PHARMA

CHAPTERWISE NOTES

Pharmaceutical Analysis

Acid-Base Titration

GENERAL PROPERTIES OF ACIDS AND BASES

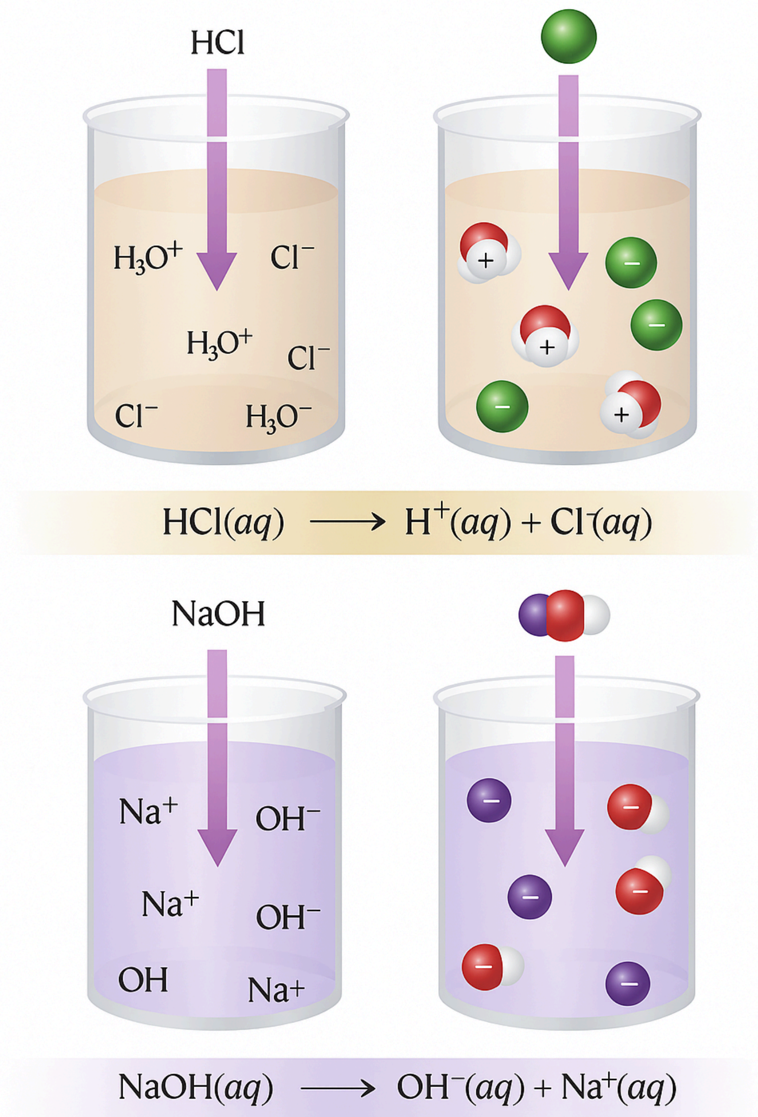
Property	Acids	Bases
pH Range	Less than 7	Greater than 7
Taste	Acids taste sour	Bases taste bitter
Reaction with Carbonates	Liberates carbon dioxide	Absorbs carbon dioxide
Litmus	Blue litmus red	Red litmus blue

ARRHENIUS THEORY

According to this concept, an acid is a compound that releases H^+ ions in water, and a base is a compound that releases OH^- ions in water. For example, HCl is an Arrhenius acid and NaOH is an Arrhenius base.

$$\mathrm{HCl}(aq) \longrightarrow \mathrm{H}^+(aq) + \mathrm{Cl}^-(aq)$$

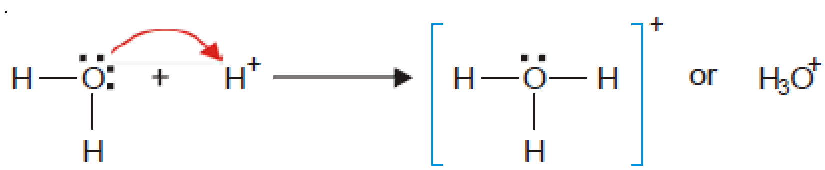
$$\mathrm{NaOH}(aq) \qquad \mathrm{OH}^-(aq) + \mathrm{Na}^+(aq)$$



Note: Here, HCl is an Arrhenius acid. NaOH is an Arrhenius base.

LIMITATIONS OF ARRHENIUS'S CONCEPT

★ The H^+ and OH^- ions produced by acids and bases, respectively, do not exist in water in the free state. They are associated with water molecules to form complex ions through hydrogen bonding. Thus, the H^+ ion forms a hydronium ion:



Hydronium ion

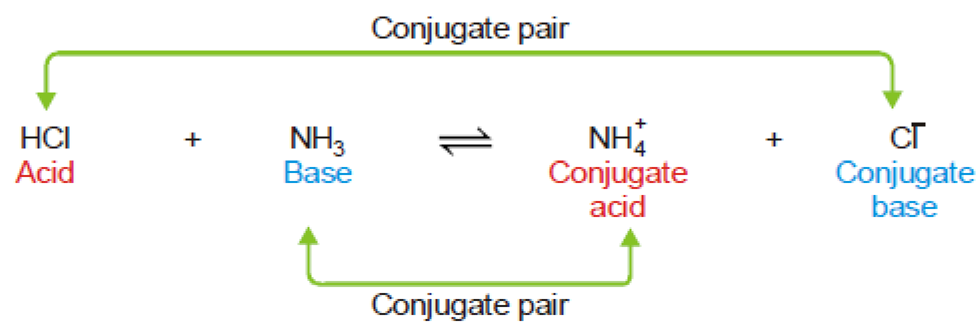
★ **Limited to water only:** Arrhenius defined acids and bases as compounds producing H+ and OH– ions in water only. But a truly general concept of acids and bases should be appropriate to other solvents as well.

BRONSTED-LOWRY CONCEPT

According to this theory, an acid is any molecule or ion that can donate a proton (H+) while a base is any molecule or ion that can accept a proton

CONJUGATE PAIRS

In an acid-base reaction the acid (HA) gives up its proton (H+) and produces a new base (A–). The new base that is related to the original acid is called a conjugate (meaning related) base. Similarly, the original base (B–) after accepting a proton (H+) gives a new acid (HB), which is called a conjugate acid.



Note: Acid gets converted to the conjugate base by donating a proton, while bases gets converted to the conjugate acid by accepting protons

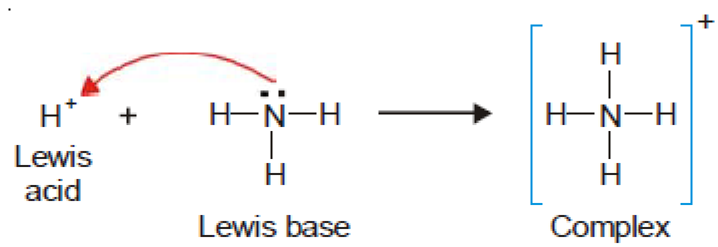
Acid		Base		Conjugate Acid		Conjugate Base
HCl	+	H_2O	$\rightleftharpoons$	H_3O^+	+	Cl^-
HNO_3	+	H_2O	$\rightleftharpoons$	H_3O^+	+	NO_3^-
HCO_3^-	+	H_2O	$\rightleftharpoons$	H_3O^+	+	CO_3^{2-}
CH_3COOH	+	H_2O	$\rightleftharpoons$	H_3O^+	+	CH_3COO^-
HCN	+	H_2O	$\rightleftharpoons$	H_3O^+	+	CN^-
H_2S	+	H_2O	$\rightleftharpoons$	H_3O^+	+	HS^-
H_2O	+	NH_3	$\rightleftharpoons$	NH_4^+	+	OH^-
H_2O	+	CO_3^{2-}	$\rightleftharpoons$	HCO_3^-	+	OH^-
H_2O	+	H_2O	$\rightleftharpoons$	H_3O^+	+	OH^-

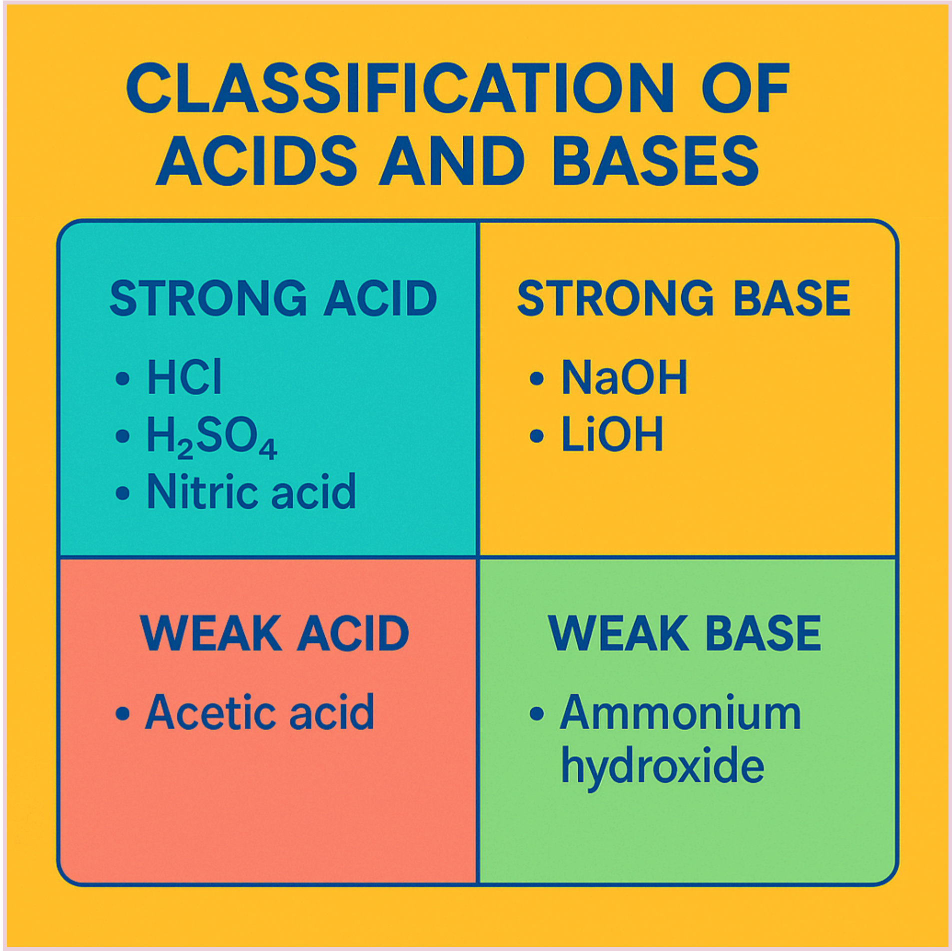
Table showing some examples of Bronsted-acids and bases

LEWIS THEORY

In the early 1930s, G.N. Lewis proposed an even more general model of acids and bases. According to Lewis's theory, an acid is an electron-pair acceptor, while a base is an electron-pair donor

For example: Proton (H+) is a Lewis acid, as it can accept an electron pair. Ammonia molecule (: (NH_3) has an electron pair that it can donate and is a Lewis base. Thus, the Lewis reaction between H^+ and NH_3 can be written as:





Neutralization Reaction in Acid–Base Titration

Definition

Neutralization is the reaction between an acid and a base to form salt and water, usually releasing heat.

Acid+Base→Salt+Water

General Reactions

- **Strong Acid + Strong Base:**

$$HCl + NaOH \rightarrow NaCl + H_2O$$

- **Weak Acid + Strong Base:**

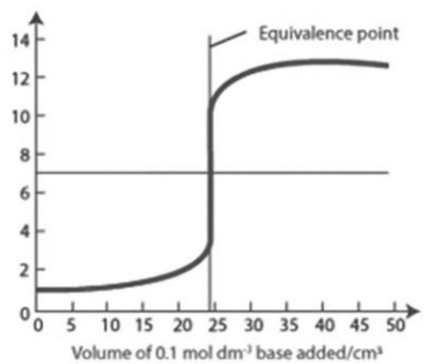
$$CH_3COOH + NaOH \rightarrow CH_3COONa + H_2O$$

Classification of Acid-Base Titration:

An acid-base titration is categorized into the following categories:

1) Titration of a strong acid Vs strong base: Let's assume that our analyte is **hydrochloric acid (HCl),** which serves as a strong acid, and the titrant is **sodium hydroxide (NaOH),** which serves as a strong base. For the titration curve of a strong acid with a strong base.

1. PH before the equivalence point is found to be acidic
2. PH at the equivalence point is found to be neutral
3. PH after the equivalence point is found to be basic

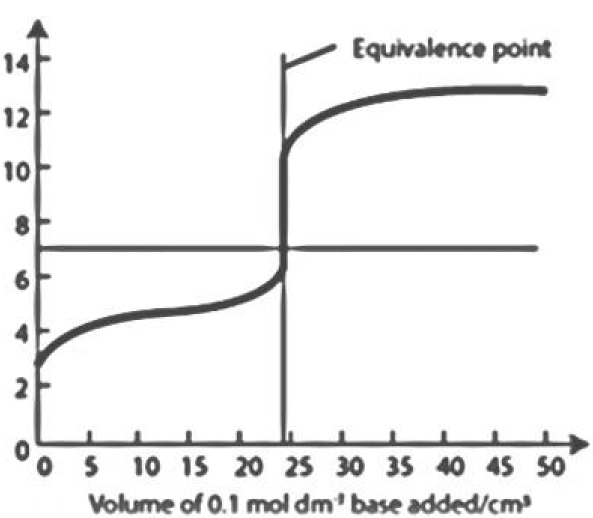


Note: Indicators used are methyl orange, methyl red, phenolphthalein, bromothymol blue, phenol red

2) Titration of a weak acid Vs strong base: Suppose our analyte is **acetic acid,** which serves as a weak acid and the titrant is **sodium hydroxide (NaOH),** which serves as a strong base.

a) PH before equivalence point is found to be Acidic
b) PH at the equivalence point is found to be Basic (pH>7).
c) PH after equivalence point is found to be Basic

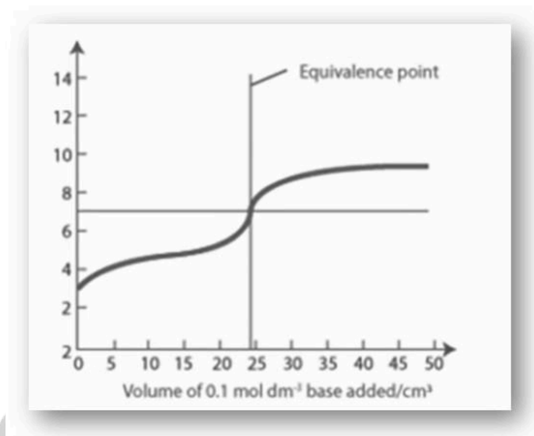
Note: Indicator used are methyl orange, methyl red, bromophenol, and bromocresol green



<u>3) Titration of a strong acid Vs weak base:</u> Let's assume that our analyte is hydrochloric acid, HCl (strong acid), and the titrant is ammonia, NH_4OH (weak base).

- PH before the equivalence point is found to be acidic
- PH at the equivalence point is found to be acidic (pH<7).
- PH after the equivalence point is found to be basic

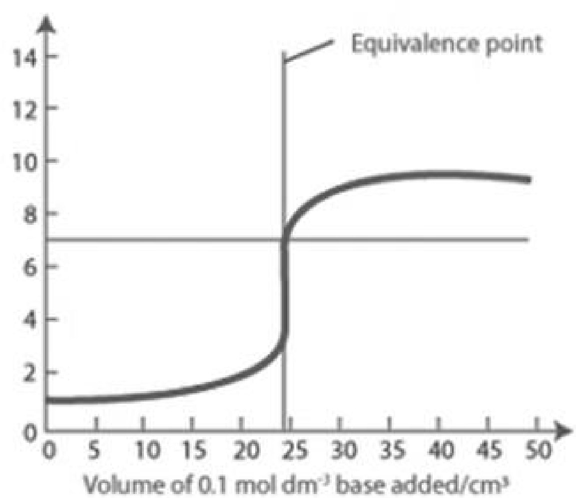
Note: Indicators used are thymolphthalein, phenolphthalein, thymol blue



4) Titration of a weak base with a weak acid:

The most common examples of this titration involve ethanoic acid (acetic acid) and ammonia.

$$CH_3COOH + NH_3 \rightarrow CH_3COONH_4$$



<u>Indicators used: Mixed indicators</u>

- ➢ **Neutral red and methylene blue**
- ➢ **Methyl green and phenolphthalein**

➢ **Thymol blue and cresol red**

Name of indicator	Color at lower pH	pH range	End-point	Color at higher pH
methyl violet	yellow	0.0 - 1.6	0.8	blue
thymol blue	red	1.2 - 2.8	2.8	yellow
methyl orange	red	3.2 - 4.4	3.7	yellow
bromophenol blue	yellow	2.8 - 4.6	4.0	blue
bromocresol green	yellow	3.8 - 5.4	4.7	blue
methyl red	red	4.2 - 6.3	5.1	yellow
bromothymol blue	yellow	6.0 - 7.6	7.0	blue
thymol blue	yellow	8.0 - 9.6	8.1	blue
phenolphthalein	colorless	8.2 - 10.0	9.3	pink/violet
alizarin yellow	yellow	10.1 - 13.0	12.5	orange/red

ACID-BASE INDICATORS

- ***Indicators are the auxiliary substances added to the conical flask that modify the colors, which signifies the completion of the titration.***
- These are generally weak acids or bases.
- There are 2 theories of acid-base indicators:

a) **Ostwald Theory/Ionization Theory**

❖ ***According to Ostwald's theory, color change is caused by the ionization of the acid-base indicator. The unionized form has a different color than the ionized form.***

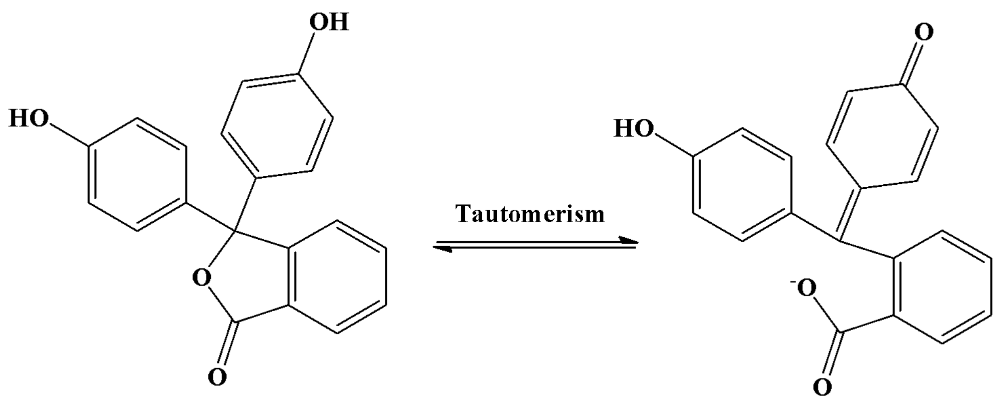
❖ For instance, if the indicator is a weak acid, then its ionization is very low in acids because of common H^+ ions.

b) **Resonance/Quinonoid theory**

❖ ***According to this theory of acid-base indicators, the color changes due to the structural changes in the indicator.***

❖ In both acidic & basic solutions, these indicators exist in different structural forms, having different colours.

- These indicators are aromatic carbon compounds & are available in 2 forms— ***Benzenoid & Quinonoid***



Benzoid form of phenolphthalein

Quinonoid form of phenolphthalein