Shree H. N. Shukla Institute of Pharmaceutical Education and Research, Rajkot

B. Pharm
Semester-III

Subject Name: Physical pharmaceutics-I
Subject Code: BP302TP

CHAPTER-5- pH, BUFFERS AND ISOTONIC SOLUTIONS

SYLLABUS:

Sorensen's pH scale, pH determination (electrometric and calorimetric), applications of buffers, buffer equation, buffer capacity, buffers in pharmaceutical and biological systems, buffered isotonic solutions.

- The course deals with the various physical and physicochemical properties, and principles involved in dosage forms/formulations.
- Theory and practical components of the subject help the student to get a better insight into various areas of formulation research and development, and stability studies of pharmaceutical dosage forms.

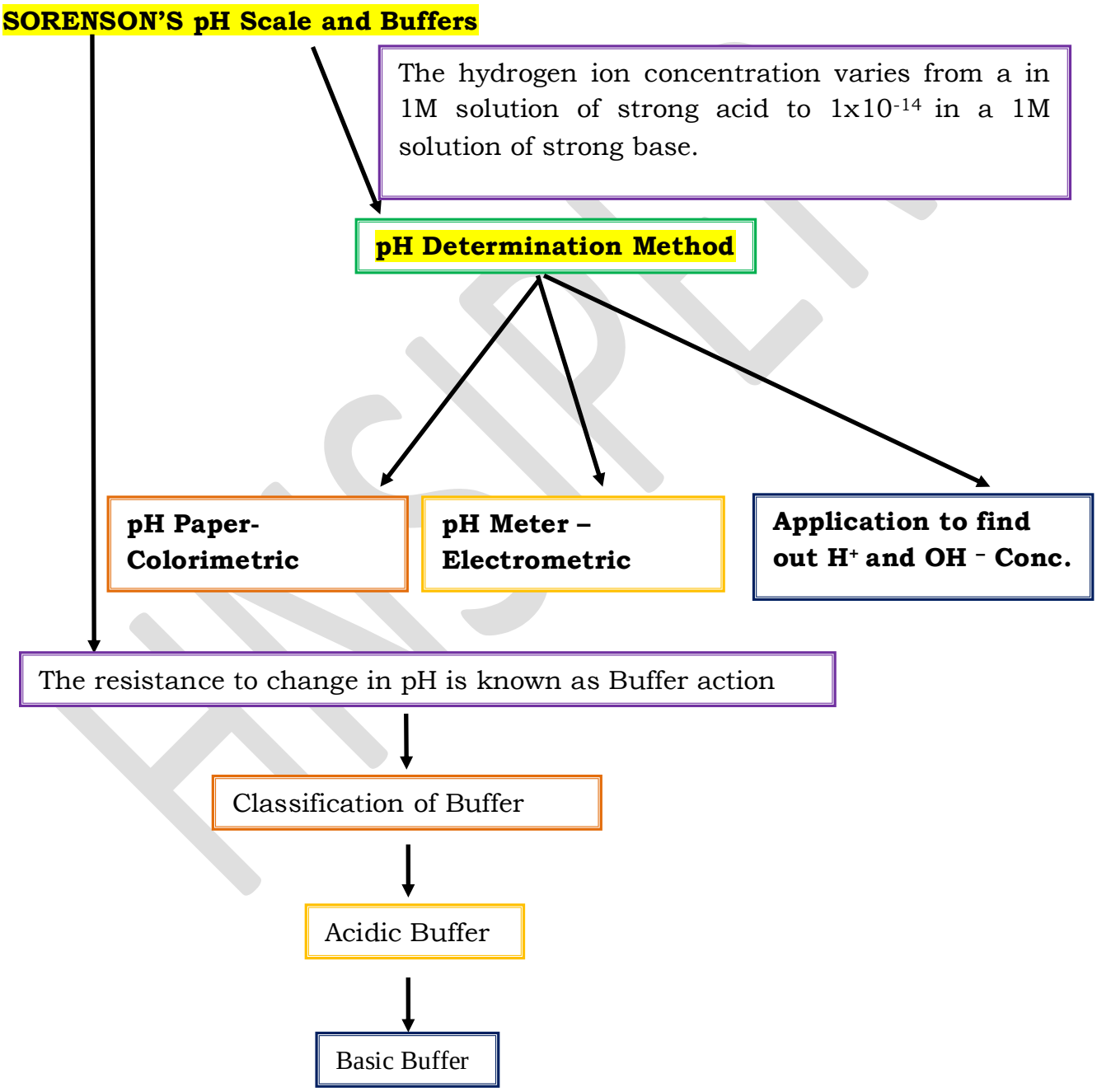
Learning objectives

- Understand the nature of the intra and intermolecular forces that are involved in stabilizing molecular and physical structure.
- Understand the differences in these forces and their relevance to different types of molecules.
- Appreciate the differences in the strengths of the intermolecular forces that are responsible for the stability structures in the different states of matter.
- Understands properties of gaseous states.

pH, BUFFERS AND ISOTONIC SOLUTIONS

TOPIC: What is pH and Buffers solution?

Ans:



DETAILING

SORENSON'S pH SCALE

- The hydrogen ion concentration varies from a in 1M solution of strong acid to $1x10^{-14}$ in a 1M solution of strong base.
- The calculations when expresses in such a way become tedious, thus, Sorenson suggested simplified method of expressing hydrogen ion concentration.
- The established the term pH, to represent hydrogen ion potential and defined it as the common logarithm of the reciprocal of the hydrogen ion concentration

$$pH = \log 1/[H^+]$$

According to Logarithm rules, $pH = \log 1 - \log [H^+]$ so $\log 1 = 0$

$$pH = 0 - \log [H^+]$$

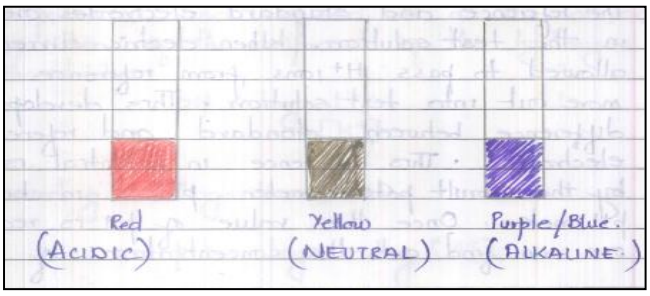
Thus $pH = - \log [H^+]$

- The pH of solution can be considered in terms of numenc scale from 0 to 14.

  Where, 7 to 0 – Degree of acidity,
- 7 to 14 – Degree of Alkalinity,
- 7 – Hydrogen & Hydroxyl ion concentration is equal is referred as neutral point.
- Neutral pH at 25 °C = 7,
- Neutral pH at 0 °C = 7.47,
- Neutral pH at 100 °C = 6.15.

1) pH Paper-Colorimetric Method:

- pH paper is a strip of special paper that is prepared by dipping the strip in different chemical compound and drying it.
- It can be used to find the approximate pH of any solution.
- These paper changes colour when immersed in acidic or basic solutions.
- To determine the pH, the pH paper is dipped in given sample solution, the colour developed in the paper is then compared with colour of chart, and the approximate pH of the solution is identified.

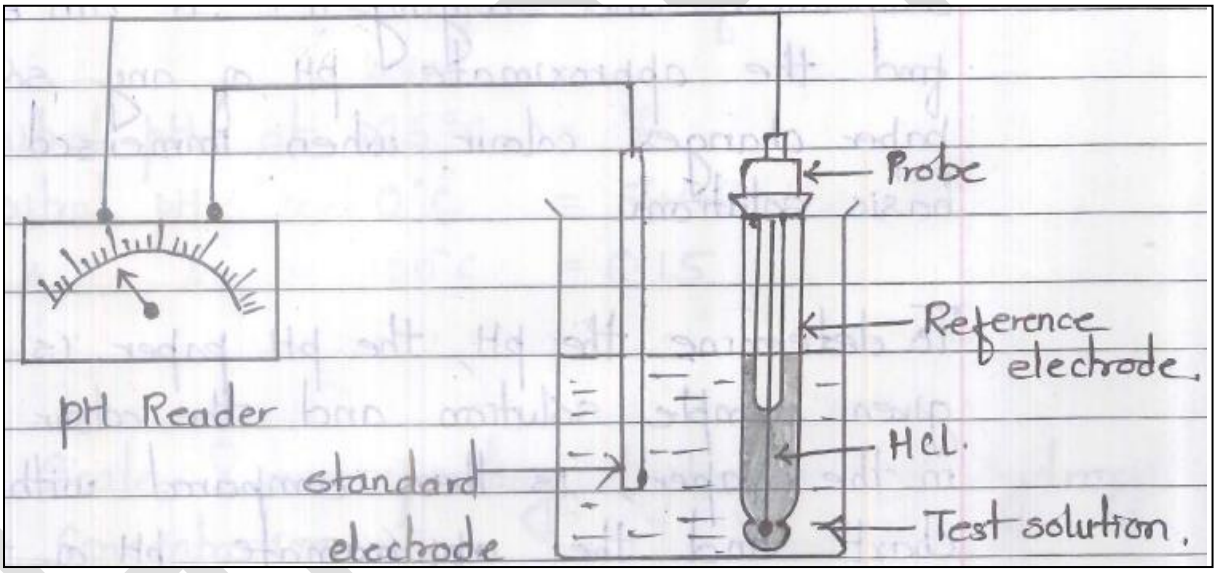


2) pH Meter – Electrometric method

- pH Meter is an electronic instrument consisting of special bulb that is sensitive to hydrogen ion that are present in the test solution.
- It consist of a) Standard electrode with known potential, b) Reference electrode enclosed in glass membrane containing HCl filled in it.

Method

- The reference and standard electrode are dipped in the test solution.
- When electric current allowed to pass H^+ ions from reference electrode more out into test solutions.
- This develops potential difference between standard and reference electrode. This difference in potential is recorded by the inbuilt potentiometer placed in between the pH meter.
- Once the value of pH is recorded, one can find out the concentration of H^+ ion.



Application:

- To find out the concentration of H^+ ion OH^- ions and bufferd to be added. To Improve the stability, solubility & Purity of given solution.

Precautions in Handling pH Meter

- For very precise measurement, the pH meter should be calibrated before each measurement.
- The calibration should be performed with least and buffer solutions with known pH e.g. pH 4 and pH 10 are used.
- After measurement, the bulb should be rinsed with dil water to remove any traces of solution, & then dry the bulb with blotting paper.
- When not in use, the bulb must be dipped in dil water to avoid dehydration of the pH sensing membrane.

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	The hydrogen ion concentration varies from a in 1M solution of strong acid to $1x10^{-14}$ in a 1M solution of strong base is called?	pH
2	The common logarithm of the reciprocal of the hydrogen ion concentration is also called ?	pH
3	Degree of Alkalinity range?	7 to 14
4	Degree of acidity range?	0 to 7
5	What is Neutral pH at 25 °C?	7
6	What is Neutral pH at 100 °C	6.15
7	pH paper of Red colour indicates?	Acidic
8	pH paper of Blue colour indicates?	Alkaline
9	Which instrument is composed of Standard electrode with known potential, b) Reference electrode enclosed in glass membrane containing HCl filled in it?	pH Meter

PHARMACEUTICAL BUFFERS

- Buffers are compounds or mixtures of compounds that by their presence in solution resist changes in pH even after the addition of small quantities of acids or alkali.
- The resistance to change in pH is known as Buffer action.

Buffers are classified as

a) Acidic Buffer: One with pH less than 7, Combination of weak acid and one of its salts-after sodium salt e.g. Ch3COOH & CH3COONa.

b) Basic Buffer:- One with pH more than 7 e.g:-Nh4OH & NH4Cl

Applications of Buffer

Maintenance of Life, Biochemical assay, In shampoos, In brasing industry, In textile industry, in baby lotions.

BUFFER EQUATION/HENDERSON HASELBALCH EQUATION

- This is also referred to as Henderson Haselbalch equation.
- This equation is use to calculate the pH of the solution or to find out the concentration of H^+ ion.
- Consider an acidic buffer containing weak acid HA and its salt BA. Dissociation of acid is given by:

$$\mathbf{HA = H^+ + A^-}$$

$$\mathbf{BA = B^+ + A^-}$$

- Dissociation of HA is at lesser extent in comparison to its salt. Salt completely dissociates increasing the value of A^-, Using law of Mass Action

$$\mathbf{K_a = [H^+]\,[A^-] \,/\, [HA]}$$

[HA] – Initial concentration

$[H^+]$ – Concentration of weak acid

$[A^-]$ – Concentration of salt

- Rearranging the equation, we get:- $H^+ = K_a\,[HA]/\,[A^-]$
- **$= K_a$ x Acid/ Salt**
- Taking log, $-\log [H^+] = -\log K_a - \log [\text{acid/salt}]$
- **Thus $pH = pK_a + \log [\text{Salt/Acid}]$....Weak Acid**
- pK_a – dissociation exponent (Negative Logarithm of K_a)
- **$pH = pK_a + \log [\text{Salt/Base}]$ .....Weak Base**
- The buffer equation is important in preparation of buffered pharmaceutical solution.
- It is satisfactory for calculation with pH range 4 to 10.

BUFFER CAPACITY

- It is defined as the resistance offered by the buffer in the change in pH on addition of small amount of acid/base.

- It is denoted by β.
- It is also known as Buffer index / Buffer efficiency / Buffer value.
- Buffer capacity is also defined as the ratio of small increment caused by strong acids or strong bases causing change in the pH on its addition.
  β = Δ B / Δ pH,
  Δ B is the small increment in gram equivalents/liter of strong base added to the buffer solution to produce a pH change of Δ pH.
- Buffer Capacity depends on 2 parameters:
  a) Concentration of salt and acid present
  b) Concentration ratio of salt to that of acid

BUFFERS IN PHARMACEUTICAL AND BIOLOGICAL SYSTEM

A) Buffers in Pharmaceutical Systems:-

Salicylic acid stored in soft glass bottles:

- Sodium ions leaches out containing with salicylic acid to form sodium salicylic and forming a buffer system i.e. Salicylic acid and sodium salicylate.
- This serves as a buffer maintaining the pH & Product remains stable.

Buffers In Biological Systems:

***In-Vivo* Biologic Buffer System**

- Blood maintained at pH 7.4 by primary buffers in plasma and secondary
- HAC – Acetic acid (Acid)
- NaAc- Sodium acetate (salt)
- This changes in the concentration of salt and acid are represented by buffer equation
- **$pH = pK_a + \log [Salt] + [Base] / [Acid] – [Base]$**
- Buffer capacity decrease rapidly as we add base and 10 greatest before adding base where [Salt]/[Acid] = 1
- Plasma- Carbonic acid/Bicarbonate & Sodium Salts of Phosphoric Acid.
- Erthrocytes- Hemoglobin/Oxyhemoglobin & Potassium salts of phosphoric acid
- Lacrimal fluid/Tears have pH of about 7.4.

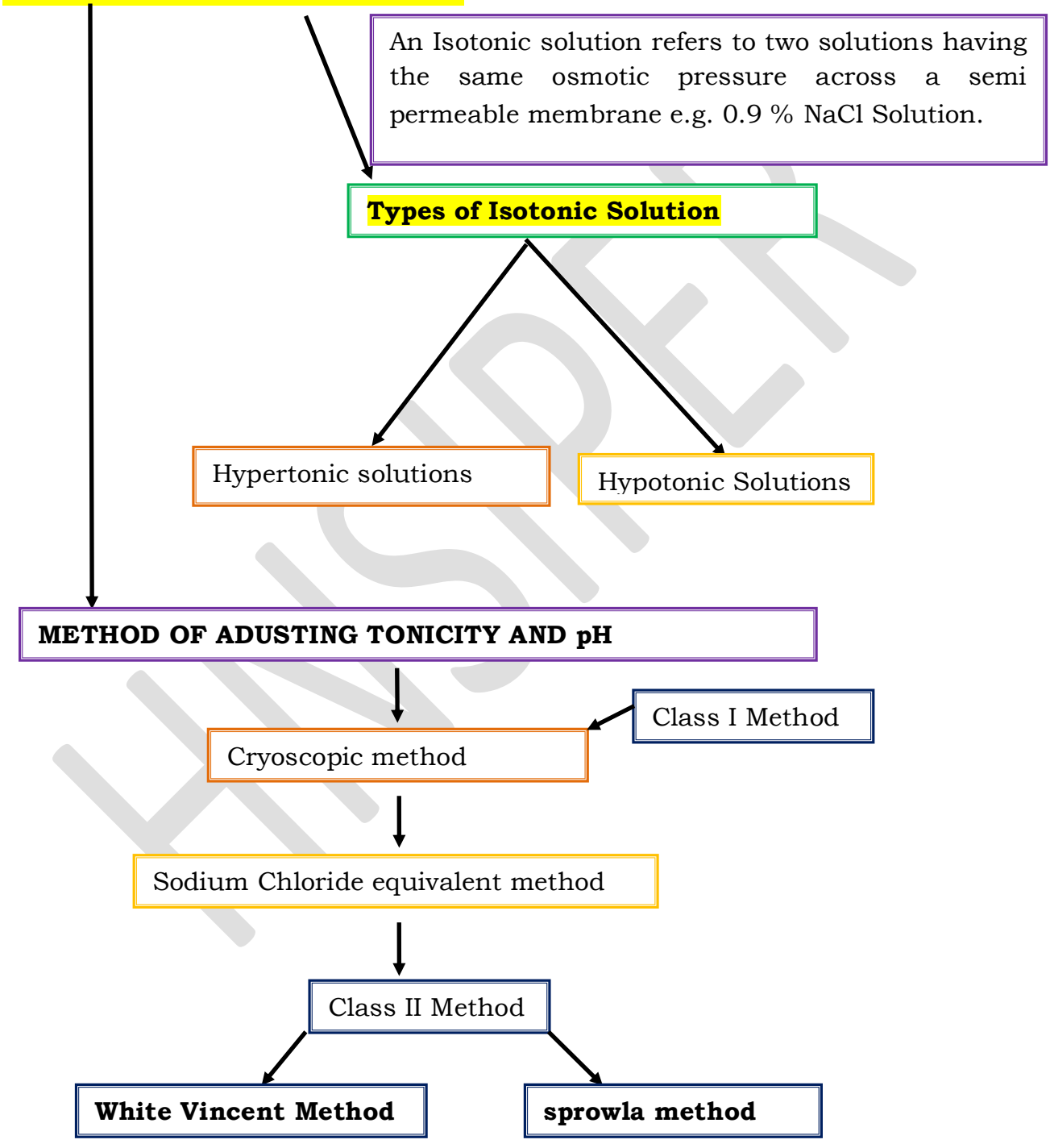
- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	What are compounds or mixtures of compounds that by their presence in solution resist changes in pH even after the addition of small quantities of acids or alkali.	Buffers
2	Buffers are classified as?	Acidic and Basic
3	Henderson Haselbalch Equation for Weak Acid is?	$pH = pK_a + \log [Salt/Acid]$
4	Henderson Haselbalch Equation for Weak Base is?	$pH = pK_a + \log [Salt/Base]$
5	Which equation is use to calculate the pH of the solution or to find out the concentration of H^+ ion.	Henderson Haselbalch Equation
6	It is defined as the resistance offered by the buffer in the change in pH on addition of small amount of acid/base is called?	Buffering Capacity
7	Buffering Capacity is denoted by?	β
8	Tears have pH of about?	7.4
9	What is Buffering Capacity equation?	$\beta = \Delta B / \Delta pH$
10	Optimum pH range of buffered pharmaceutical solution is?	4 to 10

TOPIC: What is Isotonic Solutions?

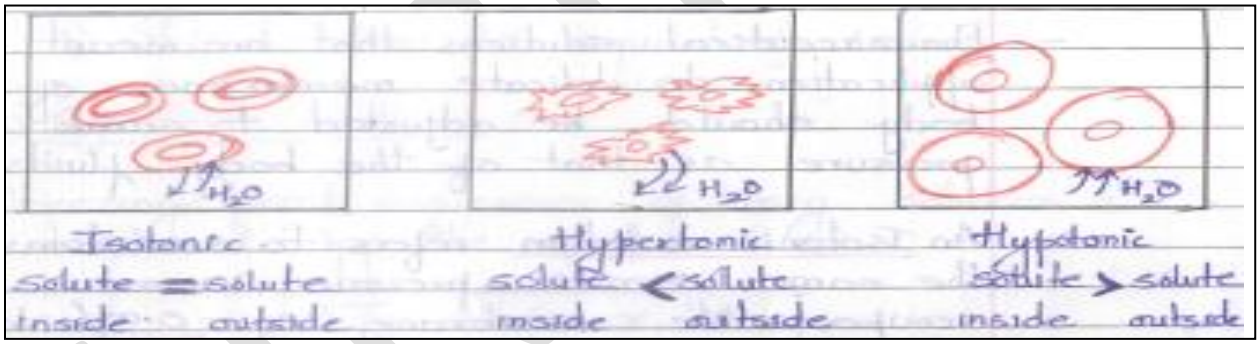
Ans:

BUFFERED ISOTONIC SOLUTIONS



BUFFERED ISOTONIC SOLUTIONS

- Pharmaceutical solutions that are meant for application to delicate membranes of the body should be adjusted to same osmotic pressure ass that of the body fluids. An Isotonic solution refers to two solutions having the same osmotic pressure across a semi permeable membrane e.g. 0.9 % NaCl Solution.
- A hypertonic solution refers to the one where the concentration of solutes is greater outside the cell than inside it e.g.: 2% NaCl solutions.
- If the RBCs are suspended in 2% NaCl solutions, the water within the cell passes through the cell membrane to dilute the surrounding salt solution.
- This cause cell shrinkage or crenation.
- A hypotonic solution refers to the one where the concentration of solute is greater inside the cell than outside it.
- If the RBCs are suspended in 0.2% NaCl solution, the water enters the cell, causing them to swell and finally burst, with the liberation of hemoglobin.
- This phenomenon is known as Haemolysis.



Tonicity: It is the concentration of only the solutes that cannot cross the membrane since these solutes exert osmotic pressure on that membrane.

Measurement of Tonicity

1) Hemolytic Method

- The effect of various solution of the drug was observed on the appearance of Red Blood Cells suspended in the solution.
- Method developed by Hunter
- A quantitative method based on the fact that a hypotonic solution liberates oxyhemoglobin in direct proportion to number of cells hemolyzed.

a) Measurement of slight temperature differences.

- It involves measurement of slight temperature differences in the vapour pressure. Freezing point of 0.9% NaCl = -0.52°C.

Calculating Tonicity Using L_{iso} Values

In case of electrolytes with both the weak and strong types freezing point depression are greater than calculated, a new factor, $L = iK_f$ is introduced

$L_{iso} = \Delta T_f / C\ \Delta T_f$ – Freezing point depression, c= Concentration of solution

METHOD OF ADUSTING TONICITY AND pH

There are several methods which are used to render the solution isotonic.

Two Methods

1. Class I Method

Sodium Chloride is added to drug solution to make it isotonic with body fluids.

2. Class II Method

Water is added to drug solution to make it isotonic with body fluids.

Class I Methods:-

a) Cryoscopic method

b) Sodium Chloride equivalent method

CRYOSCOPIC METHOD:

Freezong point depression of drug solution is determined by the equation

$\Delta T_f = L_{iso} \times 10 / Mol.Wt$

b) Sodium Chloride Equivalent Method

NaCl equivalent of drug is the amount of NaCl that has the same osmotic effect of 1g or other weight unit of the drug.

$E = 17x\ L_{iso} / M.W.$

Amount of isotonic agent required to adjust the tonicity

$X = Y/E$

X – Grams of isotonic agent required to adjust the tonicity

Y – Additional amount of NaCl for isotonicity

E – Gram of NaCl equivalent to 1g of the isotonic agent

II] Class II Methods

a) **White – Vincent Method**
b) **The sprowla method**

a) **White – Vincent Method**

Developed equation for calculating the volume v (ml) of osmotic solution prepared by mixing drug with water

$V = V_0 \times E \times 111.1$

W = Weight in grams of drug

E = NaCl equivalent

b) **The Sprorols Method**

Simplification of the White Vincent method. Table of values V can be constructed by keeping the weight of the drug fixed i.e. 0.3g in 1% solution.

One Word Question Answer

SR NO.	QUESTION	ANSWER
1	When two solutions having the same osmotic pressure across a semi permeable membrane e.g. 0.9 % NaCl Solution is called?	Isotonic solution
2	one where the concentration of solutes is greater outside the cell than inside it e.g.: 2% NaCl solutions is called?	hypertonic solution
3	one where the concentration of solute is greater inside the cell than outside it is called?	Hypotonic Solution
4	What is Sodium Chloride Equivalent Method equation?	$E= 17x\ L_{iso} / M.W.$
5	What is Freezing point depression equation?	$\Delta T_f = L_{iso} \times 10/ Mol.Wt$
6	What is White – Vincent Method equation?	$V= V_0 \times E \times 111.1$
7	If the RBCs are suspended in 0.2% NaCl solution, the water enters the cell, causing them to swell and finally burst, with the liberation of hemoglobin, this phenomenon is called?	Haemolysis
8	The concentration of only the solutes that cannot cross the membrane since these solutes exert osmotic pressure on that membrane is called?	Tonicity