



# Buffered and isotonic solutions

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# Outline



1. Henderson–Hasselbalch equation,
2. Buffer capacity
3. Maximum buffer capacity
4. Isotonic solution
5. Calculate solution tonicity
6. Tonicity adjustments.

# Objectives



1. Apply the buffer equation, also known as the Henderson–Hasselbalch equation, for a weak acid or base and its salt.
2. Discuss the factors influencing the pH of buffer solutions
3. Describe the concept of tonicity and its importance in pharmaceutical systems.
4. Calculate solution tonicity and tonicity adjustments.

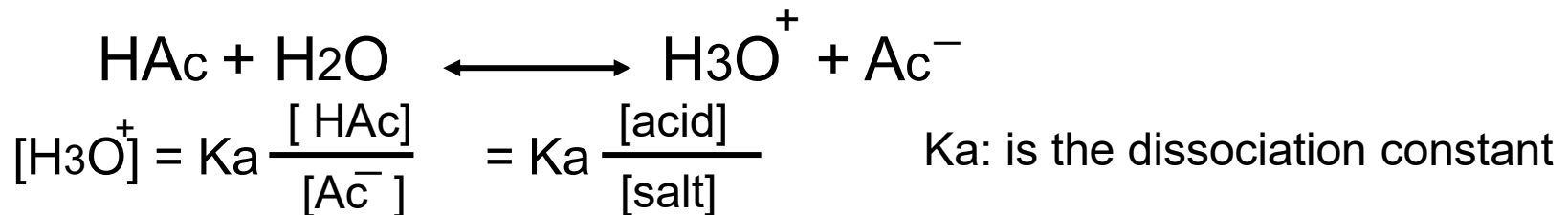
- Buffers are compounds or mixture of compounds, that by their presence in solution resist changes in PH upon the addition of small quantities of acid or alkali.
- Buffer action: is the resistance to a change in PH.
- If we add acid or base to a solution of NaCl the PH is altered considerably because there is no buffer.
- A combination of weak acid and its conjugated base (salts), or weak base and its conjugated acid (salts), act as a buffer.

- **Example .**

1 ml of 0.1 N HCl added to water the PH decreased from 7 to 3 .

1 ml of 0.1 N HCl added to a solution of acetic acid and sodium acetate in equal quantity the PH changed only by 0.09

*The buffer equation for weak acid and its salt:*



$$-\log [\text{H}_3\text{O}^+] = -\log K_a - \log [\text{acid}] + \log [\text{salt}]$$

For the buffer  $\text{PH} = \text{PKa} + \log \frac{[\text{salt}]}{[\text{acid}]}$  *Henderson-Hasselbalch equation*

$$\text{PH} = \frac{1}{2} \text{PKa} - \frac{1}{2} \log C \text{ for the PH of the acid only}$$

- Example .

what is the PH of 0.1 M acetic acid solution,  $PK_a = 4.76$ ? What is the PH after enough sodium acetate has been added to make the solution 0.1 M with respect to this salt?

Example .

What is the molar ratio,  $[salt]/[acid]$ , required to prepare an acetate buffer of PH 5.0?  $PK_a = 4.76$ .

- *The buffer equation for a weak base and its salt.*

buffer solutions are not ordinarily prepared from weak bases and their salts because of the volatility and instability of the bases and because of the dependence of their PH on PKw which is often effected by temp. changes.

$$\text{PH} = \text{PKw} - \text{PKb} + \log [\text{base}]/[\text{salt}]$$

Example :

what is the PH of a solution containing 0.1 mole of ephedrine and 0.01 mole of ephedrine hydrochloride per liter of solution? The PKb of ephedrine is 4.64.

- Some factors influencing the PH of buffer solutions
  1. Addition of neutral salts change the PH of solution by altering the ionic strength.
  2. Dilution also alter the PH of solution.
  3. Addition of water in moderate amounts not change the PH, may cause a small +ve or –ve deviation because itself can act as a weak acid or base.
  4. Temperature, example PH of acetate buffer was found to increase by increasing the temp. while PH of boric acid-sodium borate decrease with increasing the temp.



## *Buffer capacity( $\beta$ )*

buffer capacity :is the magnitude of the resistance of a buffer to PH changes.

Also known as *buffer efficiency* or *buffer index* or *buffer value*.

$$\beta = \frac{\Delta B}{\Delta PH}$$

$\Delta B$ : is the small increment in g eq./L of strong acid or base added to buffer.

$\Delta PH$ : is the change in PH due to  $\Delta B$

*So if 1 g eq. of strong acid or base is added to 1 liter buffer solution produce  $\Delta PH = 1$  so  $\beta = 1$*

- A more exact equation for buffer capacity

$$\beta = 2.3 C \frac{K_a [H_3O^+]}{(K_a + [H_3O^+])^2}$$

C: is the sum of molar conc. of weak acid and its salts.

$[H_3O^+]$  : is the hydrogen ion conc.

$K_a$  : is the dissociation constant

Example: at a hydrogen ion conc. of  $1.75 \times 10^{-5}$ , (PH= 4.76), what is the capacity of a buffer containing 0.01 mole each of acetic acid and sodium acetate per liter of solution?  $K_a = 1.75 \times 10^{-5}$

- *Maximum buffer capacity*

this occur where  $pH = pKa$  or  $[H_3O^+] = Ka$

so the equation will be

$$\beta = 2.3 C \frac{Ka [H_3O^+]}{(Ka + [H_3O^+])^2}$$

*Substituting Ka by H<sub>3</sub>O<sup>+</sup>*

$$\beta = 2.3 C \frac{[H_3O^+]^2}{(2[H_3O^+])^2}$$

$$B_{max} = C \cdot 2.3 / 4 = 0.576 C$$

Example: what is the maximum buffer capacity of an acetate buffer with a total conc. of 0.02 mole per liter

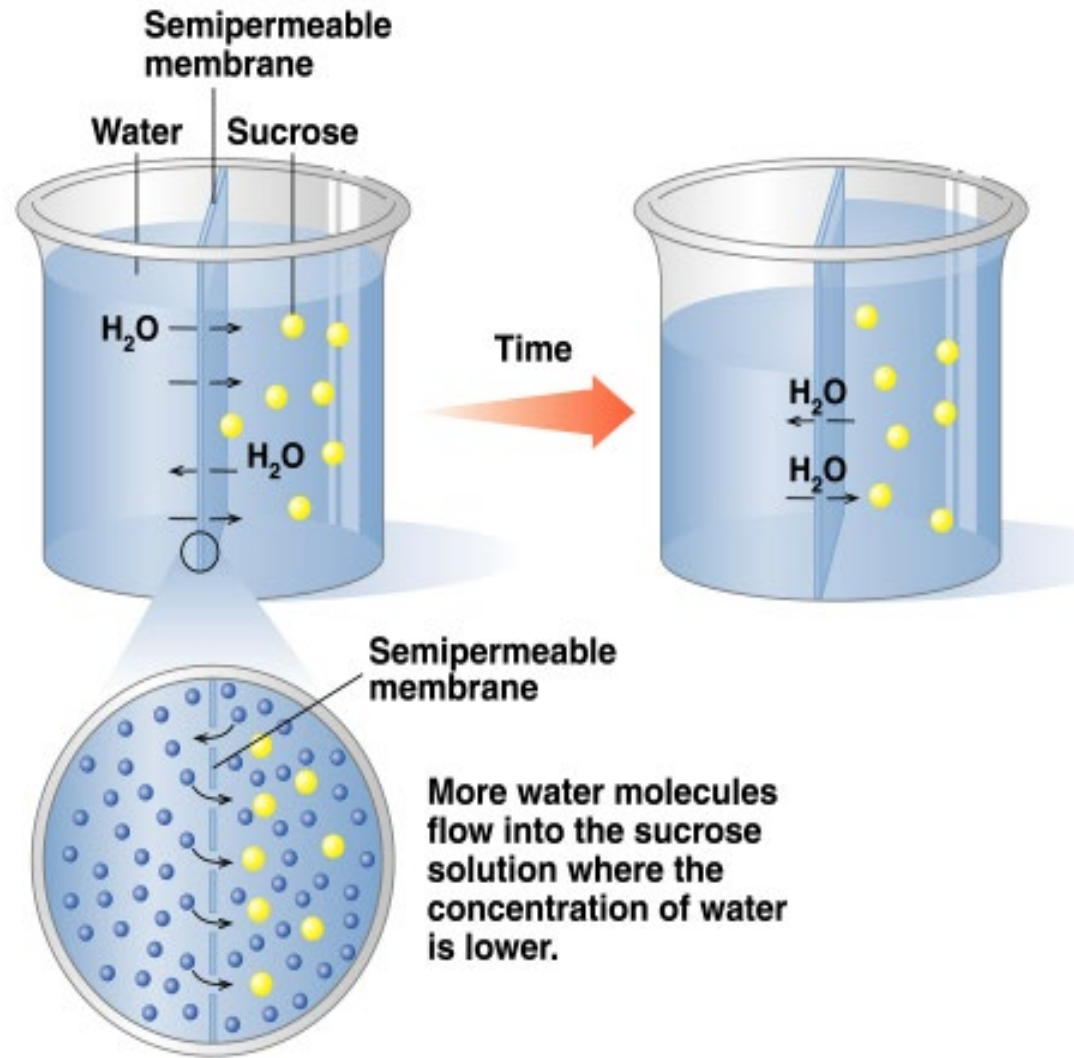
## *Buffered Isotonic solutions*

*pharmaceutical solutions that are meant for application to the eye, nasal tract, blood or other body tissues should be adjusted to approximately have the same osmotic pressure as that of body fluids, to produce no discomfort when used.*

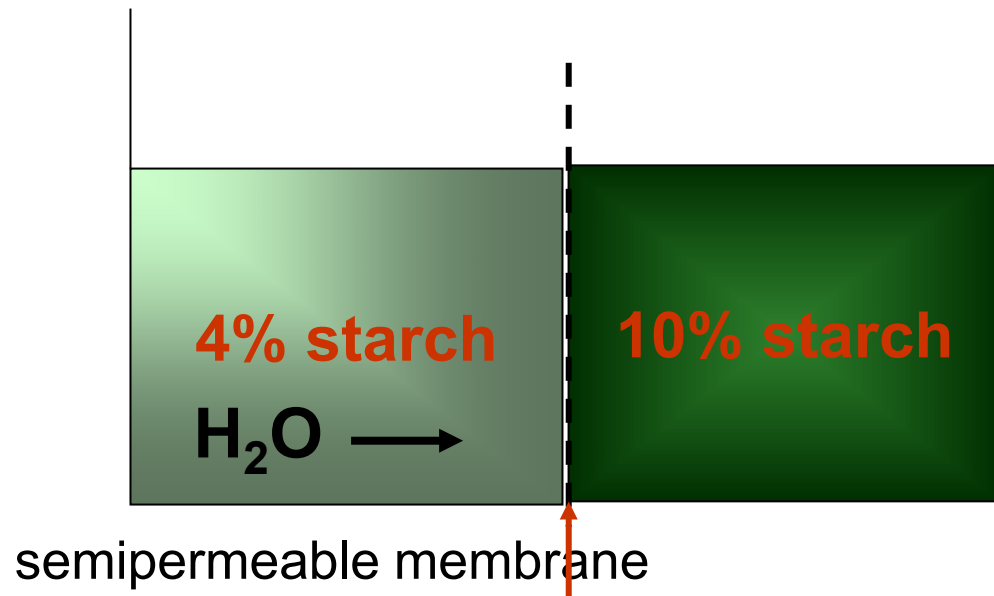
# Osmosis

In **osmosis**, water (solvent) flows from the lower solute concentration into the higher solute concentration. The level of the solution with the higher concentration rises.

The concentrations of the two solutions become equal with time.

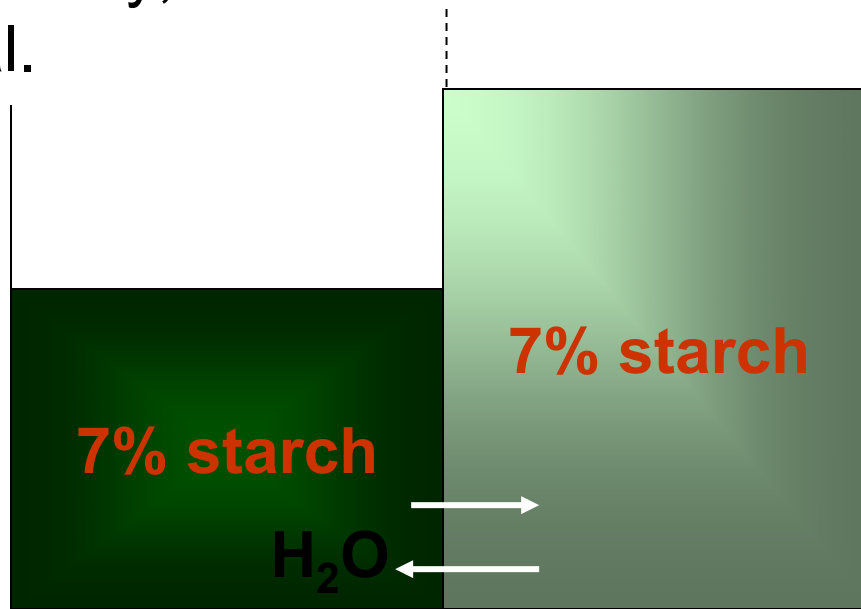


A semipermeable membrane separates a 4% starch solution from a 10% starch solution. Starch is a colloid and cannot pass through the membrane, but water can. What happens?



# Water flow Equalizes

- The 10% starch solution is diluted by the flow of water out of the 4% and its volume increases.
- The 4% solution loses water and its volume decreases.
- Eventually, the water flow between the two becomes equal.



## Osmotic pressure is

- Produced by the solute particles dissolved in a solution.
- Equal to the pressure that would prevent the flow of additional water into the more concentrated solution.
- Greater as the number of dissolved particles in the solution increases.



# Osmotic Pressure of the **Blood**

## Red blood cells

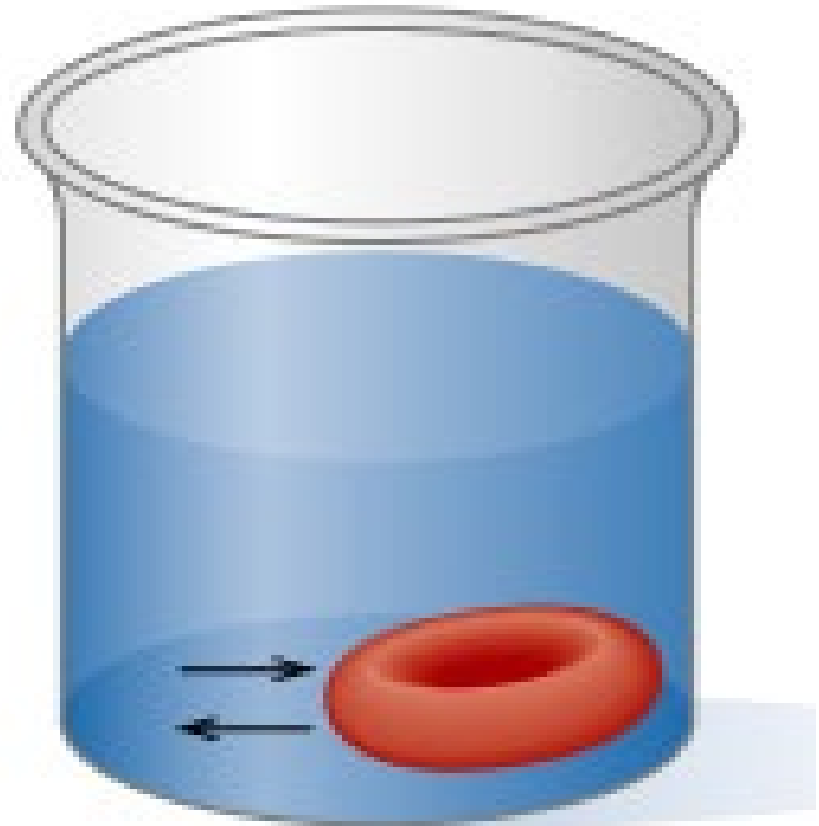
- Have cell walls that are semipermeable membranes.
- Maintain an osmotic pressure that cannot change or damage occurs.
- Must maintain an equal flow of water between the red blood cell and its surrounding environment.

# *Isotonic Solutions*

## An isotonic solution

- Exerts the same osmotic pressure as red blood cells.
- Is known as a “physiological solution”.
- Of 5.0% glucose or 0.90% NaCl is used medically because each has a solute concentration equal to the osmotic pressure equal to red blood cells.

## Isotonic solution

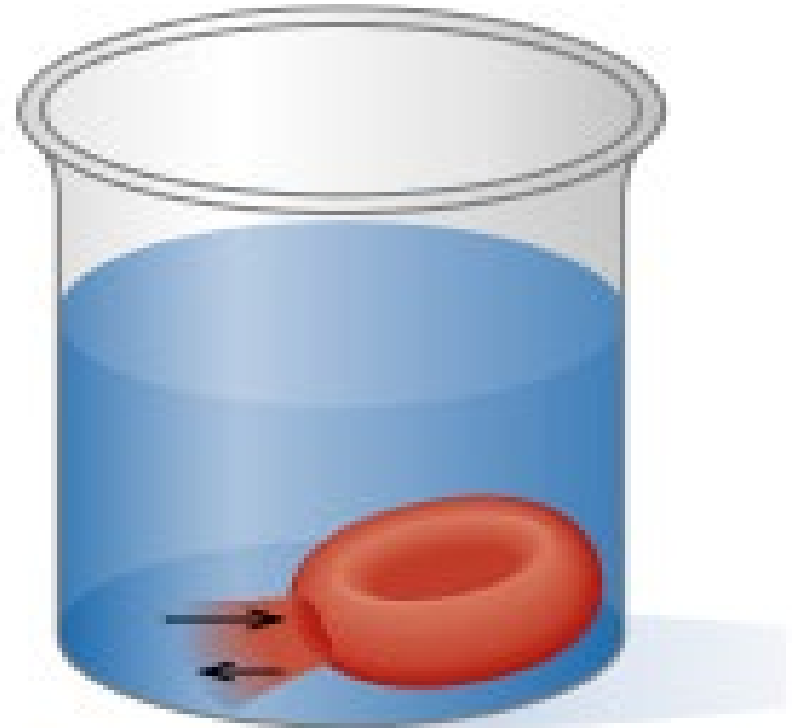


# *Hypotonic Solutions*

## A hypotonic solution

- Has a lower osmotic pressure than red blood cells.
- Has a lower concentration than physiological solutions.
- Causes water to flow into red blood cells.
- Causes hemolysis: RBCs swell and may burst.

## Hypotonic solution



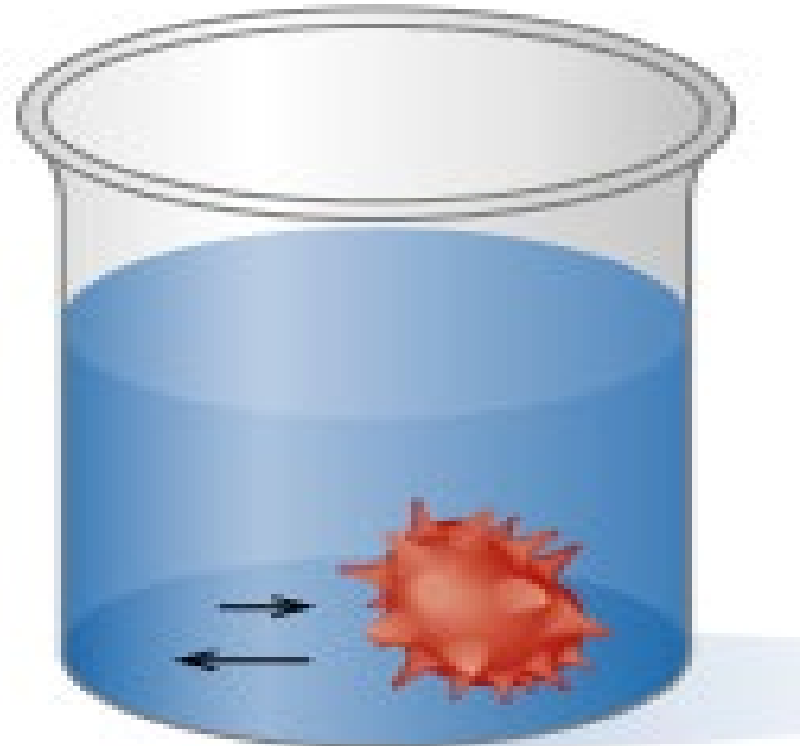
## Hemolysis

# *Hypertonic Solutions*

A hypertonic solution

- Has a higher osmotic pressure than RBCs.
- Has a higher concentration than physiological solutions.
- Causes water to flow out of RBCs.
- Causes crenation: RBCs shrinks in size.

**Hypertonic solution**



**Crenation**

## Measurement of tonicity

1. *Hemolytic method*: which is the effect of various solutions of the drug on the appearance of RBCs.
2. *By the determination of colligative properties by calculating Liso value.*

$$\Delta T_f = L C \text{ for isotonic solution } L = Liso$$

the freezing point of blood is  $-0.52$

for 0.9% NaCl which is isotonic with body fluid

$$\begin{array}{l} \Delta T_f = Liso C \quad 0.9 \text{ g} \dots\dots\dots 100 \text{ ml} \\ \quad \quad \quad \quad x \quad \quad \quad \quad \dots\dots\dots 1000 \text{ ml} \\ \quad \quad \quad \quad x = 9 \text{ g} \end{array}$$

$$n = 9 / 58.5 \text{ g/mol} = 0.154$$

NaCl is univalent ion  $Liso = 3.4$

$\Delta T_f = 3.4 \times 0.154 = 0.52$  SO FP =  $-0.52$  so 0.9% NaCl is isotonic with blood.

## *The L value:*

$$\Delta T_f = i K_f m$$

used for the colligative properties of nonelectrolyte and electrolyte solutions.

in dilute solution it can be modified slightly by

$$\Delta T_f = L c$$

$$L = i K_f$$

$c = M$  molar conc.

At a conc. of a drug that is isotonic with body fluids

$L = i K_f = L_{iso} = 1.9$  for non electrolytes

= 2.0 for weak electrolytes

= 3.4 for univalent electrolytes

- Example :

what is the FP of 1% solution of sodium propionate ( M.WT = 96 g/mol)

sodium propionate is a univalent electrolyte.

## *Methods for adjusting tonicity*

1. **Class I:** NaCl or some other substances is added to the solution of the drug to lower the FP of the solution to  $-0.52\text{ C}^\circ$  and thus make it isotonic with body fluids.

*a. cryoscopic method.*

*b. sodium chloride equivalent method.*

2. **Class II:** water is added to the drug in a sufficient amount to form an isotonic solution

*a. white- Vincent method.*

*b. Sprowles method.*



# 1. Class I

## a. cryoscopic method.

Ex. How much sodium chloride is required to render 100 ml of 1% solution of apomorphineHCl isotonic with blood serum ?  
1% of this drug have  $\Delta T_f$  of  $0.08C^\circ$

$$0.52 - 0.08 = 0.44 C^\circ$$

$$1\% \dots\dots\dots 0.58 C^\circ$$

$$x \dots\dots\dots 0.44 C^\circ$$

$$10/58.5 = 0.170$$

$$0.17 \times 3.4 = 0.58$$

$$x = 0.76 \%$$

So 1g of apomorphinHCl + 0.76 g of NaCl and water to 100 ml the solution will be isotonic.

## b. Sodium chloride equivalent method

( E value)

$$E \text{ value} = 17 \frac{\text{L iso}}{\text{M.WT}} \quad \text{M.WT of the drug}$$

**E value** is the weight of NaCl with the same freezing point depression as 1 g of the drug

Ex. Calculate E value for a new drug ( M.WT. = 187g/mole).this drug is univalent.

$$E \text{ value} = 17 \times 3.4 / 187 = 0.31$$

**E value** x **quantity of drug in the prescription** **subtracted** from 0.9 g= amount of NaCl that should be added. then the volume completed to 100 ml.

- **Example :**

solution contain 1.0 g ephedrine sulphat in 100 ml, what quantity of NaCl should be added to make the solution isotonic, how much dextrose should be added for this purpose. E value for ephedrine 0.23 and for dextrose 0.16 .

ephedrine sulphat  $1.0 \text{ g} \times 0.23 = 0.23 \text{ g}$

$0.9 \text{ g} - 0.23 = 0.67\text{g}$  of NaCl should be added.

*For dextrose or any substance used to replace NaCl for isotonicity*

$$X = \frac{\text{Additional amount of NaCl for isotonicity}}{\text{E value of it}}$$

*$X = 0.67/0.16 = 4.2 \text{ g}$  of dextrose should be added to make the solution isotonic.*

*Other agents than dextrose may of course be used to replace NaCl. It is recognized that thiomersal becomes less stable in eye drops when sodium chloride used as isotonic agent so other agents as mannitol, propylene glycol, or glycerin could serve as alternatives to sodium chloride. The conc. of these agents for isotonicity is calculated by the same equation as dextrose.*

Example: prepare 200 ml of an isotonic aqueous solution of thiomersal, M.WT 404.84g/mole. The conc. of thiomersal is 1:5000. thiomersal is univalent compound. Using propylene glycol as a preservative, propylene glycol is a non electrolyte and the M.WT= 76.09g/mol.

# Class II methods

## 1. White – Vincent method.

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

**V:** is the volume of water which when mixed with the drug give isotonic solution.

**W:** weight of the drug in gram.

**E :** sodium chloride equivalents.

**111.1:** is constant which represent the volume in ml. of isotonic solution obtained by dissolving 1 g of sodium chloride in water.

Example: make the following solution isotonic with respect to an ideal membrane.

phenacaineHCl .....0.06 g      Evalue = 0.2

Boric acid .....0.3 g      E value = 0.5

steril D.W. enough to make 100 ml

$$V = [ ( 0.06 \times 0.2) ] + [ ( 0.3 \times 0.5) ] \times 111.1$$

$$V = 18 \text{ ml}$$

so drugs are mixed with water to make 18 ml of an isotonic solution and the preparation is completed to 100 ml by adding isotonic diluting solution.

## *2. Sprowls method :*

This method depend on V which is obtained from white-vincent method. This method usually used for ophthalmic and parenteral preparation.

## Reference

MARTIN'S PHYSICAL PHARMACY AND PHARMACEUTICAL  
SCIENCES