



Buffered and Isotonic Solutions

Lecture by:
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PHYSICAL PHARMACY

1ST SEMESTER / 2026-2027



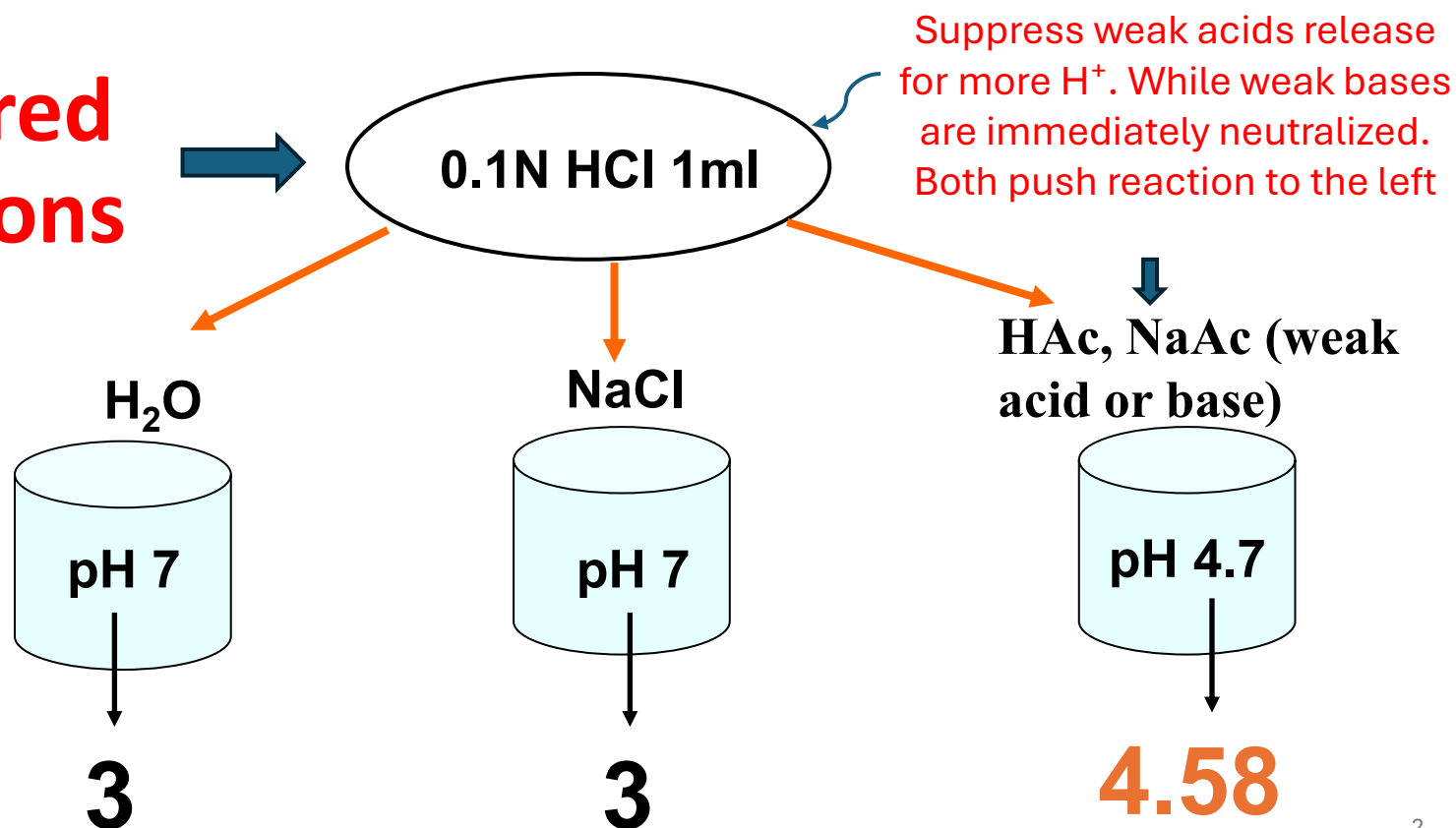


Buffers are **compounds** or mixtures of compounds that, **by their presence in solution, resist changes in pH** upon the addition of small quantities of acid or alkali.



The resistance to a change in pH is known as **buffer action**.

Buffered Solutions



Clarification

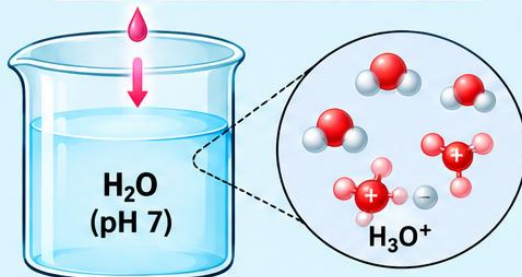
Effect of Adding Strong Acid (HCl)



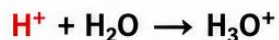
0.1 N HCl
(1 mL)

- HCl provides H^+ ions.
- In water and neutral salt solutions, H^+ remains in solution, causing a large drop in pH.
- In the buffer, the conjugate base (Ac^-) reacts with H^+ , so the pH changes only slightly.

A. Pure Water (H_2O)



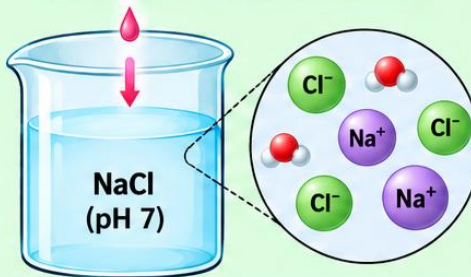
Added H^+ reacts with water:



Final pH = 3

- No buffer $\rightarrow$ cannot resist the change in pH.

B. NaCl Solution



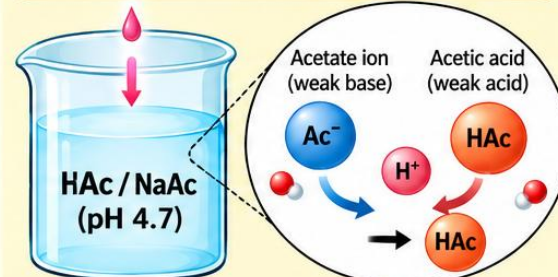
NaCl dissociates but does not react with H^+ :



Final pH = 3

- Neutral salt $\rightarrow$ provides no buffering capacity.

C. Acetate Buffer (HAc / NaAc)



Added H^+ reacts with the conjugate base:

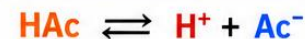


Final pH = 4.58

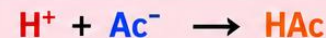
- Buffer resists the change in pH by consuming the added H^+ .

Solution	Initial pH	Final pH (after 0.1 N HCl)	Change in pH
Pure water (H_2O)	7	3	Large decrease
NaCl solution	7	3	Large decrease
Acetate buffer (HAc / NaAc)	4.7	4.58	Small decrease

Buffer Equilibrium and Response to Added H^+

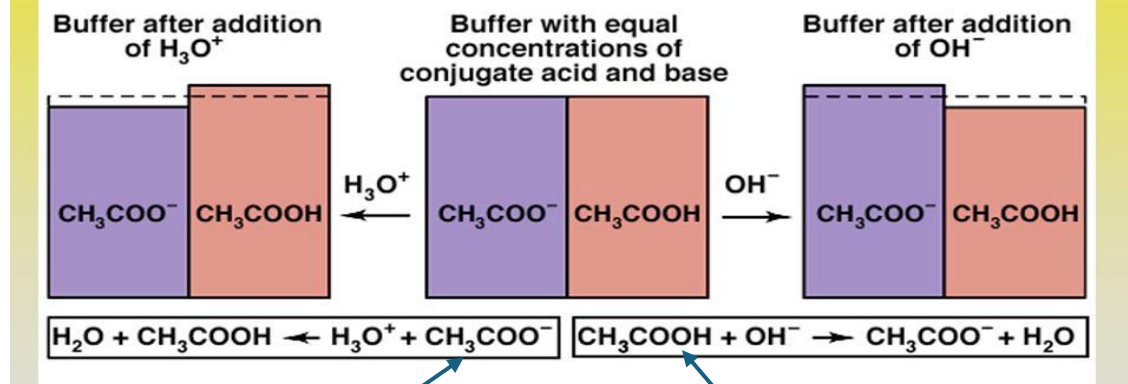


When H^+ is added, the equilibrium shifts to the left:



This consumes the added H^+ and prevents a large decrease in pH.

How a Buffer Works



Conjugate base accepts proton so neutralize added acid (remove added H^+)

Weak acid donates proton so neutralize added base (remove added OH^-)

Buffered Solutions

- Combination of a weak acid and its conjugate base



- Combination of a weak base and its conjugate acid



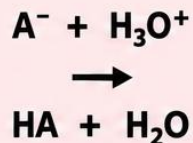
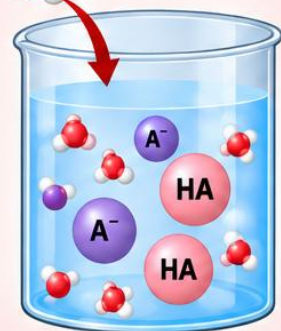
Clarification

How a Buffer Works

A buffer contains a weak acid (HA) and its conjugate base (A^-) in comparable concentrations. It resists changes in pH when small amounts of acid (H_3O^+) or base (OH^-) are added.

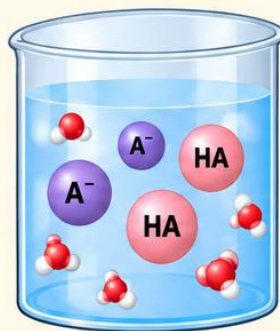
1. After addition of acid (H_3O^+)

Added H_3O^+



Conjugate base (A^-) accepts a proton to neutralize the added acid.

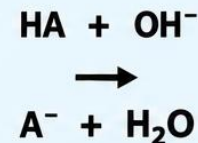
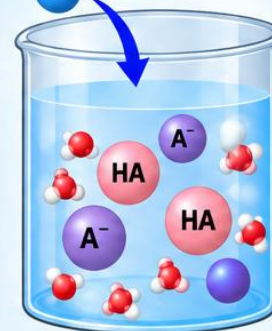
2. Buffer with equal concentrations of HA and A^- (normal condition)



Weak acid (HA) and its conjugate base (A^-) are present in comparable amounts, maintaining a nearly constant pH.

3. After addition of base (OH^-)

Added OH^-



Weak acid (HA) donates a proton to neutralize the added base.

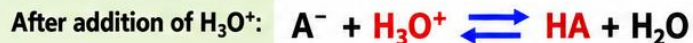
Buffer composition



Examples:

- CH_3COOH / CH_3COO^- (acetic acid/acetate)
- H_2CO_3 / HCO_3^- (carbonic acid/bicarbonate)

Buffer reactions (general)

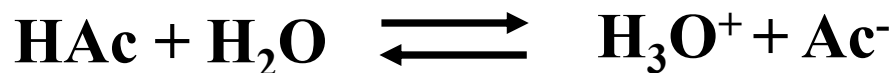


Key points

- 1 Buffer resists pH change by neutralizing added H_3O^+ or OH^- .
- 2 Most effective when $[HA] \approx [A^-]$ ($pH \approx pK_a$).
- 3 Works best for small amounts of added acid or base.
- 4 Does not prevent pH change if large amounts of acid or base are added.

The Buffer Equation

- A Weak Acid and Its Salt
- If the strong acid is added to a 0.01 M solution containing equal quantities of acetic acid and sodium acetate, the pH is **changed only 0.09 pH units** because the base (Ac-) ties up the hydrogen ions according to the reaction



$$[\text{H}_3\text{O}^+] = K_a \frac{[\text{HAc}] \text{ Acid}}{[\text{Ac}^-] \text{ Salt}}$$

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{Ac}^-] \xrightarrow{\text{salt}}}{[\text{HAc}] \xrightarrow{\text{acid}}}$$

$$-\log[\text{H}_3\text{O}^+] = -\log K_a - \log[\text{acid}] + \log[\text{salt}]$$

A Weak Acid and Its Salt

$$\text{pH} = \text{p}K_a + \log \frac{[\text{salt}]}{[\text{acid}]}$$

**Dissociation
exponent**

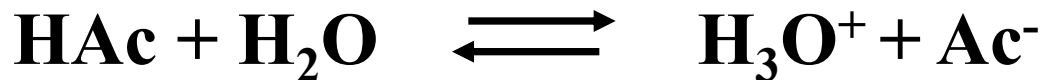
Buffer equation or
Henderson-Hasselbalch
equation

Common ion effect

*

$$K_a = \frac{[H_3O^+][Ac^-]}{[HAc]}$$

is momentarily disturbed since the acetate ion supplied by the salt increases the $[Ac^-]$



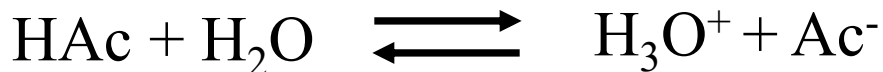
The ionization of HAc is repressed upon the addition of the common ion $[Ac^-]$

Example

- For example, when sodium acetate is added to acetic acid, the dissociation constant for the weak acid, is

$$K_a = \frac{[H_3O^+][Ac^-]}{[HAc]} = 1.75 \times 10^{-5}$$

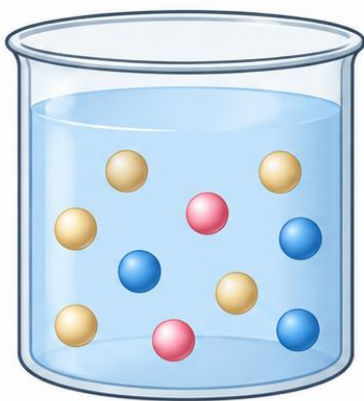
- Is momentarily disturbed because the acetate ion supplied by the salt increases the $[Ac^-]$ term in the numerator.
- To reestablish the constant K_a at 1.75×10^{-5} , the hydrogen ion term in the numerator $[H_3O^+]$ is instantaneously decreased, with a corresponding increase in $[HAc]$. Therefore, the constant K_a remains unaltered, and the equilibrium is shifted in the direction of the reactants.
- Consequently, the ionization of acetic acid is repressed upon the addition of the common ion, Ac^- . This is an example of the common ion effect.



Clarification

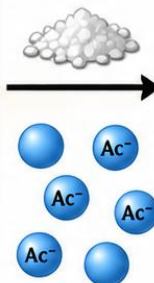
Common ion effect

1. Equilibrium of acetic acid in water

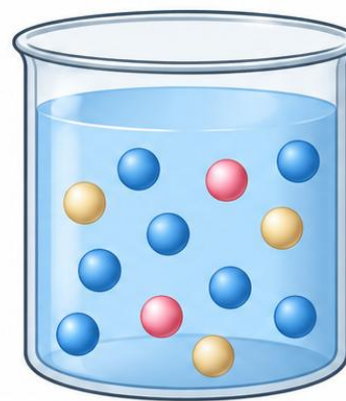


$$K_a = \frac{[\text{H}_3\text{O}^+][\text{Ac}^-]}{[\text{HAc}]}$$

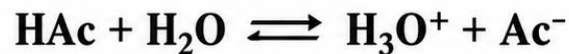
Add sodium acetate (NaAc)



2. After addition of common ion (Ac⁻)



- HAc (molecule)
- H₃O⁺ (hydronium ion)
- Ac⁻ (acetate ion)

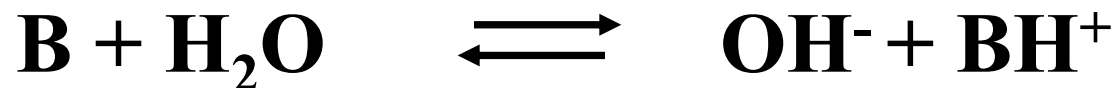


$$K_a = \frac{\overset{2}{\downarrow} [\text{H}_3\text{O}^+][\text{Ac}^-] \overset{1}{\uparrow}}{\underset{3}{\uparrow} [\text{HAc}]}$$

The ionization of HAc is repressed upon the addition of the common ion [Ac⁻]

The Buffer Equation

- A Weak Base and Its Salt



$$K_b = \frac{[\text{OH}^-][\text{BH}^+]}{[\text{B}]}$$

salt
base

$$[\text{OH}^-] = K_b \frac{[\text{B}] \text{ Base}}{[\text{BH}^+] \text{ salt}}$$

$$\downarrow [\text{H}_3\text{O}^+] \cdot [\text{OH}^-] = K_w$$

$$-\log[\text{H}_3\text{O}^+] = -\log K_w - \log 1/K_b - \log[\text{salt}]/[\text{base}]$$

- **A Weak Acid and Its Salt**

$$\text{pH} = \text{p}K_w - \text{p}K_b + \log \frac{[\text{base}]}{[\text{salt}]}$$

* **Note:**

Buffers are not ordinarily prepared from weak bases because of:

1. **Volatility & instability of the bases.**
2. **Dependence of their pH on $\text{p}K_w$, which is often affected by temp. changes.**

Example 8.2:

What is the molar ratio, $[\text{Salt}]/[\text{Acid}]$, required to prepare an acetate buffer of pH 5.0? If you know that pK_a is 4.76. Also express the result in mole percent.

$$\text{pH} = \text{pK}_a + \log \frac{[\text{Salt}]}{[\text{Acid}]}$$

$$5.0 = 4.76 + \log \frac{[\text{Salt}]}{[\text{Acid}]}$$

$$\log \frac{[\text{Salt}]}{[\text{Acid}]} = 5.0 - 4.76 = 0.24$$

$$\frac{[\text{Salt}]}{[\text{Acid}]} = \text{antilog } 0.24 = 1.74$$

- Therefore, the mole ratio of salt to acid is 1.74/1.
- Mole percent is mole fraction multiplied by 100.
- The mole fraction of salt in the salt–acid mixture is $1.74/(1 + 1.74) = 0.635$, and in mole percent, the result is 63.5%.

Factors influencing the pH of buffer solutions

1. Altering the ionic strength

- ① Addition of neutral salts
- ② Dilution (alter activity coefficients) small pH change

2. Temperature

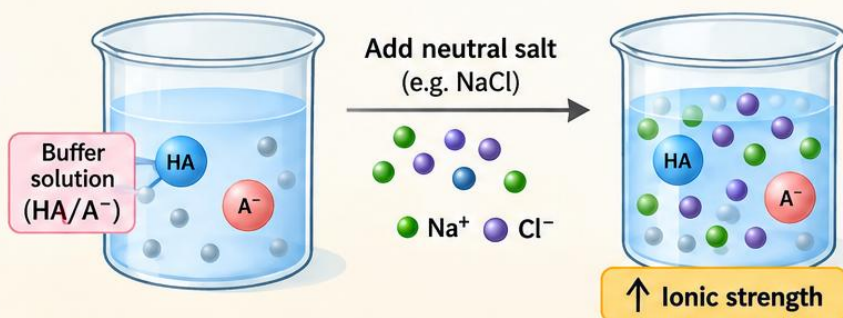
The pH of the most basic buffer was found to change more markedly with temp. than that of acid buffers, owing to K_w .

Clarification

Factors influencing the pH of buffer solutions

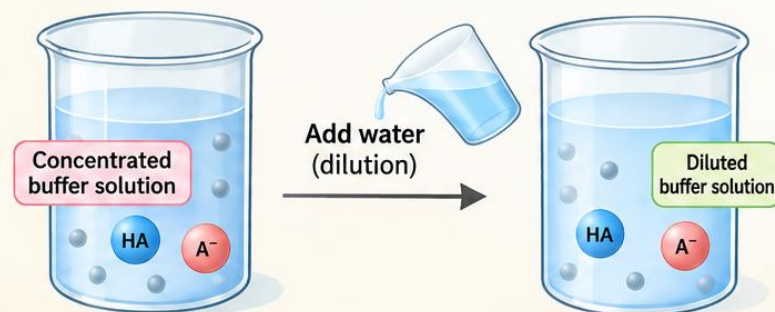
1. Altering the ionic strength

① Addition of neutral salts



Addition of neutral salts increases the ionic strength, which changes the activity coefficients of the buffer components, but causes only a **small change in pH**.

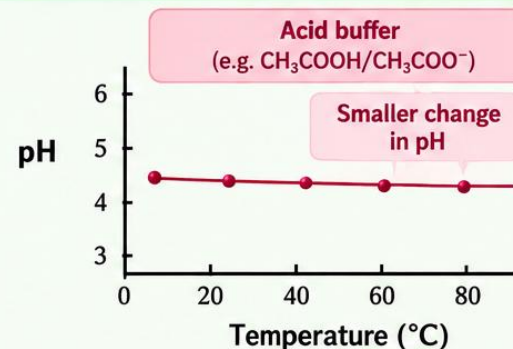
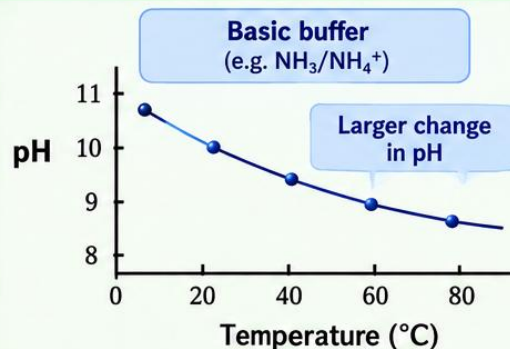
② Dilution (alter activity coefficients)



Dilution decreases the ionic strength and alters the activity coefficients of HA and A^- , resulting in only a **small change in pH**.

2. Temperature

The pH of most **basic buffers** changes more markedly with temperature than that of **acid buffers**, owing to K_w .

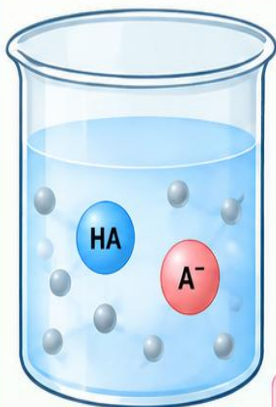


Clarification

Activity Coefficient (γ)

Activity coefficient (γ) is a factor that shows how much the behavior of an ion in a real solution differs from its concentration due to interactions with other ions.

A Dilute solution (almost ideal)

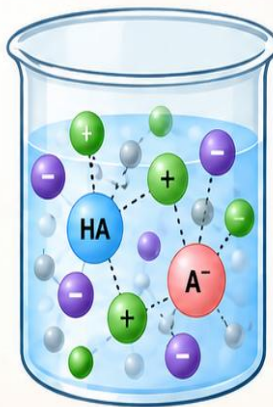


- Ions are far apart (weak interactions).
- Activity coefficient is close to 1.

$$\gamma \approx 1$$

Activity > Concentration
 $a_i \approx [i]$

B Higher ionic strength (after adding neutral salt, e.g. NaCl)

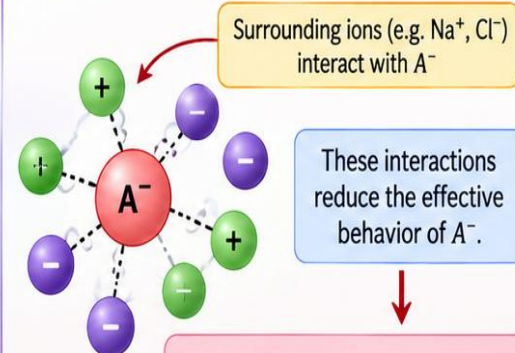


- More ions in solution (stronger interactions).
- Activity coefficient becomes less than 1 ($\gamma < 1$).

$$\gamma < 1$$

Activity < Concentration
 $a_i = \gamma[i] \quad (\gamma < 1)$

C Meaning of activity coefficient



Therefore, its activity (a) is lower than its concentration.

Mathematical expression

$$a_i = \gamma_i [i]$$

a_i = activity of the ion (M)
 $[i]$ = concentration of the ion (M)
 γ_i = activity coefficient (dimensionless)

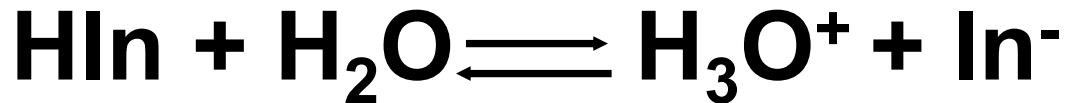
Relation to pH

$$\text{pH} = -\log a_{H^+} = -\log (\gamma_{H^+} [H^+])$$

Changes in γ (due to ionic strength or dilution) can cause a **small change in pH**.

pH indicator

- Acid indicator



Acid color (at low
pH- high H^+)

Alkaline color (at high pH- low H^+)

$$K_{\text{In}} = \frac{[\text{H}_3\text{O}^+][\text{In}^-]}{[\text{HIn}]}$$

← base
← acid

$$\text{pH} = \text{p}K_{\text{In}} + \log \frac{[\text{base}]}{[\text{acid}]} \longrightarrow 1/10 \sim 10/1$$

- * From experience, one cannot discern a change from the acid color to the salt color or conjugate base until the ratio of [base] to [acid] is about 1 to 10 (-1 acid) and from [acid] to [base] 10 to 1 (+1 base)
- * The effective range of the indicator is...

$$\text{pH} = \text{p}K_{\text{In}} \pm 1$$



Clarification

pH Indicator: Equilibrium, Equation and Effective Range

Acid form of indicator (HIn)



HIn
(acid form)

Acid color
(at low pH – high H^+)



Acid color
(at low pH – high H^+)

Alkaline color
(at high pH – low H^+)

Base form of indicator (In^-)



In^-
(base form)

Base color
(at high pH – low H^+)

$$K_{In} = \frac{[H_3O^+][In^-]}{[HIn]}$$

← base form [In^-]
← acid form [HIn]

$$pH = pK_{In} + \log \frac{[base]}{[acid]} = pK_{In} + \log \frac{[In^-]}{[HIn]}$$

$$\frac{[In^-]}{[HIn]} = 10 : 1$$



Mostly In^-
→ base color

$$\frac{[In^-]}{[HIn]} = 1 : 1$$



Transition range
→ mixed color

$$\frac{[In^-]}{[HIn]} = 1 : 10$$



Mostly HIn
→ acid color

Base color ←

$$pH = pK_{In} + 1$$

$$pH = pK_{In}$$

$$pH = pK_{In} - 1$$

→ Acid color

Effective range: **$pH = pK_{In} \pm 1$**

A visible color change is observed when one form is about **10 times** more abundant than the other (ratio **10:1** or **1:10**), so the indicator changes color over a range of $pK_{In} - 1$ to $pK_{In} + 1$.

Characteristics of colorimetric method

- ① Less accurate
- ② Less convenient but less expensive than electrometric method
- ③ Difficult to apply for the unbuffered pharmaceutical preparation (change the pH - indicator itself is acids or base)
- ④ Error may be introduced by the presence of salts & proteins

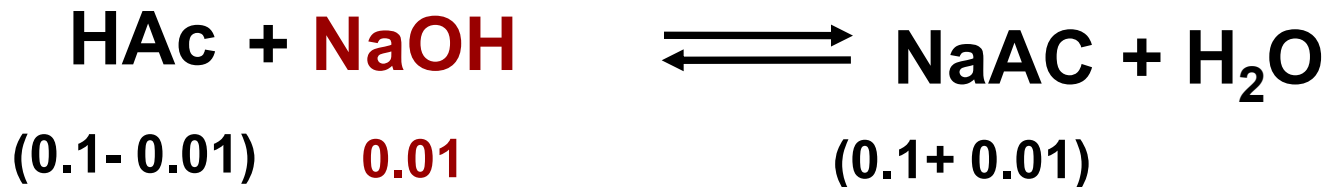
Buffer capacity

- The magnitude of the resistance of a buffer to pH changes

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

buffer capacity
= buffer efficiency
= buffer index
= buffer value

ΔB : small increment in **gram equivalents/Liter**
of **strong base (or acid)** added to the buffer
solution to produce a pH change of ΔpH



- Before the addition of NaOH

$$\text{pH} = \text{pK}_a + \log \frac{[\text{salt}]}{[\text{acid}]} = 4.76$$

- After the addition of NaOH

$$\text{pH} = \text{pK}_a + \log \frac{[\text{salt}] + [\text{base}]}{[\text{acid}] - [\text{base}]} = 4.85$$

$$\begin{aligned}
 \longrightarrow \beta &= \frac{\Delta B}{\Delta \text{pH}} = \frac{0.01}{(0.1 - 0.01)} = 0.11 \\
 &= 0.09
 \end{aligned}$$

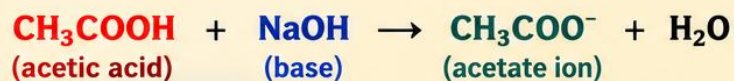
TABLE 8–2. Buffer Capacity of Solutions Containing Equimolar Amounts (0.1 M) of Acetic Acid and Sodium Acetate

Moles of NaOH Added	pH of Solution	Buffer Capacity, β
0	4.76	
0.01	4.85	0.11
0.02	4.94	0.11
0.03	5.03	0.11
0.04	5.13	0.10
0.05	5.24	0.09
0.06	5.36	0.08

- In Table 8-2, the buffer capacity is not a fixed value for a given buffer system but instead **depends on the amount of base added**.
- The buffer capacity changes as the ratio $\log([Salt]/[Acid])$ **increases** with added base. With the addition of **more sodium hydroxide**, the **buffer capacity decreases rapidly**, and, when sufficient base has been added to convert the acid completely into sodium ions and acetate ions, the solution no longer possesses an acid reserve.
- The buffer has its greatest capacity before any base is added, where $[Salt]/[Acid] = 1$, and, therefore, **pH = pKa**.

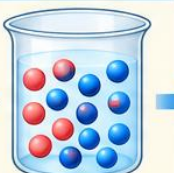
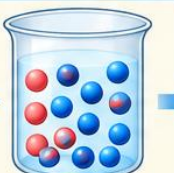
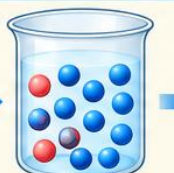
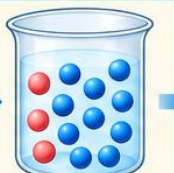
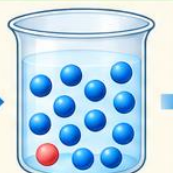
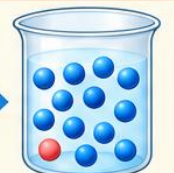
Clarification

Effect of Added NaOH on the pH and Buffer Capacity of an Acetic Acid / Sodium Acetate Buffer (0.1 M)



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

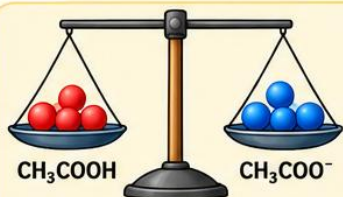
Buffer capacity (β):
amount of strong base
required to change pH
by 1 unit.

	0 mol NaOH added	0.01 mol NaOH added	0.02 mol NaOH added	0.03 mol NaOH added	0.04 mol NaOH added	0.05 mol NaOH added	0.06 mol NaOH added
							
	[Salt]/[Acid] = 1 (1 : 1)	[Salt]/[Acid] > 1 (~ 1.2 : 1)	[Salt]/[Acid] > 1 (~ 1.5 : 1)	[Salt]/[Acid] > 1 (~ 2 : 1)	[Salt]/[Acid] > 1 (~ 3 : 1)	[Salt]/[Acid] > 1 (~ 5 : 1)	[Salt]/[Acid] > 1 (~ 10 : 1)
	Maximum buffer capacity $\text{pH} = \text{p}K_a$						
Moles of NaOH added	0	0.01	0.02	0.03	0.04	0.05	0.06
pH of solution	4.76	4.85	4.94	5.03	5.13	5.24	5.36
Buffer capacity, β	(maximum)	0.11	0.11	0.11	0.10	0.09	0.08

 CH_3COOH (acetic acid)
 CH_3COO^- (acetate ion)
 Each sphere represents relative amount (conceptual).

Buffer capacity (β)

Decreases as more NaOH is added



Maximum buffer capacity

$$[\text{Salt}]/[\text{Acid}] = 1 \rightarrow \text{pH} = \text{p}K_a (4.76)$$



After enough base is added...

The weak acid (CH_3COOH) is completely converted to acetate (CH_3COO^-).

No acid reserve

→ very low buffering capacity against added base.

- The buffer capacity is also influenced by **C** (total buffer concentration), that is, the **sum of the molar concentrations of the acid and the salt**.
- The buffer capacity can be computed at any hydrogen ion concentration, at the point **where no acid or base has been added to the buffer**.

- A more exact equation for buffer capacity (1914, 1922)

$$\beta = 2.3 \cdot C \cdot \frac{K_a \cdot [\text{H}_3\text{O}^+]}{(K_a + [\text{H}_3\text{O}^+])^2}$$

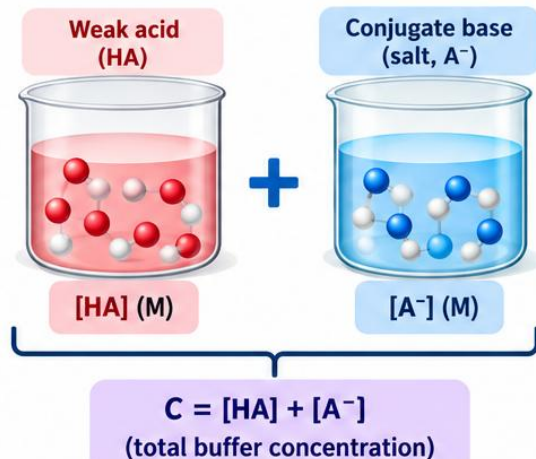
c : total buffer conc. (sum of the molar conc. of the acid & the salt)

• β ---- at any $[\text{H}_3\text{O}^+]$

Clarification

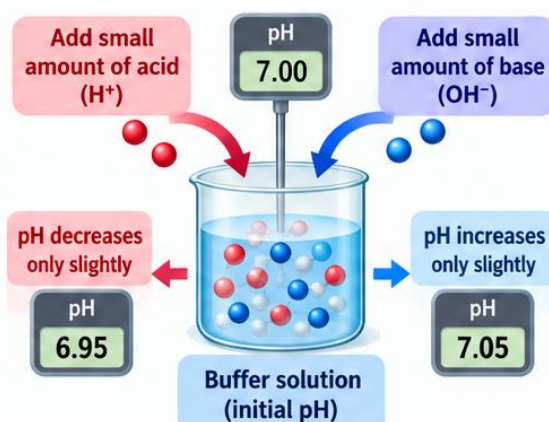
1 What is total buffer concentration (C)?

C is the **sum of the molar concentrations of the weak acid and its conjugate base (the salt)**.



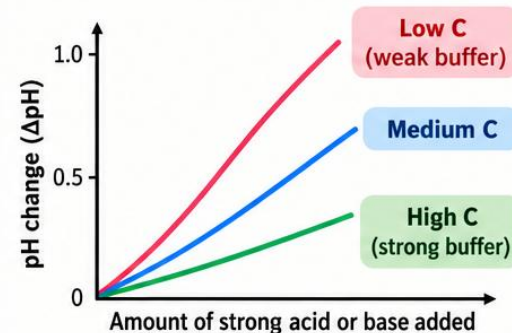
2 What is buffer capacity (β)?

Buffer capacity (β) is the amount of strong acid or base required to produce a unit change in pH. It shows the resistance of the buffer to pH change.



3 Buffer capacity depends on C

Increasing the total buffer concentration (C) increases the buffer capacity, so the pH changes less for the same amount of added acid or base.



Higher C → higher buffer capacity (β) → smaller pH change.

4 Mathematical expression for buffer capacity

The buffer capacity can be computed at any hydrogen ion concentration, at the point where **no acid or base has been added to the buffer** (initial buffer composition).

$$\beta = 2.3 \cdot C \cdot \frac{K_a \cdot [H_3O^+]}{(K_a + [H_3O^+])^2}$$

C : total buffer concentration
(sum of the molar concentrations of the acid and the salt)

β : buffer capacity
(mol L^{-1} per pH unit)

C : total buffer concentration
($[HA] + [A^-]$)

K_a : acid dissociation constant of the weak acid

$[H_3O^+]$: hydrogen ion concentration
(mol L^{-1})

- This equation gives the buffer capacity (β) at **any** $[H_3O^+]$ for the initial buffer (**no added acid or base**).

Example 8-6:

At a hydrogen ion concentration of 1.75×10^{-5} (pH = 4.76), what is the capacity of a buffer containing 0.10 mole each of acetic acid and sodium acetate per liter of solution?

The total concentration, $C = [\text{acid}] + [\text{salt}]$, is 0.20 mole per liter, and the dissociation constant is 1.75×10^{-5} .

$$\beta = \frac{2.3 \times 0.20 \times (1.75 \times 10^{-5}) \times (1.75 \times 10^{-5})}{[(1.75 \times 10^{-5}) + (1.75 \times 10^{-5})]^2} = 0.115$$

Maximum Buffer capacity

- $\beta_{\max}$ occurs where $\text{pH} = \text{p}K_a$, or $([\text{H}_3\text{O}^+] = K_a)$

$$\beta_{\max} = 2.303 \cdot C \cdot \frac{[\text{H}_3\text{O}^+]^2}{(2 [\text{H}_3\text{O}^+])^2} = \frac{2.303}{4} \cdot C$$

$$\beta_{\max} = 0.576 \cdot C$$

($\text{pH} = \text{p}K_a$)

Example 8.8: What is the maximum buffer capacity of an acetate buffer with a total concentration of 0.02 mole per liter?

$$\beta_{\max} = 0.576 \times 0.020 = 0.01152 \text{ or } 0.012$$

Characteristics of Buffer Capacity

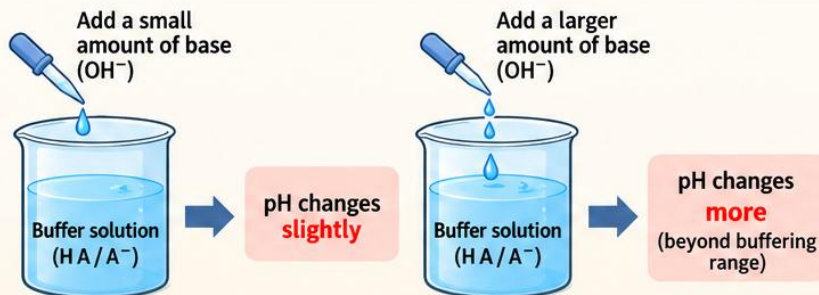
- ...is not a fixed value, but rather depend on the amount of base added
- ...depends on the value of the ratio $[\text{salt}]/[\text{acid}]$ and magnitude of the individual concentrations of the buffer components
- The greatest capacity (β_{max}) occurs where $[\text{salt}]/[\text{acid}] = 1$ and $\text{pH} = \text{pK}_a$
- Because of interionic effects, buffer capacities do not in general exceed a value of 0.2

Clarification

Characteristics of Buffer Capacity

1

Buffer capacity is not a fixed value
It depends on the amount of base added



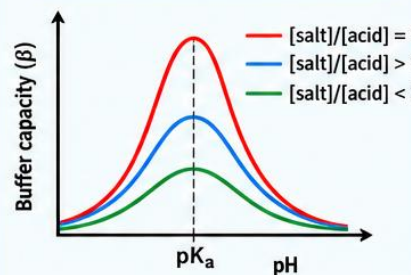
Therefore, buffer capacity depends on the **amount of base (or acid) added**.

2

Buffer capacity depends on the ratio $[\text{salt}]/[\text{acid}]$ and the concentrations of buffer components

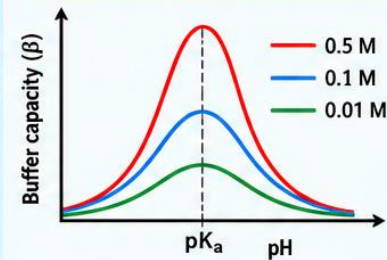
A. Effect of ratio $[\text{salt}]/[\text{acid}]$

Different ratios give different buffer capacities.



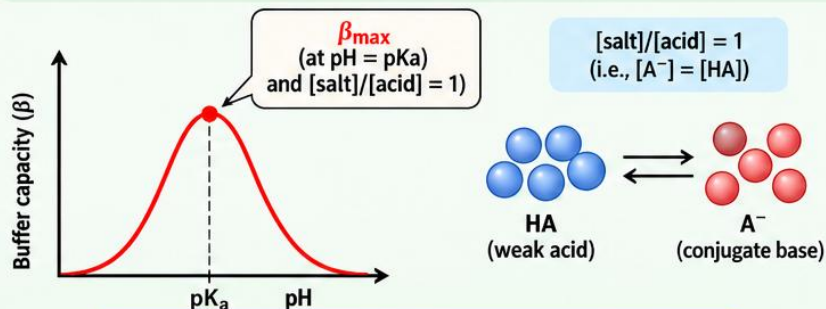
B. Effect of concentration

Higher concentrations of buffer components give higher buffer capacity.



3

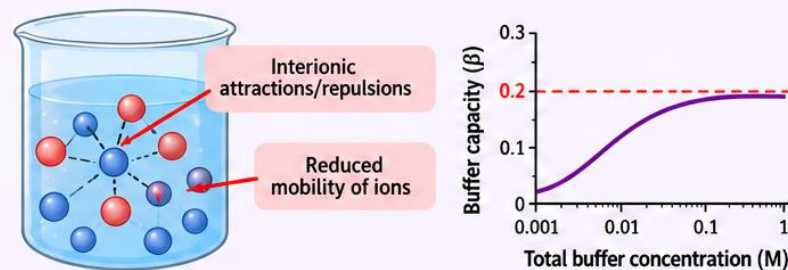
The greatest buffer capacity (β_{max}) occurs where $[\text{salt}]/[\text{acid}] = 1$ and $\text{pH} = \text{pK}_a$



Thus, the buffer resists pH change most effectively at **$\text{pH} = \text{pK}_a$** when **$[\text{salt}]/[\text{acid}] = 1$** .

4

Because of interionic effects, buffer capacities do not in general exceed a value of 0.2



At higher concentrations, ions interact with each other (**interionic effects**), which **limits the increase** in buffer capacity.

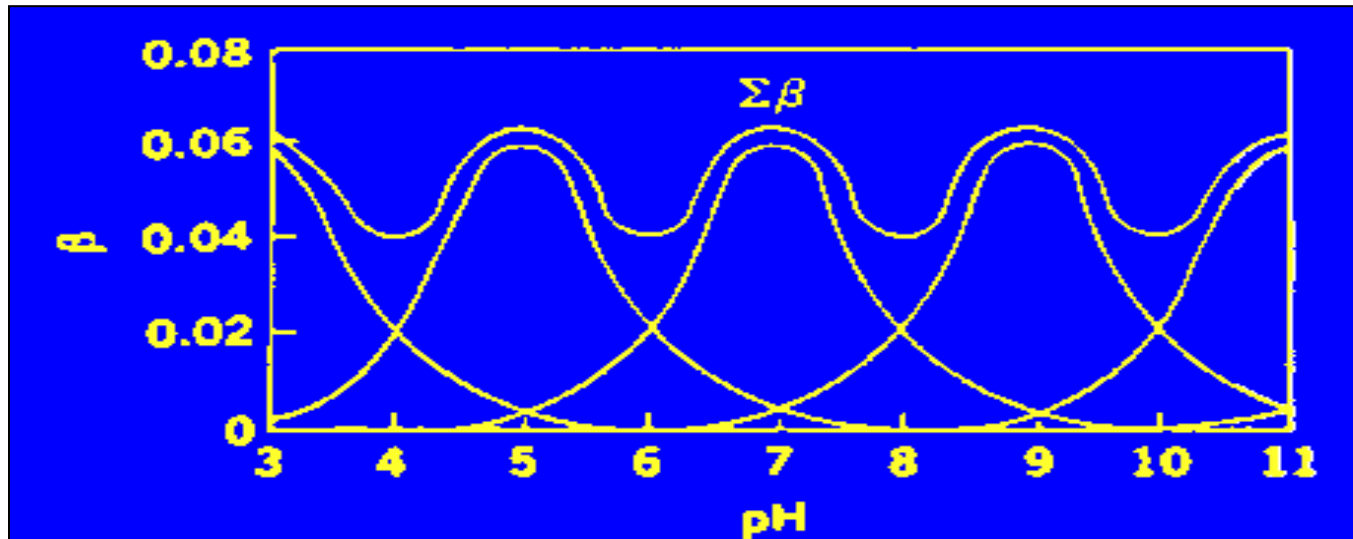
Therefore, buffer capacities typically **do not exceed 0.2**.

Universal Buffer

The buffer capacity of a combination of buffers, the **pKa values of which overlap to produce a universal buffer**.

Total buffer capacity ($\Sigma\beta$): is the sum of the β values of the individual buffers.

In this figure, it is assumed that the **maximum β 's of all buffers in the series are identical**.



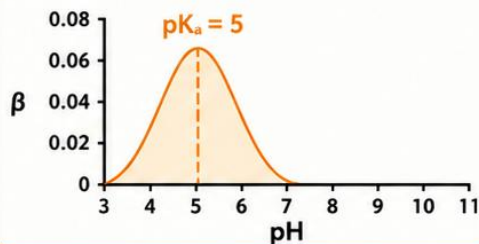
Clarification

Universal Buffer

A universal buffer is a mixture of several buffer systems with **different pK_a values** that **overlap** to provide a wide and nearly constant buffer capacity over a broad pH range.

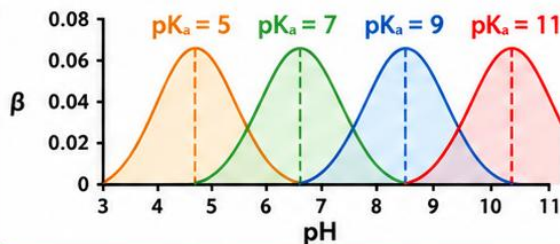
1 Individual buffers

Each buffer (a weak acid and its conjugate base) has a maximum buffer capacity (β) at its pK_a ($pH = pK_a$).



2 Multiple buffers with overlapping pK_a

Buffers with **different pK_a values** are combined so their buffer capacity curves overlap.

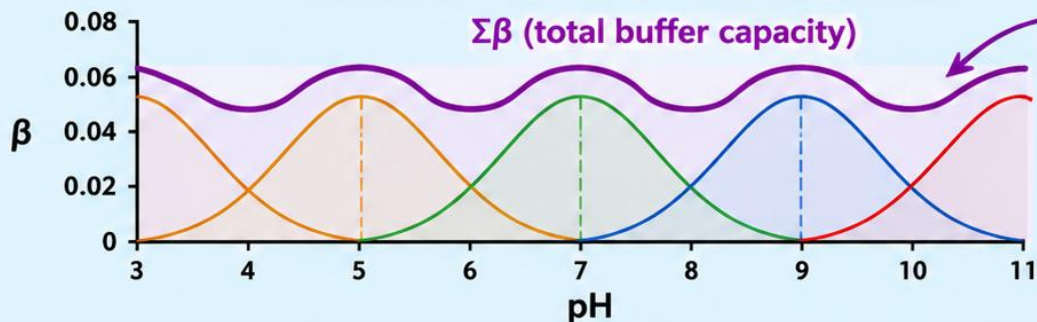


3 Total buffer capacity

The total buffer capacity ($\Sigma\beta$) is the **sum of** the β values of all individual buffers.

In this figure, the maximum β 's of all buffers in the series are assumed to be identical.

Result: Universal buffer



$\Sigma\beta$ is the sum of the β values of the individual buffers.

Because the pK_a values overlap, the total buffer capacity remains **high and relatively constant** across a wide pH range ($\approx 3-11$).

Buffers in Pharmaceutical and Biologic Systems

In Vivo Biologic Buffer Systems

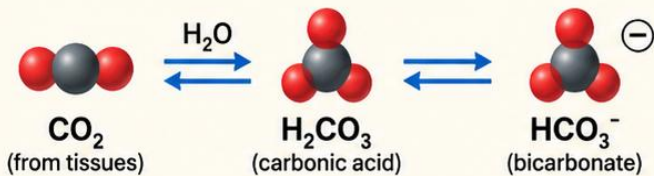
Blood is maintained at a pH of about **7.4** by:

- Primary buffers in the **plasma**: The plasma contains carbonic acid/bicarbonate and acid/alkali sodium salts of phosphoric acid as buffers.
- Secondary buffers in the **erythrocytes**: hemoglobin/oxyhemoglobin and acid/alkali potassium salts of phosphoric acid.
- **Plasma proteins**, which behave as acids in blood, can combine with bases and so act as buffers.
- It is usually life-threatening for the pH of the blood to go **below 6.9 or above 7.8**. The pH of the blood in diabetic coma is as low as about **6.8**.

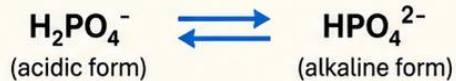
Clarification

1. Primary buffers in the **plasma**

The plasma contains carbonic acid/bicarbonate and acid/alkali sodium salts of phosphoric acid as buffers.



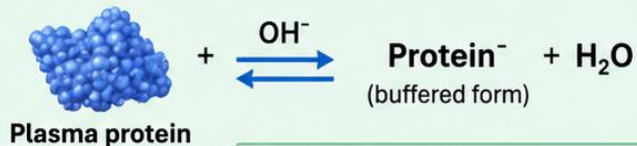
Carbonic acid / bicarbonate buffer



Acid/alkali sodium salts of phosphoric acid

3. Plasma proteins

Plasma proteins, which behave as acids in blood, can combine with bases and so act as buffers.



Blood pH

is maintained at about

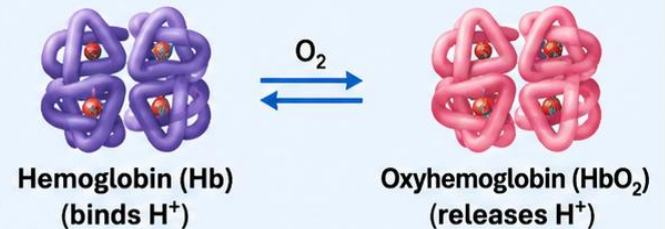
7.4

Plasma
(liquid part)

Erythrocytes
(red blood cells)

2. Secondary buffers in the **erythrocytes**

Hemoglobin/oxyhemoglobin and acid/alkali potassium salts of phosphoric acid act as buffers inside red blood cells.



Hemoglobin (Hb)
(binds H^+)

Oxyhemoglobin (HbO_2)
(releases H^+)



Acid/alkali potassium salts of phosphoric acid

4. Physiological importance

It is usually life-threatening for the pH of the blood to go **below 6.9 or above 7.8**.

The pH of the blood in diabetic coma is as low as about **6.8**.

6.9

7.8

Life-threatening
(acidosis)

Normal blood pH
~ 7.4

Life-threatening
(alkalosis)

Lacrima fluid, or tears, have been found to have a great degree of buffer capacity, allowing a dilution of 1:15 with neutral distilled water before an alteration of pH is noticed.

- The pH of tears is about 7.4, with a range of 7 to 8 or slightly higher.

Urine

- pH: 6.0 (range 4.5 –7.8)
- below normal...hydrogen ions are excreted by the kidney.
- above pH 7.4...hydrogen ions are retained by action of the kidney.

Clarification

TEARS (Lacralmal fluid)



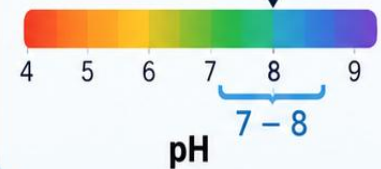
High buffer capacity

Allows a dilution of 1:15 with neutral distilled water before an alteration of pH is noticed.

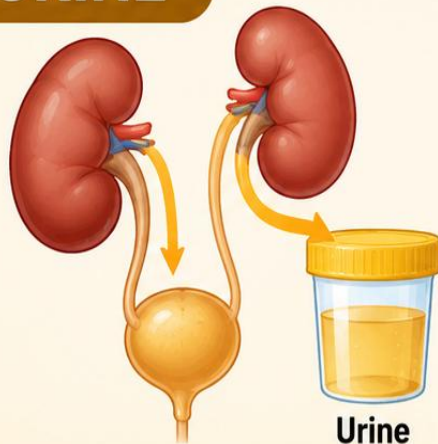
pH of tears

~7.4

(range 7 – 8
or slightly higher)



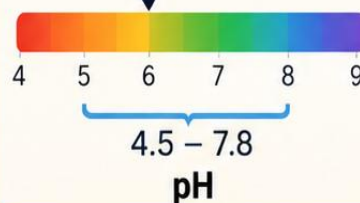
URINE



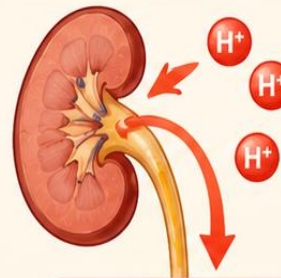
pH of urine

6.0

(range 4.5 – 7.8)

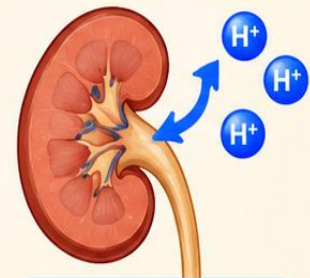


Below normal pH (< 7.4)



**H^+ excreted
by the kidney**

Above pH 7.4 (> 7.4)



**H^+ retained
by the kidney**

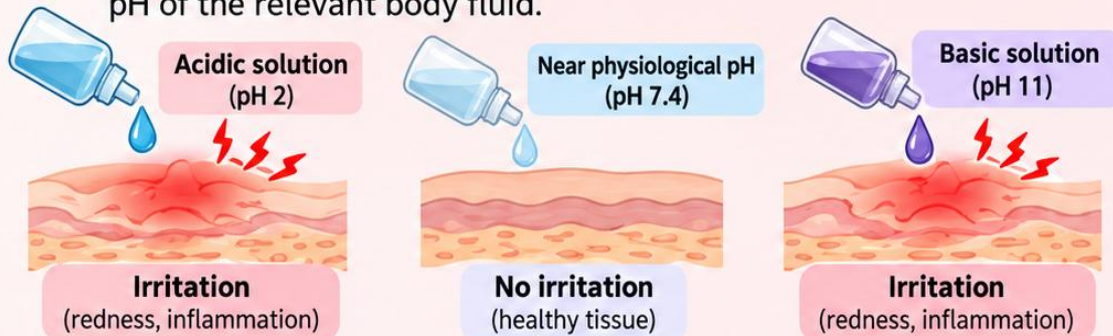
Influence of Buffer Capacity and pH on Tissue Irritation

- Solutions to be applied to tissues or administered **parenterally** are liable to cause irritation if their pH is greatly different from the normal pH of the relevant body fluid.
- Consequently, the pharmacist must consider when formulating **ophthalmic solutions, parenteral products**:
 1. its **buffer capacity** and
 2. the **volume** to be used in relation to the volume of body fluid with which the buffered solution will come in contact.
 3. The **buffer capacity of the body fluid** should also be considered.

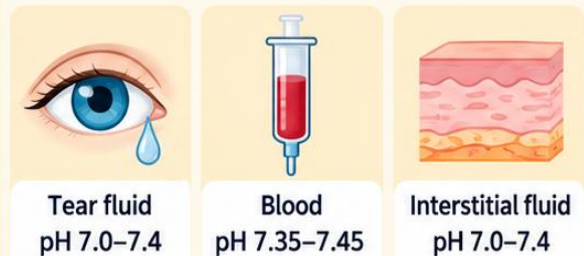
Clarification

Influence of Buffer Capacity and pH on Tissue Irritation

- 1** Solutions applied to tissues or administered parenterally are liable to **cause irritation** if their **pH is greatly different** from the normal pH of the relevant body fluid.



Normal pH of relevant body fluids



- 2** When formulating **ophthalmic solutions** or **parenteral products**, consider:

Buffer capacity



Choose an appropriate buffer system and concentration.

+

Volume to be used



Consider the volume relative to the volume of body fluid with which the solution will come in contact.

- 3** The **buffer capacity of the body fluid** should also be considered.



More susceptible to pH changes
→ higher risk of irritation.

Resists pH changes
→ lower risk of irritation.

Key Message

- ✓ Maintain pH close to the physiological pH of the target tissue or body fluid.
- ✓ Use an appropriate buffer system and concentration.
- ✓ Consider the application volume and the buffer capacity of the body fluid.

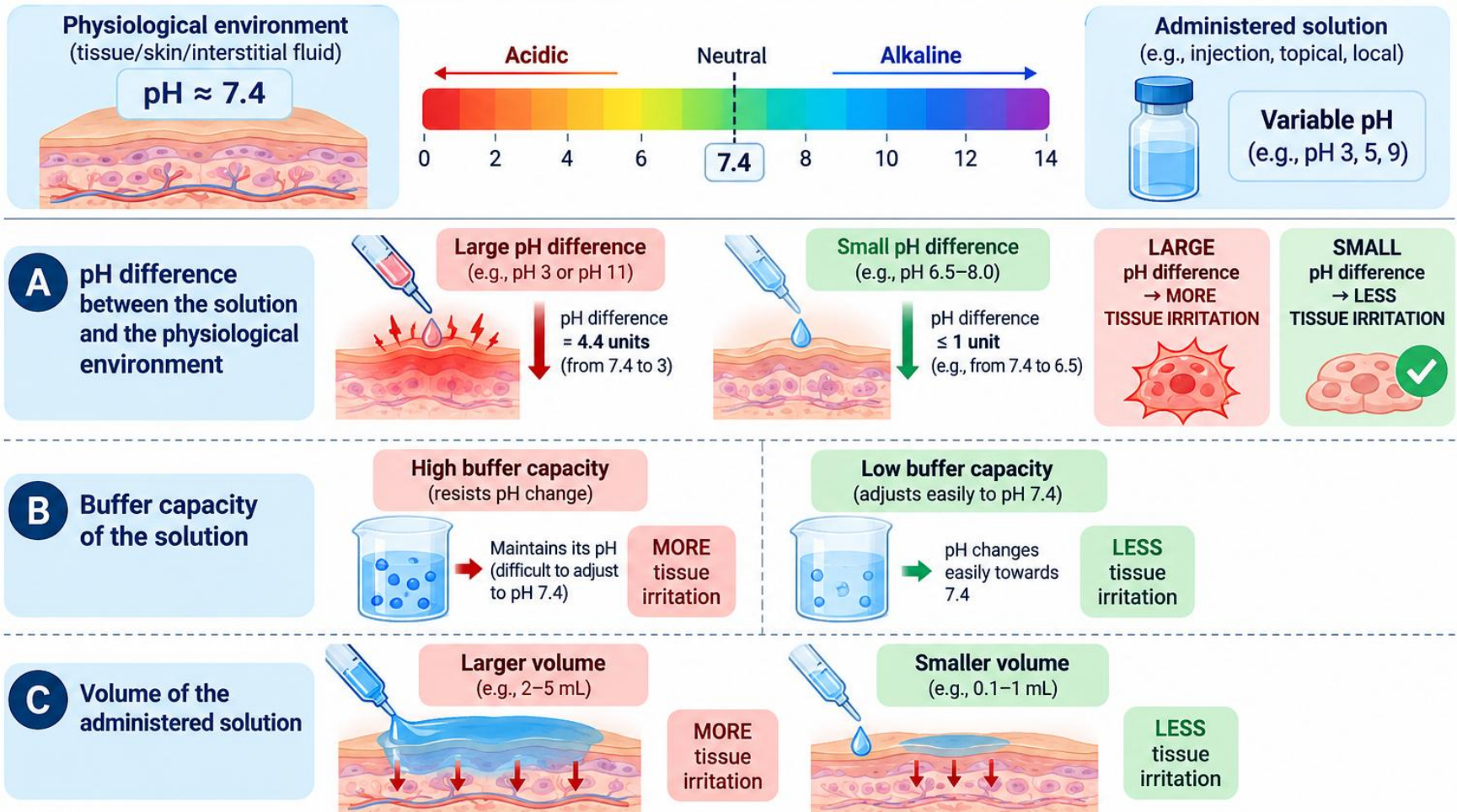
- **Tissue irritation, due to large pH differences between the solution being administered and the physiologic environment in which it is used, will be minimal :**

- A. the lower **is the buffer capacity of the solution,**

- B. the **smaller is the volume** used for a given concentration.

Clarification

Tissue irritation is minimized when the pH difference between the administered solution and the physiological environment is small, when the solution has a lower buffer capacity, and when a smaller volume is used.



- Martin and Mims found that Sørensen's phosphate buffer produced irritation in the eyes of a number of individuals when used outside the narrow pH range of 6.5 to 8, whereas a boric acid solution of pH 5 produced no discomfort in the eyes of the same individuals.
- It can be explained partly in terms of **the low buffer capacity of boric acid as compared with that of the phosphate buffer** and partly to the difference of the physiologic response to various ion species.

Clarification

Phosphate buffer (pH 6.5 – 8)



Irritation
(redness, stinging)

Observed in a number
of individuals

Boric acid solution (pH 5)



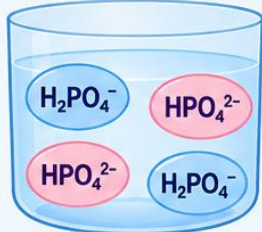
No discomfort
in the eyes

No irritation in the same
individuals

Why does this happen?

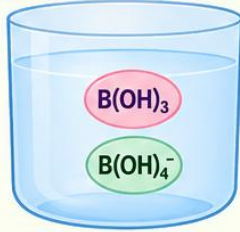
1 Low buffer capacity of boric acid

Phosphate buffer (pH 6.5 – 8)



High buffer capacity
(resists pH change)

Boric acid solution (pH 5)



Low buffer capacity
(easily changes pH)

2 Different physiologic response to ion species

Phosphate ions

At pH 6.5 – 8, higher concentration
of phosphate ions (H_2PO_4^- , HPO_4^{2-})



- Can interact with the ocular surface
- May alter tear film/osmolarity
- May trigger irritation in some individuals

Borate species

At pH 5, mainly non-ionized
boric acid (B(OH)_3) with few ions



- Lower ionic strength
- Less interaction with ocular surface
- Generally well tolerated by most individuals

Therefore, phosphate buffer (pH 6.5 – 8) may cause eye irritation in some individuals, while boric acid solution (pH 5) is usually well tolerated.



THANK

The word 'THANK' is written in a bold, white, sans-serif font on a blue rectangular background. The blue background has rounded corners on the right side. Several thin horizontal lines are present: a black line above the blue bar, a blue line below the blue bar, a black line below the dark grey bar, and a black line below the plus sign.

YOU

The word 'YOU' is written in a bold, white, sans-serif font on a dark grey rectangular background. The dark grey background has rounded corners on the right side.

+