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 referes to the lines drawn during calculation to bind quantities together

Method: High conc parts of high conc

Intermediate conc

Low conc parts of low conc

Example:

Prepare 600ml of 60%v/v alcohol from 95% v/v alcohol.

Higher concentration = 95%

Required concentration = 60%

Lower concentration = 0% (i.e. water)

So from allegation method

it is obtained: Volume of 60% alcohol solution = 600ml

95% 60 - 0 = 60 parts

↘ ↗

60

0% ↗ ↘ 95 - 60 = 35 parts

95 parts

Proof Spirits:

For excise (tax) purpose, the strength of alcohol in indicated♣ by degrees proof.

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 510F weighs 12/13th of an equal volume of water.

[N.B. Density of proof spirit = 12/13 of density of water at♣ 510F = 0.923 g/ml] 1

| 100 degree proof alcohol = 57.1% v/v alcohol |

If the strength of the alcohol is above 57.1%v/v alcohol then the solution is called “over proof”.

If the strength of the alcohol is below 57.1%v/v alcohol then the♣ solution is called “under proof”.

In India, the excise duty is calculated in terms of Rupees per litre♣ of proof alcohol.

So any strength of alcohol is required to be converted to degree♣ proof.

We shall follow the British System Conversion of strength of alcohol from %v/v to degrees proof as per Indian system.

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

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

Isotonic Solutions: Osmosis:

If a solution is placed in contact with a♣ semipermeable membrane the movement of the solvent moleculesthrough the membrane is called osmosis.

An ideal semipermeable membrane only lets the solvent♣ moleculesto 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.

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 23

Test of tonicity:♣ 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.

25 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.

Calculations for Adjustment of Tonicity:

It is difficult and time consuming to determine the osmotic♣ pressure of a solution.

So some indirect methods are adopted to compare between two isotonic solutions

Two solutions will produce same osmotic pressure if both contain the same numbers of ultimate units.

These units may be as follows: These units may be molecules in case of substances♣ those do not ionize.

These units may be ions in case of substances those♣ ionize.

These units may be both ions and unionized♣ molecules in case of weak electrolytes. 27

• Tonicity of a solution can be adjusted by the following methods:

Tf∆– Freezing point depression method ( ) – Sodium chloride equivalent method (E) – Isotonic solution V-Value method