PHYSICAL PHARMACEUTICS

UNIT-5

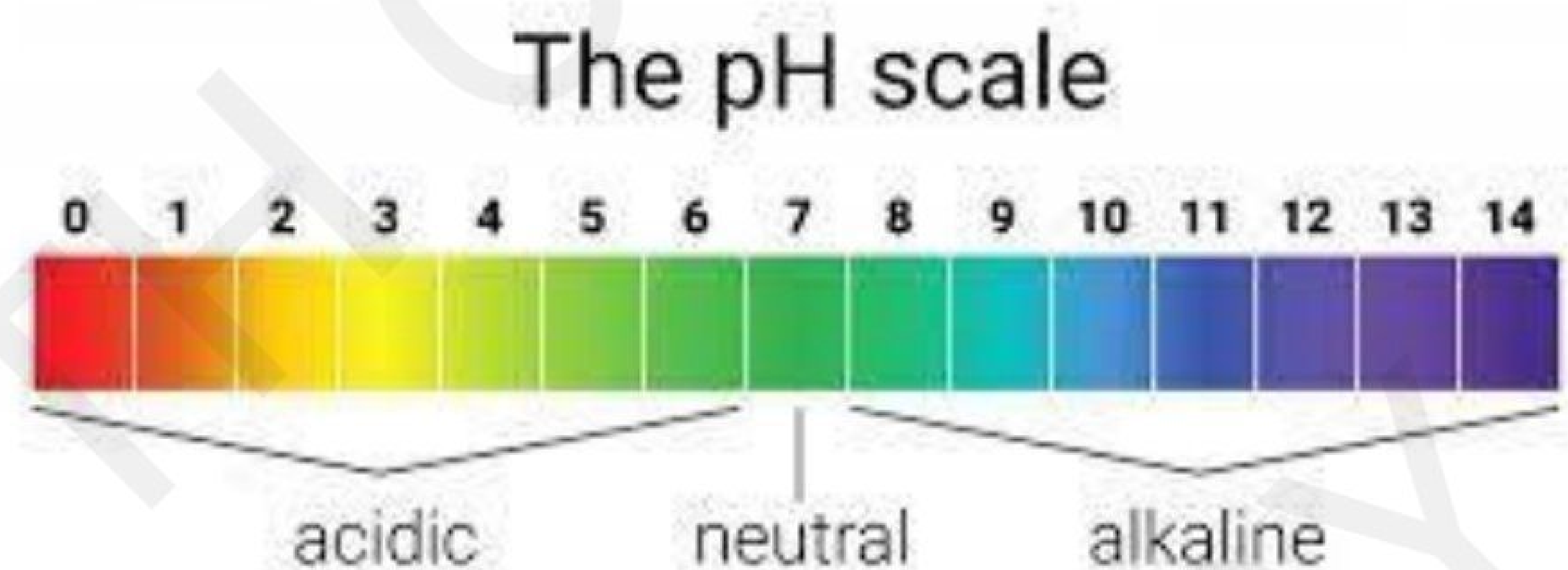
[DEPTH OF BIOLOGY]

pH, BUFFERS & ISOTONIC SOLUTIONS

SORENSEN`S pH scale

- pH- potential /power of hydrogen
- It is given by sorensen, so it is also called sorensen`s pH scale.
- p- potenz means power
- H- hydrogen
- pH defined as negative logarithm of the hydrogen ion concentration
  - **$pH = -\log [H^+]$**
  - where, log is a base −10 logarithm and [H+] is the concentration of hydrogen ions in moles per litre of solution.

- Concentration of H+ ions is a measure of it`s acidity or basicity of a aqeuous solution at specific solution
- Higher relative no of H+- acidic solution
- Higher relative no of OH- ion – basic or alkaline solution. [DEPTH OF BIOLOGY]
- The role of pH scale is to determine the acidity or basicity of any solution



[DEPTH OF BIOLOGY]

- Scale ranges from 0 to 14
- 0 at start indicates strongly acidic solution & 14 at end indicates strongly alkaline solution.
- The mid point 7 indicates the neutral point.
- ***3 regions of pH scale:***

0-7 ACIDIC

7 NEUTRAL

7-14 BASIC

DETERMINATION OF pH

- By following methods-

1. pH paper
2. Electrometric method
3. Colorimetric method

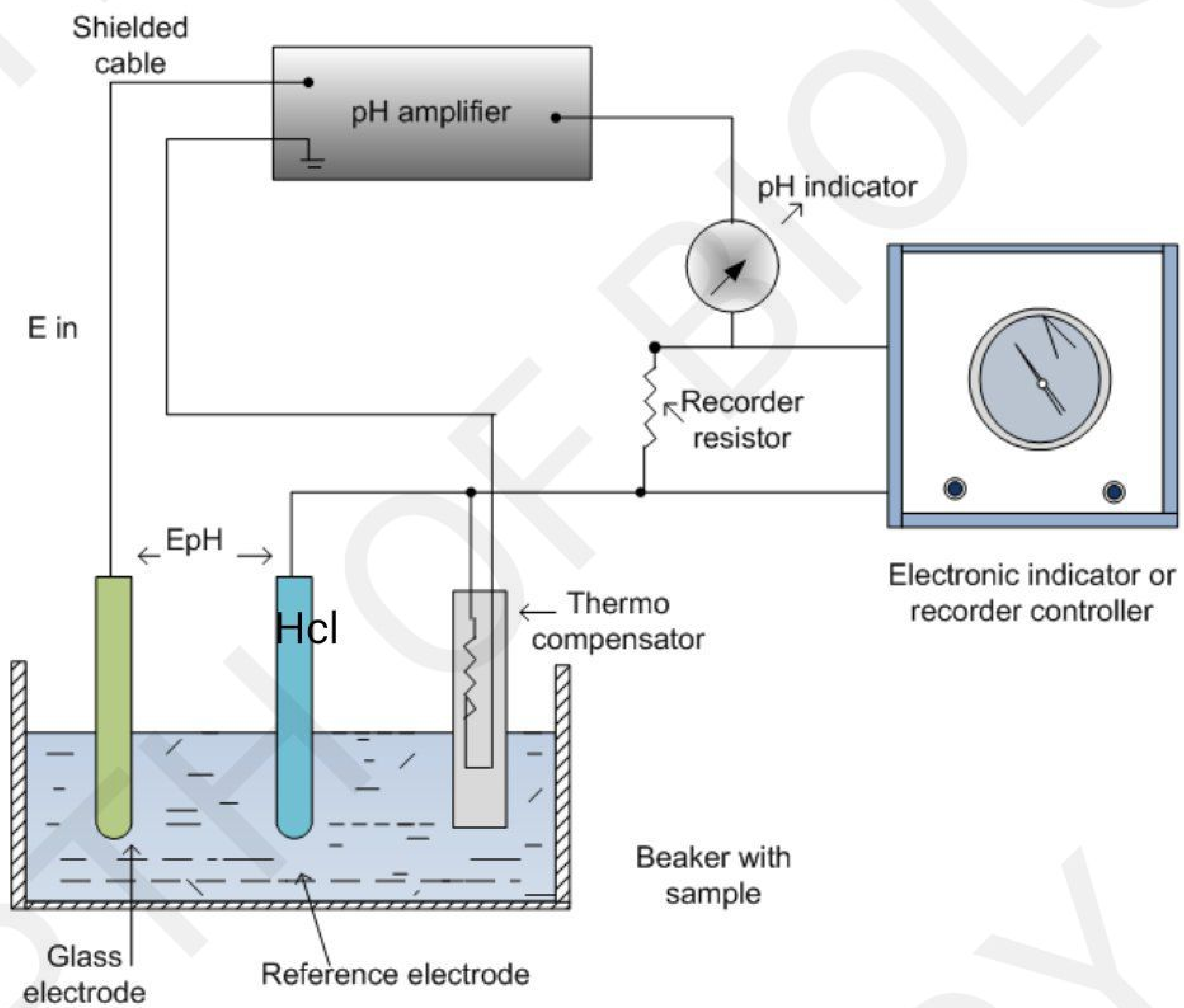
pH paper

- ➢ Take one pH paper and dip it into the sample solution.
- ➢ Compare the colour of pH paper with the standard pH measure chart
- ➢ According to the pH value the basicity or acidity is determined

ELECTROMETRIC METHOD

- Also known as pH meter
- Consists of voltmeter connected with 2 electrodes- **standard electrode** known as potential & **special electrode-** which allows migration of H+ ions & it contain reference solution of dilute HCl.
- ***WORKING-*** dip electrodes [both] in solution to be tested.
- If there`s a difference between the pH of solution & probe`s solution then it passes electric signals to a meter that display reading in pH units.

- pH reading can be altered by change in temperature. A thermocompensator is required to prevent this.



Circuit for electronic pH measurement

COLORIMETRIC METHOD

- Dip colorimetric paper in sample solution
- Compute standard colorimetric table with observed color
- pH value is obtained according to their color
- According to that we determine the acidity or basicity of solution

BUFFER SOLUTION

- Solution that are able to resist change in pH value.

TYPES

1. **Acidic Buffers –** used in acidic solution.

COMPOSITION- weak acid & its salts

Eg- $CH_3COOH + CH_3COONa$ w.a + s.b

2. **Basic Buffers –** used in basic solution

COMPOSITION – weak base & its salts

Eg- $NH_4OH + NH_4Cl$

APPLICTIONS OF BUFFER

1. BIOCHEMICAL ASSAY- enzyme activity depends on pH so the pH during enzyme assay must stay constant.

2. MAINTAINENCE OF LIFE- most biochemical processes are bound to work in narrow range of pH, the body has it`s own buffer to maintain constant pH

EG- blood contain bicarbonate buffer that keep pH close to 7.4

3. CALLIBRATE pH meter

4. TEXTILE INDUSTRY- many dyeing processes require buffer to maintain correct pH for various dyes

5. FOOD INDUSTRY- to maintain acidity & microbiological stability of food.

BUFFER EQUATION

- Used to calculate pH of buffer solution & change in pHwith addition of acid or base.

- ACIDIC BUFFER

pH of acidic buffer can be calculated by dissociation constant Ka of weak acid and the concentration of acid & salt used.

Dissociation of weak acid & salt expressed as-

$HA \rightleftharpoons H^+ + A^-$ [weak acid]

(common ion effect)

$BA \rightleftharpoons B^+ + A^-$ [its salt]

- By law of mass action

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

Taking, negative log of RHS and LHS:

$$-log\ K_a = -log\ \frac{[H^+][A^-]}{[HA]}$$

$$\Rightarrow -log\ K_a = -log\ [H^+] - log\ \frac{[A^-]}{[HA]}$$

As we know,

$$-log\ [H^+] = pH and - log\ K_a = pKa$$

The equation above can also be written as,

$$pK_a = pH - log\ \frac{[A^-]}{[HA]}$$

Rearranging the equation,

$$\Rightarrow pH = pK_a\ +\ log\frac{[A^-]}{[HA]}$$

HA- acid
&
A- salt

- This relationship is also known as ***Henderson-Hasselbalch equation.***
- Basic buffer [weak base & its salt]- in similar way buffer equation can be written as

$$pK_b = pOH - \log \frac{[BH^+]}{[B]}$$

Rearranging the equation,

$$\Rightarrow pOH = pK_b + \log \frac{[BH^+]}{[B]}$$

BUFFER CAPACITY

- Buffer capacity as a quantitative measure of resistance to pH change when H+ or OH- ions is added to the buffer solution.
- Buffer capacity is also known as acid neutralizing or alkalinity capacity.

[DEPTH OF BIOLOGY]

buffer capacity $$\beta = \frac{\Delta B}{\Delta pH}$$

ΔB: amount of acid and base add

ΔpH: how much ph change

BUFFER IN PHARMACEUTICAL SYSTEM

- Buffer play an important role in maintaining the pH of medically active compounds
- SOLUBILITY- by providing a suitable pH solubility of compounds can be frequently controlled
- PATIENT COMFORT- if the pH of injectables or preparations for external/ internal use is changed than usual then it may cause irritation so it is maintained by buffers

- Example- sorensen proposed mixture of salt of sodium phosphate for pH 6 to 8
- Mixture of boric acid and monohydrate sodium carbonate buffers with pH 5 to 9

BIOLOGICAL SYSTEM

- Body fluids have balanced pH
- Small changes in pH can alter the biochemical reaction that takes place

- So maintenance of normal range of pH is essential

BODY FLUIDS	pH VALUE	BUFFER SYSTEM
Blood	7.4- 7.5	Bicarbonate
Urine	4.5-8.0	Phosphate
Interstitial fluids	7.2-7.4	Bicarbonate
Intercellular fluid	6.5-6.9	Protein & phosphate

BUFFERED ISOTONIC SOLUTION

- Pharmaceutical buffered solutions that are meant for application of body should be adjusted same osmotic pressure as that of body fluids

- Eg- blood : 0.9% w/v NaCl solution

<u>THERE ARE 3 TYPES-</u>

1. ISOTONIC- same osmotic pressure as body fluid [0.9% NaCl].
2. HYPOTONIC- less concentration of solute (osmotic pressure) than 0.9% NaCl

3. HYPERTONIC- high concentration of solute (osmotic pressure) than 0.9% NaCl .

METHODS TO DETERMINE ISOTONICITY

1. CRYOSCOPIC METHOD- this method depends upon colligative properties of solution like freezing, boiling point, vapour pressure & temperature difference.

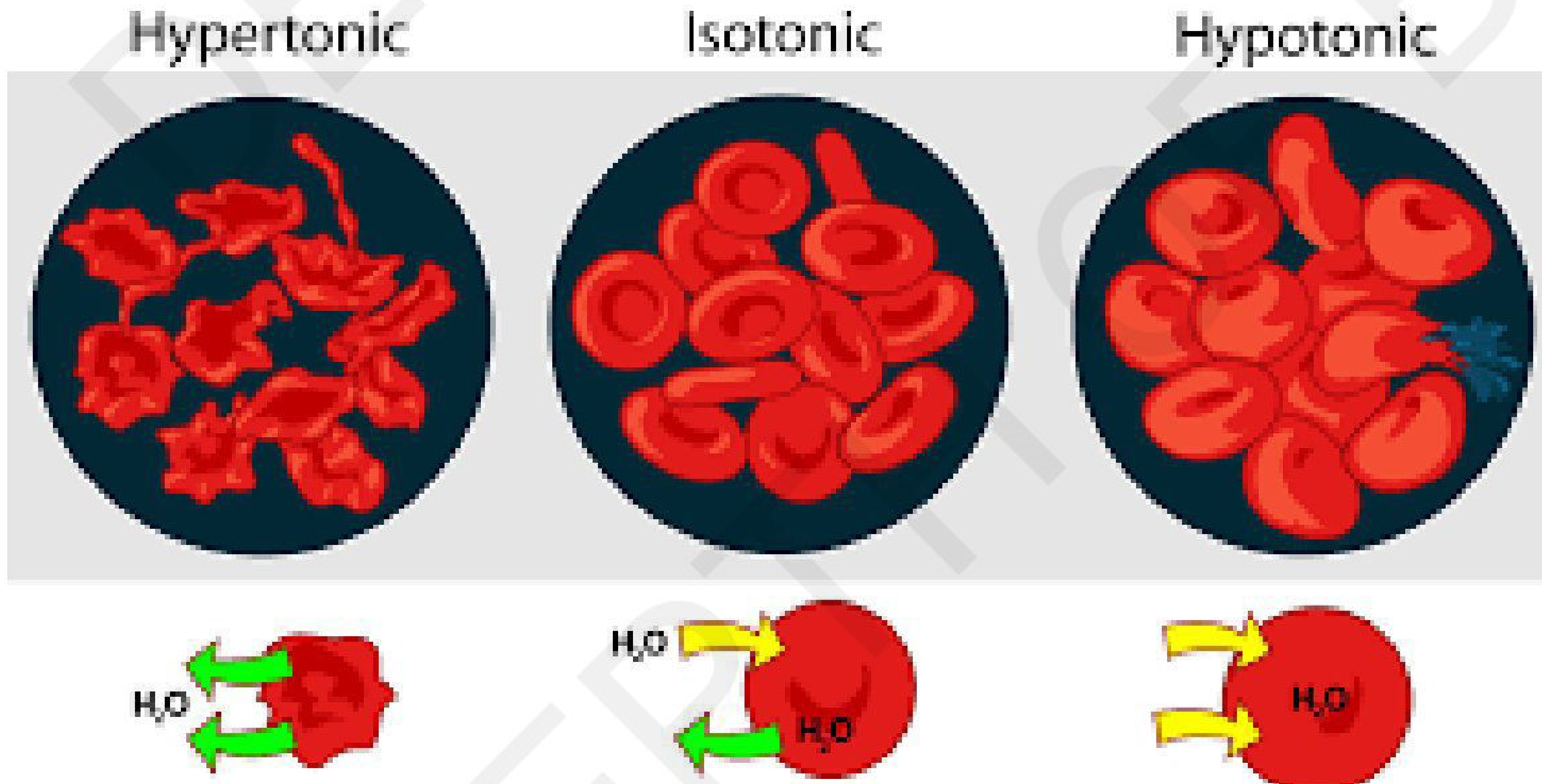
- ❖ Take 2 solution 1 standard isotonic solution [0.9%NaCl] and other is test solution
- ❖ Now compare their colligative property with standard solution & determine tonicity

- F.p. Of standard 0.9% w/v NaCl – 0.52 C

- **Same- isotonic**
- **>0.9% NaCl-hypertonic**
- **<0.9% NaCl-hypotonic**

HEMOLYTIC METHOD

- The effect of various solution of the drug was observed on the appearancd of red blood cells in suspended solution.



- According to osmosis, solvent particle move from low concentration to high concentration

1. Conc of solution > conc of RBC

So, solvent move from low to high {RBC to solution} this causes cell to shrink- **HYPERTONIC SOLUTION**

2. Conc of solution = conc of RBC

So RBC remain same- **ISOTONIC SOLUTION**

3. Conc of solution < conc of RBC

Solvent move from solution to RBC- **HYPTONIC SOLUTION**

Methods of Adjusting Tonicity

- One of several methods can be used to calculate the quantity of sodium chloride, dextrose, and other substances that may be added to solutions of drugs to render them isotonic.
- The methods are divided into two classes. In the class I methods, sodium chloride or some other substance is added to the solution of the drug to lower the freezing point of the solution to -0.52°C and thus make it isotonic with body fluids.
- Under this class are included the cryoscopic method and the sodium chloride equivalent method. In the class II methods, water is added to the drug in a sufficient amount to form an isotonic solution..

- The preparation is then brought to its final volume with an isotonic or a buffered isotonic dilution solution. Included in this class are the White–Vincent method and the Sprowls method

- ***Class I Methods*** [DEPTH OF BIOLOGY]

- ***a)Cryoscopic Method–*** The freezing point depressions of a number of drug solutions, determined experimentally or theoretically from the equation:-

for hypotonic = So, add Nacl

- ***Sodium Chloride Equivalent (E)-*** (same)
- Sodium chloride equivalent of a drug is the amount of sodium chloride that has the same osmotic effect of 1 g, or other weight unit, of the drug.
- The E value can be calculated from the L_{iso} value or freezing point depression.
- For a solution containing 1 g of drug in 1000 mL of solution

Class II Methods

Add H_2O

- a)White–Vincent Method- for hypertonic

The class II methods of computing tonicity involve the addition of water to the drugs to make an isotonic solution, followed by the addition of an isotonic or isotonic-buffered diluting vehicle to bring the solution to the final volume. Stimulated by the need to adjust the pH in addition to the tonicity of ophthalmic solutions.

White –Vincent developed a simplified equation for calculating the volume V (mls) of osmotic solution prepared by mixing drug with water.

$$V = w \times E \times 111.1$$

w is the weight in grams of the drug and E NaCl equivalent

b) The Sprowls Method

A further simplification of the method of White and Vincent method in which V value for drugs of fixed weight 0.3 g in 1% solusion are computed and constructed as a table.