

BUFFERS

Keywords:

buffer *buffer equation* *buffer capacity*

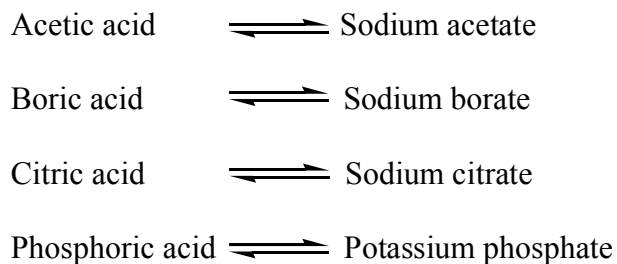
Objective(s):

- Restore understanding of buffer systems and establish importance for use.
- Develop the physicochemical relationship between weak acids and bases and buffer systems.
- Gain confidence in selecting pharmaceutical buffers.
- Define preliminary physiologic buffer systems.

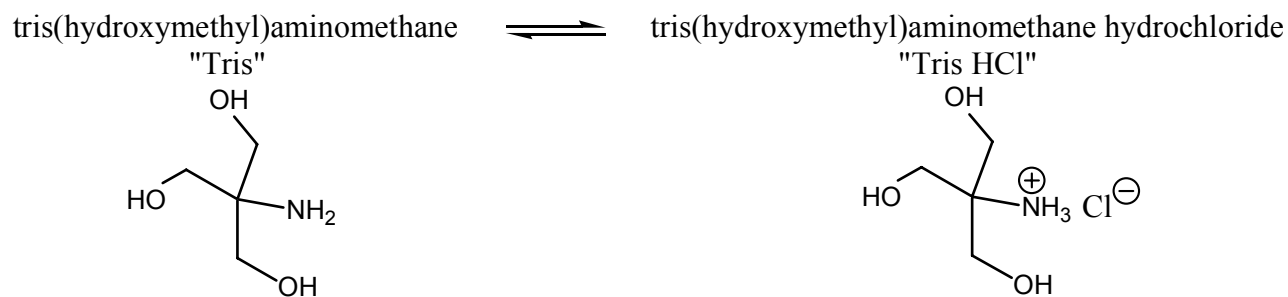
Definitions and descriptions:

Buffer – A buffer is a solution that resists pH changes when acids or bases are added to the solution. Most buffer solutions consist of a weak acid and its conjugate base (salt of the weak acid).

Examples of Weak Acid Buffer Systems.



Examples of Weak Acid Buffer System.



The pH of some ‘well known’ liquids containing buffer systems:

<u>Product</u>	<u>pH (room temp)</u>
Apple juice	3.7
Club Soda (Schwepps)	5.1
Coffee (instant)	4.7
Diphenhydramine	5.0
Distilled Vinegar	2.6
Gatorade	3.0
Ipecac	1.7
Listerine	3.9
Pepsi	2.6
Robitussin DM	2.5
Saline USP	6.8
Visine	6.3

Buffer Properties and Function:

When acids or bases are added to pure water, they immediately produce H_3O^+ or OH^- ions that decrease or increase the pH, respectively. Buffer systems resist large pH changes because added acids or bases are neutralized by the existing HA/A⁻ system (equilibrium).

Added acids are neutralized by the conjugate base (A⁻) which is converted to the acid (HA). Added bases are neutralized by the acid (HA), which is converted to the conjugate base (A⁻). Addition of acids or bases therefore change the HA/A⁻ ratio. However.....

- we know that from the Henderson-Hasselbalch (buffer) equation, changes in the HA/A⁻ ratio will also change the pH. However, the pH change is related to the *log* of the change in the HA/A⁻ ratio. Therefore, the pH change is relatively small.

Also, the assumption here is that the concentration of buffer salts exceeds that of the acid being introduced to the solution and therefore, there is a large number of “solvation ions” (halleluiah) to handle.

The Buffer Equation(s): The buffer equation is the Henderson-Hasselbalch equation adapted to consider acids and their conjugate bases leading to solutions that are resistant to pH change. The buffer equation can be used to calculate:

- the pH of a buffer solution when the HA/A⁻ ratio is known.
- the HA/A⁻ ratio required to give a buffer of a given pH.
- the pH change which results from the addition of an acid or base to a buffer solution

In most cases, you will need to know the pK_a of the weak acid to conduct these calculations.

The following forms of the buffer equation are useful for buffer calculations:

$$\text{pH} = \text{pK}_a + \log \text{B/A} \quad (\text{useful to calculate the pH of the buffer solution})$$

$$\text{pH} - \text{pK}_a = \log \text{B/A} \quad (\text{useful to calculate the ratio of base to acid})$$

$$\text{pK}_a = \text{pH} + \log \text{A/B} \quad (\text{useful to calculate the pK}_a \text{ of a buffer at a known pH})$$

$$\text{pK}_a - \text{pH} = \log \text{A/B} \quad (\text{useful to calculate the ratio of acid to base})$$

Question: Calculate the pH of a buffer solution prepared by dissolving 242 mg of Tris in 10 mL of 0.170 M HCl and diluting to 100 mL with water. [Tris: mw 121 g/mol and pK_a = 8.08 for the conjugate acid]

Buffer Capacity: The ability of a buffer system to resist pH changes is its buffer capacity and indicated by the buffer index (β):

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

where: B = strong base (in molarity) Δ = change (delta)

Buffer capacity is defined as the number of equivalents of strong base (ΔB) required to cause a one-unit change in pH (ΔpH) in 1 L of solution. The greater the buffer capacity, the smaller the change in pH from addition of a given amount of strong acid or base. Buffer capacity is dependent on the total concentration of the buffer system and on the HA/A⁻ ratio. The buffer index number is generally experimentally derived in a manner like a titration (see Table below). For example, when 0.03 moles of NaOH was added to an acetate buffer system prepared at 0.1 M, the pH expectedly increased from 4.76 to 5.03; a change of 0.27 pH units. Therefore, the equation $\beta = \delta\text{B}/\Delta\text{pH} = 0.03/0.27 = 1/9 = 0.11$

Note that the buffer capacity is highest when the smallest number of moles of NaOH are added. Also, the buffer equation can be adapted for the addition of acids, except the pH would decrease in these experiments.

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

Buffer capacity is maximal when $\text{pH} = \text{pK}_a$ and is acceptable in the range $\text{pH} = \text{pK}_a \pm 1$

Buffer capacity is increased by the following factors:

- increasing the concentration of the buffer system components (e.g. doubling the total molar concentration of the buffer system will double the buffer capacity at a given pH).
- using equimolar concentrations of the acid (HA) and its conjugate base (A^-). Buffer capacity is maximal when $\text{pH} = \text{pK}_a$ ($[\text{HA}] = [\text{A}^-]$).

Why use buffers in pharmacy?

Solubility - The *ionized* form of a drug is more water soluble than the *unionized* form. Buffers can be used to maintain a drug in its *ionized* (salt) form for aqueous solutions.

Absorption - The *unionized* form of a drug is more lipid soluble than the *ionized* form. The *unionized* form therefore penetrates biological membranes much more efficiently than the *ionized* form. buffers can also be used to maintain the drug in its *unionized* form.

Stability - pH can affect the stability of a drug in an aqueous solution. For example, ester drugs are very susceptible to hydrolytic reactions. Buffering formulations at low pH (pH 3-5) can reduce the rate of hydrolysis.

Tissue irritation - High or low pH can cause tissue irritation. Buffering a formulation to near neutral pH can reduce tissue irritation. Ophthalmic products are least irritating at pH 7-9.

Buffers and the Body:

Body fluids contain buffering agents and buffer systems that maintain pH at or near pH=7.4. Important endogenous (natural) buffer systems include carbonic acid/sodium bicarbonate and sodium phosphate in the plasma and hemoglobin, and potassium phosphate in the cells. An *in vivo* value of pH < 6.9 or pH > 7.8 can be life threatening.

Pharmaceutical solutions generally have a low buffer capacity in order to prevent overwhelming the bodies own buffer systems and significantly changing the pH of the body fluids. Buffer concentrations of between 0.05 and 0.5 M and buffer capacities between 0.01 to 0.1 are usually sufficient for pharmaceutical solutions.

Choosing the Right Pharmaceutical Buffer :

- Choose a weak acid with $\text{pH} \gg \text{pK}_a$.
- Use buffer equation to calculate ratio of acid/base needed to give required pH.
- Choose concentration needed to give suitable buffer capacity.
- Choose available ingredients considering sterility, stability, cost, toxicity.
- Use pH meter or, at least, pH indicator paper.

PHARMACEUTICAL BUFFER EXAMPLES

The following are some buffer systems that are used in the formulation of pharmaceuticals. Most pharmaceutical buffers are composed of ingredients that are found in the body (e.g. acetate, phosphate, citrate):

<u>Buffer System</u>	<u>pKa</u>	<u>buffer pH range</u>
Acetic acid/sodium acetate	4.76	3.8 to 5.6
Phosphoric acid/sodium phosphate		
H ₃ PO ₄ /NaH ₂ PO ₄	2.1(pK ₁)	
NaH ₂ PO ₄ /Na ₂ HPO ₄	7.2(pK ₂)	5 to 8
Na ₂ HPO ₄ /Na ₃ PO ₄	12.3(pK ₃)	
Citric acid/sodium citrate		
	3.1(pK ₁)	
	4.8(pK ₂)	1.2 to 6.6
	9.2(pK ₃)	
Boric acid/sodium borate	9.2	7.8-10.6

Coming up next.....

BONDING AND SOLUBILITY

PARTITION COEFFICIENTS

DISSOLUTION