TONICITY

Iso-osmotic:

Solution which produces the **same osmotic pressure** as that of the cell contents but not necessarily the same concentration of solute in question, but the **solute is permeable** through the cell membrane thereby altering the tone of the cell.

Eg. 1.8% solution of urea

Isotonic:

Iso (same) and tonic (concentration). Solutions which produce the **same osmotic pressure** as that of the cell contents and also have same salt concentration in question, **without net gain or loss of water** by both solutions, provided the cell membrane is impermeable to the solutes.

Eg. 0.9% w/v NaCl solution

5.0% w/v Dextrose solution

2.0% w/v of Boric acid solution

Difference between Osmolarity and Tonicity

• Osmolarity is a measure of the osmotic pressure of a given solution.	• Tonicity is a measure of the osmotic pressure gradient between two solutions separated by a permeable membrane.
• Osmolarity is measured in osmol/L	• Tonicity is related to concentration measurements and is expressed in terms of mol/L
• Osmolarity takes into consideration the total number of solute that penetrates and do not penetrate the membrane.	• Tonicity takes into account the concentration relating to the non-permeable solutes.
• Osmolarity often represents the analysis of the given solution.	• Tonicity is used as a measure of the external environment

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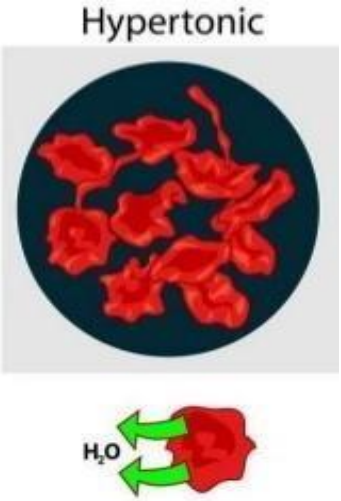
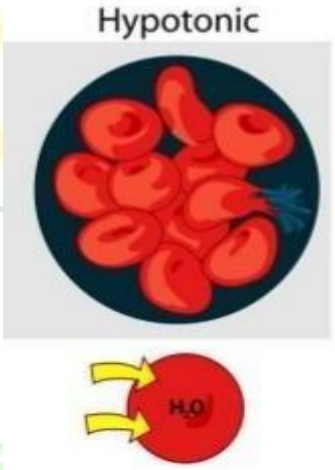
Hypertonic Solution:



- A hyper-tonic solution is one that has greater concentration than reference solution (i.e. RBCs contents)
- A hyper-tonic solution has greater osmotic pressure than that of reference solution.
- If RBCs are suspended in 2% w/v solution of NaCl (i.e. hypertonic solution) then water present within the RBCs will come out (i.e.due to osmosis, from dilute RBCs fluid to concentrated hypertonic solution) into the surroundings to dilute the NaCl solution (hypertonic solution). This exit of water from RBCs causes their shrinkage and RBCs become winkled in shape. This shrinkage of RBCs is known as "Plasmolysis".

Hypotonic Solution:



- A hypo-tonic solution is one that has lower concentration than reference solution (i.e. RBCs contents).
- A hypo-tonic solution has lower osmotic pressure than that of reference solution.
- If RBCs are suspended in 0.1% w/v solution of NaCl (i.e hypotonic solution), then water from this solution will enter the RBCs (i.e. due to osmosis, from dilute hypotonic solution to RBCs fluid) to dilute the fluid within the RBCs causing their swelling, which may later result in rupturing of RBCs and release of haemoglobin. This rupturing of RBCs is known as "Haemolysis".

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Measurement of Tonicity

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There are broadly two methods to measure tonicity:

1. Hemolytic Method: Effect of various solutions of a drug is observed on the appearance of red blood cells suspended in the solution.
2. Cryoscopic Method: Isotonicity can be measured from colligative properties of the solution. E.g. Freezing point depression method.

Isotonic Buffered Solutions:

A solution which maintains **isotonicity** and **pH** as that of body fluids.

Tonicity Adjustment Methods:

Class I methods: Cryoscopic method
Sodium chloride equivalent method

Class II methods: White Vincent Method
Sprowls method

Cryoscopic Method
(Freezing Point Depression Method)

The plasma and blood freezing point temperature = -0.52°C

- The dissolved substances in plasma or tear depress the solution freezing point below 0.52°C.
- Any solution that freeze at t = -0.52°C is isotonic with blood and tear

$$W = \frac{0.52 - a}{b}$$

Where, W = weight of substance that need to be adjusted to make it isotonic substance in g.
a = the depression of the freezing point of water produced by the medicament already in the solution.
b = the depression of freezing of water produced by 1 % w/v of the added substance.

NUMERICAL:

- How much NaCl is required to render 100ml of a 1% solution of apomorphine hydrochloride isotonic with blood serum?
  (1% solution of drug has freezing point lowering of 0.08°C)
  (1% solution of NaCl has a freezing point lowering of 0.58°C)

Solution:

In order to make drug solution isotonic, NaCl is needed to add to lower freezing point by (0.52-0.08)

W = 0.44/0.58
W = 0.758 g

So, 1 g of drug and 0.758g of NaCl in 100 ml of solution.

- ❑ Find out 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.

Solution:
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

W = 0.52-0.09/ 0.576
W = 0.746 g

Hence, by adding 0.746 gm of NaCl in 1% cocaine HCl solution, the final solution become isotonic.

Sodium Chloride Equivalent Method (E)

- Sodium chloride equivalent (E) of a drug is the amount of sodium chloride that is equivalent to 1 gm of the drug.
- The percent of sodium chloride required for adjusting the isotonicity can be calculated using the following equation.

$$PSA = 0.9 - (PSM \times E\ of\ \ medicament)$$

Where,
PSM = Percent strength of medicament
PSA = Percent of sodium chloride for adjustment of isotonicity.

Above equation is used to calculate the amount of adjusting substance (sodium chloride) required for making the solution isotonic. It is valid for 100 ml solution.

NUMERICAL: Calculate the gram of sodium chloride needed to make 30 ml of a 2% isotonic physostigmine salicilate solution using sodium chloride method.

Solution:
E value of physostigmine salicilate = 0.16
PSM =2.0 %
Volume of preparation required = 30 ml
For equation

PSM = 0.9 – (PSM E of medicament)
= 0.9 – (2.0 0.16)
= 0.9 - 0.32 = 0.58 %

The above strength is valid for 100 ml since is expressed in percent. It should be prepared from 30 ml of solution
For 100 ml of solution, sodium chloride required = 0.58
For 30 ml of solution, sodium chloride required =?

30 × 0.58/100 = 17.4/100 = 0.174 g of sodium chloride

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.
- White Vincent, from their study of need of Ph adjustment in addition to tonicity of ophthalmic solution, developed an equation
  The volume of water that should be added in given amount of drug to make isotonic solution is calculated by using:

$$V = W \times E \times 111.1$$

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

NUMERICAL: Make 50 ml isotonic solution from 0.5 gm of boric acid. E value of boric acid is 0.50.
Solution:
Given amount of boric acid = 0.5 gm
Required volume = 50 ml
E value of boric acid = 0.50
Fistly, we calculate the amount of the 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 added in 27.8 ml of water to male isotonic solution.
But, final volume that is required is 50ml. so, remaining 22.2ml of some other isotonic solution (e.g. 0.9% NaCl) are added to make up final volume 50 ml.

Sprowl Method:

Sprowls method is a simplification of White-Vincent method in which values of V for the drug of fixed weight (0.3 g) are computed and construed.
This is commonly used for ophthalmic and parental solutions.

$$V = W \times E1\% \times 111.1\ or$$

$$V = 33.33 \times E1\%$$