during storage can lead to chemical degradation or microbial growth in drug products, leading to impurities.

Contamination During Storage: Inadequate storage conditions (e.g., unsealed containers or contamination from poorly maintained storage areas) may result in the introduction of external contaminants, such as dust, microorganisms, or chemical reactions with the environment.

6. Microbial Contamination



Manufacturing and Handling: Microbial contaminants like bacteria, fungi, and yeasts can be introduced during manufacturing, especially if aseptic conditions are not properly maintained. They can also be introduced through improper handling, storage, or packaging.

Water and Airborne Contaminants: Water used in the manufacturing process or as an ingredient can be a source of microbial contamination if not properly treated. Similarly, airborne contaminants from unclean air or environments can also contribute.

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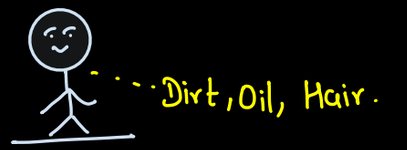
7. Human Handling and Environmental Contamination

Operator Contamination: Human operators can introduce impurities through direct contact with the drug substances during manufacturing or packaging, such as oils, dirt, or chemical residues from clothing, skin, or equipment.



Contaminants in the Production Environment: Airborne particles, dust, or particulate matter in the environment (from floor, walls, machinery) can contaminate the drug substance if good manufacturing practices (GMP) are not followed

8. Equipment and Manufacturing Tools

Residues from Equipment: Impurities can arise from equipment used in the production process, such as mixers, reactors, or filtration units. Residual chemicals from previous batches, wear-and-tear materials (e.g., metal particles), or cleaning agents used in the equipment can introduce impurities.

Leaching from Manufacturing Tools: Materials such as metals, polymers, or rubber used in the equipment or tools can leach into the drug substance.

9. Transportation and Distribution

Temperature and Environmental Conditions: Improper handling during transportation, such as exposure to inappropriate temperatures or humidity, can lead to the degradation of the drug and the formation of new impurities.

Contamination During Transit: Improper sealing, contamination from other goods, or exposure to pollutants can introduce impurities into the pharmaceutical product during transport.

Types of Impurities:

1. Organic Impurities → Related to Drug/API & Excipient.

These are chemical impurities that are often related to the active pharmaceutical ingredient (API) or excipients and may arise from the synthesis, degradation, or other processes.

-Process-Related Impurities: These impurities result from the manufacturing process and may include:

-Unreacted starting materials
-By-products from side reactions
-Residual solvents, reagents, or catalysts used in the synthesis

2. Inorganic Impurities

These include trace metals, salts, and other inorganic compounds that can arise from raw materials, equipment, or the environment during manufacturing.

Heavy Metals: Metals such as lead, arsenic, mercury, cadmium, or nickel may contaminate the drug product during manufacturing or from the raw materials. These impurities can be toxic, so their levels are strictly regulated.

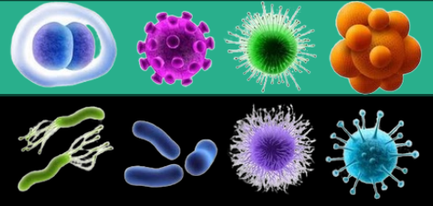
→ Raw Material, Manufacturing.

Elemental Impurities: These are trace metals (e.g., iron, aluminum, or zinc) that may be present in the API or excipients. The presence of elemental impurities is closely monitored to ensure patient safety, particularly for drugs that require parenteral administration.

→ Trace Metal Cont in A.P.I or Excipients.

Inorganic Residues: These are residues of salts or other inorganic substances that could be introduced during the manufacturing process, such as from the raw materials or the equipment used.

→ By Raw Material, Equipment.



3. Microbial Impurities

Microbial contamination can occur during manufacturing, storage, or handling, and it is especially critical for liquid formulations, injectables, and biologics.

Bacterial Contamination: Bacteria such as Pseudomonas aeruginosa or Staphylococcus aureus can contaminate injectable drugs or ophthalmic solutions.

Fungal Contamination: Yeasts and molds can contaminate drug products, especially in the case of liquid or semi-solid formulations exposed to moisture.

Endotoxins: Lipopolysaccharides from the cell walls of gram-negative bacteria that are toxic when injected. These endotoxins can cause fever and other adverse effects.

Mycoplasma: A type of microorganism that may be present in biologics or products derived from cell cultures.

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4. Physical Impurities

These refer to foreign particles or contaminants that are not chemically part of the drug product but may be introduced during manufacturing, packaging, or storage.

Glass Fragments: Small glass particles that may come from broken glass vials or packaging, especially in injectable products.

Metal Particles: These may come from the wear of equipment used during manufacturing or packaging processes (e.g., stainless steel or aluminum fragments).

Plastic Particles: These can arise from plastic containers or packaging materials and are a concern in both solid and liquid pharmaceutical products.

Dust and Fibers: These particles can be introduced during manufacturing or packaging and can affect the quality of tablets, capsules, and powder formulations.

5. Adventitious Contaminants (Coming from an External Source).

These are unintended and often incidental impurities that can be introduced from various sources during the manufacturing or packaging process.

Residual Cleaning Agents: Cleaning solutions or detergents used to clean equipment may leave residues in the final product if not properly removed.

Lubricants: Materials like magnesium stearate used to facilitate tablet formation may remain as impurities in the final product.

Cross-Contamination: Impurities introduced from other products or batches in the same manufacturing facility due to inadequate cleaning between production runs.

9. Contaminants from Packaging

Impurities may also arise from the packaging materials used for the drug product.

Leachables and Extractables: Substances that leach from plastic or rubber components of packaging materials into the drug product. These can include plasticizers, stabilizers, or other chemical residues from packaging.

Packaging Contaminants: Particles or chemicals from the packaging process, including residues from adhesives, coatings, or inks.

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Testing and Control:

Chromatographic Techniques: High-performance liquid chromatography (HPLC), gas chromatography (GC), and thin-layer chromatography (TLC) are commonly used to separate and identify impurities.

Mass Spectrometry (MS): Provides molecular weight and structural information about impurities.

Spectroscopic Techniques: Infrared (IR), nuclear magnetic resonance (NMR), and ultraviolet-visible (UV-Vis) spectroscopy help in identifying and quantifying impurities.

Microbial Testing: Ensures the product is free from harmful microorganisms.

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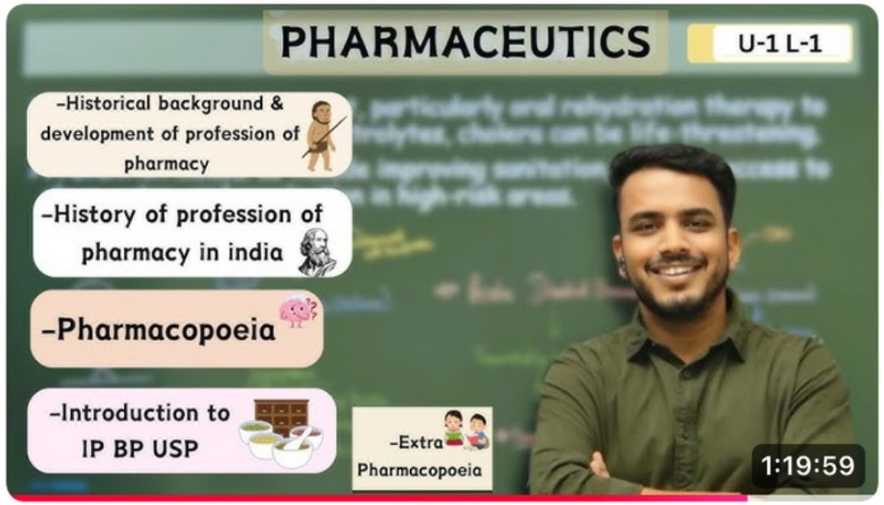
Indian Pharmacopoeia



Historical background & development of profession of pharmacy | Pharmacy as a career | Pharmacopoeia

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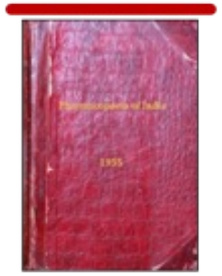
Indian Pharmacopoeia

1955 — First Edition



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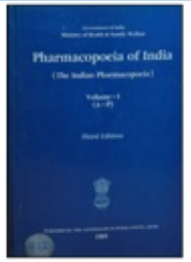
986 Monographs
Title of monographs in Latin
Supplement in 1960

1966 — Second Edition

1 Volume
890 Monographs
Title of monographs changed from Latin to English
Supplement in 1975

1985 — Third Edition



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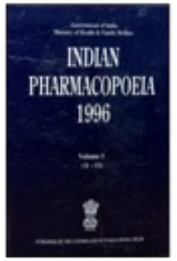

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Addenda in 2000, 2002, and 2005
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2007 — Fifth Edition

3 Volumes
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1968 Monographs
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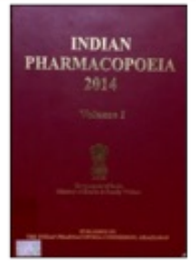

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