

## Acids, Bases and Buffers

In Earlier, Acid may be defined as any substance which has a sour taste and its aqueous solution turns blue litmus to red colour.

A base may be defined as any substance which has a bitter taste and its aqueous solution turns red litmus to blue colour.

But these could not be explained the behavior of all acids or bases.

In chemistry, acids and bases have been defined differently by three sets of theories.

### **Theories of acid and base**

#### **1. Arrhenius theory**

According to this theory an acid is a substance which dissociates to give hydrogen ions in water.

Base is a substance which dissociates to give hydroxide ions in water

Eg. Sodium hydroxide in water produces hydroxide ion



### **Limitations**

1. The definition of acid or bases are only in terms of aqueous solutions and not in terms of substance.
2. This theory is not able to explain acidic or basic in non aqueous solvents. For Ex Ammonium nitrate in liquid ammonia acts as an acid, but it does not give  $\text{H}^+$  ions.
3. This theory is not able to explain for the basic substances which does not contain  $\text{OH}^-$  ions, For Ex, Ammonia is a basic.
4. It cannot be explain acidic character of salts like  $\text{AlCl}_3$  in aqueous solutions.
5. The neutralization of acid and base in absence of solvent could not be explained.

#### **2. Bronsted and lowry theory (Proton concept)**

According to this theory, Acids are substances which is capable to donate protons  $\text{H}^+$  to any other substances. They are also called as proton donors.

For Ex



Bases are substances which can accept protons  $\text{H}^+$  from any other substances. They are also called as proton acceptors.

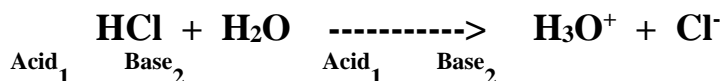
For Ex



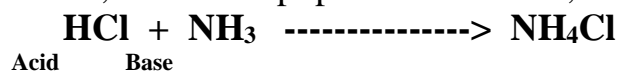


### Conjugate acid-base pair

Let us consider a reaction

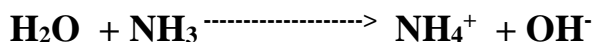


In this reaction HCl donates proton to water, therefore it is an acid. On the otherhand, water accept proton from HCl, and therefore it is a base.



Here HCl donates a proton and ammonia accepts this proton and forms ammonium chloride. So HCl is an acid and ammonia is a base. The acid-base pairs, the members of which can be formed each other mutually by gain or loss of protons are called conjugate acid-base pairs.

Water is having dual character because it can accept or donate protons.



### Limitations

1. This theory is not able to explain about the acids which do not contain proton.
2. In large no. of acid-base reactions, proton transfer is not taking place.

### 3. Lewis theory (Electron concept)

According to this theory, acids are chemical substances which accept a lone pair of electrons and are called electron acceptors. Bases are substances which donate a lone pair of electrons in solution and are called electron donors. So the process of neutralization is simply the formation of a co ordinate bond between acid and base. Eg. Combination of boron trifluoride and ammonia

In the above reaction boron trifluoride accepts the lone pair of electron donated by ammonia. So BF<sub>3</sub> is an acid and NH<sub>3</sub> is a base. They behave as acid only when a base is available to accept proton or donate electron and similarly bases

### Limitations

1. According to this theory, the strength of Lewis acids and bases is depend upon the type of reaction, it is not possible to arrange them in any order of their relative strength.
2. As Lewis acid - base reaction involves electrons, they are expected to be fast reactions, but many reactions are slow.

### Relative strength of Acids and Bases

The relative strength of an acid or base is based on the efficiency of donating or accepting protons. These properties of a substances will be affected by the environment, an acid can donate proton easily in proton accepting medium. With respect to strength there are two classes, strong and weak. Strong acids and bases are dissociate completely in aqueous media, But weak acids and bases do not dissociate completely. The relative strength of an acid or base is determined by dissociation constant K.

The dissociation constant K can be calculated by using the following formula

$$K = \frac{[\text{Concentration of products}]}{[\text{Concentration of reactants}]} \quad \text{or} \quad \frac{[\text{Concentration of ionized}]}{[\text{Concentration of unionized}]}$$

For example

HCl is a strong acid, which dissociates completely in water



The dissociation constant  $K_a = \frac{[\text{H}^+][\text{Cl}^-]}{[\text{HA}]}$

The concentration of water is not consider, because of large quantity was used. Similarly, ammonia is a base

The dissociation constant or strength of acid or base K is usually expressed in log. **pKa** is the *negative log of the equilibrium constant*

$\text{pK}_a = -\log K_a$	the negative log of the equilibrium constant for acids
$\text{pK}_b = -\log K_b$	the negative log of the equilibrium constant for bases
$\text{pK}_w = -\log K_w$	the negative log of the equilibrium constant for water

- ☐ Strong acids have a large  $K_a$ , indicating that there are more products than reactants, larger  $K_a$ , stronger acid, larger  $\text{pK}_a$ , weaker acid,

- larger  $K_b$ , stronger base, larger  $\text{pK}_b$ , weaker base

☐ Examples,

$\text{pK}_a$  value for weak acids

## The pH scale

We use the pH scale to describe how many hydrogen ions are dissolved in a solution. The pH comes from the negative log of the hydrogen ion concentration.

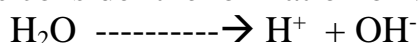
$$\text{pH} = -\log [\text{H}^+]$$

The term, p, means we have taken the negative log of something.

Similarly

$$\text{pOH} = -\log [\text{OH}^-] \quad \text{the negative log of the hydroxide ion concentration}$$

Let us consider the ionization of water



$$K = \frac{[\text{H}^+][\text{OH}^-]}{[\text{H}_2\text{O}]}$$

But the concentration of water is constant, because, in large quantity, only one molecule is dissociated.

$$K [\text{H}_2\text{O}] = [\text{H}^+][\text{OH}^-]$$

$$K_w = [\text{H}^+][\text{OH}^-] \quad \text{where } K_w \text{ is ionic product of water and its value is } 1 \times 10^{-14}$$

Take the log of both sides. Remember when you have stuff multiplied together, when you take the log, you add them.

$$\text{so } \log K_w = \log [\text{H}^+] + \log [\text{OH}^-]$$

Now multiply by -1 through the entire equation to get:

$$-\log K_w = -\log [\text{H}^+] - \log [\text{OH}^-] \quad \text{or } \text{p}K_w = \text{pH} + \text{pOH}$$

$$-\log 10^{-14} = -\log [\text{H}^+] - \log [\text{OH}^-]$$

$$14 = \text{pH} + \text{pOH}$$

So for water  $\text{pH} = 7$ , ie neutral pH.

The pH scale is from 0 to 14. The pH value is less than 7 for acid and more than 7 for base. How strong an acid is labeled as pH. The lower the pH, the stronger the acid.

## **Buffers**

A **buffer** solution is any solution that maintains an approximately constant pH in small additions of acid and base. The buffer solution consists of mixture of weak acids or bases with its salts.

### **Types of buffer solutions**

1) **Acidic buffer:** It consists of a weak acid and its conjugate base or salt. It buffers on the acidic side of neutral.

Example, Acetic acid and sodium acetate

2) **Basic buffer:** consists of a weak base and its conjugate acid or salt. It buffers on the basic side of neutral.

Example, Ammonium hydroxide and Ammonium chloride

### Properties of buffer solutions

- The pH of buffer solution remains constant.
- The pH of buffer solution does not change on dilution
- The pH does not change after addition of small quantity of acid or base
- The pH of buffer solution does not change on keeping for long time.

### Buffer actions

The resistance to **change in pH** possessed by buffer is called buffer action

#### Acid buffer action:

Let us consider Acidic buffer which is prepared by mixing acetic acid and sodium acetate in water.

**Acetic acid** is a weak acid and ionized to **acetate** ion and **hydrogen** ion to some extent only.

**Sodium acetate** is a strong electrolyte, so fully dissociated to **acetate** ion and **sodium ion**

Therefore the buffer mixture contains less amount of **hydrogen** ion and more amount of **acetate** ion.

If a little amount of **strong acid** is added to the buffer mixture the **hydrogen ion** from **strong acid**, will be attracted by **acetate ion**, and feebly ignitable **acetic acid** is formed, the acidity does not change much.

If a little amount of **strong alkali** is added to the buffer mixture, the **hydroxide ion** from alkali is neutralized by hydrogen ion of acetic acid. Therefore the **alkalinity** does not change much.

It is possible to calculate the pH of acidic buffer by Henderson-Hasselbalch equation

Let us consider the dissociation on an acid



$$K_a = \frac{[\text{H}^+][\text{A}^-]}{[\text{HA}]}$$

when expressed in logarithmic form we get:

$$\log K_a = \log [\text{H}^+] + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

multiplying both sides by -1:

$$-\log K_a = -\log [H^+] - \log \frac{[A^-]}{[HA]}$$

Consider  $pK_a = -\log K_a$ .  $pH = -\log [H^+]$

$$pK_a = pH - \log \frac{[A^-]}{[HA]}$$

multiplying by -1 through the entire equation to get rid of the - signs we get:

$$-pK_a = -pH + \log \frac{[A^-]}{[HA]}$$

Rearranging the above equation

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

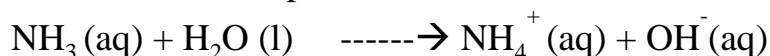
$$pH = pK_a + \log \frac{[\text{Conjugate base}]}{[\text{Acid}]}$$

Or

### Base buffer action:

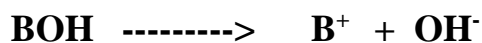
Similarly Let us consider basic buffer which is prepared by mixing ammonia and ammonium chloride in water.

Base Buffer Example:



When strong acid is added,  $NH_3$  accepts protons from incoming acid to make  $NH_4^+$ . When strong base is added,  $NH_4^+$  donates a proton to form  $NH_3$  and  $H_2O$ . pH remains the same.

It is possible to calculate the pH of acidic buffer by Henderson-Hasselbalch equation  
Let us consider the dissociation of an acid



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

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

when expressed in logarithmic form we get:

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

multiplying both sides by -1:

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

$$\text{pOH} = \text{pK}_b + \log \frac{[\text{B}^+]}{[\text{BOH}]}$$

Hence  $\text{pH} + \text{pOH} = 14$

So  $\text{pH} = 14 - \text{pOH}$

$$\text{pH} = 14 - \left( \text{pK}_b - \log \frac{[\text{B}^+]}{[\text{BOH}]} \right)$$

$$\text{pH} = 14 - \left( \text{pK}_b + \log \frac{[\text{Conjugate acid}]}{[\text{Base}]} \right)$$

### Buffer capacity( $\beta$ )

It is the effectiveness of buffer in quantity basis. It is defined as the amount of **strong acid or strong base** that must be added to the buffer to produce unit change of pH.

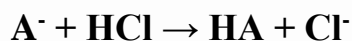
Hence  $\beta = d[B] / dpH$ .

Since, the addition of base increase the pH and addition of acid decrease the pH. The value of  $\beta$  depends on the nature of buffer and the pH, which is determined by the relative concentrations of the acid and its conjugate base. The buffer functions are best around pKa value.

$\text{pH} = \text{pK}_a$ , when  $[\text{HA}] = [\text{A}^-]$  and there are equal amount of acid and its conjugate base.

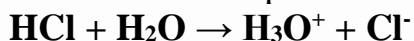
For Example

In a buffer, the more  $\text{A}^-$  and HA molecules available, after the addition of a strong acid or base will have on the pH of a system. Consider the addition of a strong acid such as HCl. Initially, the HCl donates its proton to the weak base ( $\text{A}^-$ ) through the reaction



This changes the pH by lowering the ratio  $[\text{A}^-]/[\text{HA}]$ , but as long as there is still a lot of  $\text{A}^-$  present, the change in pH will be small. But if we keep adding HCl, the weak base  $\text{A}^-$  will eventually run out.

HCl will donate its proton to water



Once the  $\text{A}^-$  is gone, any additional

This will dramatically increase the concentration  $[H^+]$  and so the pH drops.

Example

## **InVivo biologic buffer systems**

### **•Blood**

Primary buffers – Plasma

$NaHCO_3$ -- $H_2CO_3$ ,  $NaHPO_4$ -- $NaH_2PO_4$ , protein

Secondary buffers :Erythrocytes;

hemoglobin-oxyhemoglobin,  $2HPO_4$ - $KH_2PO_4$

### **•Lacriminalfluid**

-pH: 7.4 (range 7 –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.

## **Buffers in Pharmaceutical systems**

In pharmaceutical formulations, lot of buffers are used because

- ❖ Some compounds are soluble in particular pH, For ex, inorganic salts of Ferric ion, phosphates, borates are soluble in acidic media.
- ❖ The **pH of blood** is maintained around 7.4 by carbonic acid and sodium carbonate buffer system and hemoglobin buffer system.
- ❖ It is used in the **assay of enzyme activity** because the enzyme activity is maximum at a particular pH.
- ❖ Used in the **estimation of metallic salts** by complexometric titration with EDTA, as the metal complex is more stable at a particular pH.
- ❖ Certain pharmaceutical **preparations are stabilized** by suitable buffers.  
Eg. **Neutral adrenaline** eye drops stabilized by borate buffer
- ❖ **Penicillin preparations** are buffered with sodium citrate, calcium carbonate and aluminum hydroxide
- ❖ The colour of the natural dyes are maintained only on particular pH, For ex, Red colour of cherry and rasbery syrups has been maintained at acidic pH.
- ❖ Some liquid preparations was stable only on particular pH range, For ex, Ascarbic acid and penicillin are stable in acidic pH. Adrenaline injection is most stable in pH 2.5 – 5.
- ❖ Optimum pH conditions for activity of medicinal compounds are maintained. For ex, the germicidal activity of sodium hypochlorite is increased at lowering pH.
- ❖ Buffers of known pH are used as a standard in analytical lab.

### Official buffers

The buffer solution recommended by pharmacopoeia are called official buffers.

Examples,

1. **Hydrochloric acid buffer** – 0.2M KCl and 0.2M HCl (pH = 5.8 to 8.0)
2. **Phthalate buffer** - 0.2M Pot. Hydrogen phthalate and 0.2M NaOH (pH = 4.2 to 5.8)
3. **Phosphate buffer** - 0.2M pot. dihydrogen phosphate and 0.2M NaOH (pH = 5.8 to 8.0)
4. **Alkaline borate buffer**- 0.2M Boric acid, 0.2M KCl and 0.2M NaOH (pH = 8 to 10)
5. **Acetate buffer** - Ammonium acetate or Sodium acetate and acetic acid (pH = 2.8 to 5.0)

### Isotonic solution

- ❖ It is a solution which has colligative properties similar to those of body fluids. Isotonic is biological compatibility.
- ❖ An isotonic solution refers to two solutions having the same osmotic pressure across a semi permeable membrane. This state allows for the free movement of water across the membrane without changing the concentration of solutes on either side.
- ❖ They have equal concentrations of solutes and water.
- ❖ Example- Sodium chloride solution 0.9% w/v which has a Freezing point depression  $(\Delta t_f) = -0.52^\circ\text{C}$

### Hypertonic solution

- ❖ In biology, a **hypertonic solution** is one with a higher concentration of solutes outside the cell than inside the cell.
- ❖ When a cell is immersed into a **hypertonic solution**, the tendency is for water to flow out of the cell in order to balance the concentration of the solutes.
- ❖ It has a Freezing point depression  $-0.52^\circ\text{C} < t_f < 0^\circ\text{C}$
- ❖ It produce swelling and bursting of the cells (ex. Hemolysis)

### Hypotonic solution

- ❖ A hypotonic solution is any solution that has a lower osmotic pressure than another solution.
- ❖ In the biological fields, this generally refers to a solution that has less solute and more water than another solution
- ❖ It has a Freezing point depression  $t_f < -0.52^\circ\text{C}$
- ❖ It produce Shrinkage of the living cells

### Some Isotonic Buffer Solutions

### **Preparation of Isotonic Solutions**

Isotonic solution is prepared by the drug solution which have equal concentration of 0.9% w/v of sodium chloride.

### **Freezing Point Depression Method**

Amount of NaCl needed in 100mL of solution =  $[0.9 \times (0.52 - t_f)] / 0.52$

Ex. 100ml of a drug solution , How much NaCl=?  $F_p = -0.18^\circ \text{C}$

Amount of NaCl needed =  $[0.9 \times (0.52 - 0.18)] / 0.52 = 0.59\text{g}$

### **Sodium Chloride Equivalent Method**

This method is based on the calculation of Sodium Chloride Equivalent Values (**E**) and prepare the isotonic solution equivalent to 0.9% w/v concentration.

E value can be calculated by the formula  $E = 17 (\text{Liso} / \text{MW})$

For Ex ,      1 g drug = ? g sodium chloride  
                    E value?      MW=340g/mole      Liso =3.4  
                    E value= $17(3.4/340)=0.17\text{g}$

### **Measurement of tonicity**

- ❖ **Hemolytic method** - Red blood cells are applied in the tonic solution. It liberates oxyhemoglobin in direct proportion to the number of cells hemolyzed.
- ❖ Determine colligative properties like Freezing point lowering  $T_f$ , Osmotic pressure etc. Based on the values when compare with the value of isotonic solution, we can determine the tonicity.

For Isotonic solution  $T_f = 0.52^\circ \text{C}$  (Freezing point lowering)

### **Calculating Tonicity Using Liso values•**

Tonicity can be calculated by the Van'tHoff expression

### **Method of adjusting tonicity and pH**

**Class I...**add Sod. Chloride to lower the freezing point of soln. to  $-0.52^\circ$

1. Cryoscopic method
2. Sodium chloride equivalent method

**Class II...**add Water to form an isotonic soln.

1. White-Vincent method

## 2. Sprowls method

### **Cryoscopic method**

Amount of NaCl needed in 100mL of solution =  $[0.9 \times (0.52 - t_f)] / 0.52$

### **Sodium Chloride Equivalent Method**

This method is based on the calculation of Sodium Chloride Equivalent Values (**E**) and prepare the isotonic solution equivalent to 0.9% w/v concentration.

E value can be calculated by the formula  $E = 17 (\text{Liso} / \text{MW})$

### **White-Vincent Method**

It is based on the following formula

$W_i$  = weight in grams of the  $i^{\text{th}}$  solute in the formulation

$E_i$  = sodium chloride equivalent of the  $i^{\text{th}}$  solute in the formula

$v$  = volume of sodium chloride solution (0.9%) that contains 1g of NaCl (this volume is 111.1 mL)

### **Example**

#### **Sprowls' Method**

The Sprowls' value is the volume of an isotonic solution that can be prepared by the addition of enough water to 0.3 g drug

“0.3g” represents the amount of drug in a fluid ounce of 1% solution (1 fluid ounce = 0.0294L)