LECTURE 3:
Buffer & Buffer Capacity

Mohamed Akl

Assistant Prof. of Pharmaceutics

Buffer

- **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.
- **buffer action is** the resistance to a change in pH

Necessity of a buffer system

- Sometimes it is necessary that a solution of a definite pH be prepared and stored.
- The preservation of such a solution is even more difficult than its preparation.
  - If solution comes in contact with air, → it will absorb CO_2 and becomes acidic.
  - On the other hand, if solution is stored in a glass bottle, alkaline impurities from the glass may alter its pH.
- Due to these reasons, pharmaceutical solutions are buffered as the buffer solutions can maintain pH at some constant value when even small amounts of acid or base are added.

Types of Buffer solutions

- Generally, buffers are of two types;
  - Acidic buffers
  - Basic buffers

Acidic Buffers:

- It is a combination of weak acid and its salt with a strong base. i.e., Weak acid & salt with strong base (conjugate base).

Examples:

CH_3COOH / CH_3COONa

H2CO_3 / $NaHCO_3$

H3PO_4 / NaH_2PO_4

HCOOH / HCOONa

Basic Buffers:

- It is a combination of weak base and its salt with a strong acid. i.e. Weak base & salt with strong acid (conjugate acid).

Examples:

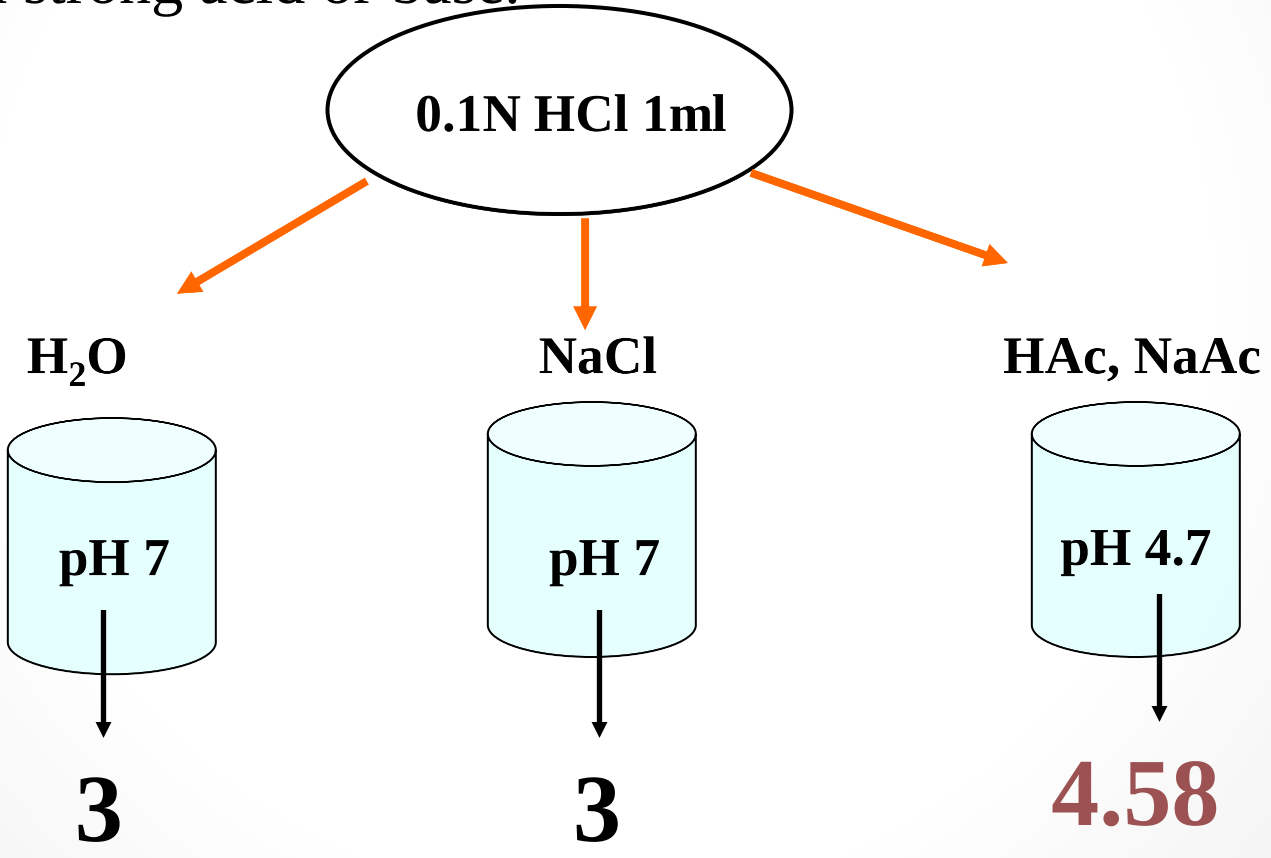
NH_4OH / NH_4Cl

NH_3 / NH_4Cl

NH_3 / (NH_4)2CO_3

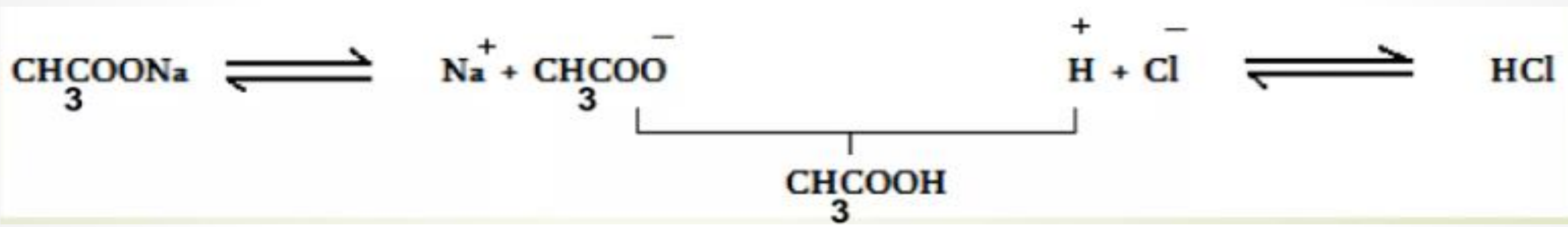
buffer Solution

buffer solution: is a system, usually an aqueous solution, that possesses the property of resisting changes in pH with the addition of small amounts of a strong acid or base.



How buffer Work?

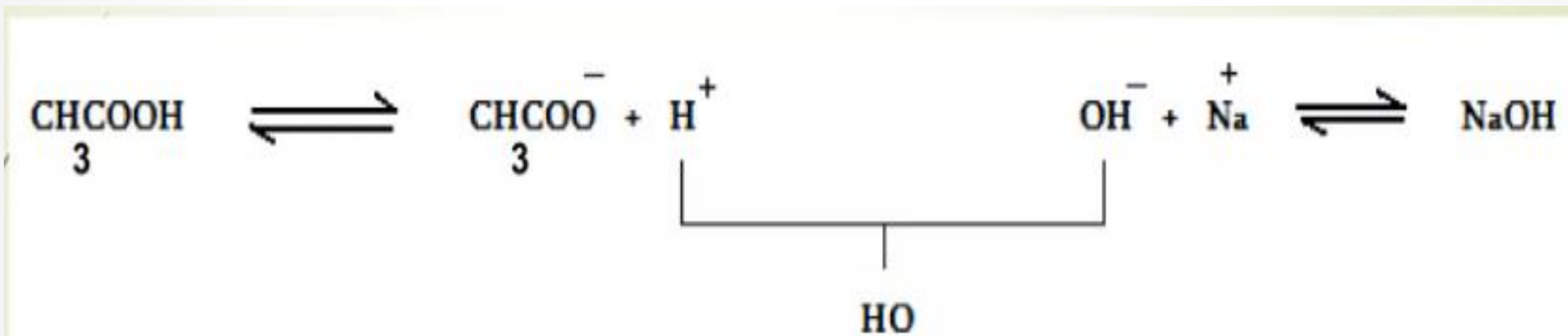
- If the strong acid is added to a 0.01 M solution containing equal quantities of acetic acid and sodium acetate, → the pH is changed only 0.09 pH units because the base Ac- ties تستوعب up the hydrogen ions according to the reaction.



- The hydrogen ions yielded by the Hcl are quickly removed as unionized acetic acid, and the hydrogen ion concentration is therefore only slightly affected (because acetic acid produced is very weak as compared to Hcl added).

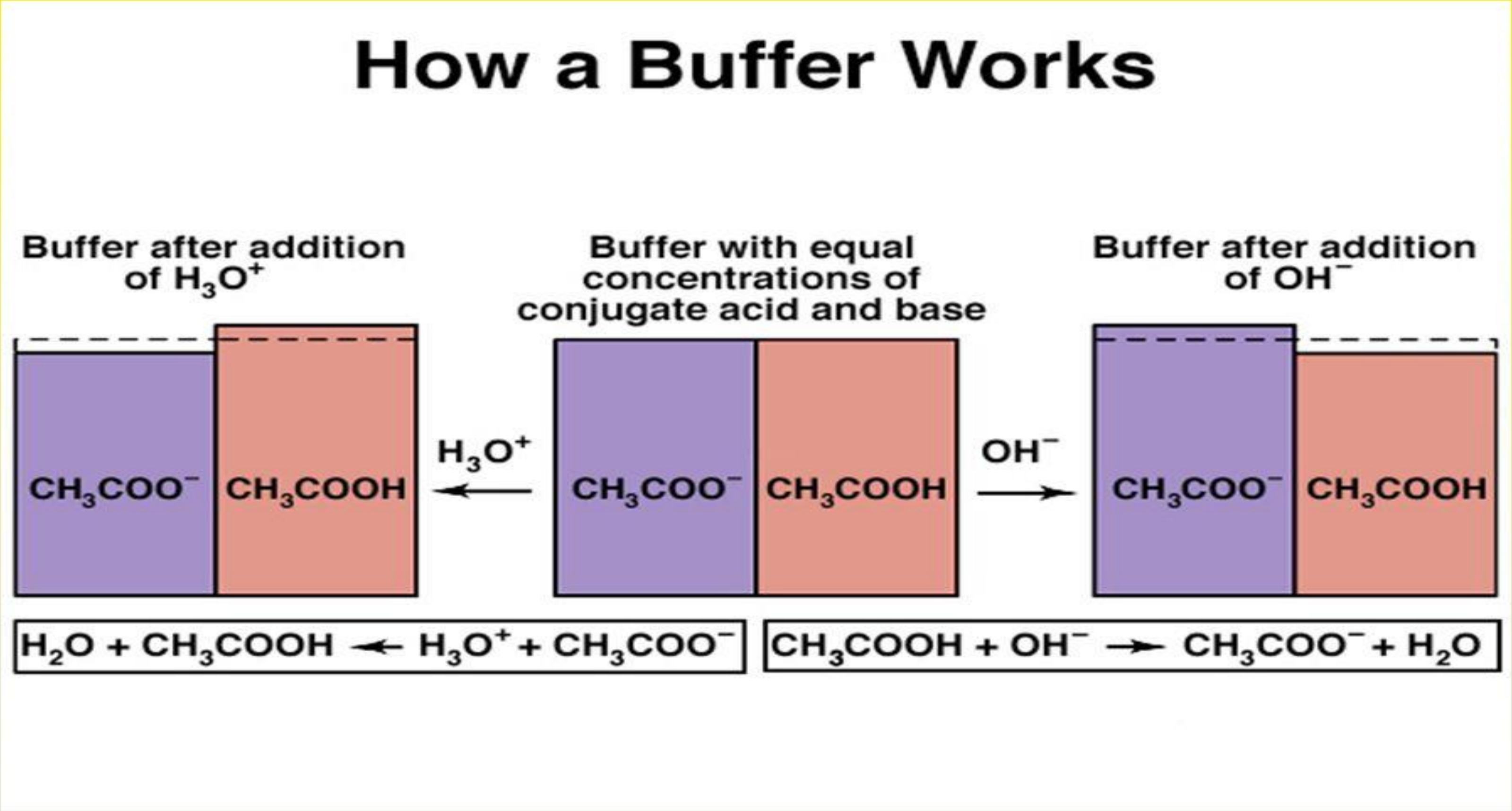
How buffer Work?

- If a strong base, sodium hydroxide, is added to the buffer mixture, → acetic acid neutralizes the hydroxyl ions and removed as water as follows:



- The supply of hydrogen ions needed for this purpose being constantly provided by the dissociation of acetic acid.

How buffer Work?



Buffer Equations

- pH = - log [H^+] , [H^+] $= 10^{-pH}$
- pOH = - log [OH^-] , [OH^-] $= 10^{-pOH}$
- pK_a = - log K_a , K_a $= 10^{-p\,Ka}$
- Acid buffer equation $$pH = pK_a + \log \frac{salt}{acid}$$
- Basic buffer equation : $$pH = pK_w - pK_b + \log \frac{base}{salt}$$
- Buffer capacity $$\beta = 2.303\ C \frac{K_a.[H^+]}{(K_a + [H^+])^2}$$
- Maximum buffer capacity $$\beta_{max} = 0.576 \bullet C$$

Buffer Equations

A Weak Acid and Its Salt

- the pH of acid buffer can be calculated from the dissociation constant, (K_a) of the weak acid and the concentrations of the acid and salt used
- $HAC \leftrightarrow H^+ + AC^-$

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

$[Ac^-]$ → salt

$[HAc]$ → acid

$$-\log[H^+] = -\log Ka - \log[acid] + \log[salt]$$

$$pH = pka + \log \frac{Salt}{acid}$$

pka → Dissociation exponent

The boxed equation → Buffer equation or Henderson-Hasselbalch equation

Common ion effect

– *** When Sod. acetate is added to acetic acid…** → the dissociation constant for the weak acid ***K_a*, is momentarily disturbed since the acetate ion supplied by the salt increases the [Ac^-] in the numerator.**

– In order to reestablish the constant K_a, the hydrogen ion term in the numerator [H^+] is instantaneously decreased, with a corresponding increase in [HAc]. → K_a remains unaltered, → the equilibrium is shifted in the direction of the reactants

$$K_a = \frac{\downarrow[H^+]\ [Ac^-]\uparrow}{\uparrow[HAc]}$$

$$HAc + H_2O \rightleftharpoons H_3O^+ + Ac^-$$

○ <u>The ionization of HAc is repressed</u> **قمع upon the addition of the common ion [Ac^-]**

Buffer Equations

• A Weak base and Its Salt

$$pH = pKw - pKb + log\ \frac{base}{salt}$$

- * **Buffers are not ordinarily prepared from weak bases because of the volatility & instability of the bases and because of the dependence of their pH on pK_w, which is often affected by temp. changes.**

Buffer Equations

Example 1: What is the pH of a buffer solution prepared with 0.05 M sodium borate and 0.005 M boric acid? The pKa value of boric acid is 9.24 at 25C.

Answer

$$pH = pka + log\frac{Salt}{acid}$$

$$pH = 9.24 + log\frac{0.05}{0.005}$$ pH = 10.24

Example 2: What is the pH of a buffer solution prepared with 0.05 M ammonia and 0.05 M ammonium chloride? The Kb value of ammonia is 1.80×10^{-5} at 25C.

$$pH = pKw - pKb + log\frac{base}{salt}$$

Buffer Equations

Prepare a buffer solution of pH 5 from acetic acid CH3COOH & CH3COONa. pka of CH3COOH is 4.7. Required pH = 5 pka = 4.7 Molar concentration of acid required = 1M, Molar concentration of base required = x M = ?

Answer

So, by putting above information in equation, we get:

- pH = pka + log[Salt] / [Acid]
- 5 = 4.7 + log [x] / [1]
- 5 – 4.7 = log x – log 1
- as log 1 = 0, □ 0.3 = log x
- x = log- 0.3 (log- means anti-log)
- x = 2
- Result → in order to prepare buffer solution of pH 5, acetic acid CH3COOH & sodium acetate CH3COO must be mixed in a ratio of 1M : 2M

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

Answer

$$pH = pka + log\frac{Salt}{acid} \qquad 5 = 4.76 + log\frac{Salt}{acid}$$

$$log\frac{Salt}{acid} = 5 - 4.76 \qquad log\frac{Salt}{acid} = 0.24$$

$$\frac{Salt}{acid} = \text{anti log } 0.24 = 1.74$$

- 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%.

Change in pH with Addition of an Acid or Base

*Calculate the change in pH after adding 0.04 mol of sodium hydroxide to a liter of a buffer solution containing 0.2 M concentrations of sodium acetate and acetic acid. The pK*a *value of acetic acid is 4.76 at 25C.*

Answer

$$pH = 4.76 + \log \frac{0.2}{0.2}, \quad pH = 4.76 + 0 = 4.76$$

- The addition of 0.04 mol of sodium hydroxide converts 0.04 mol of acetic acid to 0.04 mol of sodium acetate. Consequently, the concentration of acetic acid is decreased, and the concentration of sodium acetate is increased by equal amounts, according to the following equatio

$$pH = 4.76 + \log \frac{salt + base}{acid - base}$$

$$pH = 4.76 + \log \frac{0.2 + 0.04}{0.2 - 0.04}$$

$$pH = 4.936$$

- Because the pH before the addition of the sodium hydroxide was 4.76, the change in pH 4.94 4.76 0.18 unit,

Quantity of Components in a Buffer Solution to Yield a Specific Volume

The molar ratio of sodium acetate to acetic acid in a buffer solution with a pH of 5.76 is 10:1. Assuming the total buffer concentration is 2.2×10^{-2} mol/L, how many grams of sodium acetate (m.w. 82) and how many grams of acetic acid (m.w. 60) should be used in preparing a liter of the solution?

Answer

- Because the molar ratio of sodium acetate to acetic acid is 10:1
- the mole fraction of sodium acetate = $\frac{10}{1+10} = \frac{10}{11} = 0.909$
- the mole fraction of acetic acid = $\frac{1}{10+1} = \frac{1}{11}$
- If the total buffer concentration 2.2×10^{2} mol/L,
- the concentration of sodium acetate = 2.2×10^{-2} mol/L $\times$ 0.909 = 0.0199
- and the concentration of acetic acid = 2.2×10^{-2} mol/L $\times$ 0.0909 = 0.00199
- sodium acetate = 0.0199 × 82 = 1.64 g per liter of solution,
- acetic acid = 60 × 0.00199= 0.120 g of per liter of solution

Buffer capacity

- **...the magnitude of the resistance of a buffer to pH changes on an addition of an acid or a base**

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

the small increment in (g. equivalents/ Liter) of strong base (or acid)

buffer capacity
= buffer efficiency
= buffer index
= buffer value

- The ratio of the small increment of strong base (or acid) added to the buffer soln. to the small change in a pH (ΔpH) brought about by this addition

Buffer capacity

$$HAc + NaOH \rightleftharpoons NaAC + H_2O$$

(0.1- 0.01) 0.01 (0.1+ 0.01)

- **Before the addition of NaOH**

$$pH = pKa + \log \frac{[salt]}{[acid]} = 4.76$$

- **After the addition of NaOH**

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

$$\rightarrow \beta = \frac{\Delta B}{\Delta pH} = \frac{0.01}{0.09} = 0.11$$

Maximum Buffer capacity

$$\beta = 2.303\ C\ \frac{K_a.[H^+]}{(K_a+[H^+])^2}$$

- β_{max} **occurs where pH = pK_a, ([H_3O^+] = K_a)**

$$\beta_{max} = 2.303 \cdot C \cdot \frac{[H_3O^+]^2}{(2\,[H_3O^+])^2} = \frac{2.303}{4} \cdot C$$

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

(pH = pK_a)

Maximum Buffer capacity

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 [salt]/[acid] and magnitude of the individual concentrations of the buffer components**
- the smaller the pH change with the addition of a given amount of acid or base, **the greater the buffer capacity of the system**
- **The greatest capacity (βmax) occurs where [salt]/[acid] = 1 and pH = *pKa***
- **Because of interionic effects, buffer capacities do not in general exceed a value of 0.2**

Applications of buffers:

Buffers in Biologic Systems

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

1. **Primary buffers** in the **plasma**:
   - The plasma contains carbonic acid/bicarbonate and acid/alkali sodium salts of phosphoric acid as buffers
2. 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**.

Applications of buffers:

Lacrimal fluid, or tears,

- The pH of tears is about 7.4, with a range of 7 to 8 or slightly higher.
- it has a great degree of buffer capacity, and can tolerate preparations having pH values between 3.5 – 10.5 with little discomfort
- Out side this range (i.e. 3.5 – 10.5), increase lacrimation may occur with other complications

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.

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.**

- 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.

- **pH and solubility**

  * Influence of buffering on the solubility of base

- At a low pH : base is in the ionic form & usually very soluble in aqueous media

- As the pH is raised : more undissociated base is formed when the amount of base exceeds the limited water solubility of this form, free base precipitates from soln.

Base soln. should be buffered at a sufficiently low pH for stabilization against precipitation.

- The pKb of pilocarpine is 7.15 at 25°C. Compute the mole percent of free base present at 25°C and at a pH of 7.4 and 4.

- **Example**

$$C_{11}H_{16}N_2O_2 + H_2O \rightleftharpoons C_{11}H_{16}N_2O_2H^+ + OH^-$$

(Pilocarpine base) **(Pilocarpine ion)**

$$pH = pK_w - pK_b + \log \frac{[base]}{[salt]}$$

At pH 7.4

$$7.4 = 14 - 7.15 + \log \frac{[base]}{[salt]}$$

$$\frac{[base]}{[salt]} = 3.56 / 1$$

Mole percent of base =

3.56 / (1 + 3.56) • 100 =

78%

At pH 4.0

$$4.0 = 14 - 7.15 + \log \frac{[base]}{[salt]}$$

$$\frac{[base]}{[salt]} = 0.0014 / 1$$

Mole percent of base =

0.0014 / (1 + 0.0014) • 100 =

0.13%

Problems

1 . One desires to adjust a solution to pH 8.8 by the use of a boric acid/ sodium borate buffer what approximate ratio of acid and salt is required? pKa = 9.24

- pH =pK$_{\mathbf{a}}$ + log $\frac{salt}{acid}$, 8.88 =9.24 + log $\frac{salt}{acid}$

  log $\frac{salt}{acid} = -0.44$, $\frac{salt}{acid}$ = shift log -0.44 $= \frac{0.363}{1}$

  acid : salt = 1: 0.363

2. What is the buffer capacity of a solution containing 0.2 M acetic acid and 0.1 M sodium acetate ?

pKa = 4.76

- $pH = pK_a + \log \frac{salt}{acid}$, $pH = 4.76 + \log \frac{0.1}{0.2} = 4.45$

$$\beta = 2.303\ C\ \frac{K_a.[H^+]}{(K_a + [H^+])^2}$$

$$\beta = 2.303 \times 0.3\ \frac{10^{-4.76} \times 10^{-4.45}}{(10^{-4.76} + 10^{-4.45})^2} = 0.15$$

3. What is the pH of a solution containing 0.1 mole of ephedrine and 0.01 mole of ephedrine hydrochloride per liter of solution?

$pK_b = 4.64$

- $pH = pK_w - pK_b + \log \frac{base}{salt}$

  $pH = 14 - 4.64 + \log \frac{0.1}{0.01}$

  $= 10.36$

4. prepare a buffer soln. with capacity of 0.02 (pH = 5 , pK_a = 4.76)

Answer

(How much salt and acid)

$\beta = 2.303\ C \frac{K_a.[H^+]}{(K_a+[H^+])^2}$

$0.02 = 2.303\ C \frac{10^{-4.76} \times 10^{-5}}{(10^{-4.76}+10^{-5})^2}$

C = 0.0375 = salt + acid

pH = pKa + log $\frac{salt}{acid}$

$5 = 4.76 + \log \frac{salt}{acid}$

$\frac{salt}{acid}$ = 1.737 , salt = 1.737 acid , 1.737 acid + acid = 0.0375

acid = 0.0137

salt = 0.0375 – 0.0137 = 0.0237

Questions ?