Methods of adjustment of Isotonicity

1. Freezing Point Method:

The lachrymal secretion contains several solutes in it and has a freezing point of -0.52°C. All solutions, which freeze at -0.52°C, will be isotonic with the lachrymal fluid. Human blood plasma also freezes at this temperature and hence solutions having freezing point at -0.52°C will be isotonic with blood plasma as well.

Adjustment of tonicity is simplified if the freezing points of the medicament and the inert salt (adjusting substance) are known for various strengths of their solutions. Freezing points are usually expressed in terms of 1% solutions and one can calculate the quantity by multiplying the freezing point with the factor.

The following, equation is useful:

Freezing point of tear secretion Freezing point of drug freezing or human Blood plasma = point of the adjusting substance.

Therefore the amount of adjusting substance required may be calculated from the equation where:-

W = the weight, in g, of the added substance in 100 mL of the final solution;

a = the depression of the freezing point produced by the medicament already present in solution, calculated by multiplying the value for the medicament by the strength of the solution expressed as a percentage w/v; and

b = the depression of the freezing point of water produced by 1% of the adjusting substance.

2. Molecular Weight Method:

Freezing point of a solute depends on the concentration of the solute dissolved therein. Greater the concentration of the solute, lower is the freezing point. In other words it depends on the number of ions (more correctly, the number of effective ions), the weight of the substance and its molecular weight. The concentration for 0.9% solution of sodium chloride can be expressed in the following manner:

Where

g = No. of gram of sodium chloride (g)

n = No. of effective ions (n)

m = molecular weight of sodium chloride (m) i.e. isotonicity factor for sodium chloride is 0.03.

Since 0.9% solution of sodium chloride (normal saline) is isotonic with body fluids, 0.03 will be the isotonicity or tonicity factor for tear secretion and blood plasma as well. Thus quantities for making eye solutions can be calculated by equating the value of 0.03 with the tonicity contributed by the drug and the additive(s).

The following equation is employed for calculating the quantity of the additive(s):

where g, n and m denote the weight in gram, effective ion concentration and molecular weight of the medicament, respectively. Values followed by subscript 1 or 2 in the equation above refer to the first additive or the second additive (if present). Effective | ionic concentration can be ascertained from the following generalizations;

n = 1 for non-ionisable substances, e.g. dextrose

n = 1.5 for partially ionisable solutes in two ions, e.g. silver nitrate

n = 2 for highly ionisable solutes in two ions e.g. sodium chloride

n = 2 for partially ionisable solutes in three ions, e.g. sodium sulfate

3. Sodium Chloride Equivalent Method:

This is the simplest method and is based on the sodium chloride equivalents of various drugs. Sodium chloride equivalent of a drug represents the amount of sodium chloride equivalent to 1 g of the drug. The method avoids tedious calculation. Sodium chloride equivalents of some common drugs are given in the following table.

It can be memorized that 0.27 g of sodium chloride makes 30 mL of a 0.9% solution and that 4.1 grain of sodium chloride makes 1 fl oz. of a 0.9% solution.

4. Isotonic solution V-Values:

Another method for adjusting tonicity is based on V-values. The isotonic solution V-values for some of the commonly used drugs are given in the following Table. The V-value of a drug is defined as the volume of water in mL to be added to 0.3 g of the drug to make an isotonic solution. The addition of an

isotonic vehicle (diluting vehicle) to make 30 ml yields a 1% solution (0.3 g drug in 30 ml). Solutions prepared by this method are iso-osmotic with 0.9% sodium chloride.