Pharmaceutical Calculations

Assist.Professor pharm.
Kahtan j.Hassoun

Dilution and concentration of pharmaceutical preparations (altering products strength)

- Conditions
- Pharmaceutical preparations can be diluted or concentrated by using compatible solvent i.e.
- It is same with original solvent
- Ex.
- *If 500 mL of a 15% v/v solution are diluted to 1500 mL, what will be the percentage strength (v/v)?*
- 1500 (mL)
- 500 (mL)

- (%) ١٥
- x (%)
- x 5%, *answer.*
-

Example:

Rx

Zinc oxide 1.5
Hydrophilic petrolatum 2.5
Purified water 5
Hydrophilic ointment ad 30

How much zinc oxide should be added to the product to make a 10% zinc oxide ointment?

Sol:

1.5 30
X 100 x= 5%

100% 5 parts of 100%
10%
5% 90 parts of 5%

Relative amount 5 : 90 = 1: 18

1 18
X 30 x = 1.667g zinc oxide

Example:

castor oil	5ml
Resorcinol monoacetate	15ml
Alcohol 85 % ad	240ml

How many ml.s each of 95% v/v alcohol and water should be used in preparing the prescription?

Sol.1:

5+15 = 20 ml of cast. Oil. And resorcinol.

240 -20 = 220 ml of 85% alcohol

85% 100

X 220 x = 187 ml

95 100

187 y y = 196.84 ml of 95% alcohol.

Example:

How many ml.s of a 2.5 % w/v chlorpromazine hydrochloride injection and how many ml.s of 0.9% w/v sodium chloride should be used to prepare 500 ml of a 0.3% w/v chlorpromazine hydrochloride injection?

Sol:

$C1 \quad V1 = C2 \quad V2$

$2.5 * V1 = 0.3 * 500$

V1 = 60 ml of chlorpromazine.

500 – 60 = 440 ml of sodium chloride.

(H.W: answer this ex. With alligation alternate method.)

Isotonic solution

- When a solvent passes through a semipermeable membrane from a dilute solution in to a more concentrated one, the concentrations become equalized and the phenomenon is known as osmosis.
- Thus, osmotic pressure is the pressure responsible for this phenomenon which varies with the nature of the solute.

We have two type of solute:

١. Nonelectrolyte, its solution contains only molecules and the osmotic pressure depends on the conc. of the solute.

٢. electrolyte solution , its solution contains ions and the osmotic pressure depends on the conc. of the solute and its degree of dissociation.

Thus , solutes that dissociate present a greater no. of particles in solution and exert a greater osmotic pressure than undissociated molecules

Colligative properties; such as osmotic pressure, vapor pressure, boiling point, and freezing point depend on the no. of particles in solution therefore the change in any one of them will result in a change in the other.

Isosmotic solutions: they are two solutions have the same osmotic pressure.

Isotonic solution: a solution have the same osmotic pressure as body fluid (serum, lacrimal fluid).

Hypotonic solution: a solution have lower osmotic pressure than that of a body fluid.

Hypertonic solution: a solution have higher osmotic pressure than that of a body fluid

Most ophthalmic preparations should be isotonic or approximately isotonic to be comfort to the patient and to reduce the irritation of the eyes. Injections that are not isotonic should be administered slowly and in small quantities to minimize tissue irritation and pain. Intravenous infusions which are hypotonic or hypertonic can have adverse effects because they generally are administered in large volumes.

We can calculate the osmotic pressure depending on colligative properties especially freezing point.
Note: freezing point of both serum and lacrimal fluid is (- 0.52 ◦C)
Freezing point (or any other colligative properties) of solutions could be used for determining the tonicity of these solutions.
As we said before F.P. of body fluid is (-0.52 ◦c) so, any substance has this F.P. should be isotonic with body fluid.

Tonicity for nonelectrolyte substances

- When one gram molecular weight of any nonelectrolyte is dissolved in 1000 gm of water, the freezing point of the solution is about (-1.86 C)
- So we can calculate the weight of substance that should be dissolved in (1000 gm) of water

Example: Boric acid has m.wt = 61.8 , thus 61.8 gm when dissolved in 1000 gm of water should produce F.P. = - 1.86 ◦c therefore:

1.86/0.52=61.8g/x

X=17.3 gm of boric acid in 1000 gm of water = 1.73% (w/v) make isotonic sol.

Example: Sodium chloride in weak solution 80% dissociated (and have m.wt. = 58.5) so, 100 molecules give 180 molecules Dissociation factor (i) = 180/100 = 1.8 therefore: simple isotonic solution could be calculated as follow:

0.52 * m.wt. /1.86 * (i) = ( ) gm of solute in 1000 gm water.

X= 9.09 gm of NaCl in 1000 gm of water = 0.9% (w/v) make isotonic sol

Example

How much Sod. Chloride should be added to 0.5% w/v sol. to make it isotonic ?

0.5% 0.5 gm /100 ml water

0.9% 0.9 gm/ 100 ml water Then

0.9 – 0.5 = 0.4 gm of NaCl should be added to 100 ml 0.5% sol. to be made isotonic with body fluid.

The amount of NaCl represented by a sub. = wt. of the sub. * E value

<u>The procedure for calculating isotonic sol. With NaCl equivalent is:</u>

1. Calculate the amount of NaCl represented by the sub. In the prescription (sub. amount * E value).
2. Calculate the amount of NaCl that would be contained in a 0.9% solution of the volume of the prescription.
3. Amount of NaCl added to make the sol. Isotonic =Amount of NaCl (step 2) – amount of NaCl (step 1)
4. If an agent other than NaCl (Boric acid, dextrose …) is to be used to make isotonic solution , we will divide the amount of NaCl (step 3) by the E value of that agent.

Example:

how many grams of sodium chloride should be used in compounding the following prescription? (E value of Pilocarpine nitrate is 0.23)

Rx

Pilocarpine nitrate		0.3
Sodium chloride		q.s.
Purified water	ad	30 ml

Make isoton. Sol.

Sig. for the eye

Use of freezing point in calculation of isotonicity:

Substance to be isotonic should lower freezing point ΔT_f = - o.52

(which is the freezing point of blood and lacrimal fluid).

Example:

How many milligrams each of NaCl and dibucaine HCl are required to prepare 30 ml of 1% dibucaine HCl isotonic solution?

(ΔT_f (1% dibucaine) = - 0.08 , ΔT_f (1% NaCl) = - 0.58 **)**

Electrolytes

- A *chemical unit, the* ***milliequivalent (mEq), is now used almost exclusively in the United States*** by clinicians, physicians, pharmacists, and manufacturers to express the concentration of electrolytes in solution.

mEq = mg X Valence /Atomic, formula, or molecular weight

What is the concentration, in milligrams per milliliter, of a solution containing 2 mEq of potassium chloride (KCl) per milliliter?

Molecular weight of KCl = 74.5

Equivalent weight of KCl = 74.5

1 mEq of KCl = 1/1000 X 74.5 g = 0.0745 g = 74.5 mg

2 mEq of KCl = 74.5 mg X 2 = 149 mg/mL, *answer.*

Osmolarity:As indicated in Chapter 11, osmotic pressure is important to biologic processes that involve the
diffusion of solutes or the transfer of fluids through semipermeable membranes. The *United States Pharmacopeia2 states that knowledge of the osmolar concentrations of parenteral fluids is*
important. The labels of pharmacopeial solutions that provide intravenous replenishment of fluid, nutrients, or electrolytes, and the osmotic diuretic mannitol are required to state the osmolar concentration. This information indicates to the practitioner whether the solution is hypoosmotic,
iso-osmotic, or hyperosmotic with regard to biologic fluids and membranes.
Osmotic pressure is proportional to the *total number of particles in solution. The unit used*
to measure osmotic concentration is the *milliosmole (mOsmol). For dextrose, a nonelectrolyte,*
1 mmol (1 formula weight in milligrams) represents 1 mOsmol. This relationship is not the same with electrolytes, however, because the total number of particles in solution depends on the degree of dissociation of the substance in question. Assuming complete dissociation, 1 mmol
of NaCl represents 2 mOsmol (Na Cl) of total particles, 1 mmol of CaCl2 represents 3

Intravenous infusions

- ***Intravenous (IV) infusions are sterile,aqueous preparations administered intravenously in relatively* large volumes.**

Common I.V.infusions

- 0.9% Sodium Chloride NS (Normal Saline)
- 0.45% Sodium Chloride 1⁄2NS
- 5% Dextrose in Water D5W or D5W
- 10% Dextrose in Water D10W or D10W
- 5% Dextrose in 0.9% Sodium Chloride D5NS or D5NS
- 5% Dextrose in 0.45% Sodium Chloride D51⁄2NS or D51/2NS
- Lactated Ringer’s (0.86% Sodium Chloride, LR
- 0.03% Potassium Chloride, 0.033%
- Calcium Chloride)
- 5% Dextrose in Lactated Ringer’s D5LR or D5LR