# Pharmaceutical Calculations

## Isotonic & Buffer Solutions

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# Isotonic & Buffer Solutions

- Osmosis: Flow of a solvent (e.g. water) through a **semipermeable membrane** from a **dilute solution** into a **more concentrated** solution to **equalize the concentration** of a solute.

- Osmosis depends on the **number of particles** in the solution (depends on the dissociation of electrolytes).

- Chemical dissociation:

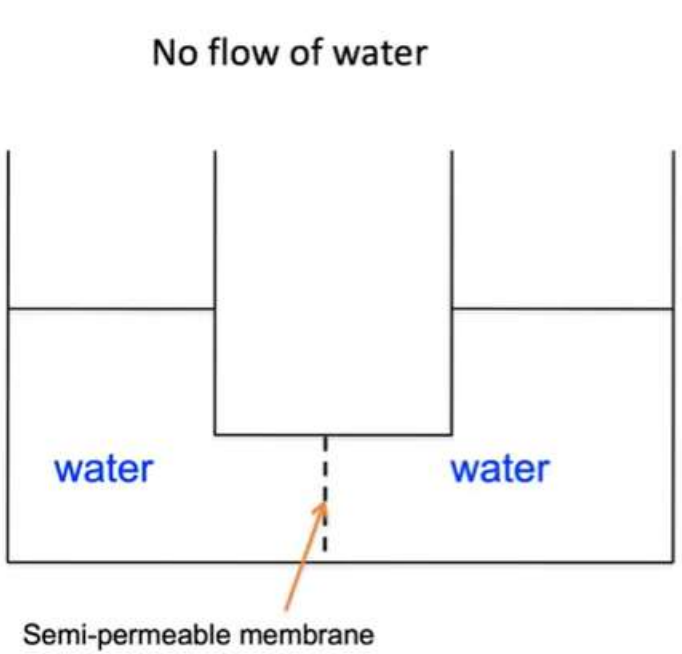
1) Non electrolyte:

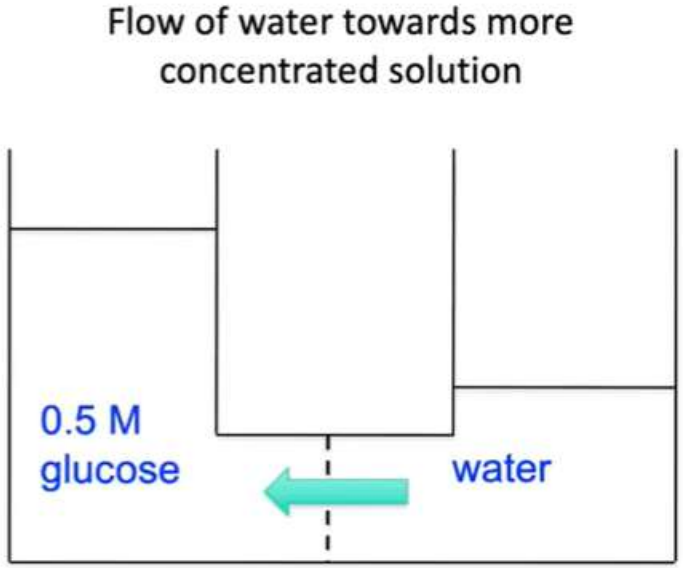
➢ **Glucose** and **sucrose do not break** down into smaller components (NO Dissociation).

2) Electrolyte:

➢ All **electrolytes can dissociate** into smaller components (e.g. **NaCl and $ZnCl_2$**).

## ❑ Flow of solvent (e.g. water through semipermeable membrane):

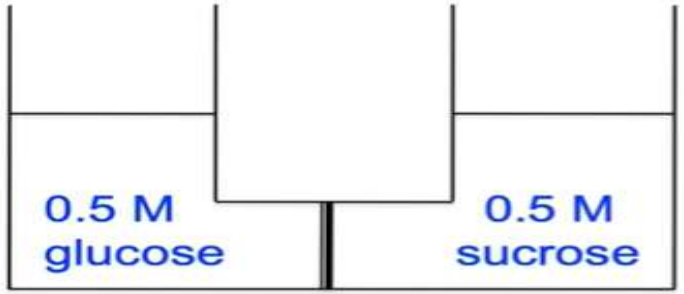



**Number of particles in 0.5 M glucose > Number of particles in water (NO particles)**

Which way will water flow when the membrane is opened?

Glucose (mw = 180)
Sucrose (mw = 342)



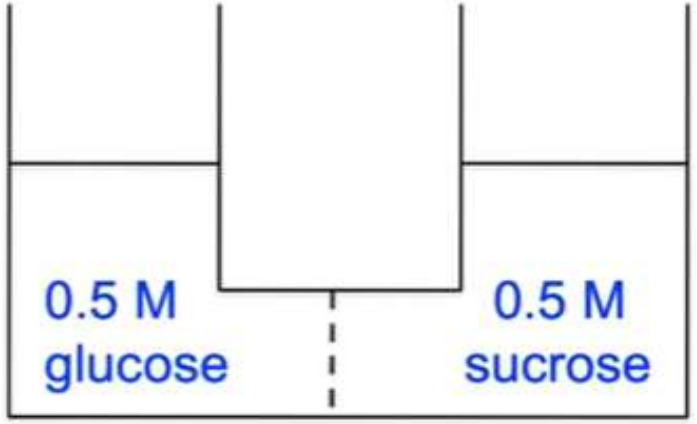

Closed membrane

A. Towards the glucose side

B. Towards the sucrose side

C. No flow

Answer: C. No flow



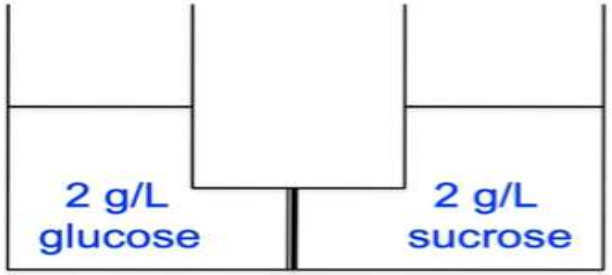

Open semi-permeable membrane

- **Both solutions are nonelectrolytes (NO dissociation).**
- **Both have the same number of particles (0.5 M = 0.5 moles / liter).**
- **The number of particles (molecules) from glucose = The number of molecules from sucrose.**
- **These solutions are called "Iso-osmolar" → they have the same osmotic force.**

Which way will water flow when the membrane is opened?

Glucose (mw = 180)

Sucrose (mw = 342)




Closed membrane

A. Towards the glucose side

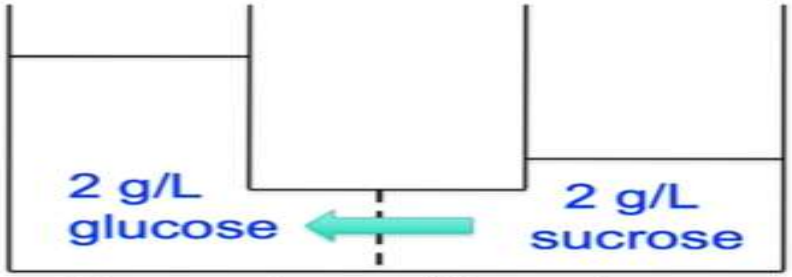
B. Towards the sucrose side

C. No flow

$$2 \text{ g/L Glu} \times \frac{1 \text{ mole}}{180 \text{ g}} \times \frac{1000 \text{ m mole}}{1 \text{ mole}} = 11.1 \text{ mM Glu.}$$

$$2 \text{ g/L Suc} \times \frac{1 \text{ mole}}{342 \text{ g}} \times \frac{1000 \text{ m mole}}{1 \text{ mole}} = 5.8 \text{ mM Suc.}$$

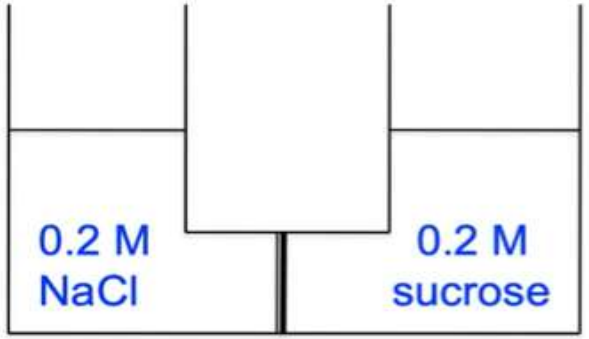
Answer: A. Towards the glucose side




Open semi-permeable membrane

Flow of water towards solution that contains more particles.

Which way will water flow when the membrane is opened?




Closed membrane

A. Towards the NaCl side

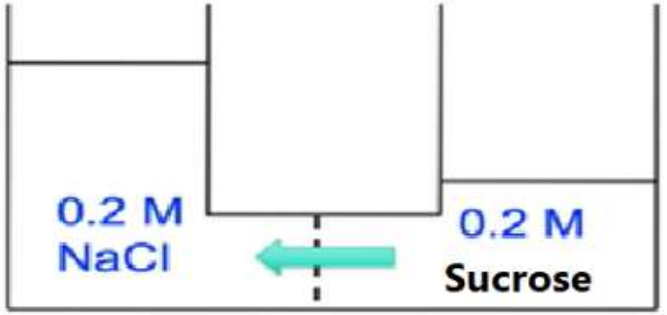
B. Towards the sucrose side

C. No flow

**0.2 M NaCl (Electrolyte) = 0.2 M $Na^+$ + 0.2 M $Cl^-$ = 0.4 M of particles**

**0.2 M Sucrose (Non-electrolyte) = NOT dissociate = 0.2 M of particles**

Answer: A. Towards the NaCl side




Open semi-permeable membrane

Flow of water towards solution that contains more particles.

## ❑ Clinical impact of osmosis and Tonicity:

- Tonicity is the ability of a solution to cause a cell to **gain or lose water** through **osmosis.**

- A solution having the **same osmotic pressure** a specific **body fluid** is called **"isotonic"** with that specific body fluid (e.g. Blood and lacrimal fluid).

- **Types of tonicity:**

1) **Hypertonic solution**: A solution of **higher osmotic pressure** than that of specific body fluid.

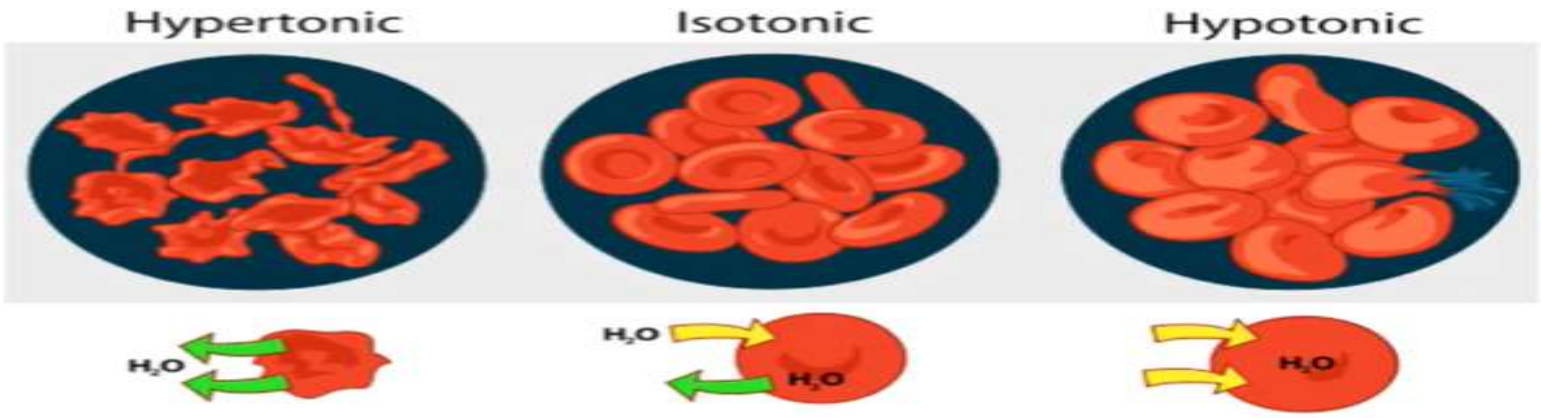
➢ Example: 20% Mannitol (To reduce cerebral edema).

2) **Isotonic solution**: A solution of the **same osmotic pressure** that of specific body fluid (e.g. 0.9% NaCl).

3) **Hypotonic solution**: A solution of **lower osmotic pressure** than that of specific body fluid.

➢ Example: 0.45% NaCl (To reduce cellular dehydration).

- Most (NOT all) pharmaceutical preparations are isotonic with body fluids.




| Solution type | Water movement | RBC effect | Result |
|---|---|---|---|
| Isotonic | No flow | Normal | — |
| Hypotonic | Flow into cell | Swelling / Rupture | Hemolysis |
| Hypertonic | Flow out of cell | Shrinkage | Crenation التحزز |

## ❑ Methods to evaluate the tonicity:

### 1) Freezing point depression (FP):

- The calculations involved in preparing an isotonic solution may be done by **comparing the colligative properties** of this solution to an isotonic solution.

- Most often a comparison of freezing points is used for this purpose, since it is generally accepted that **(- 0.52 °C)** is the freezing point of both **blood serum and lacrimal fluid**.

- Key concept: The isotonic solutions freeze at (- 0.52 °C).

- Freezing point is related to the **number of particles** in solution **(colligative property).**

- **Dissociation (Van't Hoff) factor (i)**

➢ Electrolytes dissociate to produce more particles than non-electrolytes, so

✓ **i = 1** for **non-electrolytes.**

✓ **i > 1** for **electrolytes.**

- **1 mole for a chemical** has a freezing point **FP = - 1.86 °C X (i).**
  - Since this value is negative, the result is called freezing point depression.

$$\frac{\textbf{Formula weight per liter}}{\textbf{- 1.86 °C X (i)}} = \frac{\textbf{Target weight per liter}}{\textbf{Target freezing point}}$$

- Dissociation factor (i) for electrolytes:

$$(i) = \frac{\text{Number of particles}}{\text{100 molecules}}$$

- For example, NaCl with 80% dissociation

$$(i) = \frac{\text{Number of particles}}{100 \text{ moles}} = \frac{180 \text{ total particles}}{100 \text{ moles}} = 1.8$$

- For example, $ZnCl_2$ with 80% dissociation

$$\frac{\text{Number of particles}}{100 \text{ moles}} = \frac{260 \text{ total particles}}{100 \text{ moles}} = 2.6$$

**Example 1: Boric acid (mw = 61.8) has negligible dissociation (non-electrolyte). What is an isotonic concentration (g/l) of boric acid?**

$$\frac{\text{Formula weight per liter}}{-1.86\ ^\circ\text{C X (i)}} = \frac{\text{Target weight per liter}}{\text{Target freezing point}}$$

$$\frac{61.8\ \text{g/l}}{-1.86\ ^\circ\text{C} \times 1} = \frac{X}{-0.52\ ^\circ\text{C}} = \mathbf{17.3\ g/l}$$

**Example 2: A solution of anhydrous dextrose (mw = 180) contains 25 g in 500 ml of water. What is the freezing point of this solution?**

$$\frac{\text{Formula weight per liter}}{\text{- 1.86 °C X (i)}} = \frac{\text{Target weight per liter}}{\text{Target freezing point}}$$

$$\frac{180\ \text{g/l}}{\text{- 1.86 °C x 1}} = \frac{50\ \text{g/l}}{X} = \textbf{- 0.52 °C}$$

**Example 3: What is the freezing point of 0.1% solution of $ZnCl_2$ (mw = 136.3), dissociation 80%?**

$$\frac{\text{Formula weight per liter}}{\text{- 1.86 °C X (i)}} = \frac{\text{Target weight per liter}}{\text{Target freezing point}}$$

$ZnCl_2$ concentration 0.1% = 0.1 g/100 ml = 1 g / 1000 ml (1 g/L)

$$\frac{136.3\ \text{g/L}}{\text{- 1.86 °C x 2.6}} = \frac{1\ \text{g/L}}{\text{X}}$$

**X = - 0.035 °C → NOT isotonic solution (Hypotonic solution)**

## 2) Sodium chloride equivalent (E) method:

- Sodium chloride equivalents (E) of various chemicals have been determined and can be used to formulate isotonic solutions.
- Key concept: (E) value is the **weight of NaCl equivalent to 1 gram of a substance**.
- NaCl is used as the reference electrolyte.
- **0.9% NaCl** solution is **isotonic** (0.9 g/100 ml or 9 g/L), has molecular weight (58.5) and dissociation factor **(i) = 1.8.**
- NaCl equivalents (E) are used to **determine the quantity of a substance** that has the **equivalent number of particles** as "**isotonic NaCl".**

$$(E)\ value\ of\ subtance = \frac{\left[\frac{MW\ of\ NaCl}{(i)\ NaCl}\right]}{\left[\frac{MW\ of\ substance}{(i)\ substance}\right]} = \frac{\left[\frac{58.5}{1.8}\right]}{\left[\frac{MW\ of\ substance}{(i)\ substance}\right]}$$

$$(E)\ value\ of\ subtance = \frac{58.5}{1.8} * \frac{(i)\ substance}{MW\ of\ substance}$$

**Example 1: Boric acid (mw = 61.8) has negligible dissociation (non-electrolyte). Determine E value of boric acid?**

$$\text{E value} = \frac{58.5}{1.8} \times \frac{1}{61.8} = 0.52$$

**Example 2: $ZnCl_2$ (mw = 136.3) has 80% dissociation. Determine E value?**

$$\text{E value} = \frac{58.5}{1.8} \times \frac{2.6}{136.3} = 0.62$$

**This means that {0.62 g of NaCl is equivalent to 1 g of $ZnCl_2$ }**

**Example 3: Calculate the percentage concentration of boric acid solution that is isotonic with body fluids. E value of boric acid = 0.52.**

Isotonic NaCl is 0.9% w/v (0.9 g NaCl / 100 mL) → For 100 ml we need to know how much boric acid would be equivalent to 0.9 g of NaCl.

$$\text{E value of boric acid} = 0.52 = \frac{0.52 \text{ g NaCl}}{1 \text{ g boric acid}}$$

1 g Boric acid → 0.52 g NaCl

X → 0.9 g NaCl

X = 0.9 / 0.52 = 1.73 g boric acid

Thus, we need 1.73 g of boric acid for every 100 ml of solution to make isotonic solution.

**So, the percentage concentration of boric acid is (1.73% w/v)**

**Example 4: Calculate the percentage concentration of $ZnCl_2$ solution that is isotonic. E value for $ZnCl_2$ = 0.62**

Isotonic NaCl is 0.9% w/v (0.9 g NaCl / 100 mL) → For 100 ml we need to know how much $ZnCl_2$ would be equivalent to 0.9 g of NaCl.

$$\text{E value of } ZnCl_2 = 0.62 = \frac{0.62 \text{ g NaCl}}{1 \text{ g } ZnCl_2}$$

$$1 \text{ g } ZnCl_2 \rightarrow 0.62 \text{ g NaCl}$$
$$X \rightarrow 0.9 \text{ g NaCl}$$

$X = 0.9 / 0.62 = 1.45$ g $ZnCl_2$

Thus, we need 1.45 g of $ZnCl_2$ for every 100 ml of solution to make isotonic solution.

**So, the percentage concentration of $ZnCl_2$ is (1.45% w/v)**

**Example 5: What is the tonicity of 0.2 M mannitol solution (mw = 182, E = 0.18, non-electrolyte) with respect to body fluids? Use both FP and E methods.**

**1) FP method:**

$$\text{Mannitol conc 0.2 M} = \frac{0.2 \text{ moles}}{\text{L}} \times \frac{182 \text{ g}}{1 \text{ mole}} = 36.4 \text{ g/l}$$

$$\frac{\textbf{Formula weight per liter}}{\textbf{- 1.86 °C X (i)}} = \frac{\textbf{Target weight per liter}}{\textbf{Target freezing point}}$$

$$\frac{182 \text{ g/l}}{-1.86 \text{ °C} \times 1} = \frac{36.4 \text{ g/l}}{X} \qquad \textbf{X = - 0.37 °C}$$

Decrease in FP of - 0.37 °C is less than – 0.52 °C, thus solution has fewer particles and must be **"Hypotonic".**

**2) E value method:**

Mannitol conc 36.4 g/L → 3.64 g/ 100 mL.

$$\text{E value for mannitol} = 0.18 = \frac{0.18 \text{ g NaCl}}{1 \text{ g mannitol}}$$

1 g Mannitol → 0.18 g NaCl

3.64 g Mannitol → X

X = 0.9 / 0.18 = 0.66 g NaCl

**0.66 g NaCl is less than 0.9 g NaCl, thus solution has fewer particles, and must be "Hypotonic".**

**1) To convert from molar conc (M) to g/L**

$$\mathrm{g/L} = \mathrm{Molarity\ (mol/L)} \times \mathrm{Molecular\ Weight\ (g/mol)}$$

**2) To convert from g/L to molar conc (M or mol/L)**

$$M = \frac{g/L}{MW}$$

M = mol/L  g/L = wight in gram per L  M.W = g/mol

**3) To calculate number of moles**

$$n = \frac{m}{MW}$$

n = Number of moles  m = mass of substance (g)  M.W = g/mol

| Substance | E-value |
|---|---|
| Boric acid | 0.52 |
| Dextrose (glucose) | 0.18 |
| Mannitol | 0.18 |
| Glycerin | 0.34 |
| Potassium chloride | 0.76 |
| Lidocaine HCl | 0.22 |
| Procaine HCl | 0.21 |
| Cocaine HCl | 0.16 |
| Pilocarpine HCl | 0.23 |

| Substance | E value |
|---|---|
| Phenylephrine HCl | 0.32 |
| Ephedrine HCl | 0.30 |
| Ephedrine sulfate | 0.23 |
| Atropine sulfate | 0.12 |
| Morphine sulfate | 0.15 |
| Scopolamine HBr | 0.12 |
| Pilocarpine nitrate | 0.23 |
| Apomorphine HCl | 0.14 |
| Naphazoline HCl | 0.27 |


Thank you