Program	B. Pharmacy
Semester	1st
Subject /Course	Pharmaceutical Inorganic and Analytical Chemistry
Subject/Course ID	Pharmaceutical Inorganic and Analytical Chemistry/BP106T
Module No.	02
Module Title	Acid-Base Chemistry and Buffer Systems, Major extra and intracellular electrolytes
Course coordinator	Ms. Pooja Devi
Mobile No.	8289042669
Email id	poojapooja25787@gmail.com

LO	Particular
1.	Define and explain acids, bases, buffers, pH scale, isotonicity, electrolytes, and physiological acid–base balance along with their pharmaceutical significance.
2.	Apply buffer equations to calculate pH and relate isotonicity and electrolyte balance to IV fluids, ophthalmic solutions, and replacement therapy preparations such as Sodium chloride, Potassium chloride, Calcium chloride, and ORS.
3.	Analyze the functions of major intracellular and extracellular electrolytes and evaluate their role in maintaining normal physiological and acid–base balance in the body.

Module Content Table

Sr. no.	Topic
1.	**Acid-Base Chemistry and Buffer Systems in Pharmacy** Definition of acids, bases, buffers, pH Scale and its significance, Buffer equation, calculation of pH for Buffer solution. Isotonicity and its application in IV Fluids and Ophthalmic Solutions.
2.	**Major extra and intracellular electrolytes** Functions of major physiological ions, Electrolytes used in the replacement therapy: Sodium chloride*, Potassium chloride, Calcium chloride and Oral Rehydration Salt (ORS), Physiological acid base balance.

Introduction to Acids and Bases

Acids and bases are important chemical substances that play a major role in our daily life as well as in scientific studies. The study of acids and bases began many years ago when early scientists observed the sour taste of some substances and the bitter taste of others. The word "acid" comes from the Latin word ***acidus***, meaning sour, while the word "base" was introduced later for substances that could neutralize acids. In ancient times, substances like vinegar, lemon juice, and curd were known to be acidic, whereas lime water and soap solutions were recognized as basic in nature. Over time, scientists developed different theories to explain their properties. Robert Boyle was one of the first scientists to classify substances as acids and bases based on their characteristics. Later, Svante Arrhenius explained that acids produce hydrogen ions in water while bases produce hydroxide ions. Further advancements were made by Johannes Nicolaus Bronsted and Thomas Martin Lowry, who described acids as proton donors and bases as proton acceptors. Today, acids and bases are widely used in industries, medicines, agriculture, and laboratories, making them an essential part of chemistry and everyday life.

Definition of Acids

An acid is a chemical substance that produces hydrogen ions (H^+) when dissolved in water. Acids generally have a sour taste and can turn blue litmus paper red. According to different theories, acids may also be defined as proton donors or electron pair acceptors.

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

Examples: Hydrochloric acid (HCl), sulfuric acid (H_2SO_4), nitric acid (HNO_3).

Definition of Bases

A base is a chemical substance that produces hydroxide ions (OH^-)when dissolved in water. Bases usually have a bitter taste and feel slippery to touch. They turn red litmus paper blue. According to other theories, bases may also be defined as proton acceptors or electron pair donors.

$$NaOH \rightarrow Na^+ + OH^-$$

Examples: Sodium hydroxide ($NaOH$), potassium hydroxide (KOH), calcium hydroxide ($Ca(OH)_2$).

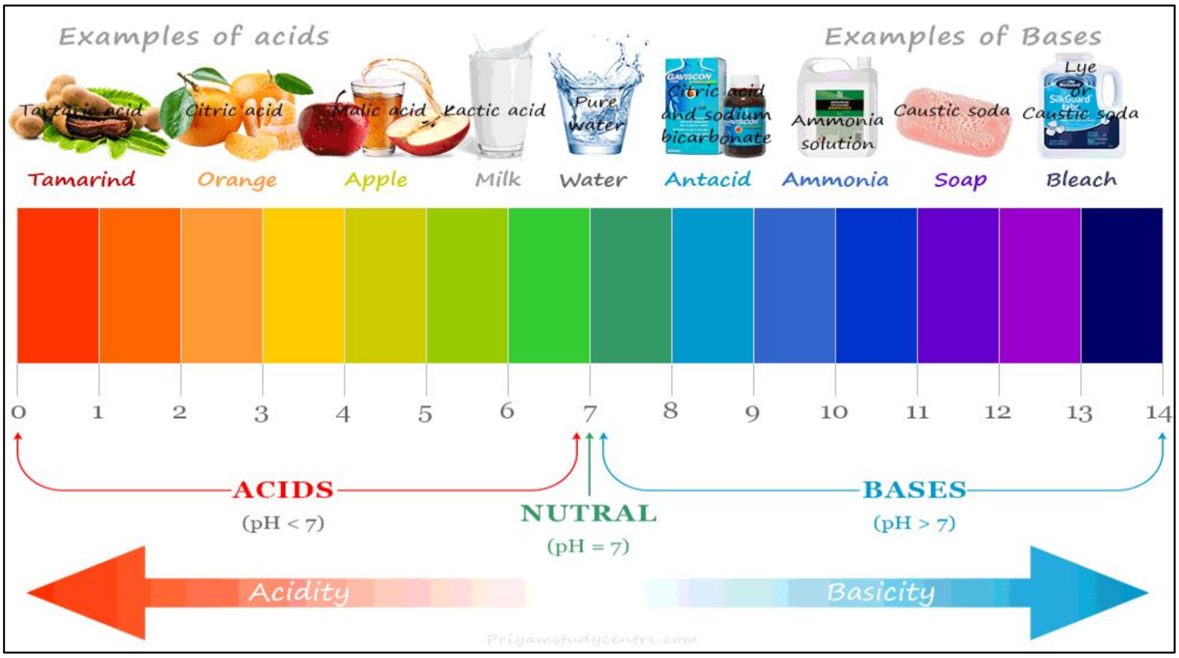


Fig. pH Scale for acids and bases

The concept of acids and bases has been explained by different scientists through various theories over time. Each theory helped in understanding the behavior and properties of acids and bases more clearly.

Earlier Concept of Acid and Base

An **acid** may be any substance which has sour taste and its aqueous solution turns blue litmus red.

A **base** may be any substance which has a bitter taste and its aqueous solution turns red litmus blue.

The earlier concept does not explain the behaviour of all acids and bases.

Arrhenius Theory

The Swedish chemist Svante Arrhenius proposed the first definition of acids and bases. (Substances A and B became known as acids and bases)

According to Arrhenius Concept, **Acid** are substance which are capable of providing Hydrogen ions (H^+, proton) when dissolved in water and **bases** are substances which are capable of providing hydroxide ions (OH^-, hydroxyl ions) in aqueous solution.

For example, Hydrochloric acid in the water, HCl undergoes dissociation reaction to produce H^+ ion and Cl^- ion, as explained below. The concentration of the H^+ ions is increased by forming hydronium ion.

$$HCl\ (aq) \rightarrow H^+\ (aq) + Cl^-\ (aq)$$

Sodium Hydroxide when dissolved in aqueous solution it gives hydroxyl ions and sodium

$$NaOH \rightarrow Na^+ + OH^-$$

According to neutralization reaction, these two ions (H^+ and OH^-) combines to form solvent (i.e. water) and a salt (NaCl). This can be referred by following equation:

$$HCl\ (acid) + NaOH\ (Base) \rightarrow NaCl\ (Salt) + H_2O\ (Water)$$

Limitations:

1. It is limited only to aqueous solution.

2. The neutralization of acids and bases in absence of solvent could not be explained.

3. It could not explain the basic nature of substances like NH_3 or Na_2CO_3 which do not contain OH- ions and acidic nature of substances like CO_2 or SO_2 which do not contain H+ ions.

Bronsted – Lowry Concept

The Bronsted–Lowry theory was proposed by Johannes Nicolaus Bronsted and Thomas Martin Lowry in 1923. According to them an acid may be defined as any hydrogen containing material (molecule or a cation or an anion) that is capable of donating a proton H^+ to any other substance. Whereas a base may be defined as any substance (a molecule, or a cation or an anion) that can accept a proton from any other substance.

In short, an acid is a proton donor and bases are a proton acceptor.

Some examples of acids are as follows:

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

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

Some examples of bases are as follows:

$$OH^- + H^+ \rightarrow H_2O$$

$$NH3 + H^+ \rightarrow NH_4$$

Conjugate Acid–Base Pairs

According to the Bronsted–Lowry theory, a conjugate acid–base pair is formed when an acid donates a proton (H^+) and a base accepts that proton. The two substances in a conjugate pair differ by one proton only.

- An **acid** loses a proton and forms its **conjugate base**.
- A **base** gain a proton and forms its **conjugate acid**.

Let us consider a reaction: Where A is acid and B is Base

$$HCl + H_2O \rightarrow H_3O^+ + Cl^-$$

(A1) (B1) (A2) (B2)

In this reaction, HCl donates a proton to H_2O and is therefore an acid. On the other hand, Water accepts a proton from HCl and is therefore a base. In the reverse reaction which is at equilibrium proceeds at the same rate as the forward reaction, the H_3O^+ ion donates a proton to Cl^- ion and hence H_3O^+ is an acid, while Cl^- ion which accepts a proton from H_3O^+ is a base. The acid base pairs, the members of which can be formed from each other mutually by the gain or loss of proton are called conjugate acid-base pairs.

Some more examples:

$$H_2SO_4 + H_2O \rightarrow H_3O^+ + HSO_4^-$$

$$CH_3COOH + H_2O \rightarrow H_3O^+ + CH_3COO^-$$

Water is having dual character because it can accept a proton or donate.

$$HCl + H_2O \rightarrow H_3O^+ + Cl^-$$

$$NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-$$

In the first reaction H_2O accepts a proton from HCl resulting to form hydronium ion H_3O^+ and thus H_2O is a base. Whereas in the second reaction H_2O donates a proton to NH_3 a base and forms hydroxide ion (OH^-) and it act as an acid. When any substance which can donate as well as accept a proton it is termed as amphoteric or amphiteric. A number of other substances, solvents etc. also exhibit amphoteric character.

Limitations:

1. It explains only proton-transfer reactions. It cannot explain reactions where no proton transfer occurs.

$$SO_2 + SO_2 \rightleftharpoons SO_2^{+} + SO_3^{2-}$$

$$Acid_1 + Base_2 \rightleftharpoons Acid_2 + Base_1$$

Thus, it can not be able to explain the reactions occurring in non-protonic solvents such as $CoCl_2$, SO_2.

2. Bronsted Lowry concept lays excessive emphasis on the proton transfer. Although it is true that most common acids are protonic in nature, yet there are many which are not.

Lewis Concept

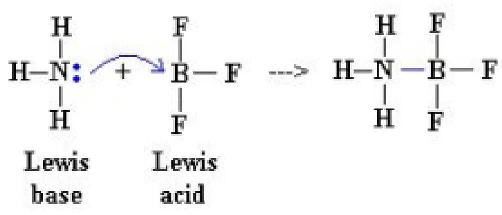
The Lewis theory of acids and bases was proposed by Gilbert N. Lewis in 1923. This theory is more general and broader than the Arrhenius and Bronsted–Lowry theories because it explains acid–base reactions that do not involve hydrogen ions or proton transfer.

According to the Lewis theory:

An acid may be defined as any species (molecule, radical or ion) that can accept an electron pair to form a coordinate bond while a base may be defined as any species (molecule, radical or ion) that can donate an electron pair to form a coordinate bond.

The chemical reaction between lewis acid and base results in a product that is described as adduct.

For example: Here, BF_3 accepts one lone pair of e- and is therefore a Lewis acid while NH_3 donates one lone pair of e^- and is therefore known as Lewis base.



Lewis Acid: H^+, NH_4^+, Na^+, K^+, Cu_2^+, Al_3^+

Lewis Base: NH_3, H_2O, OH-, Cl^-, CN^-

Limitations:

1. As lewis acid- base reactions involve electrons, they are expected to be very fast reactions. However, there are many lewis acid-base reaction which are very slow.

2. Strength of lewis acid and bases is found to depend on the type of reaction, it is not possible to arrange them in order of their relative strength.

Advantages:

1. It is widely used in coordination chemistry.
2. It explains the behavior of catalysts in industrial reactions.
3. It helps in understanding organic reaction mechanisms.
4. It explains reactions that are not covered by Arrhenius and Bronsted–Lowry theories.
5. It is the most general acid–base theory.
6. It explains both protonic and non-protonic reactions.

Importance of acids and bases in pharmacy

Acids, bases and their reaction play vital role in pharmacy practice. Some of the main application of the these are as follows:

• Acid-base neutralization reaction finds use in preparative procedures for the preparation of suitable salt, and for conversion of certain salts into more suitable forms.

• Acid-base is used in analytical procedure which is involving acid-base titrations.

• Acids and bases find use as therapeutic agents in the control of and adjustment of pH of the GI tract, body fluids and urine.

BUFFERS

A buffer solution is a solution that resists changes in pH when a small amount of acid or base is added to it. In other words, a buffer solution maintains the pH of a solution nearly constant.

Buffer solutions are very important in chemical laboratories, biological systems, and industrial processes because many chemical reactions require a fixed pH.

A buffer solution is usually made up of:

1. A weak acid and its salt with a strong base, or
2. A weak base and its salt with a strong acid.

1. Acidic Buffer Solution

An acidic buffer solution is a mixture of a weak acid and its salt formed with a strong base. The pH of an acidic buffer is less than 7. These buffers are used when an acidic medium is required.

The weak acid only partially ionizes in water, while its salt completely dissociates and provides the common ion. Due to the presence of both components, the concentration of hydrogen ions remains nearly constant.

Common Examples:

- Acetic acid (CH_3COOH) and sodium acetate (CH_3COONa)
- Carbonic acid (H_2CO_3) and sodium bicarbonate ($NaHCO_3$)

Example of Acetic Acid Buffer

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

Sodium acetate dissociates completely:

$$CH_3COONa \rightarrow CH_3COO^- + Na^+$$

The acetate ions (CH_3COO^-) from sodium acetate suppress the ionization of acetic acid due to the common ion effect. Therefore, only a small amount of hydrogen ions remains in the solution, and the pH stays stable.

Action of Acidic Buffer

When Acid is Added

If a small amount of strong acid is added, the extra hydrogen ions are consumed by acetate ions.

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

Thus, the concentration of hydrogen ions does not increase significantly.

When Base is Added

If a small amount of base is added, the hydroxide ions react with acetic acid.

$CH_3COOH + OH^- \rightarrow CH_3COO^- + H_2O$

Hence, the hydroxide ions are neutralized and the pH remains almost constant.

Uses of Acidic Buffers:

1. Used in pharmaceutical preparations.
2. Used in food preservation.
3. Maintains blood pH in biological systems.
4. Used in chemical analysis and laboratory experiments.

2. Basic Buffer Solution

A basic buffer solution is a mixture of a weak base and its salt formed with a strong acid. The pH of a basic buffer is greater than 7. These buffers are used when a basic medium is required.

The weak base ionizes only slightly, while its salt dissociates completely and supplies the common ion, helping maintain a stable hydroxide ion concentration.

Common Examples

- Ammonium hydroxide (NH_4OH) and ammonium chloride (NH_4Cl)
- Ammonia (NH_3) and ammonium chloride (NH_4Cl)

Example of Ammonium Hydroxide Buffer

$$NH_4OH \rightleftharpoons NH_4^+ + OH^-$$

Ammonium chloride dissociates completely:

$$NH_4Cl \rightarrow NH_4^+ + Cl^-$$

The ammonium ions (NH_4^+) suppress the ionization of ammonium hydroxide by the common ion effect, thereby maintaining a stable hydroxide ion concentration.

Action of Basic Buffer

When Acid is Added

If a small amount of acid is added, the hydroxide ions neutralize the added hydrogen ions.

$$OH^- + H^+ \rightarrow H_2O$$

The equilibrium then shifts to produce more hydroxide ions.

When Base is Added

If a small amount of base is added, the ammonium ions react with the added hydroxide ions.

$$NH_4^+ + OH^- \rightarrow NH_4OH$$

Thus, excess hydroxide ions are removed and the pH remains nearly constant.

Uses of Basic Buffers:

1. Used in textile and dyeing industries.
2. Used in chemical manufacturing.
3. Maintains pH in biological and industrial processes.
4. Used in analytical chemistry.

Buffer Action

The property of buffer solution is to resist any change in its pH value, even when small amount of acid or base is added to it is known as "Buffer action".

Hydrogen Ion Concentration, pH and pOH

Pure water ionises as follows:

$$H_2O \rightleftharpoons H^+ + OH^-$$

$$K = \frac{[H^+]\,[OH^-]}{H_2O}$$

$$K\,[H_2O] = [H^+]\,[OH^-]$$

$$K_w = [H^+]\,[OH^-]$$

Where K_w = Ion product constant

The ion product constant (K_w) is expressed by involving only the concentration of ionic species on right hand side of the reaction and has a constant value at 25°C of 1×10^{-14}. It can be represented as:

$$[H^+]\,[OH^-] = 1 \times 10^{-14}$$

In pure water, the concentration of both ions is equal each having the value of 1×10^{-7} M

$$[H^+] = [OH^-] = 1 \times 10^{-7}$$

The hydrogen ion concentration is greater than hydroxide ion concentration when an acid or base is added to water. The value of hydrogen ion concentration is 10^{-7}g ion/litre.

In neutral solution $[H^+] = [OH^-]$
In acid solution $[H^+] > [OH^-]$
In alkaline solution $[H^+] < [OH^-]$

pH Scale and Its Significance

The pH scale is a numerical scale used to measure the acidic or basic nature of a solution. The term "pH" stands for "potential of hydrogen" or "power of hydrogen." It represents the concentration of hydrogen ions (H^+) present in a solution. The concept of pH is very important in chemistry because it helps in determining whether a substance is acidic, basic, or neutral.

The pH scale was introduced in 1909 by the Danish chemist Sorensen while working at the Carlsberg Laboratory in Denmark. Before the introduction of the pH scale, it was difficult to express the acidity and basicity of solutions accurately. Sorensen developed the pH concept to provide a simple mathematical way to express hydrogen ion concentration in solutions. His work made the study of acids and bases easier and more systematic.

The pH of a solution is defined as the negative logarithm of the hydrogen ion concentration.

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

This equation shows that pH depends on the concentration of hydrogen ions in a solution. If the concentration of hydrogen ions is high, the pH value becomes low and the solution is acidic. If the concentration of hydrogen ions is low, the pH value becomes high and the solution is basic.

The pH scale covers from 0-14 of all the hydrogen ion concentrations. It can be measured by using the pH meter.

$[H^+]$ (mol dm^{-3})	pH	[OH] (mol dm^{-3})	pOH Basicity	Acidity, Basicity
1.0 (10^0)	0	10^{-14}	14	Increasing acidity
0.1 (10^1)	1	10^{-13}	13	
10^{-4}	4	10^{-10}	10	
10^{-7}	7	10^{-7}	7	Neutral
10^{-10}	10	10^{-4}	4	
10^{-13}	13	10^{-1}	1	
10^{-14}	14	10^{-0}	0	Increasing basicity

Significance of pH Scale

The pH scale is very important in chemistry, biology, medicine, agriculture, industries, and environmental science because many physical, chemical, and biological processes depend upon a proper pH range. The pH scale helps in determining whether a solution is acidic, basic, or neutral and also indicates the strength of acids and bases. By measuring pH, scientists and industries can control reactions and maintain suitable conditions for various processes.

1. Human Body

The human body functions properly only within a narrow pH range. Human blood has a pH of about 7.4, which is slightly basic. Even a small change in blood pH can disturb body functions and may become dangerous. The stomach contains hydrochloric acid, which has a low pH and helps in digestion by breaking down food and killing harmful bacteria.

Saliva in the mouth also has a particular pH that helps protect teeth from decay. If the pH in the mouth becomes too acidic, tooth enamel may get damaged. Therefore, toothpaste is usually basic in nature to neutralize excess acids.

2. Biological Systems

Most biological reactions occur only at a specific pH. Enzymes, which act as biological catalysts, work efficiently only within a narrow pH range. If the pH changes too much, enzymes may lose their activity and biological reactions may slow down or stop completely.

For example:

- Pepsin enzyme in the stomach works best in acidic conditions.
- Trypsin enzyme in the intestine works best in basic conditions.

Thus, maintaining proper pH is essential for normal biological functioning.

3. Agriculture

The pH of soil greatly affects plant growth. Different crops require different soil pH ranges for proper absorption of nutrients and minerals.

- Acidic soils may reduce the availability of essential nutrients.
- Highly basic soils may prevent plants from absorbing minerals properly.

Farmers test soil pH regularly and add lime to acidic soil or organic matter to basic soil to maintain proper conditions for crop production.

4. Industries

Many industrial processes require strict pH control because the quality of products depends on it. Industries such as:

- pharmaceutical industries,
- food industries,
- textile industries,
- dyeing industries,
- paper industries,
- leather industries,

All require proper pH conditions during manufacturing. In pharmaceutical industries, medicines and injections are prepared at suitable pH levels to avoid harmful effects on the human body. In food industries, pH helps maintain flavor, preservation, and quality.

5. Environmental Science

The pH of rivers, lakes, oceans, and rainwater affects aquatic life and environmental balance. Aquatic organisms can survive only within a limited pH range.

Acid rain decreases the pH of soil and water bodies, harming plants, fish, and other living organisms. Therefore, monitoring environmental pH is important for pollution control and environmental protection

6. Daily Life Substances

Many substances used in daily life have specific pH values:

- Lemon juice and vinegar are acidic.
- Soap and detergents are basic.
- Shampoo and skin-care products are prepared with balanced pH to avoid irritation.

The pH scale helps manufacturers prepare products that are safe and suitable for human use.

7. Chemical Laboratories

In laboratories, pH measurement is important for:

- carrying out chemical reactions,
- preparing buffer solutions,
- performing titrations,
- studying acid–base behavior.

Many reactions occur correctly only under controlled pH conditions.

8. Medicines

Doctors and medical laboratories measure the pH of blood, urine, and other body fluids to diagnose diseases. Abnormal pH values may indicate health problems such as kidney disorders, respiratory problems, or digestive issues.

Importance of Maintaining Proper pH

Maintaining proper pH is necessary because:

1. It ensures proper functioning of living organisms.
2. It controls chemical reactions.
3. It improves industrial product quality.
4. It protects the environment.
5. It supports healthy plant growth.

Buffer capacity

Buffer capacity is the ability of a buffer solution to resist changes in pH when a small amount of acid or base is added. It tells us **how much acid or base a buffer can neutralize** before its pH changes significantly.

Definition: Buffer capacity is defined as: "The number of moles of strong acid or strong base (H^+/OH^-) required to change the pH of 1 litre of a buffer solution by one unit."

Mathematical Expression:

$$\beta = \frac{d[B]}{dpH}$$

Where: β = buffer capacity, dB = small amount of strong base or acid added, dpH = change in pH

Buffer Equation or Henderson Hessel Bach Equation

Buffer equation is also known as Henderson Hessel Bach equation. It is used to calculate the pH of a buffer solution and the changes in pH which occurs during addition of acid or an base. With the help of this equation it is possible to calculate the pH of a buffer solution of known concentration or to make buffer solution of known pH. Two separate equations are obtained for each type of buffer, acidic and basic

pH of acidic buffer: The hydrogen ion concentration obtained from the dissociation of weak acid HA is given by equation,

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

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

Ka = equilibrium constant

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

Taking logarithms of both sides of the equation and multiplying throughout by -1 gives

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

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

$$pH = pKa + \log \frac{[\text{Conjugate base}]}{[\text{acid}]}$$

pH of an alkaline buffer: The ionisation of a weak base BOH is given by:

$$BOH \rightleftharpoons B^+ + OH^-$$

$$Kb = \frac{[B^+][OH^-]}{[BOH]}$$

$$[OH^-] = Kb \frac{[BOH]}{[B^+]}$$

$$\log [OH^-] = \log Kb + \log \frac{[BOH]}{[B^+]}$$

$$-\log [OH^-] = -\log Kb + \log \frac{[B^+]}{[BOH]}$$

$$pOH = pKb + \log \frac{[\text{conjugate acid}]}{[\text{base}]}$$

Acid Base Imbalance

The human body functions properly only within a narrow pH range. The normal pH of blood is:

$$pH = 7.35 \text{ to } 7.45$$

When the blood pH changes beyond this range, acid–base imbalance occurs.

- ✓ Decrease in blood pH below 7.35 is called **acidosis**.
- ✓ Increase in blood pH above 7.45 is called **alkalosis**.

These conditions affect enzyme activity, metabolism, nerve function, and overall body processes.

Types of Acidosis- There are two main types:

1. Respiratory acidosis
2. Metabolic acidosis

1. Respiratory Acidosis: Respiratory acidosis occurs when the lungs cannot remove enough carbon dioxide from the body.

Carbon dioxide combines with water to form carbonic acid: Increase in CO_2 causes increase in H_+ ions, lowering pH.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

2. Metabolic Acidosis: Metabolic acidosis occurs due to excess production of acids, Loss of bicarbonate ions and Failure of kidneys to remove acids.

Calculation of pH for Acidic and Basic Buffer Solutions:

The pH of buffer solutions is calculated using the **Henderson–Hasselbalch equation**.

1. pH of Acidic Buffer Solution: Let us consider acidic buffer which is prepared by mixing acetic acid and sodium acetate. Acetic acid is a weak electrolyte and sodium acetate a strong electrolyte and hence the dissociation of acetic acid get suppressed due to common ion (CH_3COO^-). The result is, the solution is having less H^+ ions and more Na^+ and CH_3COO^- ions. When a small quantity of an acid is added, H^+ ions of it combine with CH_3COO^- to form undissociated CH_3COOH. The net result is that pH does not change. When a small quantity of a base is added, OH^- ions get neutralised by acetic acid and pH does not change.

An acidic buffer contains: Weak acid and Salt of weak acid with strong base

Example:

- Acetic acid (CH_3COOH)
- Sodium acetate (CH_3COONa)

Formula for Acidic Buffer

$$pH = pKa + \log \frac{[\text{Conjugate base}]}{[\text{acid}]}$$

Where: pH = pH of buffer, pKa= negative logarithm of acid dissociation constant, salt or conjugate base = concentration of salt, acid = concentration of weak acid

Steps for Calculation

Step 1: Find the value of: pKa, concentration of acid and concentration of salt

Step 2: Substitute values into the equation.

Step 3: Solve logarithm value and calculate pH.

Numerical Example of Acidic Buffer

Calculate the pH of a buffer containing: 0.2 M acetic acid and 0.3 M sodium acetate

Given: pKa=4.76

$$pH = pKa + \log \frac{[\text{Conjugate base}]}{[\text{acid}]}$$

Substituting values:

$$pH=4.76 + \log \frac{0.3}{0.2}$$

$$pH=4.76 + \log (1.5)$$

$$\log (1.5) = 0.176$$

Therefore:

$$pH = 4.76 + 0.176$$

$$pH = 4.936$$

Thus, the pH of acidic buffer is: pH ≈ 4.94

2. pH of Basic Buffer Solution: A basic buffer contains: Weak base and Salt of weak base with strong acid

Example:

- Ammonium hydroxide (NH_4OH)
- Ammonium chloride (NH_4Cl)

Firstly, calculate pOH: $$pOH = pKb + \log \frac{[\text{conjugate acid}]}{\text{Base}}$$

Then calculate pH using:

$$pH = 14 - pOH$$

Where:

- pKb = negative logarithm of base dissociation constant
- Salt = concentration of salt
- Base = concentration of weak base

Step 1: Find: pKb, Concentration of base, Concentration of salt

Step 2: Calculate pOH using Henderson–Hasselbalch equation.

Step 3 Use pH=14−pOH to calculate pH.

Numerical Example of Basic Buffer

Calculate the pH of a buffer containing: 0.4 M ammonium hydroxide and0.5 M ammonium chloride

Given: pKb = 4.75

Substituting values: $$pOH = 4.75 + \log \frac{0.5}{0.4}$$

$$pOH = 4.75 + \log (1.25)$$

$$\log (1.25) = 0.097$$

Therefore:

$$pOH = 4.75 + 0.097$$

$$pOH = 4.847$$

Now calculate pH: $$pH = 14 - 4.84$$

$$pH = 9.153$$

Thus, the pH of the basic buffer is: pH ≈ 9.15

If salt concentration increases ⟶ pH increases. If acid concentration increases ⟶ decreases.

Buffers in Pharmaceutical System and Applications of Buffers

1. Solubility enhancement: The pH of the pharmaceutical formulations are adjusted to an optimum value so that the drug remains solubilised though out its shelf-life and not precipitated out. **E.g.** Sodium salicylate (Aspirin) precipitates as salicylic acid in acidic environment.

2. Increasing stability: To prevent hydrolysis and for maximum stability, the pH of the medium should be adjusted suitably. **E.g.** Vitamins

3. Improving purity: The purity of proteins can be identified from its solubility at their isoelectric point as they are least soluble at this point. The isoelectric pH can be maintained using suitable buffers. **E.g.** Insulin precipitates from aqueous solution at pH 5.0-6.0.

4. Optimising biological activity: Enzymes have maximum activity at definite pH values. Hence buffer of desired pH is added to the preparation.

5. Comforting the body: The pH of the formulations that are administered to different tissues of the body should be optimum to avoid irritation (eyes), haemolysis (blood) or burning sensation (abraded surface). The pH of the preparation must be added with suitable number of buffers to match with the pH of the physiological fluid. **E.g** buffer in various dosage forms.

Dosage Form	Buffer Used	Composition	Applications
Eye drops (Ophthalmic preparations)	Phosphate buffer	Sodium dihydrogen phosphate + Disodium hydrogen phosphate	Maintains pH near tears and reduces eye irritation
Eye drops (Ophthalmic preparations)	Borate buffer	Boric acid + Sodium borate	Used for soothing effect and pH maintenance
Injections (Parenteral preparations)	Phosphate buffer	Phosphate salts	Maintains physiological pH and drug stability
Oral syrups	Acetate buffer	Acetic acid + Sodium acetate	Maintains acidic pH and improves stability
Oral liquids	Citrate buffer	Citric acid + Sodium citrate	Improves taste and maintains pH
Tablets and capsules	Citrate or phosphate buffer	Citrate or phosphate salts	Enhances dissolution and stability
Nasal preparations	Phosphate buffer	Phosphate salts	Prevents nasal irritation and maintains suitable pH

Topical preparations	Acetate buffer	Acetic acid + Sodium acetate	Maintains stability of creams and lotions
Blood storage solutions	Citrate buffer	Citric acid + Sodium citrate	Prevents blood clotting
Biological products	Phosphate buffer	Phosphate salts	Maintains stable pH for proteins and vaccines
Antibiotic preparations	Citrate or phosphate buffer	Acidic/basic salts	Prevents degradation of antibiotics
Protein formulations	Phosphate buffer	Phosphate salts	Maintains protein stability and activity
Vaccine preparations	Phosphate buffer	Sodium phosphate salts	Maintains pH and effectiveness of vaccines
Dermatological preparations	Borate or phosphate buffer	Boric acid or phosphate salts	Maintains skin-compatible pH
Intravenous fluids	Bicarbonate buffer	Sodium bicarbonate + Carbonic acid	Maintains blood pH and treats acidosis

Standard Buffer Solutions: Standard buffer solution having the standard pH. They are used for reference purposes in the measurement of pH and carrying out many pharmacopeial tests which require maintenance of specified pH

The standard buffer solutions of pH ranging from 1.2-10 are possible to prepare by appropriate combinations of 0.2N HCl or 0.2N NaOH or 0.2M solution of potassium hydrogen phthalate, potassium dihydrogen phosphate, boric acid, potassium chloride. Standard buffers with pH range:

Buffer	pH
Hydrochloric acid buffer	1.2-2.2
Acid Phthalate buffer	2.2-4.0
Neutralised phthalate buffer	4.2-5.8
Phosphate buffer	5.8-8.0
Alkaline Borate buffer	8-10

Preparation of Buffer Solutions:

Weak acid with pKa = desired pH should be selected

↓

Ratio of salt and acid needed should be calculated using buffer equation

↓

Individual concentration of buffer salt and acid determined.

↓

Ingredients are dissolved in carbon dioxide free water

↓

Buffer capacity of 0.01-0.1 is adequate

↓

Concentration of 0.05-0.5 M is sufficient

↓

Allowed to establish equilibrium

↓

pH verified

Isotonicity

Pharmaceutical solutions that are meant for application to delicate membranes of body should be adjusted to same osmotic pressure as that of body fluids. Isotonic solutions cause no swelling or contraction of the tissues with which they come in contact and produce no discomfort when instilled in the nasal tract, eye blood, or other tissues.

Isotonicity is the property of a solution having the same osmotic pressure as body fluids such as blood plasma, tears, and body cells. In an isotonic solution, there is **no net movement of water** across a semipermeable membrane, so cells neither swell nor shrink.

There are three types of solutions in our body based on solute concentration:

a. Isotonic Solution: In this type of solution the concentration of solutes is the same both inside and outside the cell. Example- a small quantity of blood is mixed with a solution containing 0.9g of NaCl (normal saline) per 100ml, the cells retain the normal size.

b. Hypertonic solution: In this type of solution the concentration of solutes is greater outside the cell than inside it. Example- the red blood cells are suspended in a 2.0% NaCl solution, the water within the cells passes through the cell membrane in an attempt to dilute the surrounding salt solution. The outward passage of water causes the cells to shrink and become wrinkled.

c. Hypotonic Solution: In this type of solution the concentration of solutes is greater inside the cell than outside of it. Example- the blood is mixed with 0.2% NaCl solution or with distilled water, water enters the blood cells, causing them to swell and finally burst.

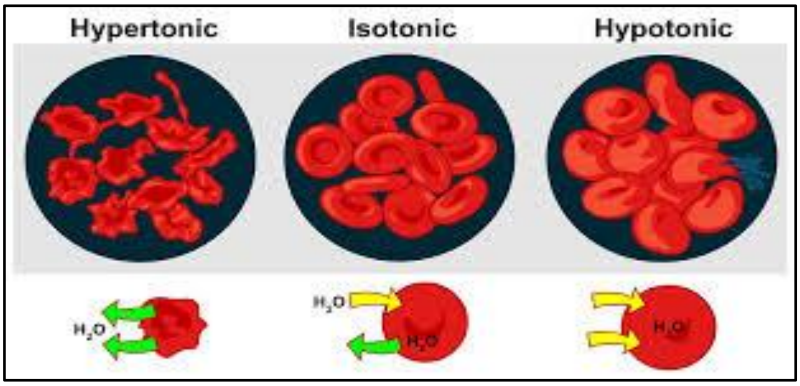


Fig. Tonicity and red blood cells

Osmolarity

Osmolarity is the measure of the total concentration of osmotically active particles present in one litre of solution.

It indicates the ability of a solution to exert osmotic pressure.

Measurement of Tonicity

There are broadly two methods to measure tonicity:

1. **Hemolytic Method:** Effect of various solutions of a drug is observed on the appearance of red blood cells suspended in the solution. RBCs are suspended in various solutions and the appearance of RBCs is observed for shrinking, swelling, bursting and wrinkling of the blood cells.

2. **Cryoscopic Method:** Isotonicity can be measured from colligative properties of the solution. E.g. Freezing point depression method. The freezing point of water is 0˚C, and when substance such as NaCl is added, the freezing point of water decreases. The freezing point of blood is -0.52˚C. Hence freezing point value of drug solution must be -0.52˚C. Then the solution shows osmotic pressure equal to blood.

Methods of adjusting isotonicity: Several methods are used in pharmaceutical preparations to adjust isotonicity. If solutions are injected or introduced in to nose and eyes, these are to be made isotonic in order to avoid haemolysis of RBCs and to avoid pain and discomfort.

Class I methods: In this 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. It includes **Cryoscopic method and Sodium chloride equivalent method**

Class II methods: In this method water is added to the drug in sufficient amount to form an isotonic solution. It includes **White-Vincent method and sprowls method.**

Cryoscopic Method (Freezing Point Depression Method): The plasma and blood freezing point temperature = -0.52°C.

- The dissolved substances in plasma or tear depress the solution freezing point below 0.52°C.
- Any solution that freeze at t = -0.52°C is isotonic with blood and tear

$$W = 0.52 - a/b$$

Where, W = weight of substance that need to be adjusted to make it isotonic substance in g.

a = the depression of the freezing point of water produced by the medicament already in the solution.

b = the depression of freezing of water produced by 1 % w/v of the added substance.

NUMERICAL: How much NaCl is required to render 100ml of a 1% solution of apomorphine hydrochloride isotonic with blood serum?

(1% solution of drug has freezing point lowering of 0.08°C)

(1% solution of NaCl has a freezing point lowering of 0.58°C)

Solution: In order to make drug solution isotonic, NaCl is needed to add to lower freezing point by (0.520.08)

W = 0.44/0.58

W = 0.758 g

So, 1 g of drug and 0.758g of NaCl in 100 ml of solution.

Sodium Chloride Equivalent Method (E)

Sodium chloride equivalent (E) of a drug is the amount of sodium chloride that is equivalent to 1 gm of the drug.

The percent of sodium chloride required for adjusting the isotonicity can be calculated using the following equation.

$$PSA = 0.9 - (PSM \times E\ of\ medicament)$$

Where, PSM = Percent strength of medicament

PSA = Percent of sodium chloride for adjustment of isotonicity.

Above equation is used to calculate the amount of adjusting substance (sodium chloride) required for making the solution isotonic. It is valid for 100 ml solution.

NUMERICAL: Calculate the gram of sodium chloride needed to make 30 ml of a 2% isotonic physostigmine salicylate solution using sodium chloride method.

Solution: E value of physostigmine salicylate = 0.16

PSM =2.0 %

Volume of preparation required = 30 ml

For equation

PSM = 0.9 – (PSM E of medicament)

= 0.9 – (2.0 0.16)

= 0.9 - 0.32 = 0.58 %

The above strength is valid for 100 ml since is expressed in percent. It should be prepared from 30 ml of solution for 100 ml of solution, sodium chloride required = 0.58

For 30 ml of solution, sodium chloride required =?

30 × 0.58/100 = 17.4/100 = 0.174 g of sodium chloride

White-Vincent Method

This method involves the addition of water to the given amount of drug to make isotonic solution, followed by the addition of some other isotonic solution (e.g. 0.9% NaCl) to make the final volume.

White Vincent, from their study of need of Ph adjustment in addition to tonicity of ophthalmic solution, developed an equation.

The volume of water that should be added in given amount of drug to make isotonic solution is calculated by using:

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

Where, V = volume of water needed to make isotonic solution

W = given weight of drug in grams

E = NaCl equivalent value of drug 1

11.1 = constant

NUMERICAL: Make 50 ml isotonic solution from 0.5 gm of boric acid. E value of boric acid is 0.50.

Solution: Given amount of boric acid = 0.5 gm

Required volume = 50 ml

E value of boric acid = 0.50

Firstly, we calculate the amount of the water that should be added in 0.5 gm of boric acid to make isotonic solution by using formula,

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

$$V = 0.5 \times 0.5 \times 111.1 = 27.8\ ml$$

So, 0.5 gm of boric acid is added in 27.8 ml of water to male isotonic solution. But final volume that is required is 50ml. so, remaining 22.2ml of some other isotonic solution (e.g. 0.9% NaCl) are added to make up final volume 50 ml.

Sprowl Method

Sprowls method is a simplification of White-Vincent method in which values of V for the drug of fixed weight (0.3 g) are computed and construed. This is commonly used for ophthalmic and parental solutions.

$$V = W \times E1\% \times 111.1\ or\ V = 33.33 \times E1\%$$

Applications of Isotonicity in Intravenous (IV) Fluids

Isotonicity is one of the most important requirements for intravenous fluids because these preparations are administered directly into the bloodstream. Blood plasma possesses a definite osmotic pressure, and IV fluids should have osmotic pressure equal to that of blood plasma. Solutions having the same osmotic pressure as blood are called isotonic solutions. If IV fluids are not isotonic, they may damage red blood cells and body tissues.

1. Prevention of Hemolysis: If a hypotonic solution is injected into the bloodstream, water enters the red blood cells through osmosis. As a result, the cells swell and may burst. This destruction of red blood cells is known as hemolysis. Hemolysis may lead to serious complications and therefore IV fluids are prepared isotonic with blood plasma to prevent this condition.

2. Prevention of Crenation: When hypertonic solutions are administered intravenously, water moves out of the red blood cells into the surrounding solution. Consequently, the cells shrink and become distorted. This process is called crenation. Crenation interferes with the normal functioning of blood cells and may cause tissue irritation and dehydration. Hence, isotonic IV fluids are necessary to avoid shrinkage of cells.

3. Maintenance of Normal Fluid and Electrolyte Balance: Isotonic IV fluids help maintain normal fluid volume and electrolyte balance in the body. They are commonly used in dehydration, blood loss, shock, and surgical conditions to restore circulating fluid volume without disturbing osmotic balance.

4. Safe Administration of Drugs: Many injectable drugs are formulated in isotonic solutions to ensure compatibility with blood and tissues. Isotonic preparations minimize pain, irritation, and tissue damage during administration. Therefore, isotonicity is essential for the safety and effectiveness of parenteral products.

Maintenance of Physiological Conditions: Isotonic IV solutions maintain normal physiological conditions in the body by preventing sudden movement of water across cell membranes. This helps preserve normal cell structure and function.

Examples of Isotonic IV Fluids: Common isotonic intravenous fluids include:

- 0.9% sodium chloride solution (normal saline)
- Ringer's lactate solution
- 5% dextrose solution

Applications of Isotonicity in Ophthalmic Solutions

Ophthalmic solutions are preparations intended for application to the eyes. The eye is a highly sensitive organ, and therefore ophthalmic preparations should be isotonic with tears to avoid discomfort and irritation. Tears possess osmotic pressure approximately equal to that of 0.9% sodium chloride solution.

1. Prevention of Eye Irritation: If eye drops are not isotonic, they may cause irritation, burning sensation, and discomfort. Hypertonic or hypotonic solutions disturb the osmotic balance of ocular tissues, leading to watering and redness of the eyes. Therefore, ophthalmic solutions are adjusted to isotonicity to ensure patient comfort.

2. Protection of Ocular Tissues: Isotonic eye preparations help protect delicate eye tissues such as the cornea and conjunctiva. Non-isotonic solutions may damage epithelial cells and affect normal eye function. Proper isotonicity prevents injury to ocular tissues.

3. Prevention of Excess Tear Secretion: When non-isotonic eye drops are instilled into the eye, they stimulate excessive tear production. Increased tearing dilutes and washes away the medication rapidly, reducing therapeutic effectiveness. Isotonic solutions reduce reflex tearing and improve retention of the drug in the eye.

4. Improvement of Drug Action: Isotonic ophthalmic solutions remain in contact with ocular tissues for a longer duration and improve absorption of medication. This enhances the therapeutic action of the drug and increases treatment effectiveness.

5. Improvement of Patient Comfort and Compliance: Comfortable ophthalmic preparations encourage proper use by patients. Isotonic eye drops do not produce pain or irritation and therefore improve patient compliance during treatment.

Examples of Isotonic Ophthalmic Solutions

- Buffered saline eye drops

- Artificial tear preparations
- Ophthalmic antibiotic solutions adjusted to isotonicity

Major Extracellular and Intracellular Electrolytes

In the body fluids, there are various inorganic and organic compounds. The concentration of these in the various compartments has been balanced in such a way that the body cells and tissues are having the same environment. In the body, various regulatory mechanisms are operative which are able control the ionic balance, osmotic balance and pH which in turn are able to maintain the concentration of solutes in various body fluids.

In a healthy person, the electrolyte concentration is maintained constant in the body fluids. If a person undergoes surgery or remain ill or remains under undesirable condition for a long time, body cannot maintain or correct the electrolyte balance, then it is done by external administration which is termed as **replacement therapy**, In this type of therapy, various combinations of products such as electrolytes, acids and bases, carbohydrates, proteins, amino acids and blood products are given to the patients as per their need.

The electrolyte concentration of body fluids has been different in various body fluid compartments. The various body fluid compartments may be put as follows:

(1) Intracellular fluid: This is the fluid which is present inside the cell, e.g., cytoplasm. It constitutes 45-50 per cent of body weight and its volume is 30 litres.

(2) Interstitial fluid: This is the fluid which is present between the cells. This constitutes 12-15 per cent of body weight and its volume is 10 litres.

(3) Plasma (Vascular fluid): This is the fluid which is present within the blood vascular system This constitutes 4-5 per cent of body weight and its volume is 3-5 litres.

Role of Major Physiological Ions

The plasma electrolyte concentrations are only able to provide a crude clue about the electrolyte status of the patient. In order to evaluate the true electrolyte picture of the body, other ancillary studies have to be carried out. Mineral salts (inorganic compounds) are necessary within the body for carrying out all body processes. They are usually needed in small quantities. The main elements are calcium, phosphorus, iron, sodium, potassium and chloride. Calcium and phosphorus are constituents of bones and teeth. In the form of haemoglobin, iron is able to convey oxygen and carbon dioxide. Sodium and potassium take part in transmission of nerve impulses and in the contraction of muscles.

Important functions served by electrolytes in general, are as follows:

(1) To control osmosis of water between body compartments.

(2) To maintain the acid-base balance needed for normal cellular activities,

(3) To generate action potentials and graded potentials and control secretion of some hormonal and neurotransmitters.

1. Sodium

Sodium (Na") is considered to be the most abundant extra-cellular ion. It constitutes nearly 90 percent of extra-cellular cations. Normal plasma sodium concentration is 136 to 142 mEq/litre. The normal intake of sodium chloride per day varies from 5 to 20 g and the daily requirement is between 3 to 5g. The excess quantity of salt consumed gets excreted in the urine. The Na^+ level in the blood is controlled by aldosterone and antidiuretic hormone (ADH).

Sodium ions are said to play important roles which are as follows:

(i) The main component of the extracellular fluid is sodium ion which is associated with chloride and bicarbonate in regulating the acid-base equilibrium.

(ii) It helps in the maintenance of osmotic pressure of various body fluids and thereby protect the body against excessive fluid loss.

(iii) It is of vital importance in preserving normal irritability of muscle and the permeability of cell.

(iv) It plays important role in the transmission of nerve impulses in the nerve fibres

Conditions under which low serum sodium level (hyponatremia) occurs can be summarised as follows:

(1) Because of loss due to excessive urination as in case of 'diabetes inspidus.

(2) Due to excessive sodium excretion in 'metabolic acidosis'.

(3) Diarrhoea and vomiting

(4) In "Addison's disease" in which there occurs a decreased excretion of hormone aldosterone which is antidiuretic in nature.

Low serum sodium level gives rise to dehydration, acidosis and excess leads to edema and hypertension.

Conditions under which a high serum sodium level exists (hypernatremia) may be put as follows

(i) severe dehydration (ii) hyper adrenalism (cushing syndrome) (iii) certain types of brain damage and (iv) excessive treatment with sodium salts.

2. Potassium

Normal plasma K^+ concentration is 3.8 to 5.0 mEq/litre. It is the most abundant cation in intra-cellular fluid. Its concentration in intra-cellular fluids is 23 times higher than in extra-cellular fluids. Active transport process is able to maintain this concentration difference. The normal intake of potassium chloride varies from 5 to 7 g per day.

Human body usually has about 2.6 g per kg body weight of potassium (K^+). The daily requirement is about 1.5 to 4.5 g. The good source of potassium in food includes milk, certain vegetables, meat and whole grains. Its deficiency generally does not take place except in certain pathological conditions. It rapidly gets absorbed from diet from gastro-intestinal tract and is rapidly excreted through kidneys.

Potassium ions are known to play an important role in

(a) The contraction of muscles, especially that of cardiac muscle.

(b) The transmission of nerve impulse.

(c) Maintaining the electrolyte composition of various body fluids.

(d) In many biochemical activities inside the cells.

(e) Helps to regulate pH by exchange against for hydrogen ions.

Elevated serum potassium levels (Hyperkalemia) are usually seen with patients who are suffering from renal failure, advanced dehydration or shock. In 'Addison's disease' there occurs an adrenal insufficiency which elevates, the serum potassium along with a high intracellular potassium symptom of hyperkalemia are mainly cardiac and C.N.S. depression.

Low serum potassium levels (Hypokalemia) develop in various conditions, which can be summarised as follows:

(a) Illness in which post-operative treatment which includes intravenous administration of solutions not having potassium for a prolong period.

(b) They have been associated with malnutrition, gastrointestinal losses, as in diarrhoea and in metabolic alkalosis.

(c) Use of diuretics like acetazolamide and chlorothiazide increase is able to increase the excretion of potassium in urine. Potassium salts are given if these drugs are to be used for a longer duration.

(d) During correction of dehydration or acidosis or alkalosis with sodium and water there occurs the depletion of potassium.

3. Calcium

The total calcium (Ca^{++}) content in body is about 22 g per kg body weight and daily requirement about 0.8 g. Most of the calcium occurs in bones and remaining is largely found in extra-cellular compartment. The main dietary sources of calcium include milk, cheese, green vegetables, egg and some fish. Calcium can be absorbed from all parts of the small intestine by an active transport mechanism.

The normal range for total plasma calcium has been 2.2-2.6 m mol/litre (i.e., 8.8-10.4 mg/100ml) Just about half of this is bound to plasma proteins, a small fraction gets complexed with citrate and phosphate and the balance amount circulates in blood as ionised calcium.

Functions of Calcium:

(a) Calcium is the major component of bones and teeth. It combines with phosphate to form calcium phosphate, which provides: Strength, Rigidity and Structural support to bones.

(b) Calcium is essential for the normal clotting of blood. It acts as an important factor in the coagulation process and helps convert prothrombin into thrombin during blood clot formation. Without sufficient calcium, blood clotting becomes slow and excessive bleeding may occur.

(c) Calcium ions are necessary for contraction of skeletal, smooth, and cardiac muscles. During muscle contraction calcium ions interact with muscle proteins and help to initiate contraction process.

(d) Calcium plays an important role in nerve conduction and transmission of impulses between nerve cells. It helps in release of neurotransmitters and proper functioning of nervous system.

(e) Calcium is essential for proper contraction and relaxation of cardiac muscles. It helps to maintain normal heartbeat, Cardiac rhythm and proper functioning of the heart.

4. Magnesium

Magnesium (Mg^{2+}) is regarded as the second most common intra-cellular electrolyte and the body's fourth most abundant cation. The adult human body having 25 g of magnesium, about 54 per cent being present in the bones along with phosphorus, about 45 per cent is in intra-cellular fluid, and about per cent is in extra-cellular fluid. Nearly about 3.3-4.9µ mol of magnesium gets excreted through the urine per day.

The daily requirement is about 350 mg. Good food source for magnesium includes various nuts, soyabeans, whole grains and sea foods. The magnesium ingested with food gets absorbed from duodenum in acidic media and this absorption is not related to magnesium stores in body.

Functions of Magnesium:

(a) Magnesium acts as a cofactor for many enzymes involved in metabolic reactions. It activates enzymes required for: Carbohydrate metabolism, Protein synthesis, Fat metabolism, Energy production.

(b) Magnesium is necessary for the formation and utilization of ATP (adenosine triphosphate), which is the main energy currency of cells. It helps in Storage of energy, Release of cellular energy, ATP-dependent reactions.

(c) Magnesium helps in transmission of nerve impulses, neuromuscular coordination and stabilization of nerve cells.

(d) Magnesium works together with calcium, sodium, and potassium to maintain electrolyte and fluid balance in the body. It is important for osmotic balance, cellular function, acid–base balance.

5. Chloride

The total chloride ion present in the body is 50m Eq per kg body weight and daily requirement is about 5 to 10 g as sodium chloride. The dietary source for chloride ion is common table salt which is used in cooking. It readily gets absorbed throughout gastrointestinal tract. Chloride jons get excreted mainly through urine and through skin during sweating.

Chloride ion is not having any important pharmacological function. However, it serves two important different body functions:

(i) Chloride ion along with sodium ion is able to maintain osmotic balance between different body fluids.

(ii) Chloride ion is able to maintain the charge balance between the body fluids, i.e., intra-cellular and extra-cellular both as they can pass through all membranes.

(iii) Chloride ions take part in formation of gastric hydrochloric acid and also in maintenance of acid-base balance. Under the normal physiological conditions there occurs no deficiency of chloride ions, but if there occurs more utilization, then deficiency can give rise to 'hypochloraemia alkalosis' causing vomiting.

(iv) Chloride is essential for the formation of hydrochloric acid (HCl) in the stomach. Hydrochloric acid which helps digestion of proteins, activates digestive enzymes such as pepsin and destroys harmful microorganisms in food.

6. Sulphate

This ion present in very small quantities in plasma and interstitial fluids. Its main dietary sources are animal and plant protein having sulphur containing amino acids such as cysteine and methionine. Sulphur ion are derived from the metabolism of these two amino acids. The organic sulphur gets oxidized to sulphate.

Sulphur containing compounds play vital role in detoxification mechanism while SH group containing organic compounds are important in tissue respiration.

7. Bicarbonate

In the extra-cellular fluid compartment, it is the second largest anion. Along with carbonic acid, it acts as one of the important buffer systems in the maintenance of the acid-base balance. A lack of bicarbonate causes the blood pH to go below 7.25 (metabolic acidosis) and an excess causes metabolic alkalosis.

8. Phosphate

Phosphate is an important mineral present in the body mainly in the form of phosphate ions. It is closely associated with calcium and is essential for the formation of bones and teeth, energy production, and many metabolic activities. Most of the phosphate in the body is present in bones and teeth, while the remaining amount is found in cells and body fluids.

Normal plasma phosphate concentration is 1.7 to 2.6 mEq/litre.

Functions of phosphate:

(i) Phosphate combines with calcium to form calcium phosphate, which provides hardness and strength to bones and teeth. It is essential for skeletal development, growth of bones and maintenance of teeth.

(ii) Phosphate is an important constituent of DNA and RNA. Therefore, it is essential for cell growth, cell division, protein synthesis and genetic functions.

(iii) Phosphate acts as an important buffer system in the body and helps maintain acid–base balance. The phosphate buffer system is represented by:

$$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$$

This system helps regulate pH of body fluids and cells.

(iv) Phosphate is a component of phospholipids, which form the structural framework of cell membranes. Thus, phosphate is essential for cell structure, cell permeability and cellular communication.

(v) Phosphate is necessary for proper functioning of muscles and nerves because it participates in energy metabolism and electrolyte balance.

Electrolytes Used in Replacement Therapy

Under the normal physiological conditions, the body mechanisms are able to adjust the electrolyte balance and no replacement becomes necessary. However, in various conditions such as prolonged fever, severe vomiting or diarrhoea, there occurs heavy loss of water and electrolytes. In order to compensate this administration of lost electrolyte in appropriate concentration of tonicity becomes essential However, there are two types of solutions of electrolytes which are used in replacement therapy.

a). A solution for rapid initial replacement: This solution is having sodium in the concentration 130-150 mEq/1, 98-110 mEq/1 of chlorine, 28-55 mEq/1 of bicarbonate, 4-12 mEq/1 of potassium, 3-5 mEq/1 of calcium and 3 mEq/1 of magnesium. These electrolyte concentrations thus closely resemble with the electrolyte concentrations which are found in extracellular fluids.

b). A solution for subsequent replacement: The electrolyte composition of such solution is 40-120 mEq/l Na, 30-105 mEq/1 Cl, 16-53 mEq/1 HCO_3, 16-35 mEq/1 K, 10-15 mEq/l Ca, 3-6 mEq/1 Mg and 0-13 mEq/1 of phosphorus.

1. Sodium Chloride

- **Chemical Formula:** NaCl
- **Molecular Weight:** 58.5
- **Category:** Electrolyte replenisher

It is having not less than 99 per cent and not more than the equivalent of 100.5 per cent of NaCl with reference to the substance dried at 130°. It contains no added substances.

Preparation: In the laboratory it is prepared from common salt (impure) in water by passing hydrochloric acid gas. The crystals are precipitated out.

$$NaOH + HCl \rightarrow NaCl + H_2O$$

Industrially, it is prepared (i) by evaporating purified saline (sea water) deposits and further purification (ii) and by purifying rock salt.

Properties: It occurs in the form of a white or colourless powder. It is odourless and having saline (salty) taste. It is soluble in water but insoluble in alcohol. It can be oxidised chemically and liberates chlorine gas.

$$2Cl + MnO_2 + 2H_2SO_4 \rightarrow Mn_2+ + SO_2 + 2H_2O + Cl_2\uparrow$$

With silver nitrate solution, it gives a white water insoluble precipitate of silver chloride which is soluble in ammonia.

$$NaCl + AgNO_3 \rightarrow AgCl\downarrow + NaNO_3$$

Identification: It gives reactions characteristic of sodium and chloride.

Test of Purity: It has to be tested for acidity and alkalinity, As, Ba, Ca and Mg, Fe and heavy metals.

Assay: The 0.1 g of the substance is dissolved in 50 ml of water in a glass stoppered flask. To it, 50 ml of 0.1 N silver nitrate solution, 3 ml of nitric acid, 5 ml of nitrobenzene and 2 ml of ferric ammonium sulphate solution are added. Now the solution is shaken well and is then titrated with 0.1 N ammonium thiocyanate solution until the water becomes reddish-yellow.

Each ml of 0.1 N AgNO3 = 0.005844 g of NaCl.

Storage: It is stored in tightly closed containers in dry place as it absorbs moisture.

Uses:

- It is a source of both sodium and chloride ions. The dosage forms are solutions, tablets and parental solutions. 0.9 per cent w/v solution is isotonic and is used as wet dressing and irrigating body cavities or tissues.
- In the form of injections and infusions it is used alone or in combination with other salts or glucose when body fluid electrolytes are depleted. Such preparations find use as electrolyte replenisher.

- Hypertonic solutions are used in conditions when there is excessive loss of sodium along with water. When hypertonic solution is given orally, it induces vomiting and thus can be used in case of poisoning as a first aid.
- It is a constituent of Ringer's solution, Ringer's injection, lactated Ringer's injection, sodium chloride and potassium chloride intravenous infusion and oral rehydration salt.

Sodium Chloride Eye Lotion (B.P.)

It contains 0.85 to 0.95 per cent w/v of NaCl.

It is prepared by dissolving sodium chloride in purified water, filtered, transferred to final container, avoiding the entry of micro-organisms and sterilised by heating in an autoclave.

Sodium Chloride Solution (B.P.)

It contains 0.9 per cent w/v sodium chloride, prepared in purified water and clarified by filtration. When normal saline is prescribed then above solution is dispensed. If the label states that it is sterile solution, then it should comply for test for sterility.

Sodium Chloride Injection

It is a sterile isotonic solution of sodium chloride in water for injection. It contains not less than 0.85 per cent and not more than 0.95 per cent w/v of NaCl. It contains no antimicrobial agents.

Composition: Sodium chloride…..9g and Water for injection sufficient to produce 1000 ml.

Preparation: The sodium chloride injection is prepared from the above ingredients by dissolving sodium chloride in water for injection, filtering and immediately sterilizing by heating in an autoclave or by filtration.

Properties: It is clear, colourless solution.

Identification: It gives reactions which are characteristic of sodium and chloride. Its pH varies from 4.5 to 7.0.

Tests for purity: It is tested for As and heavy metals.

Storage: Stored in single-dose contains of glass or plastic

2. Potassium Chloride

Potassium Chloride is an important electrolyte used in replacement therapy to treat or prevent potassium deficiency (hypokalemia). Potassium is the principal intracellular cation and is essential for proper functioning of nerves, muscles, heart, and maintenance of acid-base balance. Loss of potassium may occur due to diarrhoea, vomiting, excessive use of diuretics, dehydration, or prolonged illness. Potassium chloride is administered to restore normal potassium levels in the body.

- **Chemical Formula:** KCl
- **Molecular Weight:** 74.5

It is having not less than 99.5 per cent of KCl which is calculated with reference to the substance dried to constant weight at 105° for two hours.

Preparation:

(1) It is mainly prepared from the natural mineral, carnallite ($KCLMgCl_2.6H_2O$). The raw salt deposit is first of all grounded and then treated with hot water when the less soluble KCl crystallises out on cooling. The process has to be repeated for achieving almost complete recovery of KCI from the mother liquor and wash water.

(2) In the laboratory, it is prepared by the action of HCl on potassium carbonate or bicarbonate.

$$K_2CO_3 + 2HCl \rightarrow 2KCl + H_2O + CO_2$$

$$KHCO_3 + HCl \rightarrow KCl + H_2O + CO_2$$

Properties: It occurs as colourless prismatic or cubical crystals or as a white granular powder. The salt is odourless. It is having a saline taste. It is soluble in water, insoluble in alcohol and solvent ether. It melts at 772°. Its 10 per cent aqueous solution is neutral to litmus paper. In qualitative analysis chloride is precipitated by Ag^+, Hg^{2+} and Pb^{2+} as insoluble chloride.

Identification: A solution of KCl gives tests which are characteristic of potassium and chloride.

Tests for purity: It is tested for acidity or alkalinity, As, Ba, Ca, Mg, Fe, heavy metals, bromide, iodide and sulphate.

Assay: Potassium chloride is assayed by the argentometric titration method called Mohr's method. A 0.2 g sample is first of all dissolved in 50 ml of water. Then, it is titrated with N/10 silver nitrate solution, using potassium chromate, solution as an indicator.

Each ml of 0.1 N silver nitrate solution = 0.007455 g of KCI.

Uses:

- It finds use as an electrolyte replenisher.
- It also finds use when hypokalemia or hypochloremic alkalosis exists as has been the case after prolonged diarrhoea or vomiting. It is sometimes used as diuretic.
- Potassium chloride has been an ingredient of Sodium Chloride Compound Injection, Ringer's solution, etc. It has to be administered very cautiously, especially in cardiac and rental diseases.

- This salt is most widely used for oral replacement of potassium in the form of solution. However, the aqueous solution causes irritation of gastro-intestinal tract.
- It is used intravenously if person cannot take it orally or in cases of severe hypotassemia.
- It finds use as adjunct in treatment of Myasthenia gravis, (severe muscular weakness).
- It is a constituent of oral rehydration salt, sodium chloride and potassium chloride intravenous infusion, sodium and potassium chloride and glucose intravenous infusion, 'Ringer's injection' and Ringer's solution'.
- It also acts as antidote for digitalis intoxication.

3. Calcium Chloride

Calcium Chloride is an important electrolyte used in replacement therapy for the treatment of calcium deficiency (hypocalcemia). Calcium is essential for normal functioning of muscles, nerves, heart, blood coagulation, and bone formation. Calcium chloride is used when rapid replacement of calcium ions is required, especially in conditions such as tetany, hypocalcemia, cardiac disorders, and electrolyte imbalance.

- **Chemical Formula:** $CaCl_2$
- **Molecular Weight:** 111

Preparation: Calcium chloride is prepared by the action of hydrochloric acid on calcium carbonate or calcium hydroxide. Calcium carbonate or calcium hydroxide is treated with hydrochloric acid and the solution is filtered to remove impurities. Then the filtrate is concentrated by evaporation. Crystals of calcium chloride are obtained which are then purified and dried.

Chemical Reactions

$$CaCO_3 + 2HCl \rightarrow CaCl_2 + CO_2 + H_2O$$

or

$$Ca\,(OH)_2 + 2HCl \rightarrow CaCl_2 + 2H_2O$$

Physical Properties: It is having white crystalline powder or colorless crystals, Odorless, Highly hygroscopic and deliquescent, Freely soluble in water and alcohol

Chemical Properties: It gives calcium ion reactions and dissociates in water into calcium and chloride ions

$$CaCl_2 \rightarrow Ca^{2+} + 2Cl^-$$

Produces white precipitate with silver nitrate due to chloride ions

$$CaCl_2 + 2AgNO_3 \rightarrow 2AgCl\downarrow + Ca(NO_3)_2$$

Tests of Purity: It is Tested for Acidity or Alkalinity for Magnesium and Alkali Metals, Sulphates, Iron, Heavy Metals, Insoluble matter.

Storage: It should be stored in airtight containers or Protected from moisture because it is highly hygroscopic.

Assay: The assay of calcium chloride is carried out by complexometric titration using disodium EDTA solution. A weighed quantity of calcium chloride is dissolved in water and made alkaline with sodium hydroxide solution. An appropriate indicator such as murexide indicator is added. The solution is then titrated with standard EDTA solution until the color changes from pink to purple, indicating the end point. In this method, EDTA forms a stable complex with calcium ions. The amount of EDTA used is proportional to the quantity of calcium chloride present in the sample.

Uses:

- Calcium chloride is widely used in replacement therapy for the treatment of calcium deficiency conditions such as hypocalcemia and tetany.
- It helps maintain normal muscle contraction, nerve transmission, cardiac function, and blood coagulation.
- It is commonly administered intravenously in emergency conditions like cardiac arrest, hyperkalemia, and calcium depletion caused by massive blood transfusion.
- Calcium chloride is also used in electrolyte replacement solutions and intravenous fluids to restore electrolyte balance in the body. In pharmaceutical preparations, it serves as a source of calcium ions and is used in calcium supplements and various medicinal formulations.

4. Oral Rehydration Salts (ORS)

Oral Rehydration Salts are electrolyte preparations used to prevent and treat dehydration caused by diarrhoea, vomiting, excessive sweating, and loss of body fluids. ORS helps in restoring water and electrolyte balance in the body by replacing essential salts and glucose lost during dehydration. In ancient times, homemade ORS is used which constitutes of one tablespoon of salt, two tablespoon of sugar in 1 litre of water.
ORS works on the principle of sodium-glucose co-transport in the intestine. Glucose helps in the absorption of sodium and water from the intestinal tract, thereby correcting dehydration and electrolyte imbalance.

Preparation: ORS is prepared by accurately weighing all ingredients and mixing them uniformly under dry conditions. The powder mixture is packed in moisture-resistant sachets. Before administration, the contents of one sachet are dissolved in the specified amount of clean drinking water.
The following three preparations are usually prepared. When glucose is used, sodium bicarbonate is packed separately. The quantities given below are for preparing 1 litre solution.

Ingredients	Formula I	Formula II	Formula III
Sodium Chloride	1.0 gm	3.5 gm	3.5 gm
Potassium Chloride	1.5 gm	1.5 gm	1.5 gm
Sodium Bicarbonate	1.5 gm	2.5 gm	-
Sodium Citrate	-	-	2.9 gm
Anhydrous Glucose	36.4 gm	20.0 gm	20.0 gm
Or Glucose	40.0 gm	22.0 gm	-

The formula II and III are recommended by WHO and UNICEF for control in diarrhoeal diseases.

New Formula for Oral Rehydration Salts by WHO

A new formula for oral rehydration salts (ORS), has been released by the World Health Organization (WHO). The new formula ORS, a sodium and glucose solution, is widely used to treat children with acute diarrhoea. Since WHO adopted ORS in 1978 as its primary tool to fight diarrhoea, the mortality rate for children suffering from acute diarrhoea has fallen from 5 million to 1.3 million deaths annually.

The new improved formula is the result of extensive research sponsored by WHO's Department of Child and Adolescent Health and Development and supported by the United States Agency for International Development (USAID).

Ingredients	Quantity (grams/litre)
Sodium Chloride	2.6
Potassium Chloride	1.5
Trisodium citrate dihydrate	2.9
Glucose Anhydrous	13.5

Physiological Acid-Base Balance

Physiological acid–base balance refers to the maintenance of hydrogen ion concentration and pH of body fluids within a narrow normal range necessary for proper functioning of the body. The normal pH of blood is about 7.35 to 7.45, which is slightly alkaline. The body continuously produces acids during metabolism, and these acids must be neutralized or eliminated to maintain normal physiological functions.

If the pH of blood becomes low (high hydrogen ion concentration) acidosis results. If the pH of level becomes high (low hydrogen ion concentration), alkalosis results.

1. Buffer System

Buffer system may consist of a weak acid and the salt of that acid, which functions as a weak base. Buffer systems of the body does not allow rapid and drastic changes in the pH of a body fluid by converting strong acids and bases into weak acids and bases. Buffers are thus able to remove the excess H^+ from the body fluids but not from the body. The major buffer systems existing in the body fluids are as follows:

(i) Carbonic acid-bicarbonate buffer system: It occurs in plasma and kidneys. It is considered to be an important regulator of blood pH. If there occurs an excess of H^{-+}, the bicarbonate (HCO_3^-) ion acts as a weak base and accepts H^+ to form carbonic acid. The latter dissociates further to yield carbon dioxide and water molecules.

H^+	+	HCO_3^-	→	H_2CO_3	→	$H_2O + CO_2$
Strong acid		weak base		weak acid		

While if there occurs shortage of H^+, the carbonic acid (another component of buffer system) ionises to release more H^+ ions and maintains the pH.

H_2CO_3	→	H^+	+	HCO_3^-
Carbonic acid		strong acid		weak base

(ii) Phosphate Buffer System: It is also able to maintain physiological pH at 7.4. As the phosphate concentration is highest in intra-cellular fluid, the phosphate buffer system is considered to be an important regulator of pH in the cytosol. This system occurs in the cells and kidneys. The system consists of monohydrogen phosphate/dihydrogen phosphate (HPO_4^{2-} /$H_2PO_4^-$) anions. It is known to act in the same manner as the carbonic acid-bicarbonate buffer system acts.

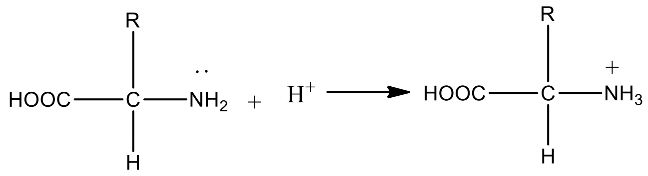
If there occurs an excess of H', the monohydrogen phosphate ion acts as the weak base by accepting the proton.

HCl	+	Na_2HPO_4	→	NaCl	+	NaH_2PO_4
Strong acid		weak base		salt		weak acid

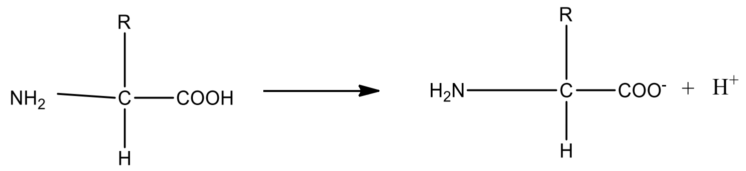
While the dihydrogen phosphate ion act as the weak acid and is able to neutralise the alkaline condition, as

NaOH	+	NaH_2PO_4	→	H_2O	+	Na_2HPO_4
Strong base		weak acid				weak base

(iii) Protein Buffer System: It is considered to be the most abundant buffer in body cells and plasma. Proteins are composed of amino acids that are having at least one carboxyl group (COOH) and at least one amino (NH_2) group. When there occurs an excess of hydrogen ions, the amino group acts as a base and accepts the proton.



While the free carboxyl group can release protons so as to neutralize an alkaline condition.



Thus, protein is able to serve both the functions of acid and base component of a buffer system because it is amphoteric in nature.

2. Elimination of some ions through urine by kidney (renal mechanism)

The third mechanism is via elimination of some ions through urine by kidney. Absorption of certain ions and elimination of others are able to control the acid-base balance of blood and thus the body fluids.

3. Through the respiratory centre (respiratory mechanism)

The control of pH also occurs though the control of respiratory centre. If it is stimulated, it alters the rate of breathing. This change in rate of breathing is able to control the removal of CO, from body fluids which gives rise to changes in pH of blood carbonic acid.

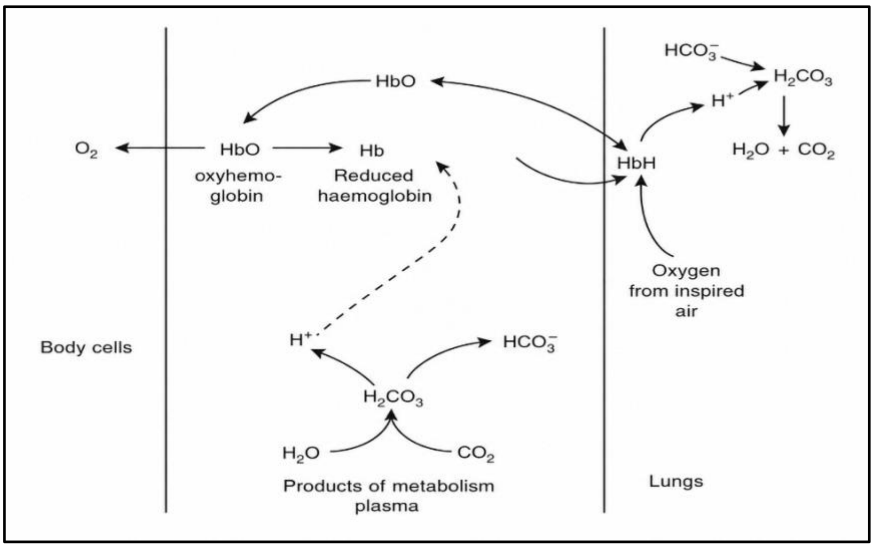


Fig. Role of Haemoglobin as a physiological buffer

Acid–Base Imbalance: Acid–base imbalance mainly occurs in two forms:

1. Acidosis: Acidosis is a condition in which the blood becomes excessively acidic and the blood pH falls below 7.35 due to excess acid formation or loss of base from the body.

2. Alkalosis: Alkalosis is a condition in which the blood becomes excessively alkaline and the blood pH rises above 7.45 due to excess loss of acid or increase in base concentration.

Points to Remember:

- ✓ **Acids** release H^+ ions, while bases accept H^+ ions.
- ✓ Buffers resist sudden changes in pH and help maintain stability of pharmaceutical preparations and body fluids.
- ✓ pH scale ranges from 0–14; pH 7 is **neutral**, below 7 is **acidic**, and above 7 is **basic**.
- ✓ Blood pH is normally maintained around 7.35–7.45 for proper physiological function.
- ✓ Henderson–Hasselbalch equation is used for buffer pH calculation.

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

- ✓ **Isotonic solutions** possess the same osmotic pressure as body fluids and are essential for IV fluids and ophthalmic solutions.
- ✓ **Hypotonic solutions** cause cell swelling, while **hypertonic solutions** cause cell shrinkage.
- ✓ **Sodium** (Na^+) is the major extracellular cation and **potassium** (K^+) is the major intracellular cation.
- ✓ **Calcium** is important for bone formation, blood clotting, and muscle contraction.
- ✓ **Chloride** helps maintain osmotic pressure and acid–base balance.
- ✓ Electrolytes regulate fluid balance, nerve impulse transmission, muscle activity, and **physiological acid–base balance**.
- ✓ Sodium chloride, Potassium chloride, Calcium chloride, and ORS are widely used in **electrolyte replacement therapy**.
- ✓ ORS helps treat dehydration by replacing lost water and electrolytes.

Case Based Learning (CBL)

Case Based Learning – 1: Dehydration and Electrolyte Imbalance

A 5-year-old child is admitted to the hospital with severe diarrhoea and vomiting for two days. The child shows signs of dehydration such as dry mouth, weakness, sunken eyes, and low blood pressure. Laboratory reports indicate low sodium and potassium levels.

→ Diarrhoea causes loss of water and electrolytes, mainly sodium and potassium. ORS contains glucose and electrolytes that help restore fluid and electrolyte balance. Sodium maintains extracellular fluid balance and nerve conduction. Potassium is important for muscle and cardiac function. Severe dehydration may disturb physiological acid–base balance, leading to acidosis.

Questions:

1. Which electrolyte imbalance is present in the patient?
2. Why is ORS recommended in this condition?
3. What is the role of sodium and potassium in the body?
4. Why is maintenance of acid–base balance important during dehydration?

Case Based Learning – 2: Dehydration and Electrolyte Imbalance

A pharmaceutical company developed an eye drop formulation. During clinical testing, patients complained of irritation and burning sensation after administration. Investigation revealed that the solution was hypertonic.

→ Isotonic solutions possess osmotic pressure similar to body fluids. Eye drops should be isotonic to avoid irritation and damage to ocular tissues. Hypertonic solutions draw water out of cells causing discomfort and shrinkage of tissues. Sodium chloride is commonly used to adjust isotonicity.

Questions:

1. What is isotonicity?
2. Why should ophthalmic solutions be isotonic with tears?
3. What problems occur with hypertonic eye drops?
4. How can isotonicity be adjusted in pharmaceutical preparations?

Problem Based Learning (CBL)

1. Buffer System and pH

A pharmacist prepared a liquid formulation with an unstable pH. After a few days, the drug degraded and patients complained of irritation. The pharmacist decided to add a buffer system to maintain the pH.

Quiz Questions

1. What is the main function of a buffer solution?

a) Increase drug solubility
b) Resist change in pH
c) Increase osmotic pressure
d) Change drug color

Answer: b) Resist change in pH

2. Which equation is used for buffer pH calculation?

a) Arrhenius equation
b) Nernst equation
c) Henderson–Hasselbalch equation
d) Boyle's law

Answer: c) Henderson–Hasselbalch equation

3. A solution with pH below 7 is:

a) Neutral
b) Basic
c) Acidic
d) Isotonic

Answer: c) Acidic

4. Normal blood pH is approximately:

a) 5.5
b) 6.0
c) 7.4
d) 8.5

Answer: c) 7.4

2. Isotonicity and IV Fluids

A patient in the hospital accidentally received a hypotonic IV solution. Soon after administration, red blood cells started swelling.

1. What happens to cells in a hypotonic solution?

a) Cells shrink
b) Cells swell
c) Cells remain unchanged
d) Cells become acidic

Answer: b) Cells swell

2. Which IV fluid is isotonic?

a) Distilled water
b) 0.9% Sodium chloride
c) 10% Sodium chloride
d) 5% Potassium chloride

Answer: b) 0.9% Sodium chloride

3. Isotonic solutions are important because they:

a) Destroy RBCs
b) Prevent irritation and cell damage
c) Increase acidity
d) Reduce drug action

Answer: b) Prevent irritation and cell damage

4. Hypertonic solutions cause:

a) Cell swelling
b) Haemolysis
c) Cell shrinkage
d) No osmotic effect

Answer: c) Cell shrinkage

Multiple Choice Questions (MCQs):

1. Which of the following defines an acid according to Bronsted-Lowry theory?
A) Proton donor
B) Proton acceptor
C) Electron donor
D) Electron acceptor
Answer: A

2. A base is defined as:
A) Proton donor
B) Proton acceptor
C) Neutral molecule
D) Salt former
Answer: B

3. The pH scale ranges from:
A) 0–7
B) 0–10
C) 0–14
D) 1–14
Answer: C

4. At 25°C, the pH of pure water is:
A) 6
B) 7
C) 8
D) 9
Answer: B

5. A buffer solution is best described as:
A) Strong acid + strong base
B) Weak acid + conjugate base
C) Strong base + conjugate acid
D) Neutral salt solution
Answer: B

6. Henderson-Hasselbalch equation is:
A) $pH = pKa + \log([A^-]/[HA])$
B) $pH = pKa - \log([A^-]/[HA])$
C) $pH = pKa + \log([HA]/[A^-])$
D) $pH = pKa - \log([HA]/[A^-])$
Answer: A

7. Buffer capacity is maximum when:
A) $pH = pKa$
B) $pH > pKa$
C) $pH < pKa$
D) $pH = 7$
Answer: A

8. Which factor affects buffer stability?

A) Temperature

B) Light

C) Ionic strength

D) All of the above

Answer: D

9. A buffer with 0.1 M acetic acid and 0.1 M sodium acetate has pH equal to:

A) 4.76

B) 7.0

C) 5.0

D) 6.5

Answer: A

10. Dilution of a buffer solution:

A) Increases buffer capacity

B) Decreases buffer capacity

C) No effect

D) Changes pKa

Answer: B

11. An isotonic solution has:

A) Same osmotic pressure as blood

B) Higher osmotic pressure than blood

C) Lower osmotic pressure than blood

D) No osmotic pressure

Answer: A

12. Hypertonic solutions cause RBCs to:

A) Swell

B) Shrink (crenation)

C) Burst (hemolysis)

D) Remain unchanged

Answer: B

13. Hypotonic solutions cause RBCs to:

A) Shrink

B) Burst (hemolysis)

C) Remain unchanged

D) Increase osmotic pressure

Answer: B

14. Common agents used to adjust isotonicity:

A) Sodium chloride

B) Dextrose

C) Glycerin

D) All of the above

Answer: D

15. Which equation is used to calculate isotonicity?

A) Henderson-Hasselbalch

B) Van't Hoff

C) Gibbs-Donnan

D) Nernst

Answer: B

16. Isotonic IV fluids prevent:

A) Hemolysis

B) Crenation

C) Both A and B

D) None

Answer: C

17. Isotonicity in eye drops is important to:

A) Prevent irritation

B) Maintain comfort

C) Avoid damage to ocular tissues

D) All of the above

Answer: D

18. These are commonly used in:

A) Oral administration

B) Parenteral administration

C) Topical creams

D) Capsules

Answer: B

19. The principal extracellular cation is:

A) Potassium

B) Sodium

C) Calcium

D) Magnesium

Answer: B

20. The principal intracellular cation is:

A) Sodium

B) Potassium

C) Chloride

D) Calcium

Answer: B

21. The major extracellular anion is:

A) Bicarbonate

B) Chloride

C) Phosphate

D) Sulfate

Answer: B

22. The major intracellular anion is:

A) Chloride

B) Bicarbonate

C) Phosphate

D) Sulfate

Answer: C

23. Sodium is primarily responsible for:

A) Muscle contraction

B) Osmotic balance and nerve impulse transmission

C) Bone formation

D) Enzyme activation

Answer: B

24. Potassium plays a key role in:

A) Maintaining resting membrane potential

B) Blood clotting

C) Oxygen transport

D) Collagen synthesis

Answer: A

25. Calcium is essential for:

A) Nerve impulse transmission

B) Muscle contraction

C) Blood coagulation

D) All of the above

Answer: D

26. Chloride helps in:

A) Acid-base balance

B) Gastric acid formation

C) Osmotic pressure regulation

D) All of the above

Answer: D

27. Sodium chloride is commonly used to treat:

A) Hyponatremia

B) Hyperkalemia

C) Hypocalcemia

D) Acidosis

Answer: A

28. Potassium chloride is used in:

A) Hypokalemia

B) Hyperkalemia

C) Hyponatremia

D) Hypernatremia

Answer: A

29. Calcium chloride is used in:
A) Hypocalcemia
B) Cardiac arrest (as stabilizer)
C) Magnesium toxicity
D) All of the above
Answer: D

30. Oral rehydration solution (ORS) contains:
A) Sodium, potassium, chloride, glucose
B) Sodium, calcium, phosphate, glucose
C) Potassium, magnesium, sulfate, glucose
D) Sodium, bicarbonate, glucose
Answer: A

31. The normal physiological blood pH is:
A) 6.8–7.0
B) 7.35–7.45
C) 7.5–8.0
D) 7.0 exactly
Answer: B

32. Respiratory regulation of pH is achieved by:
A) Excretion of H^+ ions
B) Control of CO_2 levels
C) Excretion of bicarbonate
D) Buffering by proteins
Answer: B

33. Kidneys regulate acid-base balance by:
A) Excreting H^+ ions
B) Reabsorbing bicarbonate
C) Producing ammonia
D) All of the above
Answer: D

34. The most important physiological buffer system is:
A) Phosphate buffer
B) Protein buffer
C) Bicarbonate buffer
D) Hemoglobin buffer
Answer: C

35. Which of the following is a Lewis acid?
A) NH_3
B) BF_3
C) OH^-
D) Cl^-
Answer: B

36. Which of the following is a Lewis base?
A) H^+
B) NH_3

C) BF_3

D) Al^{3+}

Answer: B

37. Which solution has the lowest pH?

A) 0.1 M HCl

B) 0.1 M NaOH

C) Pure water

D) 0.1 M NaCl

Answer: A

38. Which of the following is a strong acid?

A) Acetic acid

B) Hydrochloric acid

C) Carbonic acid

D) Phosphoric acid

Answer: B

39. Which of the following is a strong base?

A) Ammonia

B) Sodium hydroxide

C) Calcium carbonate

D) Magnesium hydroxide

Answer: B

40. Which indicator turns red in acidic medium?

A) Phenolphthalein

B) Methyl orange

C) Litmus (blue)

D) Bromothymol blue

Answer: B

41. Which indicator turns pink in basic medium?

A) Phenolphthalein

B) Methyl orange

C) Litmus (red)

D) Bromothymol blue

Answer: A

42. Which of the following salts produces an acidic solution in water?

A) NaCl

B) NH_4Cl

C) KNO_3

D) Na_2CO_3

Answer: B

43. Which of the following salts produces a basic solution in water?

A) NaCl

B) NH_4Cl

C) Na_2CO_3

D) KNO_3

Answer: C

44. Which of the following is amphoteric?

A) HCl

B) NaOH

C) $Al(OH)_3$

D) KOH

Answer: C

45. Which organ is primarily responsible for long-term regulation of blood pH?

A) Lungs

B) Kidneys

C) Liver

D) Heart

Answer: B

46. Which organ is primarily responsible for short-term regulation of blood pH?

A) Lungs

B) Kidneys

C) Liver

D) Pancreas

Answer: A

47. Which of the following is NOT a buffer system in the human body?

A) Bicarbonate buffer

B) Phosphate buffer

C) Protein buffer

D) Sodium chloride buffer

Answer: D

48. Which of the following IV fluids is isotonic?

A) 0.9% NaCl

B) 5% NaCl

C) 0.45% NaCl

D) Distilled water

Answer: A

49. Which of the following is used to treat metabolic acidosis?

A) Sodium bicarbonate

B) Potassium chloride

C) Calcium chloride

D) Sodium chloride

Answer: A

50. Which of the following solutions is considered hypotonic relative to blood plasma?

A) 0.9% NaCl

B) Distilled water

C) 5% NaCl

D) Ringer's lactate

Answer: B

Short Answer Type Questions (Objective type questions):

1. Define acids and bases with one example each.
2. What is a buffer solution? Mention its various types.
3. Define pH and write its significance.
4. Define acid in terms of Bronsted concept.
5. Define isotonicity.
6. Differentiate between hypertonic and hypotonic solutions.
7. Why are ophthalmic solutions made isotonic?
8. What are the different methods for adjusting isotonicity of solution.
9. Write the Henderson–Hasselbalch equation.
10. Explain buffer action briefly.
11. Name the major extracellular and intracellular electrolytes.
12. Write any two functions of sodium ions.
13. Write any two functions of potassium ions.
14. Mention the physiological role of calcium ions.
15. State two functions of chloride ions.
16. What is electrolyte replacement therapy?
17. Write the uses of Sodium chloride in pharmacy.
18. What is ORS? Write its uses.
19. Explain physiological acid–base balance.
20. State the importance of electrolytes in the human body.

Long Answer Type Questions

1. Define acids, bases, and buffers. Explain buffer action and discuss the pharmaceutical importance of buffer systems.
2. Describe the Henderson–Hasselbalch equation and explain the calculation of pH for buffer solutions with suitable examples.
3. Define isotonicity. Discuss isotonic, hypotonic, and hypertonic solutions and explain their applications in IV fluids and ophthalmic preparations.
4. Discuss the major extracellular and intracellular electrolytes and explain their physiological functions in the human body.
5. Explain electrolyte replacement therapy and discuss the uses of Calcium chloride, and Oral Rehydration Salts (ORS).
6. Describe physiological acid–base balance briefly.
7. Elaborate the different theories of acid and bases in detail with suitable example for each category.
8. Discuss in detail preparation, properties, uses and storage for sodium chloride and potassium chloride.