Acid and Base

History of Acids and Bases

In the early days of chemistry chemists were organizing physical and chemical properties of substances. They discovered that many substances could be placed in two different property categories:

Substance A

1. Sour taste
2. Reacts with carbonates to make CO_2
3. Reacts with metals to produce H_2

Substance B

1. Bitter taste
2. Reacts with fats to make soaps
3. Do not react with

Arrhenius Theory:

The Swedish chemist *Svante Arrhenius* proposed the first definition of acids and bases.
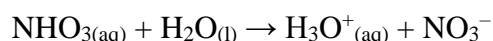
(Substances A and B became known as acids and bases)

According to Arrhenius Concept, Acid are substance which are capable of providing **Hydrogen ions (H+, proton)** when dissolved in water and bases are substances which are capable of providing **hydroxide ions (OH-, hydroxyl ions)** in aqueous solution.

For example, Hydrochloric acid in the water, HCl undergoes dissociation reaction to produce H^+ ion and Cl^- ion, as explained below. The concentration of the H+ ions is increased by forming hydronium ion.
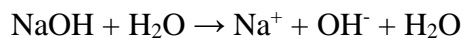
$$HCl_{(aq)} \rightarrow H^+_{(aq)} + Cl^-_{(aq)}$$

$$HCl_{(aq)} + H_2O_{(l)} \rightarrow H_3O^+_{(aq)} + Cl^-_{(aq)}$$
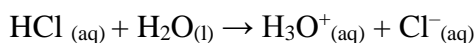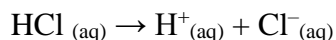
Other examples of Arrhenius acids are listed below

$$NHO_{3(aq)} + H_2O_{(l)} \rightarrow H_3O^+_{(aq)} + NO_3^-$$

In this reaction, nitric acid dissolves in aqueous water to give hydrogen and nitrate ions.

Another example of Arrhenius Base is

$$NaOH + H_2O \rightarrow Na^+ + OH^- + H_2O$$

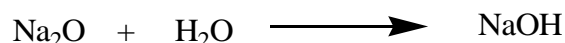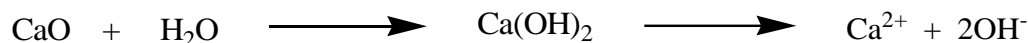**Application:**

1. Non-metallic Oxides   are arrhenius acidic in nature
    eg CO_2, SO_2, SO_3, N_2O_5, P_4O_{10}

$$CO_2 \quad + \quad H_2O \quad \longrightarrow \quad H_2CO_3 \quad \longrightarrow \quad H^+ + HCO_3^-$$

$$SO_3 \quad + \quad H_2O \quad \longrightarrow \quad H_2SO_4 \quad \longrightarrow \quad H^+ + HSO_4^-$$
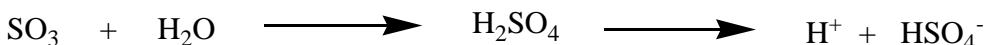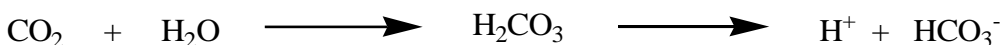
2. metallic Oxides   are arrhenius bases
    eg CaO, Na_2O

$$CaO \quad + \quad H_2O \quad \longrightarrow \quad Ca(OH)_2 \quad \longrightarrow \quad Ca^{2+} + 2OH^-$$

$$Na_2O \quad + \quad H_2O \quad \longrightarrow \quad NaOH$$

Limitations of Arrhenius theory:

- The Arrhenius theory is applicable only in aqueous solution; for example, according to the theory, HCl is an acid in the aqueous solution but not in benzene, even though it donates H^+ ion to the benzene. Also, under Arrhenius's definition, the solution of sodium amide in liquid ammonia is not alkaline, even though amide ion deprotonates the ammonia.

Bronsted -Lowry concept:

According to Bronsted-Lowry theory,

An **acid** is any substance (molecular or ionic) that can **donate a proton** to any other substance (molecular or ionic) and a **base** is any substance that can **accept a proton** from any other substance.

$$HCl \quad + \quad H_2O \quad \longrightarrow \quad H_3O^+ + Cl^-$$
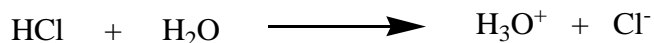
In the above example what is the Brønsted acid? What is the Brønsted base?

In reality, the reaction of HCl with H_2O is an **equilibrium** and occurs in **both directions**, although in this case the equilibrium lies far to the right.

$$\text{HCl} \quad + \quad \text{H}_2\text{O} \quad \rightleftharpoons \quad \text{H}_3\text{O}^+ \quad + \quad \text{Cl}^-$$
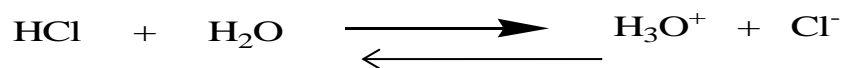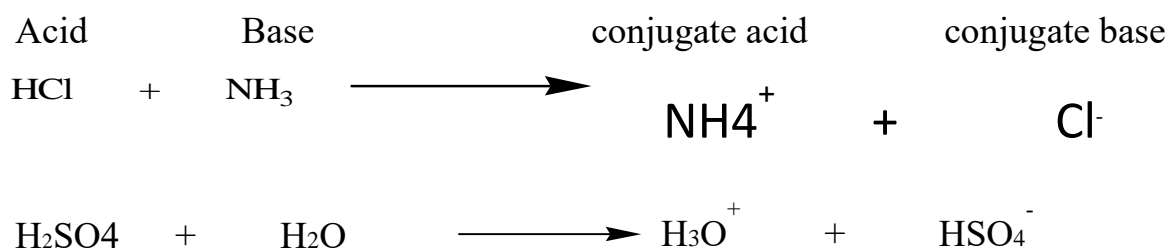
For the **reverse reaction** Cl⁻ behaves as a **Brønsted base** and H_3O^+ behaves as a **Brønsted acid**.

The Cl⁻ is called the **conjugate base** of HCl. **Brønsted** acids and bases always exist as **conjugate acid-base pairs**. Their formulas differ by only one proton.

Acid	Base	conjugate acid	conjugate base

$$\text{HCl} \quad + \quad \text{NH}_3 \quad \longrightarrow \quad \text{NH4}^+ \quad + \quad \text{Cl}^-$$

$$\text{H}_2\text{SO4} \quad + \quad \text{H}_2\text{O} \quad \longrightarrow \quad \text{H}_3\text{O}^+ \quad + \quad \text{HSO}_4^-$$

- ❑ Every Arrhenius Acid is Bronsted Acid
- ❑ Every Arrhenius Base is not Bronsted Base e.g., NaOH is Arrhenius base because it gives OH- ion in aqueous solution but not a Bronsted base because it cannot accept proton.

- ❑ **Limitations of Bronsted Lowry Concept:**
  - The protonic definition cannot be used to explain the reactions occurring in non-protonic solvents such as $COCl_2$, SO_2, N_2O_4, etc.
  - Substances like BF_3, $AlCl_3$ etc, do not have any hydrogen and hence cannot give a proton but are known to behave as acids

Lewis Acid Base:

According to Lewis Acid Base concept,

A base is an <u>electron pair donor</u> and acid is an <u>electron pair acceptor</u>.

Lewis Acids:

- Lewis acids accept an electron pair. Lewis Acids are Electrophilic meaning that they are electron attracting.

- Various species can act as Lewis acids. All cations are Lewis acids since they are able to accept electrons. (e.g., Cu^{2+}, Fe^{2+}, Fe^{3+})

- **Lewis acids- H^+, NH_4^+, Na^+, K^+, Cu^{2+}, Al^{3+}, etc.**

Lewis Bases

- Lewis Bases donate an electron pair. Lewis Bases are Nucleophilic meaning that they "attack" a positive charge with their lone pair. An atom, ion, or molecule with a lone-pair of electrons can thus be a Lewis base.

- **Lewis base- NH_3, H_2O, OH^-, Cl^-, CN^-, S^{2-}, etc.**

- The reaction of boron trifluoride with ammonia is an example.

(Lewis base)   (Lewis acid)
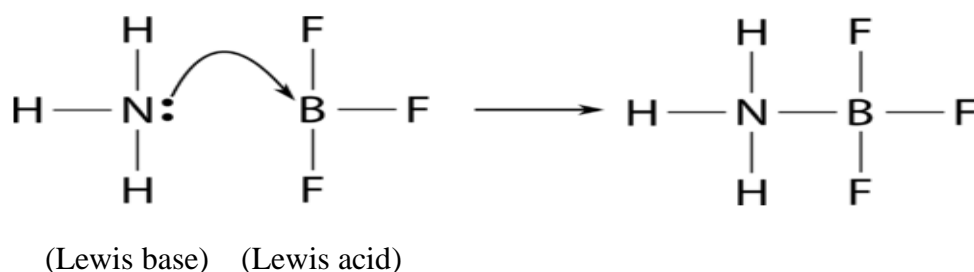
Boron trifluoride **accepts** the electron pair, so it is a **Lewis acid**. Ammonia makes available (donate) the electron pair, so it is the Lewis base.

Importance of acids and bases in pharmacy

Acids, bases and their reaction play vital role in pharmacy practice. Some of the main application of the these are as follows:

- Acid-base neutralization reaction finds use in preparative procedures for the preparation of suitable salt, and for conversion of certain salts into more suitable forms.

- Acid-base is used in analytical procedure which is involving acid-base titrations.

- Acids and bases find use as therapeutic agents in the control of and adjustment of pH of the GI tract, body fluids and urine.

Buffer

Buffers: Buffers are defined as a compound or a mixture of compounds that resists the pH upon the addition of small quantities of acid or alkali. Buffer have definite pH value. The pH will not change after keeping it for a long period of time. The pH value altered negligibly by the addition of small quantities of acid or base.

Buffer action: The resistance to a change in pH is known as buffer action. So buffers can be added to show buffer action.

Buffer capacity: The amount of acid/base required to produce a unit change in pH in a solution is called buffer capacity.

Types of buffers:
Generally buffers are of two types:
1. Acidic buffers
2. Basic buffers

There are some other buffer system:

3. Two salts acts as acid-base pair. Ex- Potassium hydrogen phosphate and potassium dihydrogen phosphate.
4. Amphoteric electrolyte. Ex- Solution of glycine.
5. Solution of strong acid and solution of strong base. Ex- Strong HCl with KCl.

1. Acidic Buffers:
An acidic buffer 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
    - ➢ H_2CO_3 / $NaHCO_3$
    - ➢ H_3PO_4 / NaH_2PO_4
    - ➢ HCOOH / HCOONa

2. Basic Buffers:
A basic buffer 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 / $(NH_4)2CO_3$

Mechanism of Buffer action:

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

In a buffer solution, the components interact with each other and produce a dynamic equilibrium. When a small quantity of acid or base is added, the dynamic equilibrium shifts and nullifies the effect of the addition.

Mechanism of Action of acidic buffers:

❑ Consider a buffer system of CH_3COOH (Weak electrolyte) and CH_3COONa (Strong electrolyte). There will be a large concentration of Na+ ions, CH_3COONa – ions, and undissociated CH_3COOH molecules.
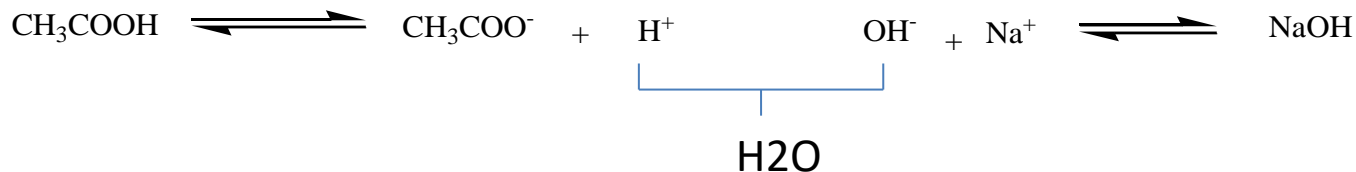
When an acid is added:

➢ If a strong acid (HCl) is added in CH_3COOH / CH_3COONa buffer, the changes that will occur may be represented as:

$$CH_3COONa \rightleftharpoons Na^+ + CH_3COO^- \qquad\qquad H^+ + Cl^-$$

CH3COOH
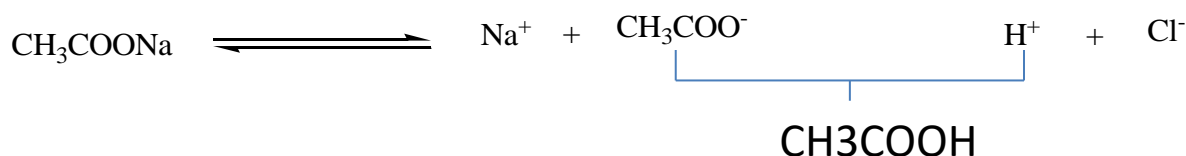
❑ The hydrogen ions yielded by the HCl are quickly removed as unionized acetic acid, and the hydrogen ion concentration is therefore only slightly affected (because acetic acid produced is very weak as compared to HCl added).

When a base is added:

➢ If a strong base (NaOH) is added in CH_3COOH / CH_3COONa buffer, the changes that will occur may be represented as:

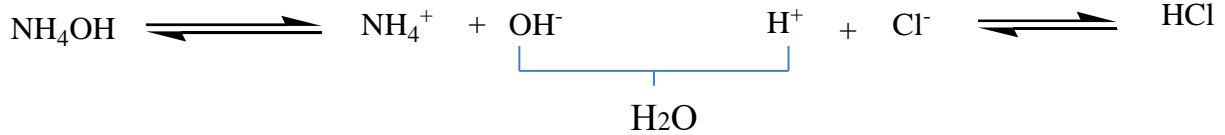$$CH_3COOH \rightleftharpoons CH_3COO^- + H^+ \qquad\qquad OH^- + Na^+ \rightleftharpoons NaOH$$

H2O

❑ The hydroxyl ions yielded by the NaoH are therefore removed as water.
The supply of hydrogen ions needed for this purpose being constantly provided by the dissociation of acetic acid.

Mechanism of Action of basic buffers:

- Consider a buffer system of NH_4OH (Weak electrolyte) and NH_4Cl (Strong electrolyte). There will be a large concentration of NH_4^+ ions, Cl^- ions, and undissociated NH_4OH molecules.
 When an acid is added:
- If a strong acid (HCl) is added in NH_4OH / NH_4Cl buffer, the changes that will occur may be represented as:

$$NH_4OH \rightleftharpoons NH_4^+ + OH^- \qquad H^+ + Cl^- \rightleftharpoons HCl$$

$$H_2O$$

- The hydrogen ions yielded by the HCl are therefore removed as water. The supply of OH^- ions needed for this is constantly provided by the ammonium hydroxide.

  When a base is added:
- If a strong base (NaOH) is added in NH_4OH / NH_4Cl buffer, the changes that will occur may be represented as:

$$NH_4Cl \rightleftharpoons Cl^- + NH_4^+ \qquad OH^+ + Na^+ \rightleftharpoons NaOH$$

$$NH_4OH$$
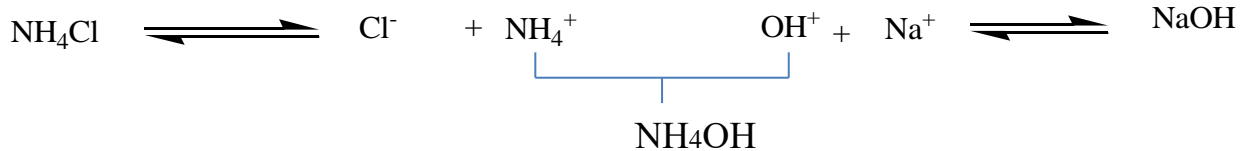
- The hydroxyl ions yielded by the NaOH are therefore quickly removed as unionized ammonium hydroxide and the pH of solution is only slightly affected.

Buffer equation-Henderson-Hasselbalch equation:

The buffer equation is also known as Henderson-Hasselbalch equation, with the help of this equation it is possible to calculate the pH of a buffer solution of known concentration or to make buffer solution of known pH.
Two separate equations are obtained for each type of buffer, acidic and basic
pH of acidic buffer: The hydrogen ion concentration obtained from the dissociation of weak acid HA is given by equation,

$$HA \rightleftharpoons H^+ + A^-$$

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

Ka = equilibrium constant
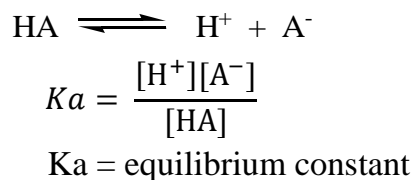
$$[H^+] = Ka \; \frac{[HA]}{[A^-]}$$

Taking logarithms of both sides of the equation & multiplying throughout by -1 gives

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

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

$$pH = pKa + \log\frac{[\text{conjugate base}]}{[\text{acid}]}$$

pH of an alkaline buffer: The ionization of a weak base BOH is given by,

$$BOH \rightleftharpoons B^+ + OH^-$$

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

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

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

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

$$pOH = pKb + \log\frac{[\text{conjugate acid}]}{[base]}$$

Now,
$$pH = 14 - pOH$$

$$= 14 - (pKa + \log\frac{[\text{conjugate acid}]}{[\text{base}]})$$

Buffer capacity:

Buffer capacity may also be defined as "*The maximum amount of either strong acid or strong base that can be added before a significant change in the pH will occur*".

The maximum amount of strong acid that can be added is equal to the amount of conjugate base present in the buffer whereas the maximum amount of base that can be added is equal to the amount of weak acid present in the buffer.

- Buffer capacity is depend on the factors:
1. The concentration of the acid or base component of the buffer (Direct relation)
2. The pH of the buffer

➢ Buffer can act best at pH = pKa and buffering range is pH = pKa +1

Or It may be defined as the moles of strong acid or strong base required to change the pH of 1000 ml of buffer solution by one unit.

❑ The magnitude of the resistance of a buffer to pH changes is referred to as the buffer capacity, β.

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

Where, **ΔB** is the small increment in gram equivalents (g Eq)/liter of strong base added to the buffer solution and **ΔpH:** change in a pH

Standard Buffer Solutions:

The standard buffer solutions of pH ranging from 1.2-10 are possible to prepare by appropriate combinations of 0.2N HCl or 0.2N NaOH or 0.2M solution of potassium hydrogen phthalate, potassium dihydrogen phosphate, boric acid, potassium chloride.

Standard buffers with pH range:

Buffer	pH
Hydrochloric acid buffer	1.2-2.2
Acid Phthalate buffer	2.2-4.0
Neutralised phthalate buffer	4.2-5.8
Phosphate buffer	5.8-8.0
Alkaline Borate buffer	8-10

Preparation of Buffer Solutions:

Weak acid with pKa = desired pH should be selected
↓
Ratio of salt and acid needed should be calculated using buffer equation
↓
Individual concentration of buffer salt and acid determined.
↓
Ingredients are dissolved in carbon dioxide free water
↓
Buffer capacity of 0.01-0.1 is adequate
↓
Concentration of 0.05-0.5 M is sufficient
↓
Allowed to establish equilibrium
↓
pH verified.

Buffers in pharmaceutical systems or Application of buffer:

1. Solubility enhancement: The pH of the pharmaceutical formulations are adjusted to an optimum value so that the drug remains solubilised though out its shelf-life and not precipitated out.
Eg. Sodium salicylate (Asprin) precipitates as salicylic acid in acidic environment.
2. Increasing stability: To prevent hydrolysis and for maximum stability, the pH of the medium should be adjusted suitably. **Eg.** Vitamins
3. Improving purity: The purity of proteins can be identified from its solubility at their isoelectric point as they are least soluble at this point. The isoelectric pH can be maintained using suitable buffers.**Eg.** Insulin precipitates from aqueous solution at pH 5.0-6.0.
4. Optimising biological activity: Enzymes have maximum activity at definite pH values. Hence buffer of desired pH is added to the preparation.
5. Comforting the body: The pH of the formulations that are administered to different tissues of the body should be optimum to avoid irritation (eyes), haemolysis (blood) or burning sensation (abraded surface). The pH of the preparation must be added with suitable amount of buffers to match with the pH of the physiological fluid.
Eg buffer in various dosage forms

Dosage Form	Application	Buffer used
Solids (Tablets, Capsules, powder)	Control pH for release. Reduce gastric irritation	Citrate buffer, Phosphate buffer
Semisolids (Creams, Ointments)	Stability	Citric acid and sodium citrate
Parenteral Products	pH maintenance (pH high: tissue, necrosis pH low: pain)	Citrates, glutamate, acetate, phthalate
Opthalamic products	Drug solubility and stability	Borates, carbonates, phosphates