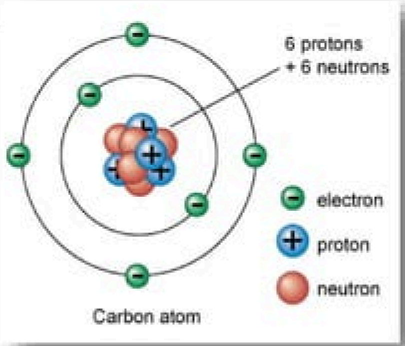
# CONTENT

# 1 and 2: Basic Concept related to Acid and Base

## CHEMICAL BONDING AND ELECTRON VALENCES

- The electrons in an atom are located at different **energy levels**.
- Electrons in the highest energy level are called **valence electrons.**
- Number of valence electrons governs an atom's bonding behavior.




***What is the <u>max number</u> of valence electrons for a full valence shell?***

Atoms are much more stable, or less reactive, with a full valence shell.

By moving electrons, the two atoms become linked. This is known as **chemical bonding.**

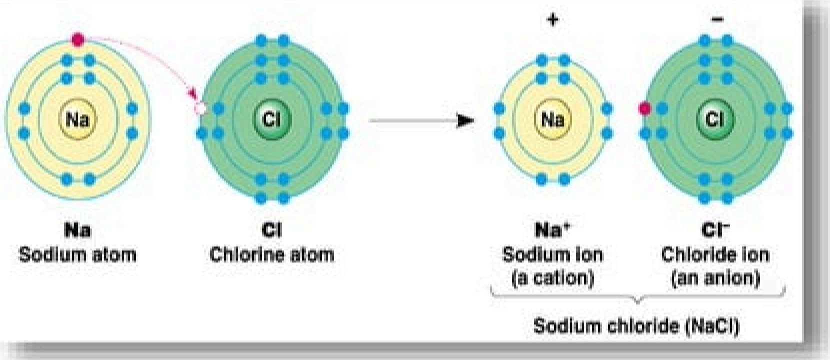
This stability can be achieved one of two ways:

- **Ionic** bond
- **Covalent** bond

# IONIC BONDS

Involves transfer of electrons between two atoms.

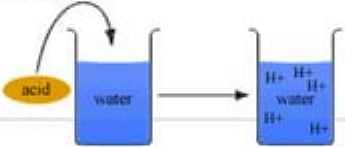
Found mainly ... inorganic compounds.



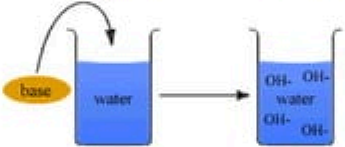

**Ion** = an atom or group of atoms which have lost or gained one or more electrons, making them negatively or positively charged.

# IONS: ACIDS & BASES

An **acid** is any ionic compound that releases **hydrogen ____ (H⁺)** in solution.

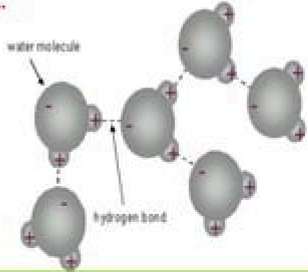



A **base** is any ionic compound that releases **hydroxide ____ (⁻OH)** in solution.



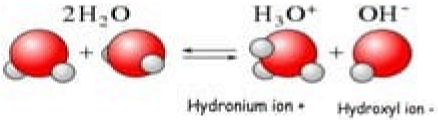

**Another important characteristic of water…**

**Water can form acids and bases**

# DISSOCIATION OF WATER

$$H_2O \Leftrightarrow H^+ + OH^-$$

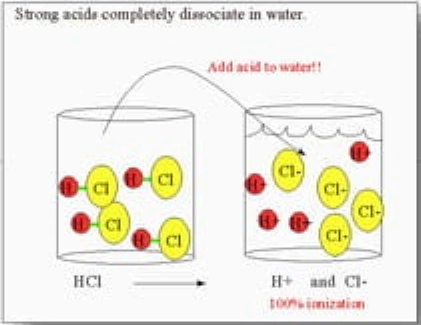


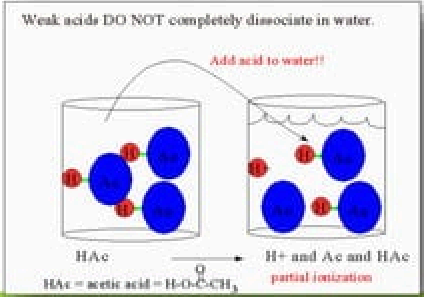

Neutral water has equal amounts of $H^+$ and $OH^-$

Acids: Excess of $H^+$ in aqueous solution

Bases: Excess of $OH^-$ in aqueous solution

Acids & bases neutralize each other.



# ACIDS AND BASES

## Acids

Act as proton donors

Electron pair acceptors

Strong acids dissociate fully in water.

Weak acids partially dissociate.

$K_a$: acid dissociation constant

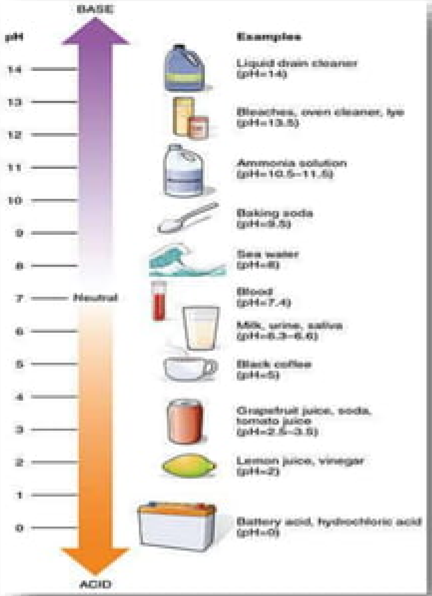
$$HA + H_2O \rightarrow H_3O^+ + A^-$$

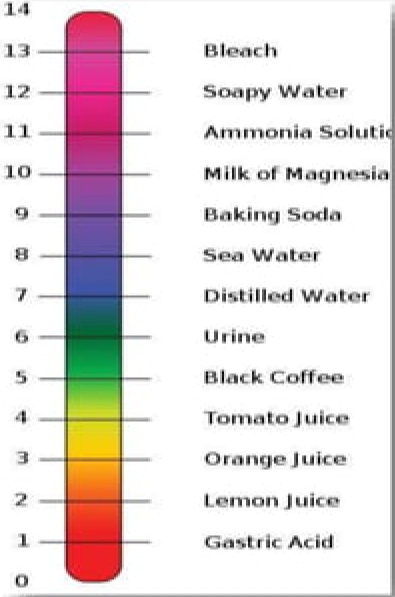
$$K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

Higher $K_a$ values mean stronger acids

## Bases

- Act as proton acceptors
- Electron pair donors
- Strong bases dissociate fully in water
- Weak bases partially dissociate
- $K_b$: base dissociation constant


BASE
pH
14
13
12
11
10
9
8
7 Neutral
6
5
4
3
2
1
0
ACID
Examples
Liquid drain cleaner (pH=14)
Bleaches, oven cleaner, lye (pH=13.5)
Ammonia solution (pH=10.5–11.5)
Baking soda (pH=9.5)
Sea water (pH=8)
Blood (pH=7.4)
Milk, urine, saliva (pH=6.3–6.6)
Black coffee (pH=5)
Grapefruit juice, soda, tomato juice (pH=2.5–3.5)
Lemon juice, vinegar (pH=2)
Battery acid, hydrochloric acid (pH=0)


14
13 Bleach
12 Soapy Water
11 Ammonia Solutio
10 Milk of Magnesia
9 Baking Soda
8 Sea Water
7 Distilled Water
6 Urine
5 Black Coffee
4 Tomato Juice
3 Orange Juice
2 Lemon Juice
1 Gastric Acid
0

**What is an Acid?**

- An acid is a substance which, when dissolved in water, releases protons.

- The extent of dissociation, that is, the amount of protons released compared to the total amount of compound, is a measure of the strength of the acid.

- For example, HCl (hydrochloric acid) is a strong acid, because it dissociates completely in water, generating free $[H^+]$ and $[Cl^-]$.

## The Hydration of Carbon Dioxide in Water

$$CO_2 + H_2O \rightleftharpoons HCO_3^- + H^+$$

$$\downarrow$$

$$H_2CO_3$$

As carbon dioxide goes into solution, carbonic acid is formed, which partially dissociates, liberating protons ($H^+$) and thus causing the solution to become **more acidic**, i.e., *lowering* the pH.

**But What's a Weak Acid?**

- Some substances, like acetic acid (vinegar!) dissociate poorly in water.
- Thus, they release protons, but only a small fraction of their molecules dissociate (ionize).
- Such compounds are considered to be weak acids.
- Thus, while 1 M HCl is pH = 0 (why?), 1 M acetic acid is only pH = 2.4…

**Weak acids thus are in equilibrium with their ionized species:**

Governed by the Law of Mass Action, and characterized by an ***equilibrium constant***:

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

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

**What is an Base ?**

A **base** is an ionic compound that releases hydroxyl ions (OH-) in solution.

Bases are also called **alkaline** substances.

Some general properties of bases include:

**Taste:** Bitter taste (opposed to sour taste of acids and sweetness of aldehydes and ketones).

**Touch:** Slimy or soapy feel on fingers.

**Reactivity:** Strong bases are caustic on organic matter, react violently with acidic substances.

**Examples:**

- **Sodium hydroxide**, NaOH, of lye or caustic soda used in oven cleaners.
- **Magnesium hydroxide**, $Mg(OH)^2$, also known as milk of magnesia, a weak base used in antacids and laxatives.

# Strong & Weak Acids - Bases

**Strong acid** – fully dissociates in water, i.e. almost every molecule breaks up to form $H^+$ ions

Some strong acids are…HCl, $H_2SO_4$, $HNO_3$

---

**Weak acid** – partially dissociates in water

Some weak acids are…carboxylic acids such as $CH_3COOH$, $C_2H_5COOH$

**Strong base** – fully dissociates in water, i.e. almost every molecule breaks up to form $OH^-$ ions

Some strong bases are….NaOH, compounds which contain $OH^-$ ions or $O^{2-}$ ions

**Weak base** – partially dissociates in water

Some weak bases…nitrogen-containing compounds, such as $NH_3$

*Strengths can be determined by the acid or base dissociation constant.*

# ACIDS AND BASES THEORY

1) ARRHENIUS THEORY – an acid which contains hydrogen and can dissociate in water to produce positive hydrogen ions

*e.g.* $HX + H_2O \leftrightarrow H^+ (H_3O^+) + X^-$

- A base reacts with a protonic acid to give water (and a salt)

*e.g.* $HCl + NaOH \rightarrow NaCl + H_2O$

2) BRONSTED-LOWRY THEORY – acids are proton donors; bases are proton acceptors

*e.g.* $HCN + H_2O \leftrightarrow H_3O^+ + CN^-$

HCN is an acid, in that it donates a proton to water. Water is acting as a base, as it accepts that proton

3) LEWIS THEORY – an acid accepts a pair of electrons; a base donates a pair of electrons

*e.g.* $HCl + NaOH \rightarrow NaCl + H_2O$

The strength of an acid depends on the extent to which is dissociates and is measured by its dissociation constant.

## ACIDS AND BASES THEORY (Continue….)

4) Lux Flood Acid Base Concept:– Oxide ion first introduced by Lux in 1929 and supported by Flood in 1947

According to, 'An acid is the oxide ion acceptor, while base is oxide ion donor.'

Ex.: $MgO + SiO_2 \longrightarrow MgSiO_3$

MgO is oxide ion donor and $SiO_2$ is oxide ion acceptor and react to form Magnesium Silicate ($MgSiO_3$)

5) Hard and Soft Acid Base Concept :–Derived by R.G. Pearson and hence called as Pearson's Principle of Hard and Soft Acid Base.

- Hard Acid: Electron acceptors with high positive e charge, small size and low polarizability (unfilled valance shell orbitals, high electronegativity)
- Soft Acid: Electron acceptors with low positive e charge, large size and high polarizability (filled valance shell orbitals, low electronegativity)
- Hard Base: Electron donors with high electronegativity, easily reducible and have low polarizability.
- Soft Base: Electron donors with low electronegativity, easily oxidizable and have high polarizability.

# pH and pOH

Important aspect for : formulation, absorption, distribution, metabolism and elimination of drugs.

❖**pH:**

Expressing the Hydrogen ion concentration $[H^+]$ or more correctly, Hydronium ion$[H_3O^+]$ concentration in solution.

pH is equal to the negative log of the molar hydrogen ion concentration.

$pH = -\log [H^+]$

pH > 7 basic

pH = 7 neutral

pH < 7 acidic

❖**pOH:**

Expressing hydroxyl ion $[OH^-]$ concentration in solution.

pOH is equal to the negative log of the molar hydroxyl ion concentration

$pOH = -\log [OH^-]$

❖**pKa:**

- Water ionizes (dissociates) slightly to yield hydronium and hydroxyl ions.
- $H_2O + H_2O \longrightarrow H_3O^+ + OH^-$
- Can also express dissociation constants in terms of logs:
- $pK_a = -\log K_a$
- ∴ the higher the $K_a$ the lower the $pK_a$
- Similarly for bases

# 3) BUFFERS

- A buffer is a solution.
- Which resist pH changes in pH upon addition of small amount of acid or bases. (near a weak acid pK value)
- Types of buffer:

a) Acid buffer solution: Composed of weak acid and its salt. Buffer has acidic pH.

b) Base buffer solution: Composed of weak base and its salt. Buffer has alkaline pH.

Buffer range: If pK is 4.8 the buffering range is 3.8 ⟶ 5.8

## The Role of Buffers:

- Certain salts, called **buffers**, can combine with excess hydrogen (H+) or hydroxide (OH-) ions.
- Produce substances less acidic or alkaline.
- Act like a chemical sponge to soak up excess acid or base, keep pH constant.
- Buffers can be "used up". Once used up, no longer help regulate pH.
- Buffers are vital to maintaining pH in organisms.
- ***Example:***

*Antacids are buffers made of the salt calcium carbonate (CaCo3).*

# 4) BUFFER EQUATION "Henderson - Hasselbalch Equation"

The Henderson–Hasselbalch **equation** relates the pH of a solution containing a mixture of the two components to the acid dissociation constant, $K_a$, and the concentrations of the species in solution.

To derive the **equation** a number of simplifying assumptions have to be made.

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

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

Take (-)Log of each $$pH = -\log K + \log\frac{[A^-]}{[HA]}$$

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

$$\frac{[\text{A}^-]}{[\text{HA}]} \text{ ratio varies from } \frac{1}{10} \Rightarrow \frac{10}{1}$$

Above and below this range there is insufficient amount of conjugate acid or base to combine with the base or acid to prevent the change in pH.

For weak acids

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

This equilibrium depends on concentrations of each component

.

If $[HA] = [A^-]$ or 1/2 dissociated

Then $$\log\frac{[A^-]}{[HA]} = \log 1 = 0$$ : pH = pK

***By definition the pK is the pH where $[HA] = [A^-]$ :***

***50% dissociated***

**Buffer** solutions achieve their resistance to pH change because of the presence of an equilibrium between the acid

HA and its conjugate base $A^-$.

and only a little is consumed in the neutralization **reaction** which results in an increase in pH.

# The buffer effect can be seen in a titration curve.

To a weak acid salt, $CH_3COO^-$, add HCl while monitoring pH vs. the number of equivalents of acid added.

or

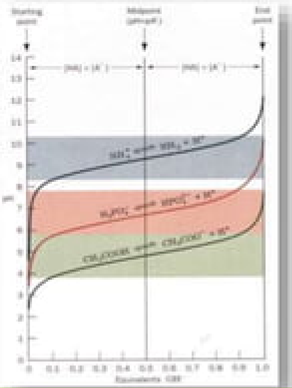
do the opposite with base.

**Buffer capacity:** The molar amount of acid which the buffer can handle without significant changes in pH.

i.e

1 liter of a 0.01 M buffer can not buffer 1 liter of a 1 M solution of HCl but

1 liter of a  1 M buffer can buffer 1 liter of a 0.01 M solution of HCl.



# 5) BUFFER CAPACITY

- **Buffer capacity** is a measure of the efficiency of a **buffer** in resisting changes in pH. Conventionally, the **buffer capacity** (β) is expressed as the amount of strong acid or base, in gram-equivalents, that must be added to 1 liter of the solution to change its pH by one unit.
- **Calculating Buffer Capacity:**

  Buffer capacity is determined through a titration, a technique in which a known volume and concentration of a base or acid is added to the analyte of unknown concentration
- **Buffer capacity is a quantitative measure** of resistance to pH change upon the addition of $H^+$ or $OH^-$ ions. It is important for river water to maintain a stable pH such that the local ecosystems are preserved in order to keep Columbus flourishing.

# 6) BUFFER IN PHARMACEUTICAL SYSTEM

**Solid Dosage Forms:** Buffers have been widely in solid dosage forms such as tablets, capsules and powders for controlling the PH of the environment around the solid particles. This has practical application for the drugs that have dissolution rate limited absorption from unbuffered solutions One of the special applications of buffers is to reduce the gastric irritation caused by the acidic drugs. For example, sodium bicarbonate, magnesium carbonate and sodium citrate antacids are used for the purpose of reducing toxicity.

**Semisolid Dosage Forms:**

Semisolid preparations such as creams and ointments undergo PH changes upon storage for long storage for a long time, resulting in its reduced stability. Hence; buffers such as citric acid and sodium citrate or phosphoric acid/sodium phosphate are included in these preparations so as to maintain their stability

**Parenteral Products:**

Use of buffers is common in the parenteral products. Since the PH of blood is 7.4,these products are required to be adjusted to this PH. Change in PH to higher side (more than 10) may cause tissue necrosis while on lower side (below 3) it may cause pain at the site of action. Commonly used buffers include citrate, glutamate, phthalate and acetate. The PH optimization is generally carried out to have better solubility, stability and reduced irritancy of the product.

**Ophthalmic Products:**

The purpose of buffering some ophthalmic solution is to prevent an increase in PH can affect both the solubility and the stability of the drug. The decision whether or not buffering agents should be added in preparing on ophthalmic solution must be based on several considerations. Normal tears have PH of about 7.4 and posses some buffer capacity.

# 7) BUFFER PREPARATION

There are a couple of ways to **prepare** a **buffer** solution of a specific pH.

**There are three ways to prepare a buffer solution.**

1. Weak acid and its salt
2. Weak acid and strong base
3. Salt of weak base and strong acid

In the first method, **prepare** a solution with an acid and its conjugate base by dissolving the acid form of the **buffer** in about 60% of the volume of water required to obtain the final solution volume.

| PH Value | Method of Preparation |
|---|---|
| 1 | 100 mL 0.2M KCl + 268 mL 0.2M HCl |
| 3 | 100 mL 0.1M sodium hydrogen phthalate + 44.6 mL 0.1M HCl |
| 5 | 100 mL 0.1M sodium hydrogen phthalate + 45.2 mL 0.1M NaOH |
| 7 | 100 mL 0.1M sodium dihydrogenate phosphate + 58.2 mL 0.1M NaOH |
| 9 | 100 mL 0.025M Borax + 9.2 mL 0.1M HCl |
| 11 | 100 mL 0.05M sodium bicarbonate + 45.4 mL 0.1M NaOH |
| 13 | 100 mL 0.2M KCl + 264 mL 0.2M NaOH |

# 8) BUFFER STABILITY

- ✓ Treat buffer solutions with care
- ✓ The typical shelf-life for commercial technical buffers is 2 years unopened and 3-6 months open.
- ✓ The typical shelf-life for alkaline buffers is 1 month open.
- ✓ Alkaline buffer= Change with dissolved air and form carbonic acid which decresed pH of the solution.
- ✓ Alkaline shelf-life= only one month
- ✓ Maintained at 25°C
- ✓ Preserved in colored bottle
- ✓ Storage condition maintain for inhibition of growth of micro organism.


# 9) BUFFER ISOTONIC SOLUTION

- A solution containing 0.9% of sodium chloride is practically isotonic with blood plasma and is regarded as standard.
- A solution containing more than 0.9% sodium chloride is called 'hypertonic'.
- A solution containing less than 0.9% sodium chloride is called 'hypotonic'.

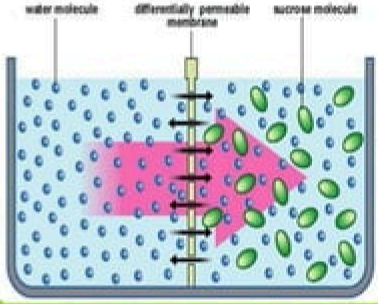
- **Osmosis** : the diffusion of solvent molecules from a region of lower solute concentration to a region of higher solute concentration through a semi- permeable membrane.
- **Semi- permeable membrane:** membranes which allow solvent molecules to pass through but resist the passage of dissolved substances.
- Excess of solvent molecules passing in one direction creates a pressure called **'Osmotic pressure'**

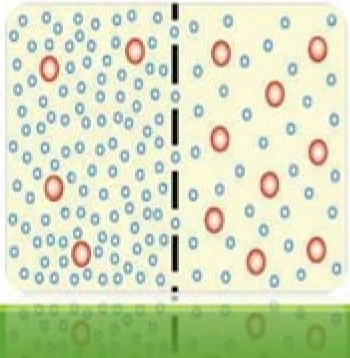
# 9) BUFFER ISOTONIC SOLUTION

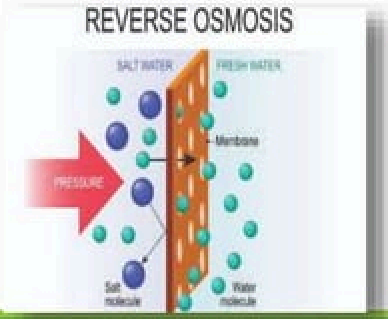
- The red blood cell membrane is not impermeable to all drugs; that is, it is not a perfect semipermeable membrane.
- Thus, it will permit the passage of not only water molecules but also solutes such as urea, ammonium chloride, alcohol, and boric acid.
- These solutes are regarded as solvent and they do not exert an osmotic pressure on the membrane (the solutions are isosmotic but not isotonic)
- A 2.0% solution of boric acid has the same osmotic pressure as the blood cell contents when determined by the freezing point method and is therefore said to be isosmotic with blood.
- The molecules of boric acid pass freely through the erythrocyte membrane, however, regardless of concentration.
- As a result, this solution acts essentially as water when in contact with blood cells. Because it is extremely hypotonic with respect to the blood, boric acid solution brings about rapid hemolysis.
- Therefore, a solution containing a quantity of drug calculated to be isosmotic with blood is isotonic .
- Accordingly, a 2.0% boric acid solution serves as an isotonic ophthalmic preparation.

## Tonicity Osmolality and Osmolarity

**Tonicity Osmolality and osmolarity** :- are colligative properties that measure the concentration of the solutes independently of their ability to cross a cell membrane. Tonicity:- is the concentration of only the solutes that cannot cross the membrane since these solutes exert an osmotic pressure on that membrane. Tonicity is not the difference between the two osmolarities on opposing sides of the membrane. A solution might be hypertonic, isotonic, or hypotonic relative to another solution. A solution containing a quantity of drug calculated to be isosmotic with blood is isotonic only when the blood cells are impermeable to the solute (drug) molecules and permeable to the solvent, water.

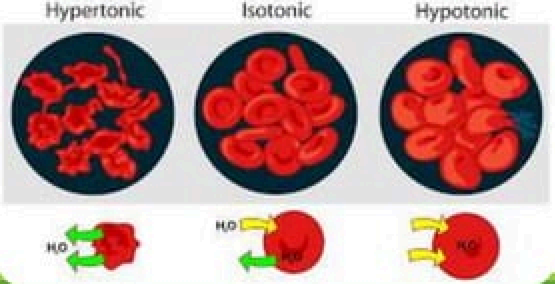




# BUFFERED ISOTONIC SOLUTIONS

- Pharmaceutical solutions that are meant for application to delicate membranes of the body should also be adjusted to approximately the same osmotic pressure as that of the body fluids.
- **Isotonic solutions cause no swelling or contraction of the tissues** with which they come in contact and produce no discomfort when instilled in the eye, nasal tract, blood, or other body tissues.
- Isotonic sodium chloride is a familiar pharmaceutical example of such a preparation.
- The need to achieve isotonic conditions with solutions to be applied to delicate membranes is dramatically illustrated by mixing a small quantity of blood with aqueous sodium chloride solutions of varying tonicity.




- **Iso- osmotic solutions**: solutions having same osmotic pressure. (all Isoosmotic solutions are not necessarily isotonic)
- **Paratonic solutions:** solutions with different osmotic pressure.

**a) Isotonic:**

- If a small quantity of blood is mixed with a solution containing 0.9 g of NaCl per 100 mL, the cells retain their normal size.
- The solution has essentially the same salt concentration and hence the same osmotic pressure as the red blood cell contents

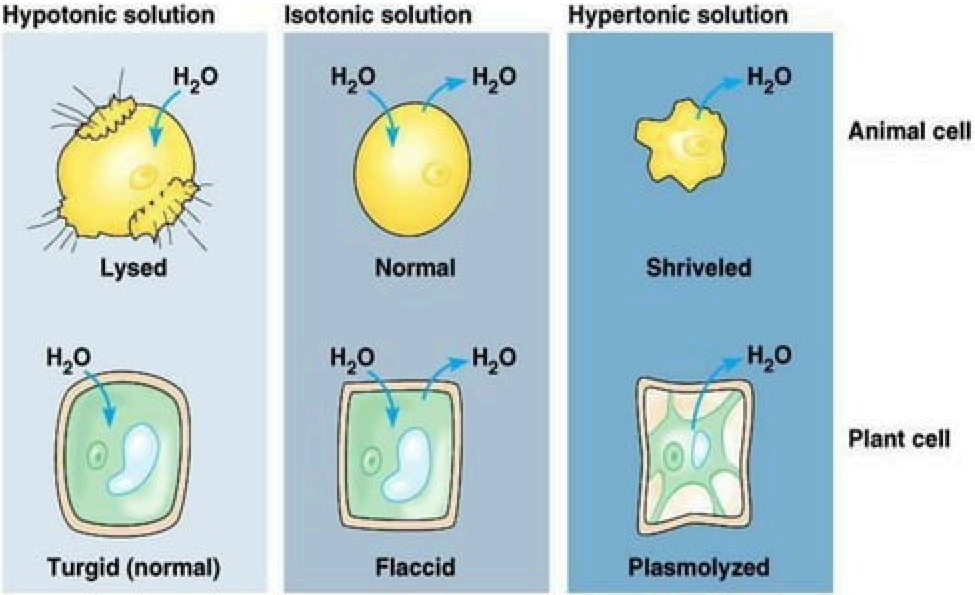
**b) Hypertonic:**

- If the red blood cells are suspended in a 2.0% NaCl solution, the water within the cells passes through the cell membrane in an attempt to dilute the surrounding salt solution.
- This outward passage of water causes the **cells to shrink** and become wrinkled or crenated.

**c) Hypotonic:**

If the blood is mixed with 0.2% NaCl solution or with distilled water, water enters the blood cells, causing them to **swell and finally burst, with the liberation of hemoglobin**.

The salt solution in this instance is said to be with respect to the blood cell contents. Finally, This phenomenon is known as hemolysis .


Hypotonic solution
Isotonic solution
Hypertonic solution
H2O
H2O
H2O
H2O
Animal cell
Lysed
Normal
Shriveled
H2O
H2O
H2O
H2O
Plant cell
Turgid (normal)
Flaccid
Plasmolyzed

# 10) MEASUREMENT OF TONICITY

**Measurement Of Tonicity**

- Hemolytic Method
- Measurement of slight temperature difference
- Calculating Tonicity Using L iso Value

Refer the link:

1) https://ijarbs.com/pdfcopy/oct2016/ijarbs28.pdf

2) http://www.uobabylon.edu.iq/eprints/publication_12_28202_1273.pdf

# 11) CALCULATION AND METHODS OF ADJUSTING ISOTONICITY

## GENERAL PRINCIPLES FOR ADJUSTMENT OF ISOTONICITY

1. Parenteral preparations should be isotonic with blood plasma (depending on the route of administration).

   i. intravenous injection- isotonicity is always desirable.

   ii. Subcutaneous injection- not essential. Intramuscular- hypertonic.

   iii.

   iv. Intrathecal injection- isotonic

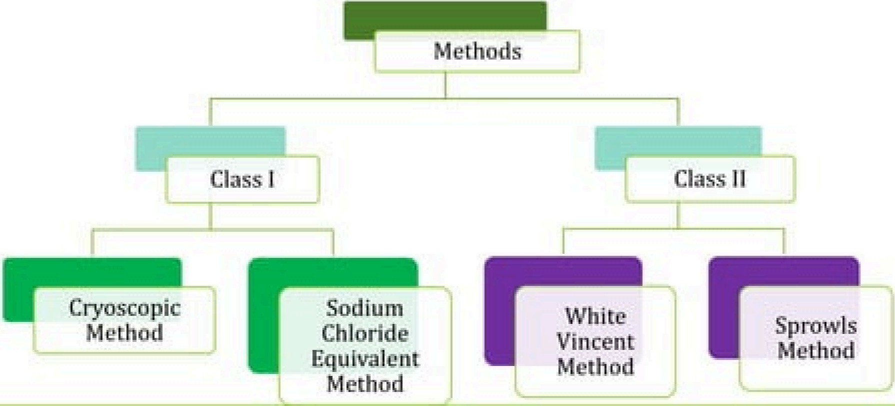
2. Nasal drops- should be isotonic.

3. Ophthalmic preparations- should be isotonic.

# 11) CALCULATION AND METHODS OF ADJUSTING ISOTONICITY

CALCULATIONS FOR SOLUTIONS ISOTONIC WITH BLOOD AND TEARS.

1. Method based on freezing point data.
2. Method based on molecular concentration.
3. Graphic method based on vapour pressure and freezing- point depression.
4. Method based on sodium chloride equivalent.



# Measurement Of Tonicity

- The tonicity of solutions may be determined by one of the following two methods:
- 1) Haemolytic Method .
- 2) Colligative Method

## Haemolytic method:

- The acting principle of this method is the observation of the effect of various solutions of drugs on the appearance of RBCs when suspended in those solutions. If, there is no change in size and shape of RBCs when immersed in test solution on observing with microscope, then this solution is isotonic to the blood.
- This method can be made more accurate by using a hematocrit, which is a centrifuge head in which a graduated capillary tube is held in each of the two arms.

- One capillary tube (tube A) is filled with blood diluted with 5 ml of 0.9% w/v NaCl (isotonic solution).
- The other capillary tube (tube B) is filled with blood diluted with an equal volume i.e. 5ml of test solution.
- Both tubes are centrifuged (i.e. rotated at high speed).
- After centrifuge, the blood cells are concentrated at one end of the capillary tubes and the volume occupied by the cells (i.e. PCV -Packed Cell Volume) is measured.
- Finally, the PCV of test solution tube (tube B) is compared with PCV of isotonic solution tube (tube A), and following inferences are made.

## RESULTS:

- If PCV of test solution (tube B) is same as that of tube A, then test solution is regarded as isotonic.
- If RBCs volume (i.e. PCV) of tube is more than that of tube A, then test solution is regarded as hypotonic solution (increase in PCV is due to swelling of RBCs, which occurs in case of hypotonic solution).
- If RBCs volume (i.e. PCV) of tube is less than that of tube A, then test solution is regarded as hypertonic solution (decrease in PCV is due to shrinkage of RBCs, which occurs in case of hypertonic solution).

# Colligative Method:

- It has been determined that solutions having same tonicity exhibit similar behavior with respect to their colligative properties such as lowering of vapour pressure, depression in freezing point, etc. Hence, tonicity of a solution may be determined by determining its colligative properties.

For making isotonic solutions, the quantities of substances to be added may be calculated by following methods:

- Based on molecular concentration
- Based on freezing point data
- Based on sodium chloride equivalent (E) value
- White-Vincent method

# Based on molecular concentration

***1% molecular concentration:***

- If one gram molecule (i.e. one gram molecular weight) of a substance is dissolved in 100 ml of water, the resulting solution will be of 1% molecular concentration. For example, the molecular weight of boric acid is 62, so if 62 gms (i.e. one gram molecular weight) of boric acid is dissolved in 100 ml of water, the resulting solution will have 1% molecular concentration.
- For non-ionizing substance, an aqueous solution having 1% molecular concentration, depresses the freezing point to - 18.6 C°, and freezing point of plasma is - 0.52 C°. So, by using this information, we can calculate the molecular concentration of blood plasma as follows;

- A depression of - 18.6 C° in freezing point of solution is due to = 1% Molecular concentration
- A depression of 1 C° in freezing point of solution is due to = 1 / - 18.6 % Molecular concentration
- A depression of - 0.52C° in freezing point of plasma is due to = 1 /- 18.6 x - 0.52

= 0.03% Molecular concentration

- So, molecular concentration of plasma is 0.03%. Therefore, any solution having the molecular concentration of 0.03% will be isotonic with blood (having the same concentration - which means isotonic).

- The formula for calculating the w/v percent of ionizing and non-ionizing substances required to make isotonic solutions with blood plasma is as follows;
- **For non-ionizing substances**
- W / V % of substance required = 0.03% x Gram molecular weight
- **For ionizing substances**
- W/V % of substance required = 0.03% x Gram molecular weight / no. of ions yielded by the molecule

## Find the proportion of Boric Acid required to make a solution isotonic. The molecular weight of boric acid is 62, and it is a non-ionizing substance

Solution:

- By applying formulae for non-ionizing substances;
- W/V % of boric acid required to make isotonic solution = 0.03% x gram molecular weight

⍰ = 0.03 x 62 = 1.86

- So, 1.86 gms of boric acid is required to make 100ml isotonic solution.

## Find the proportion of Sodium sulphate required to make a solution isotonic. The molecular weight boric of sodium sulphate is 148, and it is an ionizing substance.

By applying formulae for ionizing substances;

- *W/V % of* ionizing substance required to make isotonic solution = 0.03% x gram molecular weight / no. of ions

  - $Na_2SO_4 \longrightarrow 2Na + SO_4$

- So, total no. of ions produced by sodium sulphate = 3
- W/V % of $Na_2SO_4$ required to make isotonic solution = 0.03% x gram molecular weight / no. of ions
- = 0.03 % x 148 / 3 = 1.48
- *S0,* 1.48 gm of sodium sulphate is required to make 100ml isotonic solution.

## Based on freezing point data

- Body fluids such as blood plasma and lachrymal secretions have a freezing point of - 0.52 C° due to different solutes present in them. 0.9% solution of NaCl (isotonic solution) also has freezing point of
- 0.52 C . Hence, all solutions which freeze at - 0.52 *C°* will be isotonic with these fluids.

- Adjustment to the tonicity of solutions is simplified if the freezing point of *1%* solution of substance whose tonicity is to be adjusted (i.e. unadjusted solution) and freezing point of 1% solution of adjusting substance are known. The freezing points are usually expressed in terms of 1% solution which can be noted from the reference table.

- The quantity of the adjusting substance needed for making the solution isotonic with blood may be
- calculated from the general formula given below;
- Amount of adjusting substance required = - 0.52 -a /b
- Where,
- a = freezing point of 1% solution of un-adjusted solution
- b = freezing point of 1% solution of adjusting substance

Find the amount of sodium chloride required to render *1%* solution of cocaine hydrochloride isotonic with blood plasma. The freezing point of 1% w/v solution of cocaine hydrochloride is - 0.09 *C°*, and that of 1% NaCl is-0.576 *C°*.

- In this example,
- Unadjusted solution (whose tonicity is to be adjusted) is *1%* cocaine HCl
- Adjusting substance is NaCl
- Freezing point of 1% w/v solution of cocaine HCl (unadjusted solution) = a = - 0.09 *C°*
- Freezing point of *1%* w/v solution of NaCl (adjusting substance) = b = - 0.576 *C°*

Amount of adjusting substance required = - 0.52 -a /b

- *= -0.52-(-0.09) /-0.576 = 0.746 gms*
- Hence, by adding 0.746 gms of NoCl in 1% cocaine HCl solution, the final solution becomes isotonic.

# Based on Sodium Chloride equivalent (E)

Sodium chloride equivalent i.e. (E) of a drug is defined as;

- "The grams of Sodium chloride that will produce the same osmotic effect as 1 gm of that drug."
  - For example, potassium chloride has sodium chloride equivalent (E) value of 0.76 gm NaCl / gm of KCl-. This means 0.76 gm of NaCl produce the same osmotic effect as 1 gm of KCl.
- To make a solution of a particular drug isotonic with blood plasma, the sodium choride equivalent value (E) of that drug is noted from the reference table. This E value is multiplied with the %age of the drug solution, and result so obtained is subtracted from 0.9%. The difference in value so obtained is the amount of NaCl needed to adjust the tonicity of the solution to isotonic value.
- Amount of NaCl required = 0.9% - {%age of solution × E)

Find the amount of sodium chloride needed to make a - solution of 0.5% of KCI isotonic with blood plasma. Sodium chloride equivalent value (E) of KCI is 0.76.

- Given solution (not isotonic) = 0.5% KCI
- E value of KCI = 0.76 So, by applying formula,
- Amount of NaCI required = 0.9 - (%age of drug × E)

⍰ = 0.9-(0.5 x 0.76)

⍰ = 0.9 -0.38 = 0.52 gm —> Hence, 0.52 gm of NaCI must be added in 0.5% KCI solution to make it isotonic.

## White-Vincent method

- This method involves the addition of water to the given amount of drug to make isotonic solution, followed by the addition of some other isotonic solution (e.g. 0.9% NaCl) to make the final volume.
- The volume of water that should be added in given amount of drug to make isotonic solution is calculated by using following formula;
- V = W x E x 111.1
- Where, V = volume of water needed to make isotonic solution
- W = given weight of drug in grams
- E = NaCl equivalent value of drug
- 111.1 = constant

# Make 50ml isotonic solution from 0.5 gm of boric acid. E value of boric acid is 0.50.

- Given amount of boric acid = 0.5 gm
- Required volume = 50 ml*
- E value of boric acid = 0.50
- Firstly, we calculate the amount of water that should be added in 0.5 gm of boric acid to make isotonic solution by using formula,
- $V = W \times E \times 111.1$
- $V = 0.5 \times 0.5 \times 111.1 = 27.8$ ml
- So, 0.5 gm of boric acid is dissolved in 27.8 ml of water to make isotonic solution.
- BUT, final volume that is required is 50 ml. so, remaining 22.2ml (50 - 27.8 = 22.2) of some other isotonic solution (e.g. 0.9% NaCl) are added to make up final 50 ml volume.