

## BUFFERED ISOTONIC SOLUTIONS

- Pharmaceutical solutions that are meant for application to delicate membranes of the body should be adjusted to same osmotic pressure as that of the body fluids.

- An Isotonic solution refers to 2 solutions having the same osmotic pressure across a semipermeable membrane. eg:- 0.9% NaCl solution

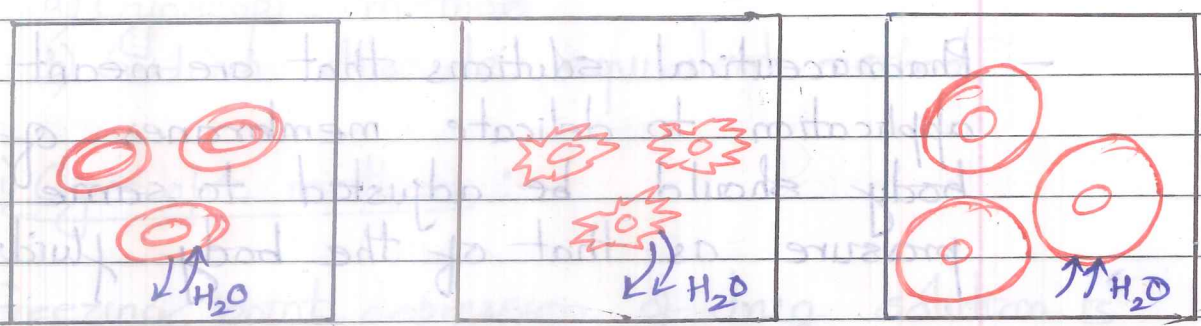
- A Hypertonic solution refers to the one where the concentration of solutes is greater outside the cell than inside it. eg:- 2% NaCl soln.

If the RBCs are suspended in 2% NaCl solution, the water within the cell passes through the cell membrane to dilute the surrounding salt solution. This causes cell shrinkage or crenation.

- A Hypotonic solution refers to the one where the concentration of solute is greater inside the cell than outside it. eg:- 0.2% NaCl sln.

If the RBCs are suspended in 0.2% NaCl solution, the water enters the cell, causing them to swell & finally burst, with the liberation of hemoglobin. This phenomenon is known as Hemolysis.





Isotonic                      Hypertonic                      Hypotonic  
 solute = solute              solute < solute              solute > solute  
 inside      outside              inside      outside              inside      outside

- Tonicity :-  
 Is the concentration of only the solutes that cannot cross the membrane since these solutes exert osmotic pressure on that membrane.

\* Measurement of Tonicity

1) Hemolytic method

- The effect of various solution of the drug was observed on the appearance of red blood cells suspended in the solutions.
- method developed by Hunter.
- A quantitative method based on the fact that a hypotonic solution liberates oxyhemoglobin in direct proportion to number of cells hemolyzed.

2) Measurement of slight temperature differences

- It involves measurement of slight temperature differences from differences in the vapour pressure.

Freezing point of 0.90% NaCl =  $-0.52^{\circ}\text{C}$ .



STUDENT'S NAME		TOTAL MARKS OBTAINED
CLASS	SUBJECT	
ROLL NO.	DATE	

### 3) Calculating Tonicity using Liso Values.

In case of electrolytes with both the weak & strong types are always greater freezing point depressions are greater than calculated, a new factor,  $L = iK_f$  is introduced.

$$L_{iso} = \frac{\Delta T_f}{c}$$

$\Delta T_f$  - freezing point depression  
 $c$  - conc. of solution.

eg:- Liso value of 0.90% NaCl (0.154M), having  $\Delta T_f = 0.52^\circ C$  is 3.4.

$$L_{iso} = \frac{0.52}{0.154} = 3.4$$

### \* Methods of Adjusting Tonicity & pH.

There are several methods which are used to render the solution isotonic.

#### 2 Methods

(Class I method)

Sodium chloride is added to drug solution to make it isotonic with body fluids.

(Class II method)

Water is added to drug solution to make it isotonic with body fluids.



## Class I methods :-

- Cryoscopic method
- Sodium chloride equivalent method.

### a) Cryoscopic method :-

Freezing point depression of drug solution is determined by the equation

$$\Delta T_f = \frac{L_{iso} \times 10}{\text{Mol. wt.}}$$

Example :-

How much NaCl is required to render 100 ml of 1% solution of apomorphine HCl isotonic with blood

Given  $\Delta T_f$  of NaCl =  $0.52^\circ$

$\Delta T_f$  of 1% apomorphine HCl =  $0.08^\circ$ .

$\Delta T_f$  of 0.9% NaCl =  $0.52^\circ$

$\therefore \Delta T_f$  of 1% NaCl =  $0.58^\circ$

To reduce the freezing point =  $\Delta T_f$  of NaCl -  $\Delta T_f$  ApoHCl  
 $= 0.52 - 0.08$

By the method of proportion,

$$\frac{1\%}{x} = \frac{0.58^\circ}{0.44^\circ}$$

$$x = 0.76\%$$

Thus by dissolving 1g of apomorphine HCl & 0.76g of sodium chloride in sufficient  $H_2O$  to make 100 ml solution.



STUDENT'S NAME		TOTAL MARKS OBTAINED
CLASS	SUBJECT	
ROLL NO.	DATE	

## b) Sodium Chloride Equivalent method.

Sodium chloride equivalent of drug is the amount of NaCl that has the same osmotic effect of 1g or other weight unit of the drug.

$$E = \frac{17 \times L_{iso}}{\text{Mol. wt.}}$$

Amount of isotonic agent required to adjust the tonicity

$$X = \frac{Y}{E}$$

X - grams of isotonic agent required to adjust the tonicity

Y - additional amount of NaCl for isotonicity

E = Gram of NaCl equivalent to 1g of the isotonic agent.

## II) Class II Methods :-

- White - Vincent method
- The Sprowls method.

### a) White - Vincent method.

- developed equation for calculating the volume V (mls) of osmotic solution prepared by mixing drug with water.

$$V = w \times E \times 111.1$$

w = weight in grams of drug  
E = NaCl equivalent.

b) The Sprouls Method:-

- Simplification of the White Vincent method.
- Table of values V can be constructed by keeping the weight of the drug fixed i.e. 0.3g in 1% solution.

$$F = \frac{W \times L \times 100}{M \times 1000}$$

Amount of solvent required to adjust the quantity

$$V = \frac{X}{F}$$

X - grams of active agent required to adjust the quantity

V - additional amount of solvent required to adjust the quantity  
 F = amount of solvent equivalent to 1% of the active agent

Class II Methods:-

- a) White - Vincent method
- b) The Sprouls method

White - Vincent method - developed equation for calculating the volume V (ml) of isotonic solution prepared by mixing drug with water

$$V = \frac{W \times E \times 100}{M \times 1000}$$

W - weight in grams of drug  
 E = NaCl equivalent of drug