Unit- V

pH, Buffers and Isotonic solutions

Buffers:

Buffers are defined as a compound or a mixture of compounds that resists the pH upon the addition of small quantities of acid or alkali. Buffer have definite pH value. The pH will not change after keeping it for a long period of time. The pH value gets altered negligibly by the addition of small quantities of acid /base.

Buffer action:

The resistance to a change in pH is known as buffer action. So buffers can be added to show buffer action.

Buffer capacity:

The amount of acid/base required to produce a unit change in pH in a solutionis called buffer capacity.

Applications of Buffers:

❖ **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.

❖ **Increasing stability:**

To prevent hydrolysis and for maximum stability**,** the pH of the medium

should be adjusted suitably.

❖ **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.

❖ **Optimising biological activity:**

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

❖ **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 amount of buffers to match with the pH of the physiological fluid.

Buffer systems:

The buffer systems are classified as followings

a. Weak acid and its conjugate base, i.e. salt of week acid with a strong base.

Example- acetic acid and sodium acetate.

b. Weak base and its conjugate acid, i.e. salt of week base with a strong acid.

Example- ammonium hydroxide and ammonium chloride.

c. Two salts acts as acid-base pair.

Example- Potassium hydrogen phosphate and potassium dihydrogen phosphate.

d. Amphoteric electrolyte.

Example- Solution of glycine.

e. Solution of strong acid and solution of strong base.

Example- Strong HCl with KCl.

Some important buffer system and their pH is given below in table-3.

Table-3: Some important buffer system and their pH.

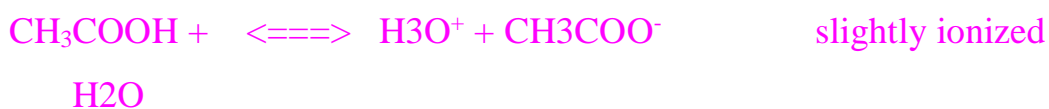| System	pH
HCl and KCl	1.2 to 2.2
HCl and potassium hydrogen phthalate	2.2 to 4.0
Sodium hydroxide and potassium hydrogen phthalate	4.2 to 5.8
Boric acid and sodium carbonate monohydrate	5.0 to 9.0
Potassium dihydrogen phosphate and sodium hydroxide	5.8 to 8.0
Boric acid, sodium hydroxide and potassium chloride	8.0-10.0

Buffer action of acidic buffer:

Consider an acid buffer, i.e. acetic acid and sodium acetate. The ionization equation are written as:

Strong electrolyte:

$$CH_3COONa \xrightarrow{\text{H}_2\text{O}} Na^+ + CH_3COO^- \qquad \text{completely ionized}$$

Weak acid:

$$CH_3COOH + H_2O \iff H_3O^+ + CH_3COO^- \qquad \text{slightly ionized}$$

Therefore, the solution contains very few H_3O^+ ions, but has an excess sodium ions and acetate ions. When a small amount of acid is added, the H_3O^+ ions present in the solution react with CH_3COO^- as

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

Since added free H_3O^+ ions are not available, pH does not change. When a small amount of base is added, the hydroxyl ions furnished by the base are neutralised by acetic acid as:

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

Since added free OH^- ions are not available, pH does not change. Thus buffer action is maintained when a small amount of acid or base is added. This process continues until entire acetate ions or acetic acid is consumed, action is not unlimited.

The mechanism of buffer action of acid-base pair (example is phosphate buffer) is similar to that mentioned above. In phosphate buffer, weak acid conjugate base are involved, i.e. ion $H_2PO_4^-$ serves as weak acid and $H_2PO_4^{2-}$ acts as its conjugate base.
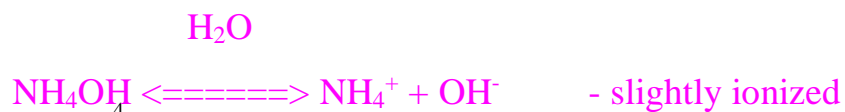
Buffer Action of Alkaline Buffer:

Buffer action of a mixture of a weak base and its salt, for example ammonium hydroxide and ammonium chloride, is considered. The ionization equation is written as:

Strong electrolyte:

$$NH_4Cl \xrightarrow{H_2O} NH_4^+ + Cl^- \quad \text{- completely ionised}$$

Weak base:

$$NH_4OH \xrightarrow{H_2O} \text{<======> } NH_4^+ + OH^- \quad \text{- slightly ionized}$$

Therefore, the solution contains very few OH$^-$ ions, but has an excess of ammonium ions and chloride ions.

When a small amount of acid is added, the H$_3$O$^+$ ions obtained from acid react with NH$_4$OH as

$$H_3O^+ + NH_4OH \Longleftrightarrow NH_4^+ + 2\ H_2O$$

Since added free H$_3$O$^+$ ions are not available, pH does not change.

When a strong base is added, the hydroxyl ions furnished by the base are neutralised by NH$_4^+$ as:

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

Since added free OH$^-$ ions are not available, pH does not change. Thus buffer action is maintained when a small amount of acid or base is added. This process continues until entire ammonium hydroxide or ammonium ions are consumed. Hence buffer action is not unlimited.

Ampholytic Substances:

Ampholytes and amphoteric electrolytes are the substances that capable of acting both as an acid and a base. For example, glycine, like an acid as shown below.

$$NH_2CH_2COOH + H_2O \Longleftrightarrow NH_2CH_2COO^- + H_3O^+$$
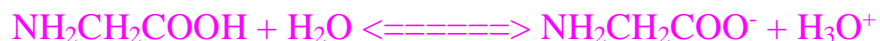
Glycine also behaves as a base as shown below.

$$NH_2CH_2COO^- + H_3O^+ \Longleftrightarrow {}^+NH_3CH_2COO^- + H_2O$$

These doubly charged ions are known as zwitter ions or dipolar ions he above system reacts with H$_3$O$^+$ ions or OH$^-$ ions and nullify the influence of the added substances.

Buffer equation-Henderson-Hasselbalch equation:

The buffer equation is also known as Henderson-Hasselbalch equation. Two separate equations are obtained for each type of buffer, acidic and basic. Buffer equation is developed based on the effect of salt on the ionization of a weak acid, when the salt and acid have a common ion.

An acid buffer, acetic acid and sodium acetate, is considered for deriving the buffer equation. The ionization equilibrium equation for weak acid (acetic acid) may be shown as:

Weak acid:

$$CH_3COOH + H_2O <====> H_3O^+ + CH_3COO^- \quad \text{-slightly ionized}$$
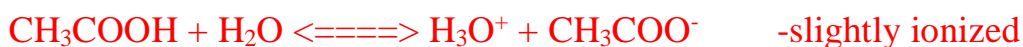
Applying the Law of Mass Action, the acid dissociation constant (Ka) is written as:

$$Ka = [H_3O^+] [CH_3COO^-]/ [CH_3COOH] = 1.75 \times 10^{-5} \quad (1)$$

When sodium acetate is added to acetic acid, equation (1) is momentarily disturbed. Since, salt also supplies the acetate ion, the term $[CH_3COOH]$ in the numerator increases.

In order to re- establish the constant Ka at 1.75×10^{-5}, the hydronium ion $[H_3O^+]$ in the numerator instantaneously decreases. In other words, the equilibrium is shifted in the direction shown below.

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

In other words, common ion, $[CH_3COO^-]$ repressed ionization of acetic acid. This is an example of common ion effect.

The pH of the final solution may be obtained by rearranging equation (1).

$$[H_3O^+] = Ka [CH_3COOH] / [CH_3COO^-] \quad (2)$$

Since, the acid is weak and ionizes slightly, $[CH_3COOH]$ may remain unaltered.

Hence, $[CH_3COOH] = [acid]$.

Since salt is completely ionized, the entire $[CH_3COO^-]$ may be obtained directly from the salt and be written as [salt].

Hence, $[CH_3COO^-]$ = [salt].

Substituting them in equation (2) gives:

$$[H_3O^+] = Ka\ [acid] / [salt] \qquad (3)$$

Taking logarithm of equation (3) and reversing the signs give:

$$- \log [H_3O^+] = - \log Ka - \log [acid] / [salt] \qquad (4)$$

But $pH = -\log [H_3O^+]$ and $pKa = -\log Ka$.

By substituting these values in equation (4) gives:

$$pH = pKa + \log [acid] / [salt] \qquad (5)$$

Equation (5) is known as buffer equation or Henderson-Hasselbalch equation for acid buffer.

Similarly buffer equation for a solution containing weak base and the corresponding salt may be derived in a similar manner.

Equation for the calculation of $[OH^-]$ may be written as:

$$[OH^-] = Kb\ [base]/[salt] \quad (6)$$

Henderson-Hasselbalch's equation for basic buffers is:

$$pH = pKw + pKb + \log[salt]/[acid] \qquad (7)$$

Applications:

❖ For a definite pH solution, it is essential to add salt and acid (or base) to water in a desired ratio. This ratio is determined by Henderson-Hasselbalch equation.

❖ Since salt and acid are added in the preparation of a buffer solution, their concentrations are known. Using this data, the resultant pH of a solution can be calculated using buffer equation.

❖   Equations (5) and (7) permit the calculation of the percent of drug ionized (or ionized) in the solution. This knowledge is important in predicting the drug absorption, because only unionized molecules can penetrate cell membranes (lipid in nature) more readily than ionized molecules.

❖   The pKa of various drugs can be determined from pH of solutions

❖   The solubility of a substance at any pH can be predicted provided intrinsic solubility and pKa are known.

❖   A suitable sält forming substance can be selected based on Henderson Hasselbalch equation.