لجان الدفعات

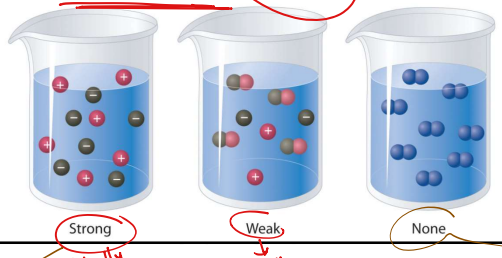
PHYSICAL PHARMACY

MORPHINE ACADEMY

Solutions of electrolytes

Solutions of electrolytes

- An electrolyte is a substance that ionizes when dissolved in suitable ionizing solvents such as water.
- This includes most soluble salts, acids, and bases.
- Electrolytes in solution have the capacity to conduct electricity through a process known as *electrolysis*
- Electrolytes can be classified as *strong electrolytes* and *weak electrolytes.*
- Strong electrolytes ionize completely (~100%), while weak electrolytes ionize only partially (1–10%).



high electrical conductivity.

partially

ions + many unionized molecules

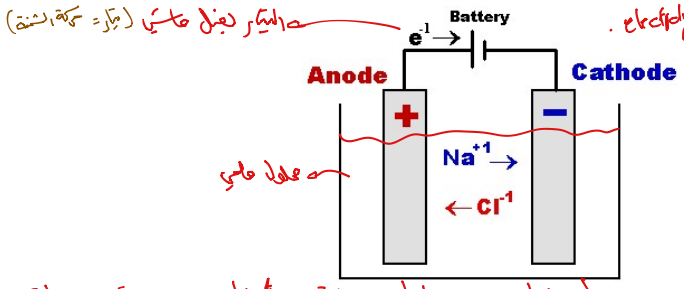
low conductivity.

no mobile ions.

∴ ↑ mobile ions → ↑ electrical conductivity

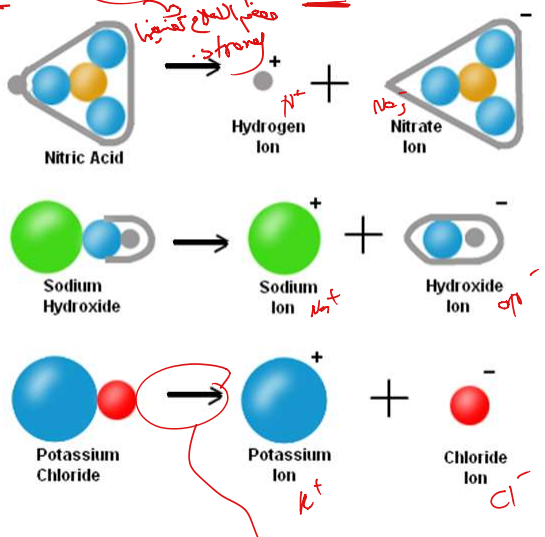
Solutions of electrolytes

- Electrolytes in solution have the capability to conduct electricity through a process known as *electrolysis*



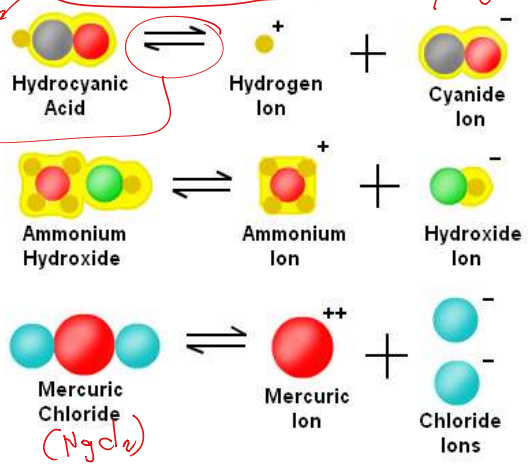
Solutions of electrolytes

- Strong electrolytes includes strong acids (e.g.HNO_3), strong bases (e.g. NaOH), and most salts (e.g. KCl).



Solutions of electrolytes

- Weak electrolytes include weak acids (e.g. CH_3COOH), weak bases (e.g. NH_3), and slightly soluble salts (e.g. AgCl).



Colligative properties

1. osmotic pressure (π).
2. Freezing-point depression.
3. Boiling-point elevation.
4. vapor-pressure lowering.

- Van't Hoff observed that the osmotic pressure (π) of dilute solutions of nonelectrolytes such as sucrose and urea, can be expressed by the equation:

$$\pi = RTc$$

- R: Gas constant, T: absolute temperature, c: concentration in mole/L
- However; he found that solutions of electrolytes gave osmotic pressures approximately two, three, and more times larger than expected from this equation.
- Van't Hoff Introduced a correction factor (i) to account for the irrational behavior of ionic solutions, he wrote:

$$\pi = iRTc$$

- The (i) factor approximately equals the number of ions formed upon dissociation (e.g. 2 for NaCl, 3 for $CaCl_2$, and 4 for $FeCl_3$).

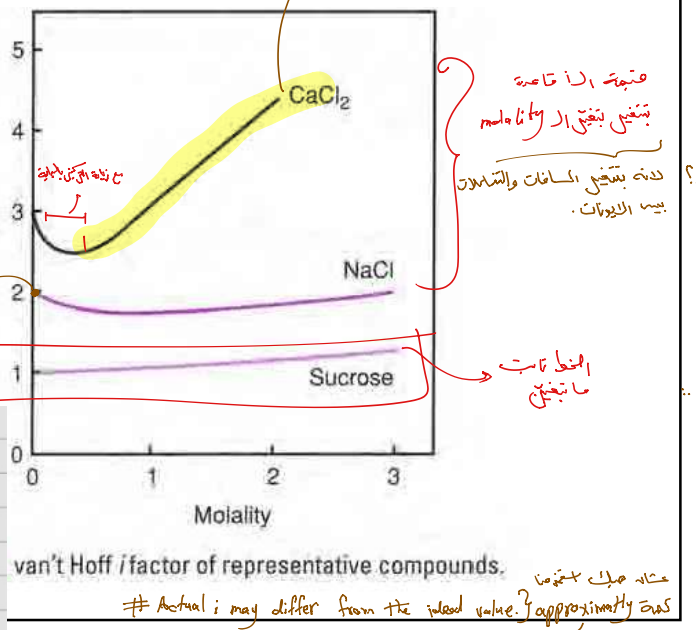
$NaCl \rightarrow Na^+ + Cl^- \Rightarrow i = 2$

$CaCl_2 \rightarrow Ca^{+2} + 2Cl \Rightarrow i = 3$

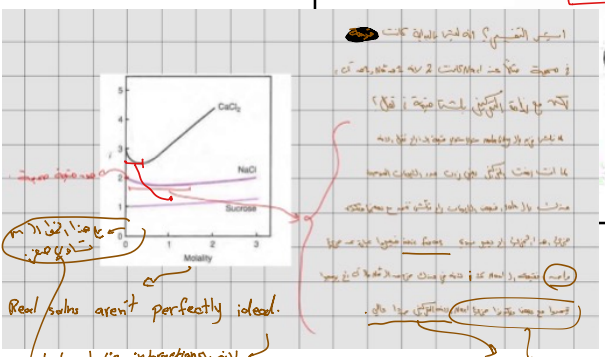
$FeCl_3 \rightarrow Fe^{+3} + 3Cl \Rightarrow i = 4$

$FeCl_3 > CaCl_2 > NaCl > sucrose$

Colligative properties



van't Hoff *i* factor of representative compounds.



Real solns aren't perfectly ideal.

Colligative properties

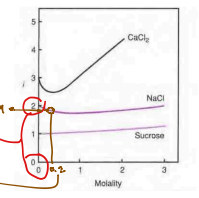
Example:

What's the osmotic pressure of a 2.0 m solution of sodium chloride at 20°C?

Answer: the i factor for a 2 m solution of sodium chloride as observed in the figure is about 1.9

$\pi = iRTm$

$= 1.9*0.082*293*2 = 91.3$ atm



Colligative properties

- The Van't Hoff factor can be used to express the four colligative properties for solutions of electrolytes and concentrated solutions of nonelectrolytes.

$$\Delta p = 0.018 i p_1^{o} m$$

$$\Delta T_f = iK_f m$$

$$\Delta T_b = iK_b m$$

$$\pi = iRTm$$

- The first equation applies only to dilute aqueous solutions

$$X_2 = \frac{\Delta p}{p_1^o} \cong \frac{n_2}{n_1} = \frac{\frac{1000}{18}}{\frac{m}{55.5}} = 0.018m$$

Electrolyte Dissociation

Arrhenius theory

- Both strong and weak electrolytes are fully dissociated into ions at infinite dilution (extremely dilute solutions in which solute-solute interactions are negligible).
- At moderately concentrated solutions, Arrhenius differentiated between strong and weak electrolytes by the fraction of the molecules ionized: the *degree of dissociation (α)*.
- A strong electrolyte was one that dissociated into ions to a high degree and a weak electrolyte was one that dissociated into ions to a low degree.
- Arrhenius determined the degree of dissociation (α) directly from conductance measurements

Electrolyte Dissociation

Arrhenius theory

Example:

Calculate the degree of ionization of 0.1 m acetic acid providing that its freezing point is -0.188°C.

Answer: Acetic acid dissociates into two ions, so v = 2.

To calculate i:

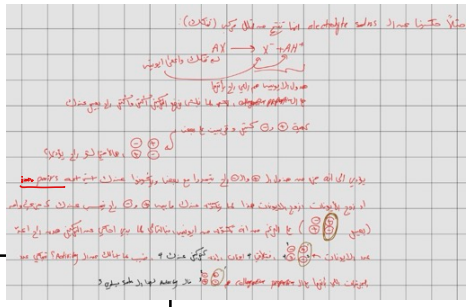
$$i = \frac{\Delta T_f}{k_f m}$$

= 0.188/ (1.86*0.1)= 1.011

It is possible now to calculate the degree of ionization:

$$\alpha = \frac{i - 1}{v - 1}$$

= (1.011-1)/ (2-1) = 0.011 or 1.1%



Activity and Activity Coefficient

- The large number of oppositely charged ions in solutions of strong electrolytes influence one another through interionic attractive forces.
- For solution of nonelectrolytes, regardless of concentration, the number of ions is small and the interionic attractive forces are insignificant.
- As for strong electrolytes, ions can associate at high concentrations into groups known as ion pairs. Thus the values of the freezing point depression and the other colligative properties are less than expected for solutions of unhindered ions. Consequently, a strong electrolyte may be completely ionized, yet incompletely dissociated into free ions.
- One may think of the solution as having an "effective concentration" or, as it is called, an **activity**.

Activity and Activity Coefficient

- The activity (a), in general, is less than the actual or stoichiometric concentration of the solute (m), not because the strong electrolytes are partly ionized, but rather because some of the ions are effectively "taken out of play" by the electrostatic forces of interaction.
- At infinite dilution in which the ions are so widely separated that they do not interact with one another, the activity **a** of an ion is equal to its concentration:

$$a = m$$

- As the concentration of the solution is increased, the ratio becomes less than unity because the effective concentration or activity of ions becomes less than the molal concentration. This ratio is known as the practical activity coefficient (γ), thus:

$$a = \gamma m$$

high concentration + strong electrolytes : مثل #

strong ⇒ α↑

ions close together ⇒ interionic interactions ↑ ⇒ ion pairs تقل

γ < 1 ⇐ a < m

infinite dilution is ideal

m = c ⇐ γ = 1 ⇐ interactions → 0

0 < γ ≤ 1

γ = 1 → Dilute conc.

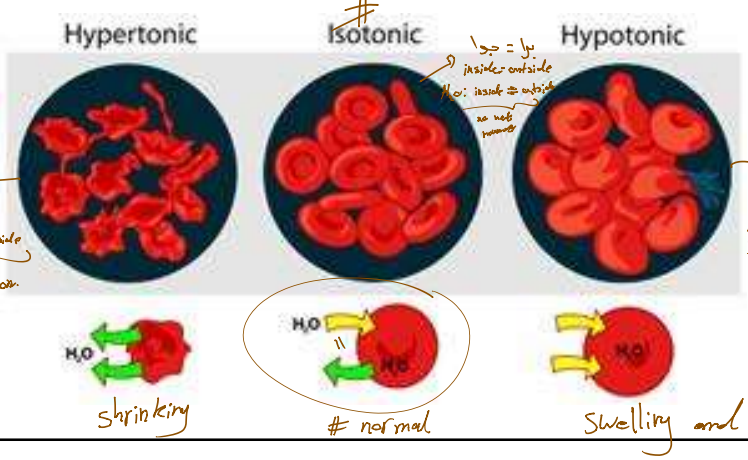
γ or γ < 1 → at exist interionic interactions.

Isotonic Solutions

انتقال الـ solvent من منطقة ذات تركيز منخفض من solutes إلى منطقة ذات تركيز عالي من solutes عبر semipermeable membrane

Introduction

- The need to achieve isotonic conditions with solutions to be applied to delicate membranes is dramatically illustrated by mixing a small quantity of blood with aqueous sodium chloride solutions of varying tonicity.



non-penetrating solutes

isotonic = equal π, not equal amounts of solute or solvent.

$\pi_{inside} = \pi_{outside}$ ⇒ no net movement of H_2O

amount of solute inside = amount of solute outside

isotonic

lower solute conc. → high solute conc.

H_2O: outside → cell

Hemolysis

inside < outside

H_2O: cell → outside

Crenation

↑ effective conc. of osmotically active particles (non-penetrating solutes) → ↑ π

① Hypertonic: $\pi_{outside} > \pi_{inside}$

② Hypotonic: $\pi_{outside} < \pi_{inside}$

③ Isotonic: $\pi_{outside} \simeq \pi_{inside}$

Introduction

- The solutions that cause no swelling or contraction of the tissues and produce no discomfort when instilled in the eye, nasal tract, blood, or other body tissues is termed **isotonic.**
- Isotonic sodium chloride NaCl (0.9%) is a familiar pharmaceutical example of such a preparation.

Isosmotic Solutions

- Osmolality and osmolarity are colligative properties that measure the concentration of the solutes independently of their ability to cross a cell membrane.
- The unit to express the amount of osmotically active particles in a solution is the osmole or milliosmole:

Number of osmoles = Number of moles × n

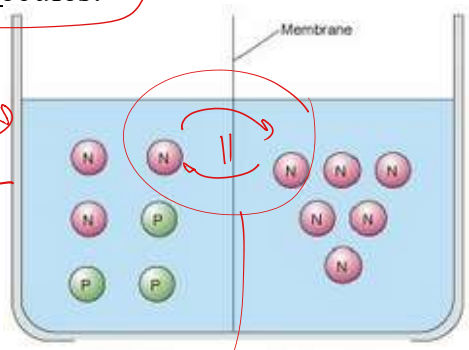
- Where ***n*** is the number of species into which the solute is dissolved

$1\ \text{Osmol} = 10^3\ \text{mOsmol}$

- **Osmolarity** is the number of osmoles of solute per L of solution
- **Osmolality** is the number of osmoles of solute per kg of solvent

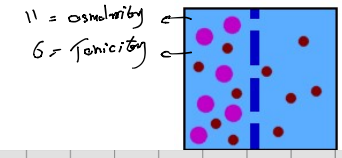
Isosmotic Solutions

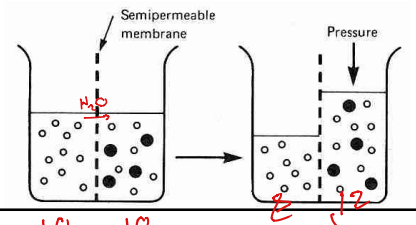
- When two solutions are separated by a perfect semipermeable membrane and there is no net movement of solvent molecules across the membrane, the solutions are isosmotic (i.e. have equal osmotic pressure or osmolarity).
- Perfect semipermeable membrane is permeable only to solvent molecules.



Isosmotic Solutions

- When two isosmotic solutions contain solutes that cannot cross the biological membrane, they are described as isotonic with respect to that membrane.
- Tonicity is a measure of the effective osmotic pressure gradient of two solutions separated by a semipermeable membrane.
- Osmolarity takes into account the total concentration of penetrating solutes and non-penetrating solutes, whereas tonicity takes into account the total concentration of only non-penetrating solutes

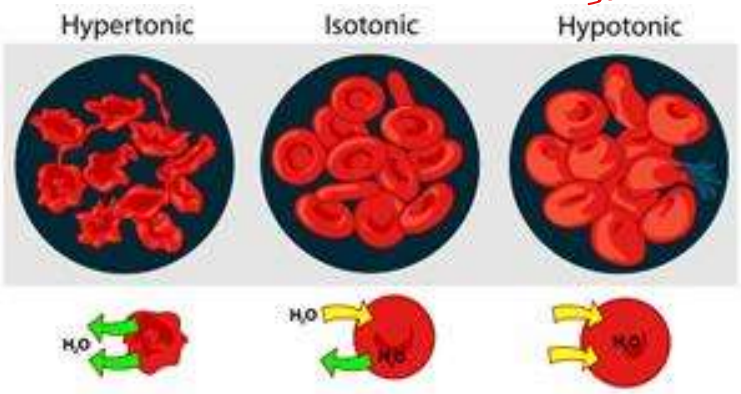




Measurement of Tonicity

Hemolytic method

- The effect of various solutions of the drug is observed on the appearance of red blood cells suspended in the solutions.



Measurement of Tonicity

Cryoscopic Method

- The tonicity is determined from ΔT_f of the solution, which is determined theoretically from the equation $\Delta T_f = K_f c$.
- For solutions of electrolytes, a new factor **($L = iK_f$)** is used:

$$\Delta T_f = L\,c$$

- The L value for solutions that is isotonic with body fluids is written as L_{iso}

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

- For sodium chloride the concentration of isotonic solution is 0.9% w/v = 0.154 M:

$$L_{iso} = 0.52\ ^{o}C / 0.154 = 3.4$$

Measurement of Tonicity

Cryoscopic Method

TABLE 8–3
AVERAGE L_{iso} VALUES FOR VARIOUS IONIC TYPES*

Type	L_{iso}	Examples
Nonelectrolytes	1.9	Sucrose, glycerin, urea, camphor
Weak electrolytes	2.0	Boric acid, cocaine, phenobarbital
Di-divalent electrolytes	2.0	Magnesium sulfate, zinc sulfate
Uni-univalent electrolytes	3.4	Sodium chloride, cocaine hydrochloride, sodium phenobarbital
Uni-divalent electrolytes	4.3	Sodium sulfate, atropine sulfate
Di-univalent electrolytes	4.8	Zinc chloride, calcium bromide
Uni-trivalent electrolytes	5.2	Sodium citrate, sodium phosphate
Tri-univalent electrolytes	6.0	Aluminum chloride, ferric iodide
Tetraborate electrolytes	7.6	Sodium borate, potassium borate

*From J. M. Wells, J. Am. Pharm. Assoc. Pract. Ed. 5, 99, 1944.

Methods of Adjusting Tonicity

Cryoscopic method

- In the cryoscopic method, 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.
- The freezing point depressions (ΔT_f) of drug solutions can be determined experimentally or theoretically.

Methods of Adjusting Tonicity

Cryoscopic method

Example

How much NaCl is required to render 100 mL of a 1% solution of apomorphine hydrochloride isotonic with blood serum?

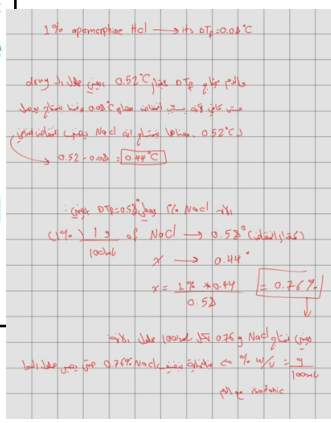
1% solution of the drug has a ΔT_f of 0.08°C.

1% solution of NaCl has a ΔT_f of 0.58°C.

To make this solution (ΔT_f = 0.08°C) isotonic with blood (ΔT_f = 0.52°C), sufficient NaCl must be added to reduce the freezing point by an additional 0.44°C (0.52°C - 0.08°C).

$$\frac{1\%}{X} = \frac{0.58°C}{0.44°C} \Rightarrow X = 0.76\%$$

Thus, 0.76% NaCl will lower the freezing point by 0.44°C and will render the solution isotonic.



Methods of Adjusting Tonicity

NaCl equivalent method

- The sodium chloride equivalent (E) of a drug is the amount of sodium chloride that has the same osmotic effect of 1 g of the drug.
- E value can be obtained theoretically from L_{iso} value and Molecular weight of the drug.

Osmotically Equivalent : $\Delta T_{f,drug} = \Delta T_{f,NaCl}$

Methods of Adjusting Tonicity

NaCl equivalent method

- For a solution of 1 g of drug in 1000 ml of solution

$$c = \frac{1\ g}{MW} \quad \Rightarrow \quad \Delta T_f = L_{iso}\frac{1\ g}{MW}$$

- For a solution of NaCl with the same freezing point depression as the drug solution

$$\Delta T_f = 3.4\frac{E}{58.45} \quad \Rightarrow \quad \frac{L_{iso}}{MW} = 3.4\frac{E}{58.45}$$

$$\boldsymbol{E = 17\frac{L_{iso}}{M.Wt}}$$

Methods of Adjusting Tonicity

NaCl equivalent method

Example 1

Calculate the approximate *E* value for a new amphetamine hydrochloride derivative (M.Wt =187). The drug is a uni-univalent salt with a L_{iso} value of 3.4.

$$\boldsymbol{E = 17\frac{L_{iso}}{M.Wt}}$$

$$\boldsymbol{E} = 17 \times \frac{3.4}{187} = 0.31$$

unitless

Methods of Adjusting Tonicity

NaCl equivalent method

Example 2

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? E value for the drug is 0.23

The quantity of the drug is multiplied by its NaCl equivalent, *E*:

Ephedrine sulfate: 1 g × 0.23 = 0.23 g

The ephedrine sulfate has contributed a weight of material osmotically equivalent to 0.23 g of NaCl.

Because a total of 0.9 g of NaCl is required for isotonicity, 0.67 g (0.90 - 0.23 g) of NaCl must be added.

Methods of Adjusting Tonicity

NaCl equivalent method

Example 3

How much dextrose would be required to make the solution in example 2 isotonic instead of NaCl?

Because the sodium chloride equivalent of dextrose is 0.16, then:

$$\frac{\mathbf{1\ g\ dextrose}}{\mathbf{0.16\ g\ NaCl}} = \frac{X}{\mathbf{0.67\ g\ NaCl}}$$

X = 4.2 g of dextrose

Methods of Adjusting Tonicity

White-Vincent Method

- White and Vincent developed a simplified equation for calculating the volume V (mls) of isotonic solution prepared by mixing the drug with water.

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

w: weight (g) of the drug.

E: NaCl equivalent

Methods of Adjusting Tonicity

White-Vincent Method

Example

How to make 30 mL of a 1% solution of procaine HCl isotonic with body fluid? NaCl equivalent for procaine HCl is 0.21

Weight of the drug = 30 × 1% = 0.3 g

$V = w \times E \times 111.1$

$V = 0.3 \times 0.21 \times 111.1 = 7$ ml

7 ml of water is added to the drug to make it isotonic, then enough isotonic diluting solution is added to make 30 mL of the finished product.