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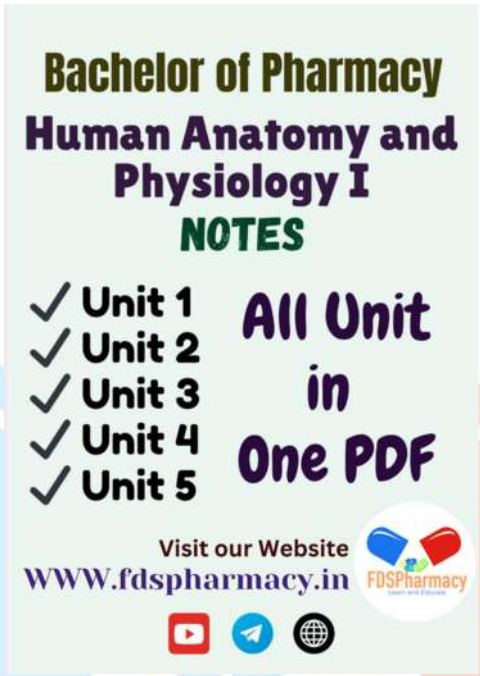
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PHARMACEUTICAL INORGANIC CHEMISTRY

UNIT 2

TOPIC :

- **Acids, Bases and Buffers :** Buffer equations and buffer capacity in general, buffers in pharmaceutical systems, preparation, stability, buffered isotonic solutions, measurements of tonicity, calculations and methods of adjusting isotonicity.

Acids and Bases

Acid :

→ An acid is a chemical substance that has the ability to donate a proton (H^+ ion) or accept an electron pair, depending on the theory used. Acids usually have a sour taste, turn blue litmus red, and react with bases to form salts and water.

Base :

→ A base is a substance that can accept a proton (H^+ ion) or donate an electron pair, depending on the theory applied. Bases usually have a bitter taste, slippery feel, turn red litmus blue, and neutralize acids to form salts and water.

Theories of acids and bases

There are 3 theories , explaining the comcept of acids and bases

- ➲ Arrhenius theory
- ➲ Bronsted Lowry theory
- ➲ Lewis theory

Theory	Acid	Base
Arrhenius	H+ Producer	OH- Producer
Bronsted lowry	H+ donar	H+ acceptor
Lewis	Electron pair acceptor	Electron pair donar

Arrhenius Theory

- The most commonly used concept of acids and bases was develop by Savante Arrhenius in 1884 termed as Arrhenius theory
- According to this theory an acid is a substance which dissociates in Aqu. Solution produce hydrogen ion on other hand a base is a

substance which dissolve in aqueous solution to produce hydroxyl ion (OH-)

For example

- HCl is an Arrhenius acid HCL H+ + Cl-
- NaOH is an Arrhenius base NaOH OH- + Na+

- Arrhenius theory was the first scientific theory that had given defination for acid and base as well as classified them It is the simplest theory and is useful in case of aqueous solution

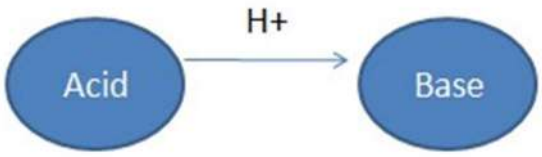
Limitations

- ❖ Acid and base have been defined only in terms of solution and not as a solid substance
- ❖ This theory also failed to explain the neutralistation of acid & base in the absence of solvent
- ❖ There are many basic substance (few organic substance) which do not have oh ions but are basie in nature this fact could not be explained by Arrhenius theory
- ❖ Acidic properties of many salts could not be explained by this theory

Bronsted Lowry theory

→ In 1923 J.N Bronsted and J.M Lowry was introduced a new concept of acid and base

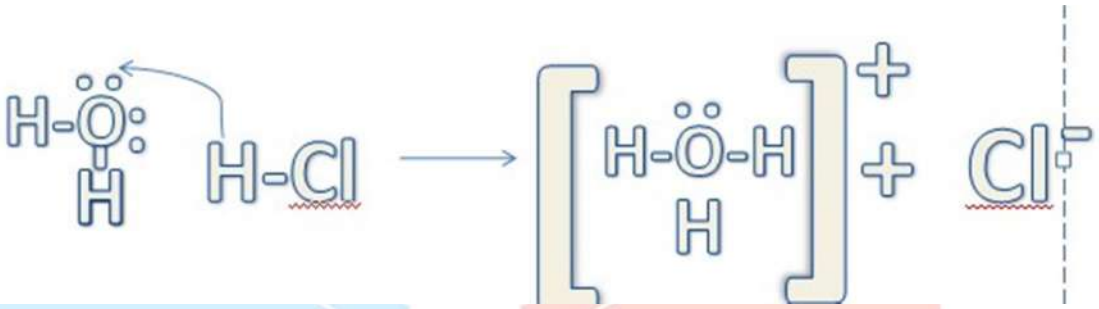
→ According to the theory an acid is any mol or ion that can donate a proton (h+) and base is any mol or ion that can accept a proton H+



An acid is a proton donor While base is a proton acceptor

- ➢ A base qualifying Bronsted lowry concept is termed as Bronsted lowry base or Bronsted base
- ➢ Where an acid qualifying Bronsted lowry concept is termed as Bronsted lowry acid or Bronsted acid

- **For example :-** On dissolving dry HCl gas in water , each molecule of HCl produces hydronium ion (H_3O^+)by donating a proton to a water molecule



There fore it can be concluded that water which accept a proton is a bronsted base where HCl gas which donate a proton is a Bronsted.

Advantages

- Much wider scope Bronsted lowry concept of acid and base cover wider range of molecules and ions accepting proton (base) or donating proton (acid)
- Where arrhenius concept of acid & base involve only those substance which release H+ or OH- ions in aqueous solution
- Not limited to aqueous solution Arrhenius concept is limited only to aqueous solution Bronsted lowry theory not only covers aqueous sol but also gas phases
- Release of OH- not necessary to qualify as a base Bronsted base is a substance which accept a proton, where Arrhenius base is a substance which release OH- ions in aqueous solution

Limitations

- Bronsted lowry theory of acid & base is based on transfer on proton commonly most of the acids as protonic in nature but some are not
- There are many acid base chemical reaction in which proton transfer not occurs

Lewis Theory of Acids & Bases

- This method of Acid & Base was given by G.N Lewis in the early 1930
- He defined Acid is an electron pair acceptor
  - Base is an electron pair donar
- In this theory the Lewis acid & Lewis base share an electron pair given by base result in the formation of a covalent or coordinate bond between them
- This resultant compaired bounded with a covalent bond is known as a complex
  - A + B = A-B
  - LA LB Complex

According to this concept

- Lewis base are anion or molecule having a long pair of electron
- Lewis Acid are cation or molecule lacking of electron pair

Advantages

- ★ It included the defination given by both Arrhenius and Bronsted Lowry.
- ★ The lewis concept explain the acidic & basic nature on the basis of transfer or gain of electron accompanied by loss/donation of electron pair.

Limitations

- ❖ Lewis acid and base can not arranged in their order of strength as their strength depend on the reaction type
- ❖ Lewis acid and base reaction are explained are excepted to be very fast but to the involvement of electron but some of there reaction slow

Buffers

→ A buffer is a solution that resists changes in pH when a small amount of acid or base is added.

Types of buffers

- Buffers are of basically two types :
  - Acidic Buffer
  - Basic Buffer

1. Acidic Buffer

→ An acidic buffer is a buffer solution that maintains an acidic pH and is prepared by mixing a weak acid with its salt of a strong base.
→ **Example** : Acetic acid (CH_3COOH) + Sodium acetate (CH_3COONa)

2. Basic Buffer

→ A basic buffer is a buffer solution that maintains a basic (alkaline) pH and is prepared by mixing a weak base with its salt of a strong acid.
→ **Example:** Ammonium hydroxide (NH_4OH) + Ammonium chloride (NH_4Cl)

Buffer Capacity

- Buffer capacity is defined as the amount of strong acid or base (in moles) that must be added to 1 liter of a buffer solution to change its pH by one unit.
- It is also known as Buffer Index , Buffer Value , Buffer Efficiency , Buffer Coefficient,
- It can be expressed as

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

Where,

B = Buffer Capacity

ΔA/ΔB= Amount of Acid or Base added

ΔPH = Change in pH

Factors Affecting Buffer Capacity :

1. **Concentration** – Higher concentration = higher buffer capacity
2. **pH relative to pKa** – Best when pH ≈ pKa
3. **Ratio of acid to base** – Optimal when [Salt]/[Acid] ≈ 1

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 calaulate the buffer equation for an Acidic Buffer.

For Acidic Buffer

The PH of acidic buffer can be calculated from the dissociation constant (ka) of the weak acid and it salt.

Let's take HA (weak acid) and BA (Salt)

$HA \leftrightarrows H^+ + A^-$ (weak acid)

$BA \leftrightarrows B^+ + A^-$ (Salt)

By applying law of mass action

$Ka = [H^+][A^-] / [HA]$

$[H^+] = Ka[HA] / [A^-]$

$[H^+] = Ka\,[Acid] / [Salt]$

Taking (-log) on both sides,

$-\log [H^+] = -\log [Ka\,[Acid] / [Salt]]$

$-\log [H^+] = -\log Ka - \log [Acid] / [Salt]$

Now

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

$pKa = -\log Ka$

$pH = pK_a + \log [salt] / [Acid]$

For Basic Buffer

$pH = pK_b + \log [salt] / [Acid]$

Buffers in pharmaceutical systems

→ A buffer is a solution that resists significant changes in pH when small amounts of acid or base are added.
It typically contains a weak acid and its salt (acidic buffer) or a weak base and its salt (basic buffer).

Applications of Buffers in Pharmaceutical Systems

- Maintain pH of Drug Formulations
- Enhance Drug Solubility
- Improve Bioavailability
- Prevent Irritation
- Ensure Compatibility with Biological Systems

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 tonicity solution

❖ Isotonic Solution

- An isotonic solution is one that has the same osmotic pressure as body fluids (e.g., blood, tears, plasma).
- There is no net movement of water into or out of cells, so cells retain their normal shape and size.

❖ Hypertonic Solution

- A hypertonic solution has a higher osmotic pressure than body fluids due to a higher concentration of solutes.
- Water moves out of the cells, causing cells to shrink (crenation).

❖ Hypotonic Solution

- A hypotonic solution has a lower osmotic pressure than body fluids due to a lower solute concentration.
- Water moves into the cells, causing cells to swell and possibly burst (hemolysis).

Measurment of Tonicity

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

- Cryoscopic / Colligative Methods
- Haemolytic Methods

1. **Cryoscopic / Colligative Methods**
    - This method is based on the colligative properties of the solution such as Freezing Point, boiling 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

2. **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, Soluent partides move from area of low concentration to area of high concentration.
    - In Haemolytic method. first we dissolue 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 e 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

→ We can make solution isotonic by using two methods

1. Class Ist - Cryoscopic & sodium Chloride Equivalent
2. Class lInd - White Vincent & sprowls method

Class Ist

a. Cryoscopic method (freezing point depression method) :

→ This method is used for hypotonic solution, ie. concentration of solution is less than 0.9% w/v Nacl.

→ Sodium Chloride (NaCl) is added to solution to make it isotonic.

$$W\% = (0.52 - a)/b$$

Where

- W = amount of adjusting substance
- a = freezing point of 1% solution of unadjusted solution.
- b = freezing point of 1%. Solution of adjusting solution.

b. Sodium Chloride Equivalent (E) :

→ This is used for hypotonic solution, In this add sodium chloride in solution to make it isotonic

$$E = 17 \times Liso / M$$

Where

- E = Sodium Chloride Equivalent / Amount of Nacl required.
- Liso = Liso constant value
- M = Molecular weight of drug solution.

Class II[nd]

→ This method is used for hypertonic solution le. concentration of solution is more than 0.9% w/v Water is added to solution to make it isotonic

a. While-Vincet method:-

$$V = W \times E \times 111\text{-}1$$

Where

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

b. Sprowls Method

This is basically simplification of White- Vincent Method

In this we set W = 0.3

$$V = 0.3 \times E \times 111\text{-}1 \quad \text{or} \quad V = 33.33 \times E$$