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PHYSICAL PHARMACEUTICS - I

UNIT 5

TOPIC :

- **pH, buffers and Isotonic solutions :** 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.

pH, buffers and Isotonic solutions

Sorensen's pH Scale

- The pH scale was introduced to simplify the wide range of hydrogen ion concentrations found in aqueous solutions.
- It was developed by Danish biochemist Søren Peter Lauritz Sørensen in 1909.
- Sørensen defined pH as the negative logarithm (base 10) of the hydrogen ion concentration.

Definition of pH

$$\boxed{pH = -\log_{10}[H^+]}$$

- Here, $[H^+]$ represents the **molar concentration of hydrogen ions** in a solution.
- The pH scale provides a **numerical value** to determine the **acidity or basicity** of a solution.

Understanding the pH Scale

- The pH scale ranges from 0 to 14.
- It is logarithmic, meaning a change of 1 pH unit = 10× change in hydrogen ion concentration.

pH Value	Nature of Solution	Remarks
0 – 6.9	**Acidic**	More hydrogen ions $[H^+]$
7	**Neutral**	Pure water
7.1 – 14	**Basic (Alkaline)**	More hydroxide ions $[OH^-]$

Examples

pH	Substance	Type
1	Gastric acid	Strong acid
3	Orange juice	Weak acid
7	Pure water	Neutral
9	Baking soda solution	Weak base
13	Bleach	Strong base

Significance of the pH Scale

- Helps in determining acidity or basicity of a solution.
- Plays an important role in:
  - Biological processes (e.g., enzyme activity)
  - Pharmaceutical formulations
  - Industrial and lab-based reactions
- Maintaining correct pH is critical in body fluids like blood (pH ~7.35–7.45).

Importance of pH in Pharmacy

1. **Drug Solubility**
   - Many drugs are weak acids or bases, and their solubility is pH-dependent.
2. **Drug Stability**
   - Hydrolysis and oxidation rates vary with pH.
   - Example: Penicillin degrades faster at high pH.
3. **Formulation Compatibility**
   - pH affects preservative efficacy, color stability, and taste masking.
4. **Biological Absorption**
   - Absorption depends on drug ionization, which is influenced by pH (as per the Henderson-Hasselbalch equation).
5. **Buffer Systems**
   - Buffers are used to maintain pH in formulations for stability and patient comfort (e.g., eye drops, injections).

Measurement of pH

1. pH Paper (Litmus/Universal Indicator)
   - Quick, approximate method using color change.
2. pH Meter (Electrometric Method)
   - Accurate measurement using glass electrode and reference electrode.

pH Determination

- The pH of a solution indicates its hydrogen ion concentration and is a crucial parameter in pharmaceutical formulation, analysis, stability, and drug absorption. Accurate pH determination is vital in the manufacturing and testing of dosage forms like tablets, injections, eye drops, etc.
- pH can be determined using the following two main methods:

1. Electrometric Method (Using a pH Meter)

Principle

- This method measures the electrical potential (voltage) generated by a glass electrode that is sensitive to hydrogen ion concentration. The potential difference is directly related to the pH of the solution.

Components

- Glass electrode (pH-sensitive)
- Reference electrode (usually calomel or silver/silver chloride)
- pH meter (measures the voltage and converts it to pH)

Procedure

1. Calibrate the pH meter with standard buffer solutions (usually pH 4, 7, and 10).
2. Rinse the electrodes with distilled water and immerse them into the test solution.

3. Wait for the reading to stabilize and record the pH.

Advantages

- Highly accurate and precise
- Suitable for clear, turbid, or colored solutions
- Can be used for very small volumes

Applications in Pharmacy

- Measuring pH of injectables, eye drops, oral liquids
- Monitoring buffer solutions
- Ensuring product stability and compatibility

2. Colorimetric Method (Using Indicators)

Principle

- This method is based on the color change of a pH indicator dye, which changes its color depending on the pH range of the solution.

Types

- Litmus paper (acid/base)
- Universal indicator (broad pH range)
- Specific pH indicators (methyl orange, phenolphthalein, bromothymol blue)

Procedure

1. Add 1–2 drops of the indicator to the test solution.
2. Observe the color change.
3. Compare the color with a standard pH color chart.

Advantages

- Quick and simple
- Useful for approximate pH estimation
- No special equipment needed

Limitations

- Less accurate (only gives a rough estimate)
- Not suitable for colored or turbid solutions
- Indicator choice limited to specific pH ranges

Buffers

- A buffer is a solution that resists changes in pH when small amounts of acid or base are added to it.
  It helps in maintaining a constant pH, which is important for biological systems and pharmaceutical formulations.

Composition of Buffers

A typical buffer contains:

1. A weak acid and its conjugate base (e.g., acetic acid + sodium acetate)
   OR
2. A weak base and its conjugate acid (e.g., ammonia + ammonium chloride)

Types of Buffers

1. Acidic Buffers:

- Contain a weak acid + its salt with a strong base
- pH is less than 7
- Example: Acetic acid + Sodium acetate

2. Basic Buffers:

- Contain a weak base + its salt with a strong acid
- pH is more than 7
- Example: Ammonia + Ammonium chloride

Applications of Buffers

1. In Pharmaceutical Formulations:

Buffers are widely used in pharmaceutical products to:

- Maintain stability of the active ingredient by controlling the pH.
- Enhance solubility of drugs which are pH-dependent.
- Improve bioavailability by keeping the drug in its ionized or unionized form.
- Protect drugs from hydrolysis or degradation which may occur at unfavorable pH levels.

2. In Parenteral Preparations (Injectables):

- Buffers are used to adjust and maintain the pH of injections.
- Ensures the solution is isotonic and non-irritating to body tissues.
- Maintains drug activity and compatibility during storage.
- Example: Phosphate buffers in insulin and other injectable formulations.

3. In Ophthalmic Preparations (Eye Drops):

- The pH of eye drops is adjusted close to physiological pH (7.4) using buffers.
- Prevents eye irritation and ensures patient comfort.
- Maintains stability and activity of the drug.
- Example: Borate buffer in eye drops.

4. In Oral Formulations (Syrups, Tablets, Solutions):

- Buffers help to mask unpleasant tastes by controlling pH.
- Improve chemical stability of solutions and suspensions.
- Help to maintain pH-sensitive drugs in active form.

5. In Biological and Diagnostic Systems:

- Buffers are used in biological assays, enzyme activity studies, and diagnostic kits to maintain constant pH.
- Essential for protein folding, DNA/RNA stability, and enzyme reactions.
- Example: Tris buffer in electrophoresis.

6. In Drug Absorption and Bioavailability:

- Some drugs are absorbed better at specific pH values.
- Buffers help maintain optimal pH in the stomach or intestine to enhance absorption.
- Used in controlled-release and enteric-coated tablets to provide pH targeting.

7. In Cosmetic and Personal Care Products:

- Buffers stabilize creams, lotions, shampoos, and toothpastes.
- Prevent microbial growth by maintaining slightly acidic pH.
- Protect sensitive ingredients from degradation.

8. In Industrial Applications:

- Buffers are used in fermentation, water purification, and electroplating processes.
- Maintain constant pH during industrial chemical reactions.

Buffer Equation (Henderson-Hasselbalch Equation)

- The Henderson-Hasselbalch equation is used to calculate the pH of buffer solutions made from a weak acid and its conjugate base or a weak base and its conjugate acid.

1. For Acidic Buffers

- (A mixture of a weak acid and its salt with a strong base)

Equation:

$$\boxed{\mathrm{pH} = \mathrm{pKa} + \log\left(\frac{[\mathrm{Salt}]}{[\mathrm{Acid}]}\right)}$$

- pKa = negative log of acid dissociation constant (Ka)
- [Salt] = concentration of conjugate base (e.g., sodium acetate)
- [Acid] = concentration of weak acid (e.g., acetic acid)

2. For Basic Buffers

- (A mixture of a weak base and its salt with a strong acid)

Equation:

$$\boxed{\mathrm{pH} = 14 - \mathrm{pKb} + \log\left(\frac{[\mathrm{Base}]}{[\mathrm{Salt}]}\right)}$$

Or you can first calculate **pOH:**

$$\boxed{\mathrm{pOH} = \mathrm{pKb} + \log\left(\frac{[\mathrm{Salt}]}{[\mathrm{Base}]}\right)}$$

Then,

$$\mathrm{pH} = 14 - \mathrm{pOH}$$

Applications of Buffer Equation:

→ Calculate pH of buffer solutions

→ Design buffers for pharmaceutical formulations

→ Adjust pH for maximum drug solubility or stability

→ Used in biological buffers to maintain physiological pH

Buffer Capacity (β)

Buffer capacity is defined as the ability of a buffer solution to resist changes in pH upon the addition of a small amount of acid or base.

Mathematically, it is expressed as:

$$\beta = \frac{dB}{d(pH)}$$

Where:

- β = Buffer capacity
- dB = the number of moles of strong acid or base added per liter of buffer
- $d(pH)$ = change in pH caused by the addition

Explanation

- A buffer solution consists of a weak acid and its conjugate base (or vice versa).
- When a strong acid (H^+) or strong base (OH^-) is added to a buffer, it reacts with the buffer components, minimizing pH change.
- Buffer capacity tells us how much acid/base the buffer can neutralize before its pH begins to change significantly.

Units

- Buffer capacity has units of mol/L per pH unit, i.e., $mol \cdot L^{-1} \cdot pH^{-1}$.

Factors Affecting Buffer Capacity

1. **Concentration of Buffer Components:**
   - Higher the concentration of acid and conjugate base → **greater buffer capacity**.
   - A **1 M buffer** resists pH changes more than a **0.1 M buffer**.
2. **Ratio of Acid to Base:**
   - Buffer capacity is **maximum when pH = pKa**, i.e., when [**acid**] = [**base**].
   - At this point, the buffer is equally capable of neutralizing added acids or bases.
3. **Type of Buffer System:**
   - Stronger weak acids and their conjugate bases (with suitable pKa near the desired pH) offer **better buffering** at specific pH ranges.

Buffers in Pharmaceutical and Biological Systems

1. Role of Buffers in Pharmaceutical Systems:

a. pH Stability of Drugs

- Many drugs are pH-sensitive and degrade in acidic or alkaline conditions.
- Buffers help maintain a constant pH, improving shelf-life and stability.

b. Solubility Enhancement

- Solubility of many drugs depends on pH.
- Buffers ensure the drug remains in the ionized or unionized form as needed for maximum solubility.

c. Bioavailability

- Buffers adjust pH to enhance drug absorption.
- For instance, enteric-coated tablets use buffering to release drug in the intestines (alkaline pH).

d. Parenteral Products

- Injectable drugs must be near physiological pH (around 7.4) to avoid irritation.
- Buffers like phosphate buffer are used in injections (e.g., insulin).

e. Ophthalmic and Nasal Formulations

- Buffers keep the formulation pH compatible with body fluids (e.g., tears have pH ~7.4).
- Prevent eye irritation or nasal discomfort.

f. Controlled Drug Release

- Some buffering agents are used in controlled-release formulations to modulate drug release rate by maintaining a constant microenvironmental pH.

2. Role of Buffers in Biological Systems

a. Maintenance of Blood pH

- Blood has a buffering system (mainly bicarbonate buffer) to maintain pH around 7.35–7.45.
- This is essential for enzyme activity, oxygen transport, and cellular function.

b. Enzyme Functionality

- Most enzymes function optimally at a specific pH.
- Buffer systems in cells and tissues help maintain pH for enzymatic reactions.

c. Digestive System

- Stomach maintains acidic pH (~1.5–3.5) for digestion using gastric acid and mucosal buffering.
- Intestine maintains alkaline pH using bicarbonate from pancreas.

d. Urinary pH Regulation

- Kidneys regulate acid-base balance via phosphate and ammonium buffers in urine.
- Helps in excretion of metabolic acids and reabsorption of bicarbonate.

Buffered Isotonic Solutions

➢ Buffered isotonic solutions are pharmaceutical buffer solutions that are specially adjusted to have the same osmotic pressure as body fluids, such as blood, tears, or plasma. These solutions are used for administration into the body (e.g., injections, eye drops) to prevent irritation or damage caused by osmotic imbalance.

Types of Solutions (Based on Tonicity)

Type of Solution	Definition	Example	Effect on Body Cells
Isotonic	A solution having **same osmotic pressure** as body fluids.	0.9% NaCl	No net movement of water. Cells remain normal.
Hypotonic	A solution with **lower solute concentration** (lower osmotic pressure) than body fluids.	0.45% NaCl	Water enters cells → cells **swell or burst**.
Hypertonic	A solution with **higher solute concentration** (higher osmotic pressure) than body fluids.	3% NaCl	Water leaves cells → cells **shrink or crenate**.

Examples of Isotonic Solutions

- 0.9% Sodium Chloride (Normal Saline)
- 5% Dextrose in Water (D5W)
- Lactated Ringer's Solution
- Buffered eye drops and injections adjusted to isotonicity

Importance of Buffered Isotonic Solutions in Pharmacy:

1. Prevents irritation or damage to tissues during administration.
2. Maintains shape and integrity of red blood cells and epithelial cells.
3. Ensures proper drug absorption and minimizes pain or inflammation.
4. Commonly used in:
    - Injectables
    - Ophthalmic (eye) preparations
    - Nasal sprays
    - IV fluids