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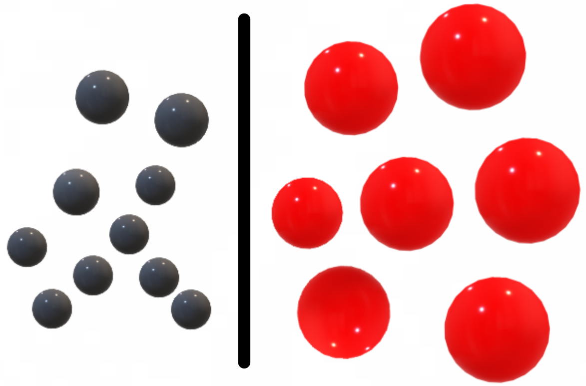
Physical Pharmacy

Isotonic Solutions

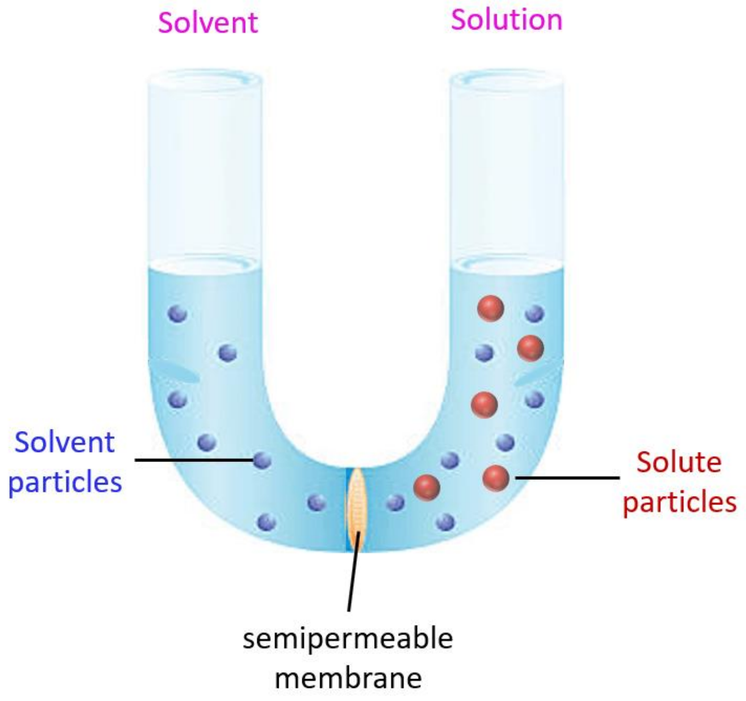


Isotonic solutions

Osmosis:

- Diffusion of a solvent through a semipermeable membrane from a less concentrated solution into a more concentrated solution is called the **osmosis**

- Osmotic pressure: The pressure that must be applied to the side of the concentrated solution to prevent the flow of the pure solvent into the solution is called the osmotic pressure of the solution



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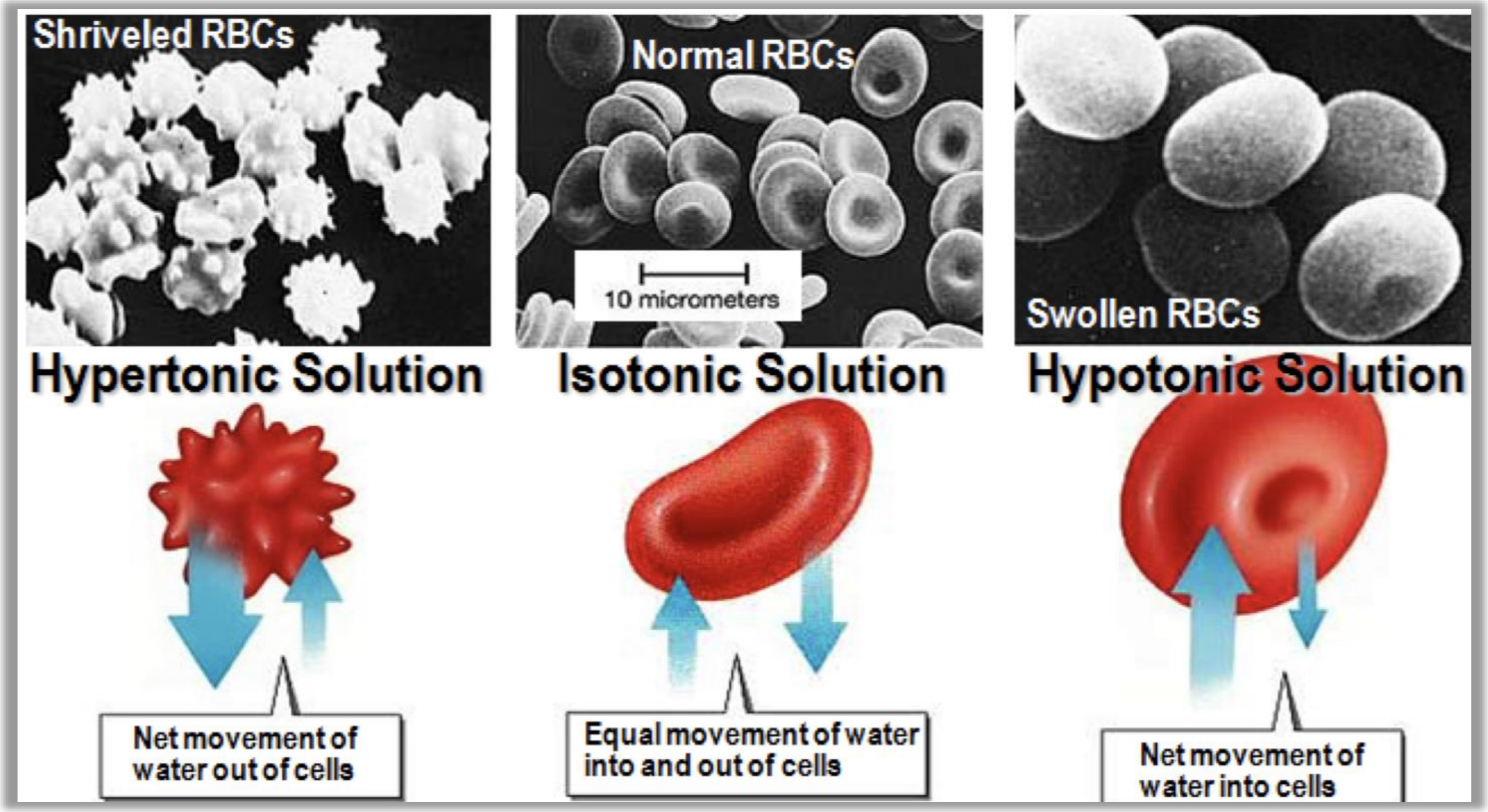
Isotonic solutions

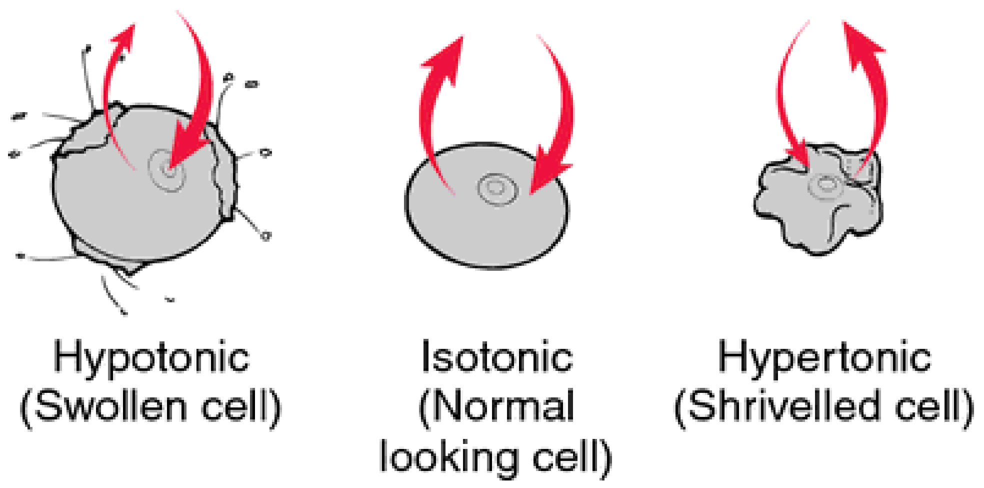
Osmosis:



Isotonic solutions

Clinical importance of osmotic effects:

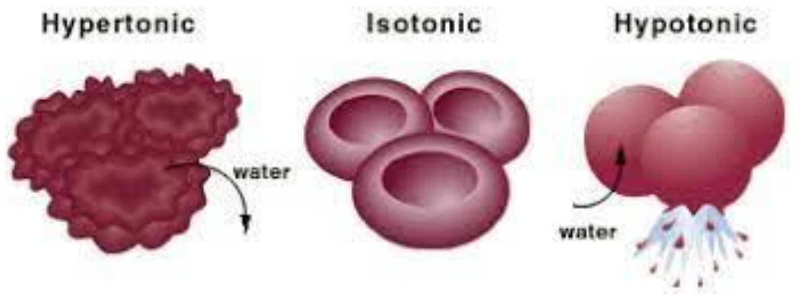
- Osmotic pressure is important from a biological viewpoint since the physiological membranes (e.g., red blood cell membranes) are semipermeable membranes.
- The effect of osmotic pressure on the red blood cells (RBC) can be demonstrated by suspending them in a solution of e.g.,



Isotonic solutions

Clinical importance of osmotic effects

- 5% sodium chloride solution which is of greater osmotic pressure than their contents.
- The water in the RBC's will then pass through the semipermeable cell membranes into the saline solution.
- The cells will consequently experience loss of water, and will shrink .



Isotonic solutions

CLINICAL IMPORTANCE OF OSMOTIC EFFECTS

- Suspended in a 0.2 % sodium chloride solution (lower osmotic pressure), the water from the solution will penetrate through the cell walls into the cells causing them to swell, to increase in size and eventually to break, to release hemoglobin.

- This process is called **hemolysis**.

Isotonic solutions

Types of solutions according to tonicity

1. **Hypertonic solution** : a solution with a greater concentration of solute outside the cell compared to the concentration of solute inside the cell

- **MORE WATER IN CELL**
- **Over time, cell loses water**

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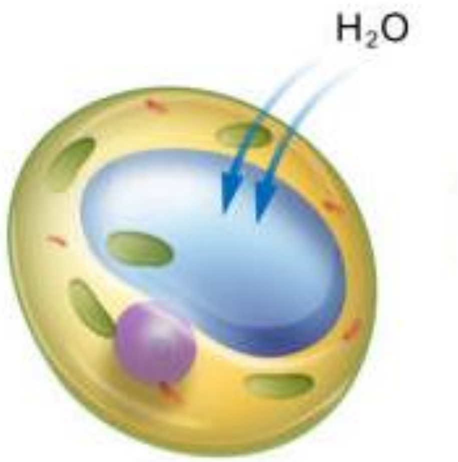
Isotonic solutions

Types of solutions according to tonicity

2. **Hypotonic solution:** a solution with a lesser concentration of solute outside the cell compared to the concentration of solute inside the cell

- **LESS WATER IN CELL, more solutes in cell.**
- **over time, cell gains water**



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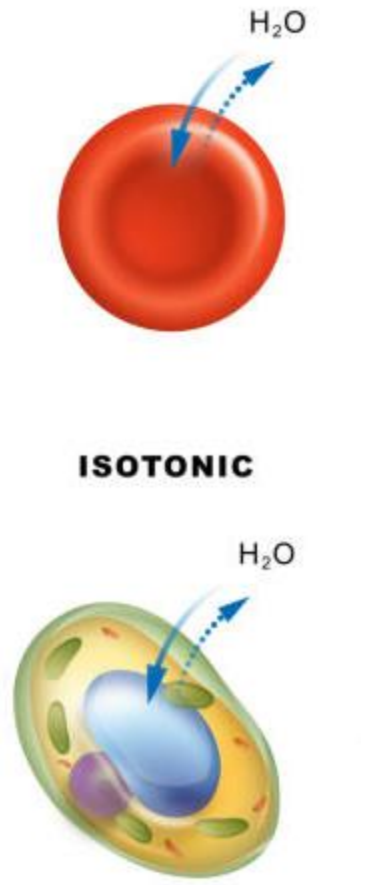
Isotonic solutions

Types of solutions according to tonicity

3. **Isotonic solution:** a solution with an equal concentration of solute outside the cell compared to the concentration of solute inside the cell



- **No change in cell volume**
- **Example: a single human red blood cell is placed in a 0.9% saline (salt) solution**

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Isotonic solutions

Types of solutions according to tonicity

- Isotonic solutions cause no swelling or contraction of the tissues with which they come in contact and produce no discomfort when instilled in the eye, nasal tract, and blood such as isotonic sodium chloride.

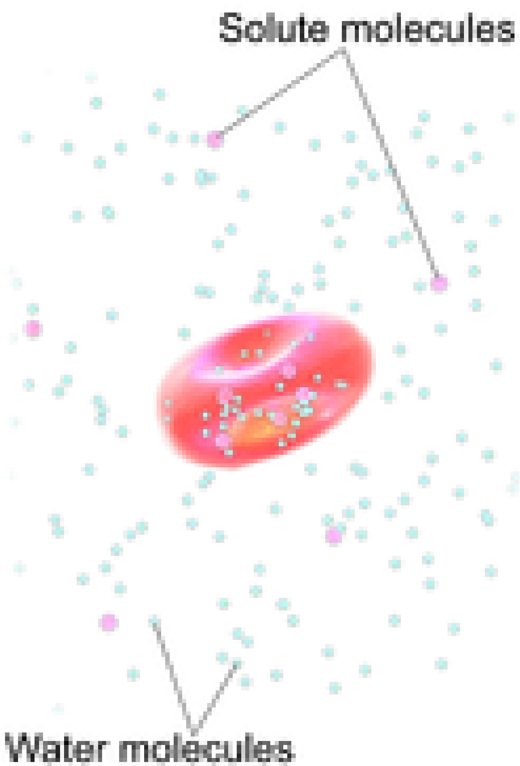
- The solution has essentially the same salt concentration and hence the same osmotic pressure as the red blood cell contents and is said to be isotonic with blood.

- Pharmaceutical buffers must usually be made isotonic so that they cause no swelling or contraction of biological tissues, which would lead to discomfort in the patient being treated.

Isotonic solutions

Measurement of Tonicity:2 methods

- First, a quantitative method based on the fact that a hypotonic solution liberates oxyhemoglobin in direct proportion to the number of cells hemolyzed.
- By such means, the van't Hoff i factor can be determined.
- The second approach used to measure tonicity is based on any of the methods that determine colligative properties



Isotonic Solution
(No Osmotic Flow)

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Isotonic solutions

Measurement of Tonicity:2 methods

- The freezing point of both human blood and lacrimal fluid is **-0.52°C.**

- This temperature corresponds to the freezing point of a 0.90% NaCl solution, which is therefore considered to be isotonic with both blood and lacrimal fluid.

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Isotonic solutions

Calculating Tonicity Using L_{iso} Values

- The modification of van’t Hoff expression of freezing point depression, $\Delta T_f = i K_f m$ by substituting molar concentration (c) and by writing i K_f as L, so that :

$$\Delta T_f = Lc$$

- L value computed from experimental data for drugs, it varies with concentration of solution.

- At concentration of drug that is isotonic with body fluids, L called $\mathbf{L_{iso}}$.

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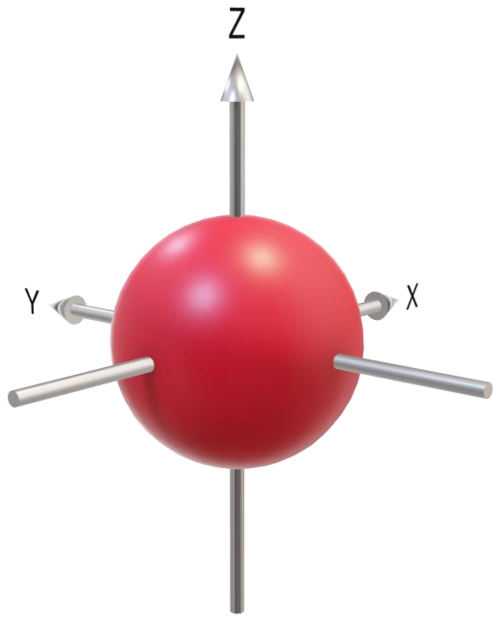
Isotonic solutions

Calculating Tonicity Using L_{iso} Values

- The L value equal to :
- L_{iso} for nonelectrolyte =1.9 (sucrose)
- L_{iso} for weak electrolyte =2 (zinc sulfate)
- L_{iso} for uni-univalent electrolyte=3.4 (NaCl)
- L_{iso} for uni-divalent electrolyte=4.3 (Na2SO4)
- L_{iso} for di-divalent electrolyte=4.8 (MgSO4)
- The L_{iso} values can also be used for calculating sodium chloride equivalents and Sprowls V values



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Isotonic solutions

Example

What is the freezing point lowering of a 1% solution of sodium propionate (molecular weight 96)? Because sodium propionate is a uni-univalent electrolyte, its L_{iso} value is 3.4, The molar concentration of a 1% solution of this compound is 0.104.

Answer :

$\Delta T_f = Lc$

$= 3.4 \times 0.104 = 0.35\ °C$

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Isotonic solutions

Methods of Adjusting Tonicity

- The methods are divided into two classes:

1. Class I :

- In the class I methods, sodium chloride or some other substance is added to the solution of the drug to lower the freezing point of the solution to -0.52°C and thus make it isotonic with body fluids.

- This class includes:

  A. **Cryoscopic method**
  B. **Sodium chloride equivalent method**

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Isotonic solutions

Methods of Adjusting Tonicity

2. Class II methods

- In this class water is added to the drug in a sufficient amount to form an isotonic solution.
- This class includes:

A. White–Vincent method
B. Sprowls method

Isotonic solutions

Class I Methods

A. Cryoscopic Method

- Calculate the amount of sodium chloride (1% solution has freezing point depression = o.58) required to make the lowering in the freezing point of the solution equals -0.52°C by using the freezing point depression produced by 1% of the drug available in books (experimentally measured).

Isotonic solutions

Example

How much sodium chloride is required to render 100 mL of a 1% solution of apomorphine hydrochloride isotonic with blood serum, 1% solution of the drug has a freezing point lowering of 0.08°C. ?

Answer :

0.52°C - 0.08°C = 0.44°C

1% NaCl has a freezing point lowering of 0.58°C

1/X =0.58/0.44=0.76%

Thus, 0.76% sodium chloride will lower the freezing point the required 0.44°C and will render the solution isotonic, The solution is prepared by dissolving 1.0 g of apomorphine hydrochloride and 0.76 g of sodium chloride in sufficient water to make 100 mL of solution.

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Class I Methods

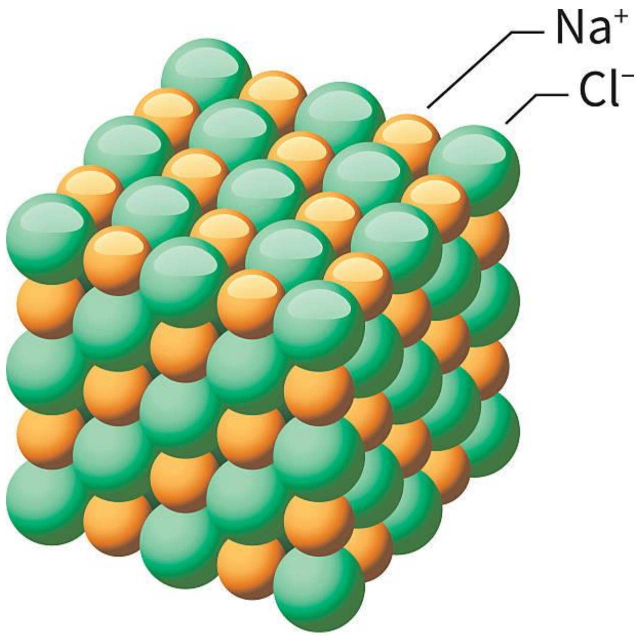
B. Sodium Chloride Equivalent Method

- Is the amount of sodium chloride that is equivalent to (i.e., has the same osmotic effect as) 1 g, or other weight unit, of the drug.

- The sodium chloride equivalents E for a number of drugs are listed in Tables.

- **E** value for a new drug can be calculated using following equation

  $E = 17\ (L_{iso}/M.Wt)$



Isotonic solutions

Example

Calculate the approximate E value for a new amphetamine hydrochloride derivative (molecular weight 187).Because this drug is a uni-univalent salt, it has an L_{iso} value of 3.4.

Answer :

E= 17(3.4/187) = 0.31

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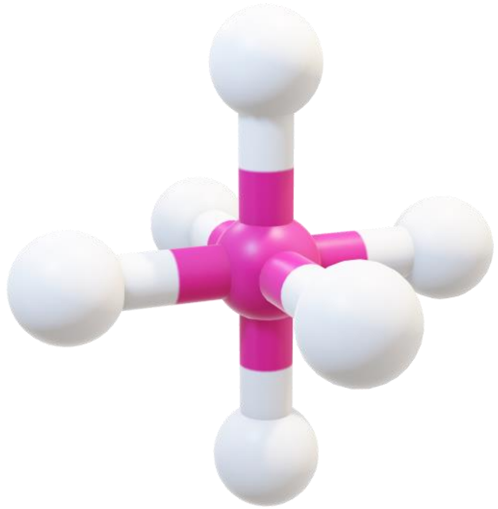
Isotonic solutions

B. Sodium Chloride Equivalent Method

- Calculations for determining the amount of sodium chloride or other inert substance to render a solution isotonic involve multiplying the quantity of each drug in the prescription by its sodium chloride equivalent and subtracting this value from the concentration of sodium chloride that is isotonic with body fluids, namely, 0.9 g/100 mL.



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Isotonic solutions

Example

A solution contains 1.0 g of ephedrine sulfate in a volume of 100 mL, What quantity of sodium chloride must be added to make the solution isotonic? How much dextrose would be required for this purpose?

Answer :

The quantity of the drug is multiplied by its sodium chloride equivalent, E, giving the weight of sodium chloride to which the quantity of drug is equivalent in osmotic pressure:

Ephedrine sulfate: 1.0 g x 0.23 = 0.23g

Isotonic solutions

Example

A solution contains 1.0 g of ephedrine sulfate in a volume of 100 mL. What quantity of sodium chloride must be added to make the solution isotonic? How much dextrose would be required for this purpose?

Answer :

The ephedrine sulfate has contributed a weight of material osmotically equivalent to 0.23 g of sodium chloride. Because a total of 0.9 g of sodium chloride is required for isotonicity,

0.90 - 0.23 g= 0.67 g of NaCl must be added.

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Isotonic solutions

Example

A solution contains 1.0 g of ephedrine sulfate in a volume of 100 mL. What quantity of sodium chloride must be added to make the solution isotonic? How much dextrose would be required for this purpose?

Answer :

If one desired to use dextrose instead of sodium chloride to adjust the tonicity, the quantity would be estimated by setting up the following proportion, Because the sodium chloride equivalent of dextrose is 0.16,

1g dextose / 0.16 g NaCl = X/0.67g NaCl

X= 4.2 g of dextrose

Isotonic solutions

Class II Methods

A. White–Vincent Method

- Calculate the volume of water required to make a solution isotonic.

1. **Multiply the weight of drug by E value**

2. **2. Since 0.9 g NaCl in 100ml water, so calculate the volume of water for calculated equivalent weight**

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Isotonic solutions

Example

to make 30 mL of a 1% solution of procaine hydrochloride isotonic, E=0.21?

Answer :

1. 0.3X0.21=0.063g

2. 0.9g NaCl / 100ml =0.063g/ v

   V= 7.0 ml

Or simply by using V=W x E x 111.1

So the isotonic solution prepared by dissolving 0.3 g procaine hydrochloride in 7.0 ml water and an isotonic solution is added to make 30 mL of the finished product.

Isotonic solutions

Class II Methods

B. The Sprowls Method

- A further simplification of the method of White and Vincent was introduced by Sprowls.
- He recognized that equation ($V = W \times E \times 111.1$) could be used to construct a table of values of V when the weight of the drug, w, was fixed (0.3g).
- **Note: Example 8-15&16 in book are required**

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Thank You !

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