PHARMACEUTICAL CALCULATIONS

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Weights & Measures:

- There are two systems of weights and measures:
  - ✓ The Imperial System
  - ✓ The Metric System

THE IMPERIAL SYSTEM

- ***It is an old system of weights and measures.***

Measurements of weights in imperial system :

- Weight is a measure of the gravitational force acting on a body and is directly proportional to its mass.
- The imperial systems are of two types:

  (a) Avoirdupois system

  (b) Apothecarie ssystem

AVOIRDUPOIS SYSTEM

- In this system pound (lb) is taken as the standard of weight (mass).

1 pound avoir (lb) = 16 oz avoir oz is pronounced as ounce.

1 pound avoir (lb) = 7000 grains (gr)

APOTHECARY OR TROY SYSTEM

- In this system **grain (gr)** is taken as the standard of weight (mass).
- 1 pound apoth (lb) = 12 ounces
- 1 pound apoth (lb) = 5760 grains (gr)
- 1 ounce = 8 drachms
- 1 drachm = 3 scruples
- 1 scruple = 20 grains (gr)

MEASUREMENTS OF VOLUMES

- 1 gallon (c) = 4 quart
- 1 quart = 2 pint (o)
- 1 pint (o) = 20 fluid ounce
- 1 fluid ounce = 8 fluid drachm
- 1 fluid drachm = 3 fluid scruple
- 1 fluid scruple = 20 minims

THE METRIC SYSTEM

- '**Kilogram**' is taken as the standard weight (mass)

1 kilogram (kg)	= 1000 grams (g)	Kilo = 1000	Greek word
1 hectogram (hg)	= 100 grams (g)	Hecto = 100	Greek word
1 dekagram (dg)	= 10 grams (g)	Deka = 10	Greek word
1 gram (g)	1 gram (g)		
1 decigram (dcg)	1/10 gram (g)	Deci = 1/10	Latin word
1 centigram (cg)	1/100 gram (g)	Centi = 1/100	Latin word
1 milligram (mg)	1/1000 gram (g)	Milli = 1/1000	Latin word
1 microgram (µg)	10^{-6} gram (g)	Micro = 10^{-6}	
1 nanogram (ng)	10^{-9} gram (g)	Nano = 10^{-9}	

MEASUREMENTS OF VOLUMES

- ‘Litre’ is taken as the standard of volume.
- 1 liter (L, lit) = 1000ml
- 1 microliter (µl) =1/1000 ml

PERCENTAGE SOLUTIONS

- The concentration of a substance can be expressed in the following three types of percentages:
- **Weight in volume (w/v):** Required to express concentration of a solid in liquid.
- **Weight in weight (w/w):** Required to express concentration of a solid in solid mixture.
- **Volume in volume (v/v):** Required to express concentration of a liquid in another liquid.

PERCENTAGE SOLUTIONS

Weight in volume (w/v)

Solute: 1part by weight

Solvent : 100 parts by volume

- In this case the general formula for 1%(w/v) is:

Solute: 1 g

Solvent: upto 100 ml

PERCENTAGE SOLUTIONS

Weight in volume (w/v)

Exercise: Calculate the quantity of

Sodium chloride required for 500ml

of 0.9% solution

ANS: 0.9% w/v solution of NaCl= 0.9 g NaCl / 100 ml

So 500 ml solution will contain 0.9g NaCl / 100 ml solution* 500 ml

= 0.9 * 500 /100

=4.5 g NaCl

PERCENTAGE SOLUTIONS

Weight in weight (w/w)

In this case the general formula for 1%(w/w) is:

		The formula is actually:	
Solute	1part by weight	Solute	1 g
Solvent upto	100 parts by weight	Solvent up to	100 g

Volume in volume (v/v)

In this case the general formula for 1%(w/w) is:

		The formula is actually:	
Solute	1part by volume	Solute	1 ml
Solvent upto	100 parts by volume	Solvent upto	100 ml

CONVERSION TABLE

Domestic Measure	Metric System	Imperial system
1 drop	0.06ml	1 minim
1 teaspoonful	5 ml	1 fluid drachm
1 desert spoonful	8 ml	2 fluid drachm
1 tablespoonful	15 ml	4 fluid drachms
1 wineglassful	60 ml	2 fluid ounces
1 teacupful	120 ml	4 fluid ounces
1 tumblerful	240ml	8 fluid ounces

WEIGHT MEASURE CONVERSION

- 1 kg = 2.2 pounds (lb)
- 1 ounce apoth = 30 g
- 1 pound avoir = 450 g
- 1 grain = 65 mg

CALCULATION BY ALLEGATION METHOD

This types of calculation involves the **mixing of two similar preparations, but of different strengths, to produce a preparation of intermediate strength.**

- The name is derived from the Latin *alligatio,* meaning the act of attaching and hence refers to the lines drawn during calculation to bind quantities together.

CALCULATION BY ALLEGATION METHOD

There are two alligation methods :

1. **Alligation Medial** :

- Involves calculating the weight average percentage strenght of a mixture of two or more substances of known quantity and conc.
- In other words, this methods calculates the amount of active ingredients in each substance in the compound and then calculates the active ingredients per cent present in whole compound.
- The quantities are expressed in a common denomiation of either weight or volume

CALCULATION BY ALLEGATION METHOD

There are two alligation methods :

2. **Alligation Alternate** :

- This rapid method involves determining the proportions in which substances of different strengths are mixed to yield a desired strength or concentration.
- Once the proportion is known, the exact amounts of substances required can be calculated.

CALCULATION BY ALLEGATION METHOD

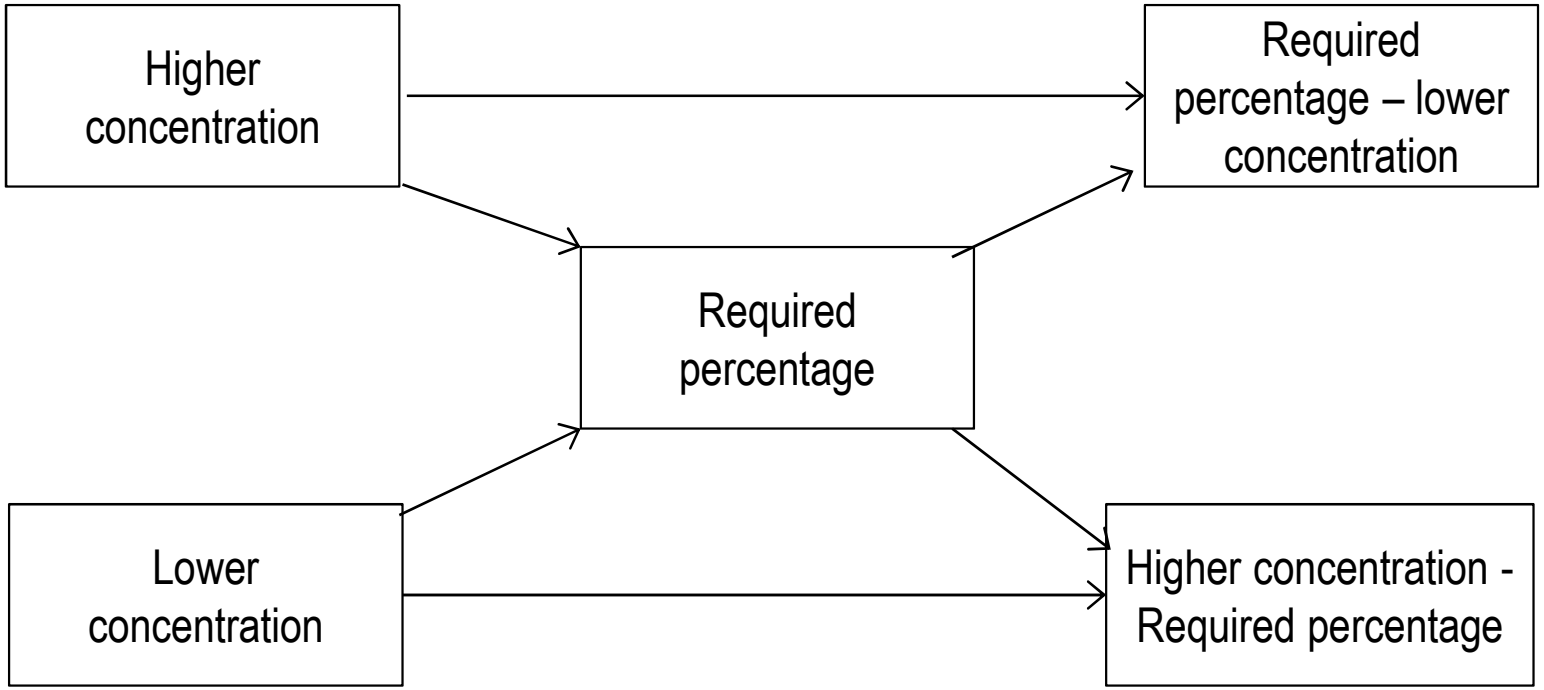
There are two alligation methods :

2. Alligation Alternate :

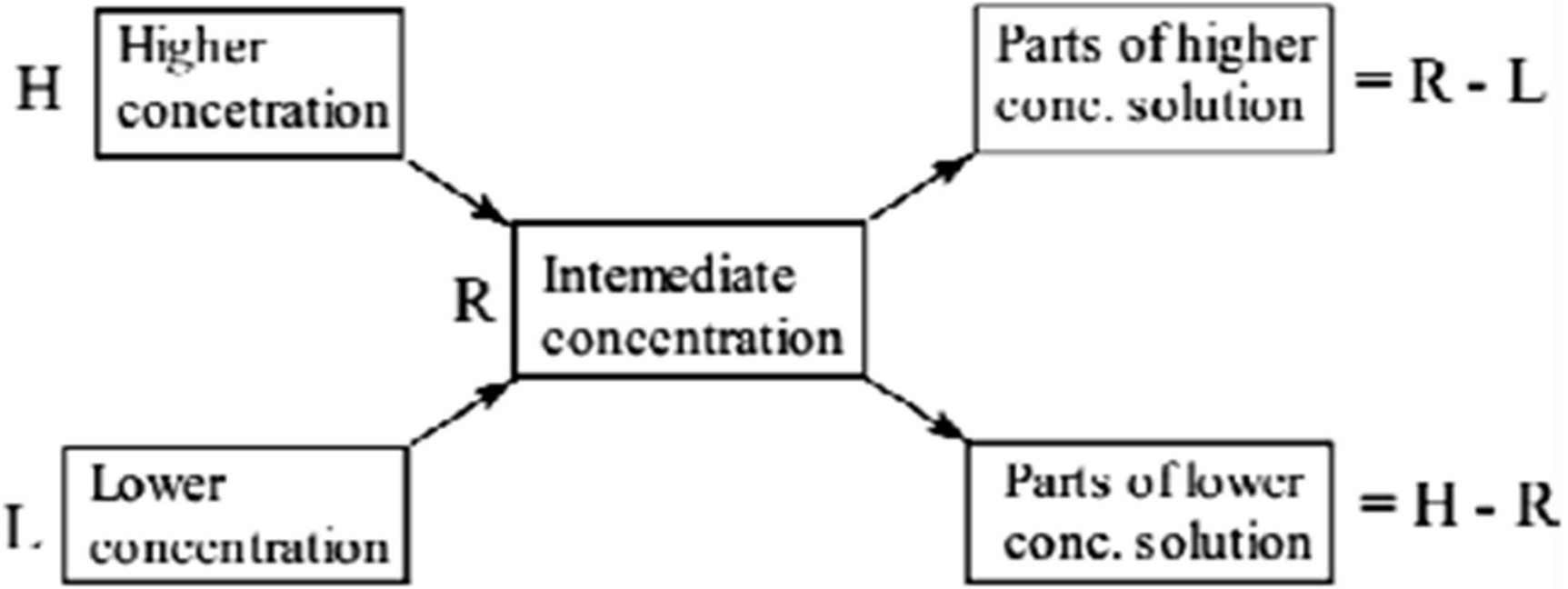
The steps involved:

1. The required percentage or concentration is placed in the centre
2. The percentage of the substance with the lower strength is placed on the lower left hand side
3. The percentage of the substance with the higher strength is placed on the upper left hand side
4. The required percentage is subtracted from the lower percentage, and the obtained difference is placed on the upper right hand side
5. The higher percentage is subtracted from the desired percentage, and the obtained difference is placed on the lower right hand side

CALCULATION BY ALLEGATION METHOD

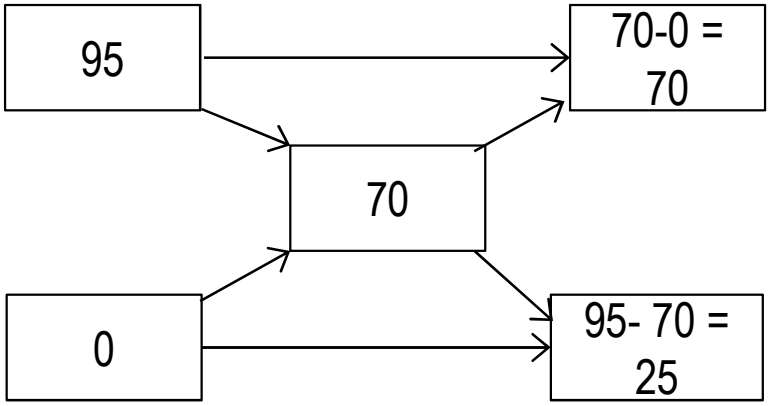


- Method:


H
Higher concetration
R
Intemediate concentration
L
Lower concentration
Parts of higher conc. solution
= R - L
Parts of lower conc. solution
= H - R

CALCULATION BY ALLEGATION METHOD

Problem 1: Calculate the volume of 95 % alcohol required to prepare 600 ml of 70% alcohol



Given:

- Volume required = 600 ml
- Percentage of alcohol required 70 %
- Percentage of alcohol to be used = 95 %

Ans: 70 parts of 95 % alcohol and

25 parts of water will produce 70%

Qty of 95 % alcohol required = 600*70 / 95 = 442.10 ml

Qty of water required = 600* 25/ 95 = 157.90 ml

CALCULATION BY ALLEGATION METHOD

Problem 2: Calculate the amount of 70%, 60%, 40% and 30% alcohol that should be mixed to get 50% alcohol

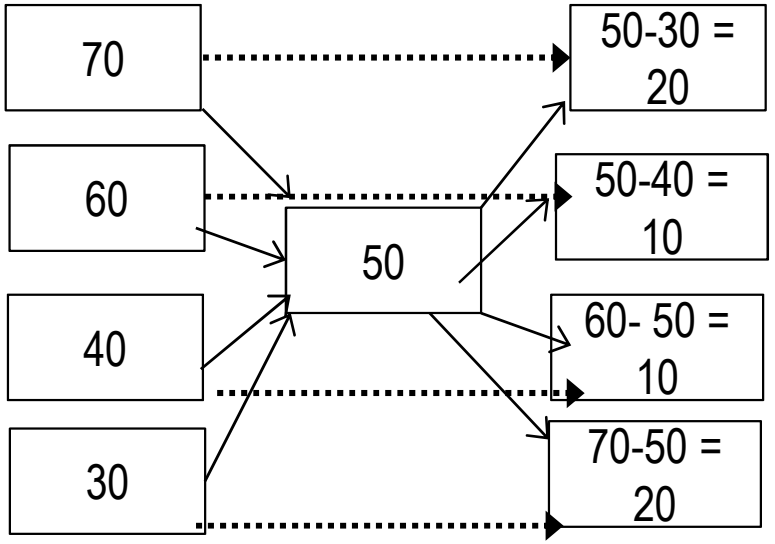
Solution: When 20 parts of 70% alcohol,

10 parts of 60% alcohol,

10 parts of 40 % alcohol

20 parts of 30% alcohol are mixed together

The resulting solution will produce 50% alc.



= (20 X 70) + (10 X 60) + (10 X 40) + (20 X 30)

= 1400 + 600 + 400 + 600 = 3000

PROOF SPIRIT

- For excise (tax) purpose, the strength of alcohol in indicated by degrees proof. That is Alcohol strength is calculated in terms of proof spirit
- The US System: Proof spirit is 50% alcohol by volume (or 42.49% by weight).
- The British / Indian system: Proof spirit is 57.1% ethanol by volume (or 48.24% by weight).
- Definition: Proof spirit is that mixture of alcohol and water, which at 51ºF weighs 12/13th of an equal volume of water.
- [N.B. Density of proof spirit = 12/13 of density of water at 51ºF = 0.923 g/ml]
- The strength value above proof strength is expressed as **OVER PROOF (O/P)**
- The strength value above proof strength is expressed as **UNDER PROOF (U/P)**

PROOF SPIRIT

Conversion of strength of alcohol from %v/v to degrees proof as per Indian system.

$$\text{Strength of alcohol} = \frac{\%\text{v / v strength}}{57.1\%\text{v / v}} \times 100$$

Conversion of strength of alcohol from degrees proof to %v/v as per Indian system.

$$\text{Strength of alcohol in \%v/v} = \frac{\text{Strength of alcohol in degree proof} \times 57.1}{100}$$

PROOF SPIRIT

Problem 1: Convert 90% v/v alcohol into proof spirit

Solution : As 57.1% alcohol corresponds to 100 volumes of proof spirit,

1 volume of 57.1% v/v alcohol = 100/57.1 = 1.753 volumes of proof spirit

90 volumes of ethyl alcohol = 90 X 1.753 = 157.77 volumes of proof spirit

i.e. 100 L (or ml) of 90% alcohol are equal to 157.77 L (or ml) of proof spirit

The proof strength of 90%^ alcohol = 157.77 – 100 = 57.77

ISOTONIC SOLUTION

- ***Osmosis:*** If a solution is placed in contact with a semipermeable membrane the movement of the solvent molecules through the membrane is called osmosis.
- An ideal semipermeable membrane only lets the solvent molecules to pass through it but not the solute molecules.
- The biological membranes are not ideal semipermeable membranes.
- They are selectively permeable; they give passage to some solutes while stop the passage of others. In case of biological membranes another term tonicity is used.
- ***Isotonicity:*** A solution is isotonic with a living cell if there is no net gain or loss of water by the cell, when it is in contact with this solution

ISOTONIC SOLUTION

- If a living cell is kept in contact with a solution and there is no loss or gain of water by the cell then the solution is said to be **isotonic with the cell**.
- It is found that the osmotic pressure of 0.9%w/v NaCl solution is same as blood plasma. So 0.9%w/v NaCl solution is isotonic with plasma.
- ***Tonicity:***

A. Isotonic: When a solution has same osmotic pressure as that of 0.9%w/v NaCl solution.

B. Paratonic: ***Not isotonic***

(a) Hypotonic: The osmotic pressure of the solution is higher than 0.9%w/v NaCl solution

(b) Hypertonic: The osmotic pressure of the solution is lower than 0.9%w/v NaCl solution

ISOTONIC SOLUTION

- A red blood corpuscle is placed in a solution and after some time it is viewed under microscope.

Observation	Conclusion	Mechanism
The shape and size of the cell remained unchanged	The solution is isotonic	Osmotic pressure of the cell fluid and the solution are same. No movement of water occurs across the cell membrane.
The size of the cell increased(swelling) and may burst.	The solution is hypotonic.	Osmotic pressure of the cell fluid is more than the solution. Water molecules moved from the solution to the interior of the cell, so the cell swelled.
The size of the cell is reduced(shrinks) or shrinked.	The solution is hypertonic.	Osmotic pressure of the cell fluid is less than the solution outside. Water molecule moved from the interior of the cell to the solution.

IMPORTANCE OF ADJUSTMENT OF TONICITY IN PHARMACEUTICAL DOSAGE FORMS

- **Solution for intravenous injection:** The injection must be isotonic with plasma, otherwise the red blood corpuscle may be haemolysed.
- **Solution for subcutaneous injection**: Isotonicity is required but not essential, because the solution is coming in contact with fatty tissue and not in contact with blood.
- **Solution for intramuscular injection:** The aqueous solution may be slightly hypertonic. This will draw water from the adjoining tissue and increase the absorption of the drug.
- **Solution for intracutaneous injection:** Diagnostic preparations must be isotonic, because a paratonic solution may cause a false reaction.

IMPORTANCE OF ADJUSTMENT OF TONICITY IN PHARMACEUTICAL DOSAGE FORMS

- **Solutions for intrathecal injection:** Intrathecal injections are introduced in the cavities of brain and spinal chord. It mixes with the cerebrospinal fluid (CSF). The volume of CSF is only 60 to 80ml.
- **Solutions for nasal drops:** Aqueous solutions applied within the nostril may produce irritation if it is paratonic. So nasal drops must be isotonic with plasma.
- **Solutions for ophthalmic use:** Only one or two drops of ophthalmic solutions are generally used. So it is not essential for eyedrops to be isotonic. Slight paratonicity will not produce great irritation because the eyedrops will be diluted with the lachrymal fluid

TONICITY ADJUSTMENT

- Tonicity of isotonic solutions is adjusted by employing osmotic pressure as these solutions are usually iso-osmotic
- Pharmacist does not usually received a prescription for paratonic solution
- Tonicity can be adjusted by introducing an inert material into the solution, provided this material is compatible with the drug
- The methods by which isotonicity can be calculated are:

1. Freezing point method
2. Molecular Weight method

TONICITY ADJUSTMENT

1. Freezing point method

- In lacrymal fluid, anumber of solutes which freeze at -0.52ºC are present, hence all the solutions with freezing point of -0.52ºC will be isotonic with lachrymal fluid

- Similarly, human blood plasma also exhibits the same freezing point, thus, the solutions freezing at -0.52ºC will be isotonic with it

TONICITY ADJUSTMENT

1. Freezing point method

- Tonicity adjustment can be eased if the freezing point of the drug and the inert salt is known for various strenght of their solutions.
- Tables providing this information are maintained by the pharmacists and the same information can also be obtained from the standard texts.
- Freezing points in this case are expressed in terms of 1% solutions and the quantity can be determined by multiplying the freezing points with the factor.

TONICITY ADJUSTMENT

1. Freezing point method

Freezing point of the tear secretion or Human blood plasma	=	Freezing point of the drug + Freezing point of the adjusting substance

.....Eq (1)

TONICITY ADJUSTMENT

1. Freezing point method

Example : 200 ml of an eye wash containing 1% of boric acid is to be dispensed. (F.P. of 1% boric acid = -0.29ºC and F.P. of 1% solution of NaCl = -0.58ºC)

On applying the equation 01:

-0.52 = -0.29 + (-X)

X = 0.52-0.29 = 0.23 i.e. NaCl sufficient to produce a freezing point lowering of 0.23ºC is required

It is given that 1% NaCl lowers the freezing point by 0.58ºC, thus, NaCL required to produce lowering of 0.23ºC will be:

1X0.23/ 0.58 = 0.39g/100 ml or 0.39%

Thus, the working formula for 200 ml of the eyewash will be:

TONICITY ADJUSTMENT

Contd…

Boric Acid (1%, for 200 ml) = 1 X 2= 2 gm

Sodium Chloride (0.39% for 200ml) = 0.39X2 = 0.78g

Purified water sufficient to produce 200 ml

However, if pharamcist has been asked to dispense 200 ml of eyewash of boric acid, the calculation will be follows:

Lowering of 0.29ºC in F.P. is produced by 1 gm of boric acid

Therefore, lowering of 0.52ºC in F.P. is produced by 1X0.52/ 0.29 = 1.8kg

Hence, 1.8g of boric acid is required for making 100ml of an eyewash and working formula will be:

Boric Acid (1.8% for 200ml) = 1.8*2 = 3.6 g

Purified water sufficient to produce 200ml

TONICITY ADJUSTMENT

2. Molecular Weight Method

- A solution's freezing point inversely depends on the concentration of the solutes dissolved in it. Thus, greater solute concentration lowers the freezing point of the solution.
- This indicates that freezing point is a function of the concentration of gram moes of the solute.
- It can also be said that freezing point depends on the no. od ions, the drug weight and its molecular weight.

:

TONICITY ADJUSTMENT

2. Molecular Weight Method

- **For a 0.9% solution of sodium chloride the concentration can be expressed as :**

$$\frac{\{\text{No. of grams of NaCL X No. of effective ions}\}}{\text{Molecular Weight of NaCl}} = \text{Isotonic factor or Isotonicity}$$

- **In other words : g X n / m = IsotonicFactor OR**

0.9X 2 / 58.5 = 0.03 (Isotonic factor for NaCl)

TONICITY ADJUSTMENT

2. Molecular Weight Method

- Isotonicity of 0.9% NaCl (normal saline) is similar to those of body fluids. Thus, 0.03 will be the isotonicity or tonicity factor for tear secretion and blood serum.
- The quantities for making eye solution can calculated by equating the 0.03 value with the tonicity factor of the drug and additive(S)
- The equztion for calculating the additive quantity :

$$0.03 = \frac{g \times n}{m} = \frac{g_1 \times n_1}{m_1} = \frac{g_2 \times n_2}{m_2}$$

TONICITY ADJUSTMENT

2. Molecular Weight Method

- Where, g = Weight in gram

  n = Effective ion concentration

  m = molecular weight of the medicament


Thank
You