PHYSICAL PHARMACEUTICS-I

UNIT 5 NOTES

pH, BUFFER & ISOTONIC SOLUTION

- SORENSON'S PH SCALE
- pH DETERMINATION
- APPLICATION OF BUFFER
- BUFFER EQUATION
- BUFFER CAPACITY
- BUFFERS IN PHARMACEUTICAL AND BIOLOGICAL SYSTEMS
- BUFFERED ISOTONIC SOLUTION

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pH

- In 1909 Sorenson, a Danish chemist, introduced the concept of pH as a convenient way of expressing acidity or basicity.

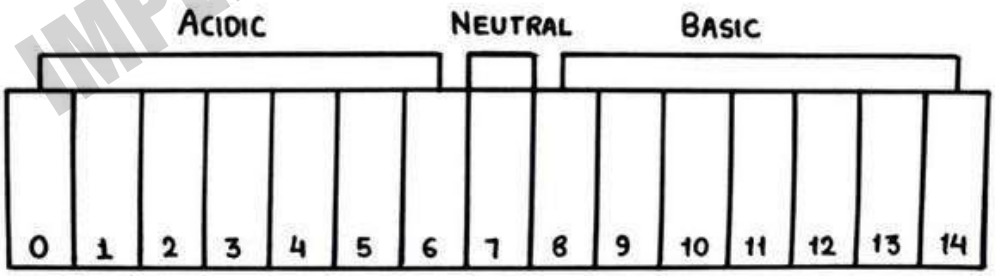
pH = Potential / Power of Hydrogen

- pH is simply defined as negative logarithm of hydrogen ion concentration

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

pH Scale

- The pH scale measures how acidic or basic a substance is
- The scale ranges from 0-14 with 7 being neutral, A pH less than 7 is acidic & greater than 7 is basic.



pH Determination

- Accurate determination of pH is essential in pharmaceutical formulations to ensure stability, solubility and compatability of drugs.
- The two main methods used in pH determination are :

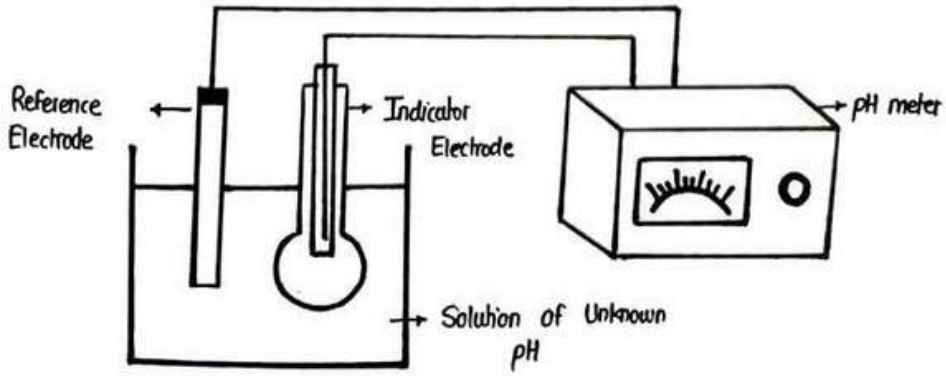
① Electrometric Methods
② Colorimetric Methods

Electrometric Method

- The electrometric method is the standard and most accurate technique for determining the pH of a solution.
- This method measures pH electrically using a pH meter, which determines the potential difference between a reference electrode and an indicator electrode immersed into the test solution.

Principle

The core principle of electrometric method is pH meter first calculate potential difference b/w electrodes & then relate it to the pH of the solution.



Calorimetric Method

Principle

- In this method, pH indicators are used which change colour depending on the hydrogen ion concentration of the solution.
- The pH is determined by comparing the colour of the test solution with that of the standard buffer solution of known pH.

Procedure

- Add few drops of suitable pH indicator to the test solution.
- Compare the colour developed with standard pH color chart or buffer standards.
- The matching colour indicates the approximate pH of the solution.

Example Of Indicators

- Methyl Orange
- Phenolphthalein
- Bromomethyl Blue

Advantages

- Simple, Quick & inexpensive.
- Requires no complex equipment.

Disadvantages

- Less accurate than electrometric method.
- Provide only approximate pH value.

APPARATUS

- Glass Electrode (sensitive to H^+ concentration)
- Reference Electrode (calomel or silver/ chloride electrode
- pH Meter

PROCEDURE

- Calibrate the pH meter using standard buffer solutions.
- Rinse the electrodes with distilled water & immerse them into the test solution.
- The pH meter measures the potential difference generated b/w electrodes.
- The corresponding pH value is directly displayed on the pH meter.

ADVANTAGES

- Highly accurate and precise.
- Suitable for colourless , turbid or viscous solutions.
- Can be used for continuous pH monitoring.

DISADVANTAGES

- Requires regular calibration
- Electrodes need careful handling

BUFFERS

- Buffers are the solutions that resist change in their pH when a small amount of acid or base added in it.
- They can neutralize small amount of acid or base

Types Of Buffers

Buffers are of basically two types :

① Acidic Buffer
② Basic Buffer

Acidic Buffers

An acidic buffer is a combination of weak acid and its salt with strong base

$CH_3COOH + CH_3COONa$

Basic Buffers

A basic buffer is a combination of weak base and its salt with strong acid.

$NH_4OH + NH_4Cl$

BUFFER CAPACITY

- The amount of Acid / Base required to produce a unit change in pH of a buffer solution is known as Buffer Capacity.
- It is also known as
  - Buffer Index
  - Buffer Value
  - Buffer Efficiency
  - Buffer Coefficient
- It can be expressed as follows :

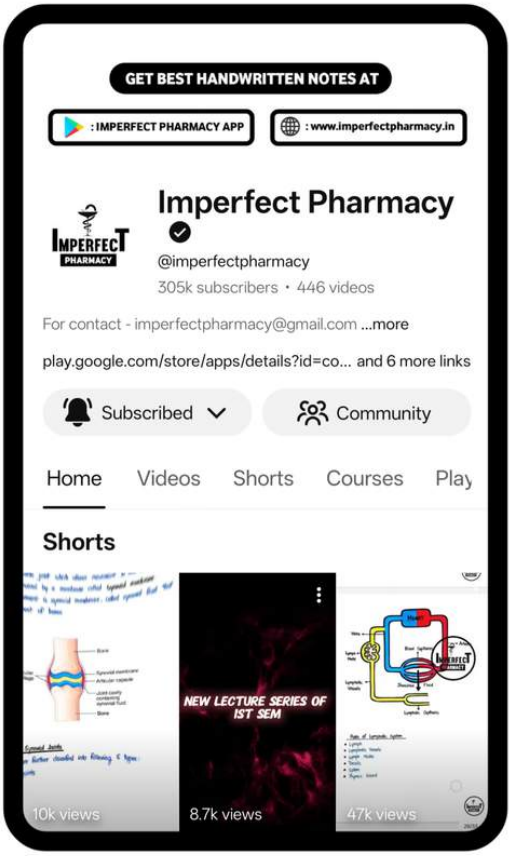
$$\beta = \frac{\Delta A / \Delta B}{\Delta pH}$$

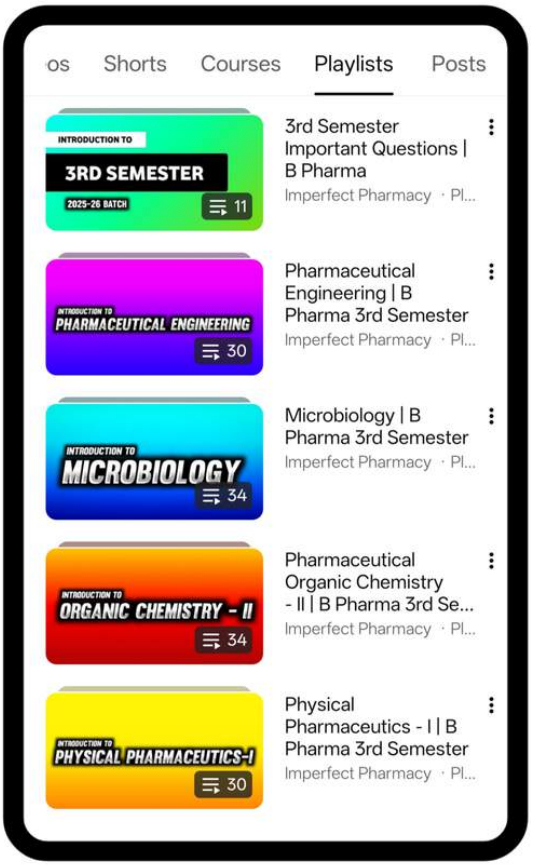
- Here in the above equation
- β = Buffer Capacity
- $\Delta A / \Delta B$ = Amount of Acid or Base added
- ΔpH = Change in pH

Factors Affecting Buffer Capacity

- The concentration of HA & A^- in a solution
- Total Buffer Concentration
- Temperature
- Ionic Strength

FOR LECTURE VIDEOS VISIT OUR CHANNEL





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BUFFER ACTION

- Buffer action basically describes the mechanism of action of buffers means how buffers actually works to resist change in their pH if we add small amount of Acid or Base.
- Here we have to see :

① Mechanism of action of Acidic Buffers

② Mechanism of action of Basic Buffers

MECHANISM OF ACTION OF ACIDIC BUFFERS

- Lets consider a acidic buffer system of CH_3COOH & CH_3COONa
- Now these CH_3COOH & CH_3COONa will dissociate like this :

CH_3COONa	$\longrightarrow$	$CH_3COO^- + Na^+$
CH_3COOH	$\rightleftharpoons$	$CH_3COO^- + H^+$

① If we add an Acid (HCl)

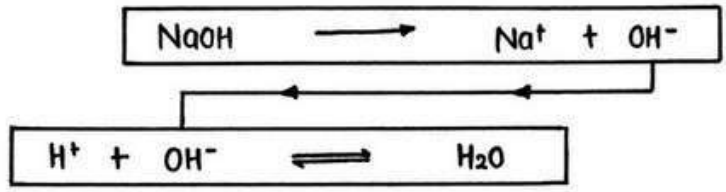
If we add HCl into the above buffer solution then first HCl will dissociate into H^+ and Cl^- & these H^+ ions will react with CH_3COO^- ions and form CH_3COOH which is already present in the solution, i.e., no any other extra compound formed & that's how the pH of the buffer solution remains unchanged.

$$HCl \longrightarrow H^+ + Cl^-$$

$$H^+ + CH_3COO^- \rightleftharpoons CH_3COOH$$

② If we add a Base (NaOH)

Now again if we add a Base NaOH in the above Acidic Buffer Solution then NaOH will dissociate into Na^+ & OH^- and these OH^- reacts with H^+ ions and form water which doesn't affect the pH of the solution.

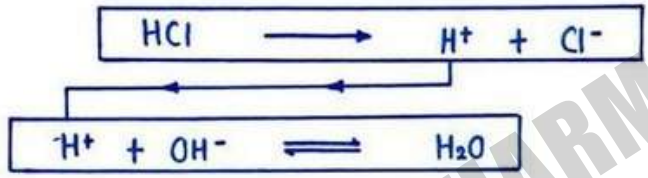


Mechanism Of Action Of Basic Buffers

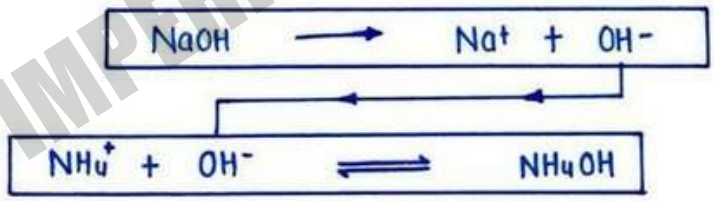
Lets consider a basic buffer system of NH_4OH & NH_4Cl
Now they will dissociate like this

NH_4OH	$\rightleftharpoons$	$NH_4^+ + OH^-$
NH_4Cl	$\longrightarrow$	$NH_4^+ + Cl^-$

① If we add an Acid (HCl)



② If we add a Base (NaOH)



BUFFER EQUATION

- Buffer Equation is also known as Handerson - Hasselbalch Equation.
- It is mainly used to calculate the pH of a buffer solution.
- Let's calculate the buffer equation for an Acidic Buffer.

FOR ACIDIC BUFFER

- As we know that Acidic Buffer contains weak acid and its salt, let's consider a weak acid 'CH_3COOH', now :

$$CH_3COOH \rightleftharpoons CH_3COO^- + H^+$$

- Now here in the above equation, if we assume CH_3COO^- as A^- then we can write the above equation as

$$HA \rightleftharpoons H^+ + A^-$$

- Now here HA → Acid
  A^- → Salt

Why A^- represented as Salt ?

As we know that An Acidic Buffer contains a weak acid and salt of it with a strong base, If we take example of CH_3COOH & CH_3COONa. then they will dissociate as follows :

CH_3COOH	$\rightleftharpoons$	$CH_3COO^- + H^+$
CH_3COONa	$\longrightarrow$	$CH_3COO^- + Na^+$

- Now here in this equation, CH_3COOH is a weak acid and it will dissociates partially & further its dissociation is slowed down or depressed by the addition of salt CH_3COONa (due to common ion effect), hence the maximum number of CH_3COO^- in the above equation is coming from CH_3COONa and that's why this CH_3COO^- is represented as 'Concentration of Salt'.
- And since we assume this $CH_3COO^- = A^-$

  Hence $A^- =$ Salt

- Now, we have :

$$HA \rightleftharpoons H^+ + A^-$$

- After applying Law of Mass Action

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

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

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

- Here K_a = Dissociation Constant
- and as we already saw, $HA \longrightarrow$ Acid

  $A^- \longrightarrow$ Salt

- So, we can write the above equation like

$$[H^+] = K_a \frac{[Acid]}{[Salt]}$$

Taking -log on both sides we get,

$$-\log [H^+] = -\log \left(K_a \frac{[Acid]}{[Salt]} \right)$$

continued ....

$$-\log [H^+] = -\log ka - \log \frac{[Acid]}{[Salt]}$$

- Now $-\log [H^+] = pH$
- & similarly we can write $-\log ka = pka$
- so the equation can be written as :

$$pH = pka - \log \frac{[Acid]}{[Salt]}$$

- Or, we can write like :

$$pH = pka + \log \frac{[Salt]}{[Acid]}$$

- And similarly the buffer equation for Basic Buffer can be written as :

$$pOH = pka + \log \frac{[Salt]}{[Base]}$$

Buffered Isotonic Solution

- A buffered isotonic solution is a solution that maintains the same pH & isotonicity as body fluids.
- Buffered Isotonic Solution combines both buffering and isotonic properties.
- They are used for various medical & biological properties.

Tonicity

- The word Tonicity is simply defined as concentration of a solution as compared to another solution.
- In Pharmaceutical system, Buffer solutions that are meant for application inside the body must have the same osmotic pressure or same concentration as that of body fluids / blood.

Tonicity / Concentration of Blood = 0.9% w/v of NaCl

Types of Solutions (As per Tonicity)

There are basically 3 types of solutions as per tonicity :

① Isotonic Solutions
② Hypotonic Solutions
③ Hypertonic Solutions

Isotonic Solution

A solution whose concentration or osmotic pressure is equal to the 0.9 %. w/v of NaCl solution is known as Isotonic Solution.

Hypotonic Solution

A solution whose concentration or osmotic pressure is less than 0.9 %. w/v of NaCl is known as Hypotonic Solution.

Hypertonic Solution

A solution whose concentration or osmotic pressure is greater than 0.9 %. w/v of NaCl solution is known as Hypertonic Solution.

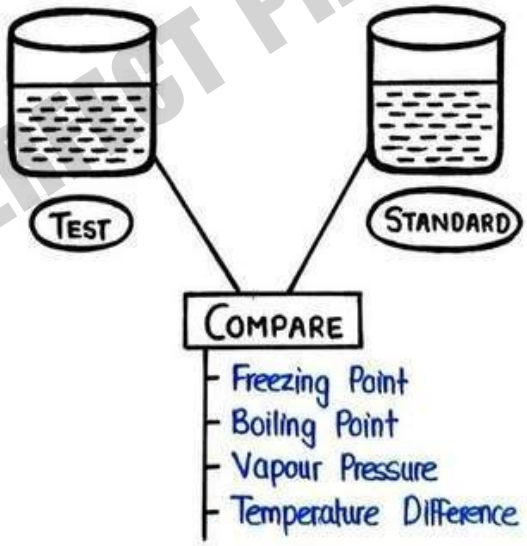
Measurment / Determination Of Tonicity

The tonicity of a solution may be determined by any 1 one of the two following methods :

① Cryoscopic / Colligative Methods
② Haemolytic Methods

Cryoscopic / Colligative Method

- This method is based on the colligative properties of the solution such as Freezing Point , bioling point , vapour pressure and temperature difference
- In this method , we basically compare the colligative properties of our Test Solution with Standard Isotonic Solution .

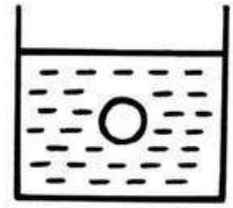


After Comparison , If

- Test = Standard : Isotonic
- Test < Standard : Hypotonic
- Test > Standard : Hypertonic

Haemolytic Method

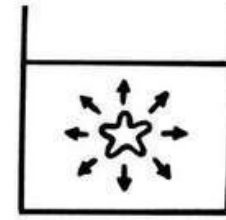
- In this method ; we determine the tonicity of the solution on the basis of appearance of Red Blood Cells suspended in the solution.



- We know that according to Osmosis , Solvent particles move from area of low concentration to area of high concentration.
- In Haemolytic method . first we dissolve the red blood cell in the given test solution , then following 3 condition can be occured.

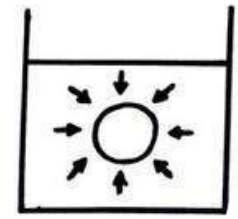
CONDITION - I (Cell Shrinkage)

If the concentration of solution is more than concentration of blood cell , then solvent will move from blood to the solution and this will cause cell shrinkage and solution will be 'Hypertonic'



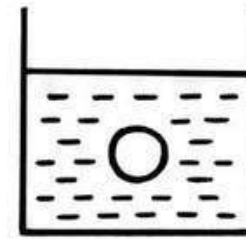
CONDITION - II (Cell Swelling)

If the concentration of solution is less than concentration of blood cell , then solvent will move from solution to the blood cell & this will cause cell swelling and solution will be 'Hypotonic'



CONDITION - III (No Change)

If the concentration of solution is equal to the concentration of blood cell, then there will be no net movement of solvent and due to this there will be no change in the size of blood cell or it will remain constant and the solution will be Isotonic.



METHODS OF ADJUSTING TONICITY

There are mainly two methods for adjusting tonicity of solutions :

① Class I (For Hypotonic)

② Class II (For Hypertonic)

CLASS - I

- This method is basically used to adjust the tonicity of Hypotonic solutions.
- In this we mainly used Sodium Chloride to make solution Isotonic.
- It includes

(i) Cryoscopic / Freezing Point Depression Method

(ii) Sodium Chloride Equivalent Method

Cryoscopic Method

$$W\% = \frac{0.52 - a}{b}$$

Here,
- w = Amount of adjusting substance
- a = Freezing Point of 1% solution of Un-adjusted solution
- b = Freezing Point of 1% solution of Adjusting substance

Sodium Chloride Equivalent Method

$$E = \frac{17 \times Liso}{M}$$

Here
- E = Sodium Chloride Equivalent
- Liso = Liso Value (Constant)
- M = Molecular Weight of Drug Solution

CLASS - II

- This method is basically used to adjust the tonicity of Hypertonic Solutions.
- In this, we basically add water to make solution Isotonic.
- It includes :

(i) White - Vincent Method

(ii) Sprowls Method

White - Vincent Method

$$V = W \cdot E \times 111.1$$

Here
- V = Volume of Isotonic solution prepared by mixing drug with water
- W = Weight of Drug in Gram
- E = Sodium Chloride Equivalent

Sprowls Method

- This is basically simplification of White - Vincent Method.
- In this we set W = 0.3

$$V = 0.3 \times E \times 111.1 \quad \text{or} \quad V = 33.35\,E$$

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