Physical Pharmacy Laboratory
2nd stage
College of Pharmacy

Lab.5 : Buffer solutions

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Definition of a buffer solution

- **A buffer solution** is a solution that resists significant changes in pH when small amounts of a strong acid or strong base are added.
- Buffers are important in pharmacy because pH can affect drug stability, solubility, absorption, and compatibility with biological tissues.

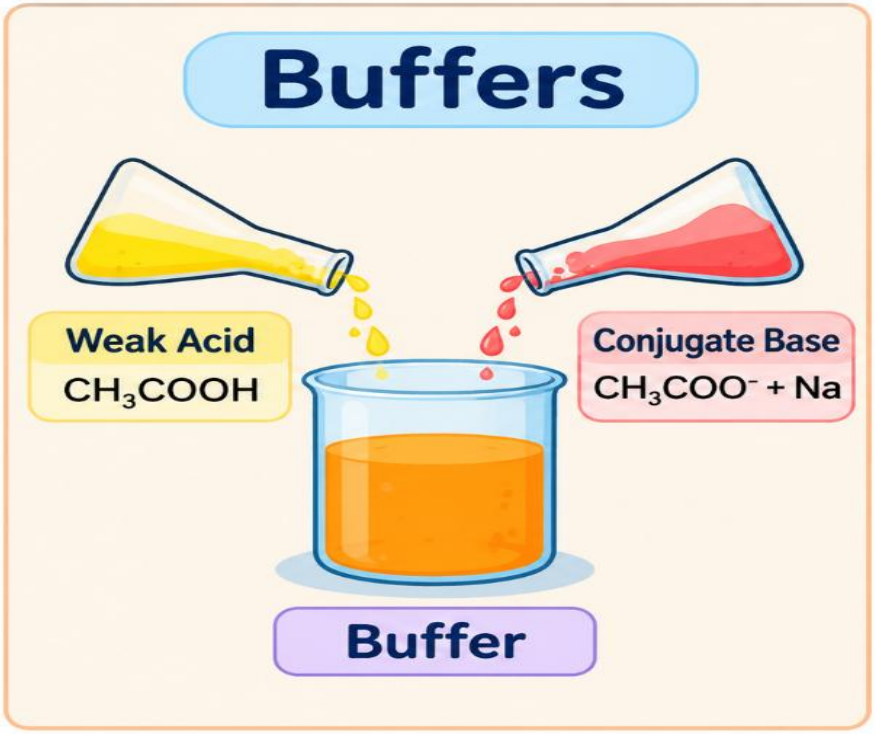
Composition of buffer solutions

- A buffer usually consists of one of the following pairs:

  1. Weak acid and its conjugate base (salt).

  Example**: acetic acid** and **sodium acetate**.

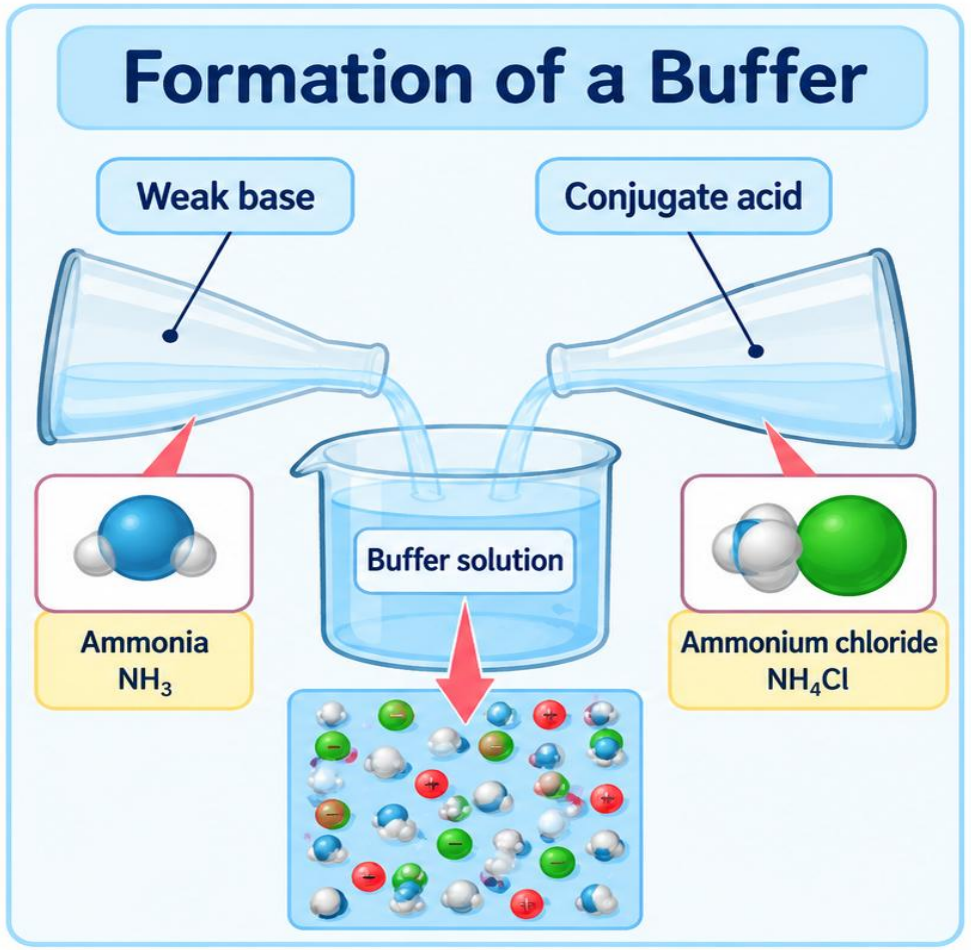
- Weak acid: CH_3COOH
- Conjugate base: CH_3COO^-
- Salt: CH_3COONa



2. Weak base and its conjugate acid (salt).

- Example: **ammonia** and **ammonium chloride.**

- Weak base: NH_3
- Conjugate acid: NH_4^+
- Salt: NH_4Cl



- A buffer **works** because one component reacts with added acid, while the other reacts with added base.

➢ A buffer **does not prevent all pH changes**. It reduces them, provided the amount of added acid or base does not exceed its **buffering capacity**.

Difference between buffer and non-buffer solutions

- Consider two solutions:
  - Solution A: **10 mL of distilled water**.
  - Solution B: **5 mL of 0.01 M acetic acid mixed with 5 mL of 0.01 M sodium acetate**.
    - ❑ Both solutions receive 1 mL of 0.1 N HCl.
    - ❑ The **water** has almost no buffering capacity, so the added acid causes a substantial **pH decrease**.
    - ❑ The **acetate buffer** resists this change because acetate ions react with the added hydrogen ions.
    - ❑ The exact pH changes depend on the solution volumes, concentrations, and initial conditions.

Mechanism of buffer action

- The acetate buffer is used to explain how buffers resist changes in pH.
- The weak acid partially ionizes in water:

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

- Sodium acetate dissociates almost completely:

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

The acetate ions CH_3COO^- act as the conjugate base, while acetic acid CH_3COOH acts as the weak acid.

A. When a strong acid is added

The added H_3O^+ ions react with acetate ions to form weakly ionized acetic acid.

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

Result: The increase in acidity is reduced, so the pH decreases only slightly.

B. When a strong base is added

The added OH^- ions react with acetic acid to form acetate ions and water.

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

Result: The increase in basicity is reduced, so the pH increases only slightly.

- **The conjugate base removes added acid, while the weak acid removes added base.**

Conjugate bases of weak acids

Acid	Conjugate Base	Sodium Salt
HCN	CN^-	NaCN
H_2SO_3	HSO_3^-	$NaHSO_3$

Conjugate acids of weak bases

Base	Conjugate Acid	Chloride Salt
NH_3	NH_4^+	NH_4Cl
CH_3NH_2	$CH_3NH_3^+$	CH_3NH_3Cl

Buffer equations

A. Buffer containing a weak acid and its salt

The Henderson–Hasselbalch equation is:

$$\mathrm{pH} = \mathrm{p}K_a + \log \frac{[\mathrm{Salt}]}{[\mathrm{Acid}]}$$

Where:

- pH = acidity or basicity of the solution.
- $\mathrm{p}K_a$ = negative logarithm of the acid dissociation constant.
- $[\mathrm{Salt}]$ = concentration of the conjugate base.
- $[\mathrm{Acid}]$ = concentration of the weak acid.

For an acetate buffer:

$$\mathrm{pH} = \mathrm{p}K_a + \log \frac{[\mathrm{CH_3COO^-}]}{[\mathrm{CH_3COOH}]}$$

When the concentrations of the acid and its salt are equal:

$$\mathrm{pH} = \mathrm{p}K_a$$

While the pH of the weak acid alone can be calculated as:

$$pH = \frac{1}{2} pKa - \frac{1}{2} \log C$$

Where, C is the molar concentration of the weak acid.

B. Buffer containing a weak base and its salt

For a weak base and its conjugate acid salt:

$$\mathrm{pOH} = \mathrm{p}K_b + \log \frac{[\mathrm{Salt}]}{[\mathrm{Base}]}$$

Then calculate pH using:

$$\mathrm{pH} = \mathrm{p}K_w - \mathrm{pOH}$$

$$\mathrm{pH} = 14.00 - \mathrm{pOH}$$

- Here, the salt supplies the conjugate acid of the weak base.

Calculation note: Use concentrations or, where appropriate, the ratio of the numbers of moles of the two buffer components. When mixing solutions of different concentrations, calculate theactual amounts before applying the equation.

Examples of Application of buffer equations

What is the pH of 0.1 M acetic acid solution, pKa= 4.76? What is the pH after enough sodium acetate has been added to make the solution 0.1 M with respect to this salt?

Calculation of pH of acetic acid solution :

$$pH = \tfrac{1}{2}\, pKa - \tfrac{1}{2} \log C \qquad pka = 4.76 \qquad C = 0.1M$$

$$= 2.38 + 0.50 = 2.88$$

Calculation of pH of the buffer:

$$pH = pKa + \log [salt]/[acid]$$

$$pH = 4.76 + \log (0.1/0.1) = 4.76$$

What is the molar ratio, [Salt]/[Acid], required to prepare an acetate buffer of pH 5.0? Also express the result in *mole percent* (pKa= 4.76)?

pH= pKa + log [salt]/[acid]

5.0 = 4.76 + log [salt] / [acid]

Log [salt] / [acid] = 5.0 - 4.76 = 0.24

[salt] / [acid] = antilog 0.24 = 1.74

What is the pH of a solution containing 0.10 mole of ephedrine and 0.01 mole of ephedrine hydrochloride per liter of solution? Since the pK_b of ephedrine is 4.64

$$pH = pKw - pKb + \log [base]/[salt]$$

$$pH = 14.00 - 4.64 + \log (0.10 / 0.01)$$

$$pH = 9.36 + \log 10 = 10.36$$

Measurement of pH

- The pH of a buffer can be measured by two main methods.

A. Colorimetric method

- This method estimates pH by observing color changes.

1. Chemical pH indicators

- These are substances that change color over a characteristic pH range. Their colors depend onthe relative amounts of their protonated and deprotonated forms.
- For an acidic indicator:

$$HIn + H_2O \rightleftharpoons In^- + H_3O^+$$

- HIn: protonated form, usually the acidic color.
- In^-: deprotonated form, usually the basic color.

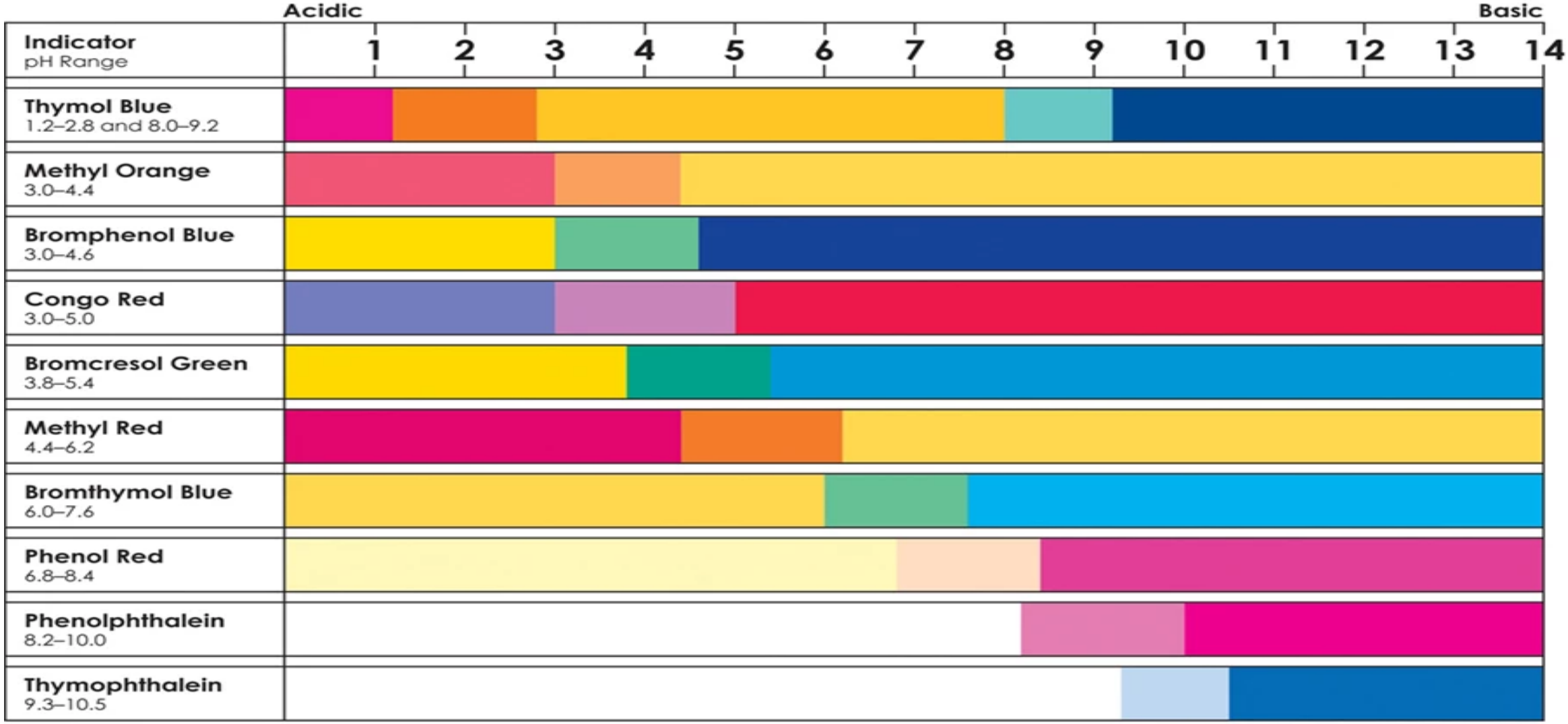
The actual colors depend on the particular indicator.

When acid is added, the increased hydronium-ion concentration shifts the equilibrium toward HIn. When base is added, hydronium ions are consumed and the equilibrium shifts toward In^-.

Example: Methyl red

- It may considered as W.A. or W.B. that acts like buffers & also exhibit color changes as their degree of dissociation varies with pH.
  - Acidic color: red.
  - Basic color: yellow.
  - Transition range: approximately pH 4.4–6.2.
  - The exact observed color depends on the pH and the indicator's transition range.

pH Indicator Chart



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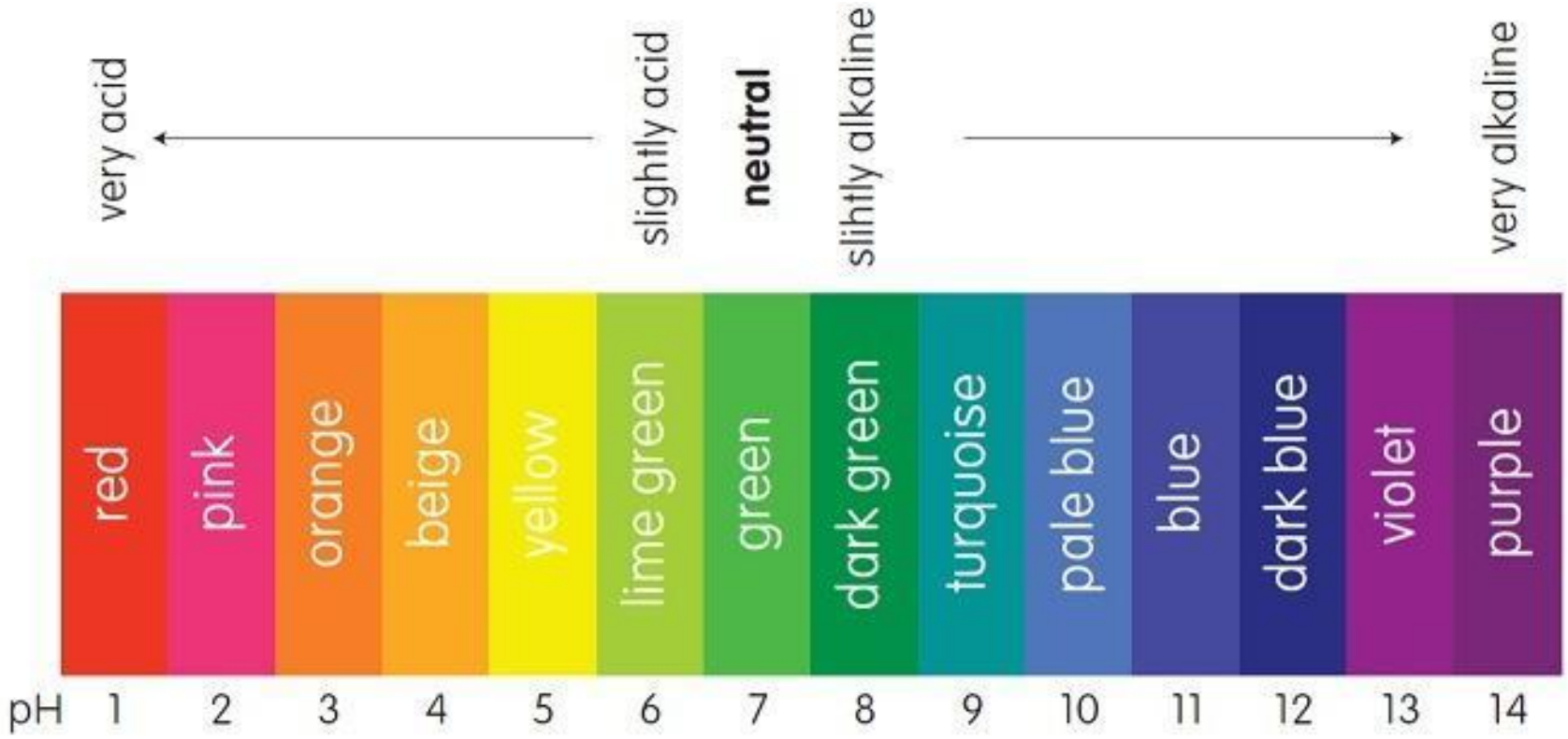
2. pH indicator paper

- Indicator paper changes color when exposed to a solution. Its color is compared with a reference chart to estimate pH.

How to use pH paper

1. Dip the indicator paper into the solution, or transfer a drop of solution onto it.
2. Observe the resulting color.
3. Compare it with the manufacturer's reference chart.
4. Record the approximate pH.



B. Electrometric method (pH meter)

- A pH meter measures pH using an electrode system that responds to hydrogen-ion activity.
- It generally provides a more precise numerical pH value than colorimetric methods when properly calibrated and used.



Procedure

1. Calibrate the pH meter using standard buffer solutions, commonly pH 4.00, 7.00, and/or 10.00, as appropriate.
2. Rinse the electrode with distilled or deionized water and gently blot it dry.
3. Immerse the electrode in the test solution, ensuring the sensing bulb and junction are properly immersed.
4. Record the pH and temperature, if required.
5. Rinse the electrode after measurement and store it according to the manufacturer's instructions.

B. Electrometric method (pH meter)

Advantages

I. More accurate and precise than indicator paper.
II. Provides a direct numerical pH reading.
III. Suitable for colored or turbid solutions that may be difficult to assess visually.

Limitations

I. Requires calibration and proper electrode maintenance.
II. Electrode readings are affected by **temperature** and may be affected by sample composition.
III. The electrode is **fragile** and requires appropriate storage



Buffer capacity

- **Buffer capacity** describes the ability of a buffer to resist a change in pH when acid or base is added.
- It depends on both the total concentration of the buffer components and their relative concentrations.
- A commonly used expression is:

$$\beta = \frac{\Delta B}{\Delta \mathrm{pH}}$$

Where:

- ΔB = amount of strong acid or strong base added per liter of buffer, expressed in equivalents per liter.
- $\Delta \mathrm{pH}$ = resulting change in pH.

For an acid addition, the pH decreases; for a base addition, the pH increases. Buffer capacity is conventionally reported as a positive quantity, with units of $\mathrm{eq\,L^{-1}\,pH^{-1}}$.

Interpretation:

- High buffer capacity: a larger quantity of acid or base is needed to change the pH by one unit.
- Low buffer capacity: a smaller quantity of acid or base causes a greater pH change.
- Buffer capacity is generally **greatest** when the weak acid and conjugate base **concentrations** are similar, provided the total buffer concentration is sufficient.

Factors affecting buffer capacity (β)

1. **[Salt]/[Acid] ratio**

When [Salt]/[Acid] =1, (pH = pKa) it indicated **maximum buffer capacity**

$$(\beta_{max}) = 0.576\ C$$

2. total concentrations of acid and salt

- When **increase** the **concentration** of the acid and the base, it will **increase** the buffer capacity

3. Addition of strong acid or base

Examples of pharmaceutical buffer systems

A. Sorensen phosphate buffer

- This system uses two stock solutions:

  M/15 **sodium dihydrogen phosphate**.

  M/15 **disodium hydrogen phosphate**.

- These are **mixed in different proportions** to obtain the desired pH.
- Here, M/15 means approximately 1/15 mol/L.

B. Acetate buffer

- This system uses:
  - Solution A: 0.2 M acetic acid.
  - Solution B: 0.2 M sodium acetate.
- **Different volumes of A and B are mixed**, and water is added to obtain a final volume of 100 mL.
- The ratio of the two components determines the approximate pH, while their total concentration influences buffer capacity.

Practice problems

1. Calculate the pH of the buffer solution if the molar concentration of phenobarbital is 0 03 M and that of sodium phenobarbital is 0 02 M The pKa for phenobarbital is 7 4
2. An acetate buffer contains 0.20 M sodium acetate and 0.10 M acetic acid. Calculate thepH using pKa = 4.76.
3. A buffer contains equal concentrations of acetic acid and sodium acetate. If pKa =4.76, calculate the pH.