Solutions of nonelectrolytes

Solutions

- Solution is a mixture of two or more components that form a homogenous molecular dispersion (one phase).
- It consists of one or more solutes dissolved in one or more solvents.
- Solute molecules or ions are "dissolved" and uniformly distributed in the solvent medium.

Solutions

- A true solution is a single phase system.
- NaCl and water, ethanol and water
  - Form a solution (one phase) ⟹ **a solution**
- Talc and water
  - Form a suspension (two phase) ⟹ **not solution**
- Oil and water
  - Form an emulsion (two phase) ⟹ **not solution**

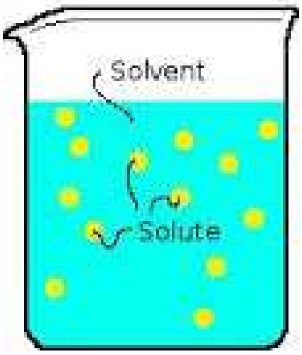
Solutions are composed of:

- **Solute:** is the substance that dissolves which may be solid, liquid, or gas.
- **Solvent:** is the substance that does the dissolving which may be solid, liquid, or gas.

Solutions

Which the solvent and which is the solute?

- **Solvent:** component in greater extent.
- **Solute:** component in minor extent.
- **Note:** When a solid is dissolved in liquid, it is the solute irrespective of relative amount.

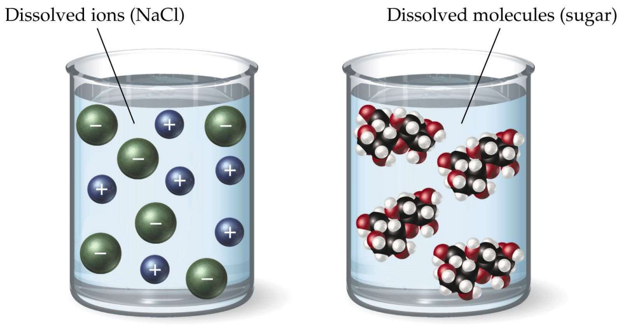


Types of Solutions

Solute	Solvent	Solution	Example
Gas	Gas	Gas	Air (O_2 in N_2)
Gas	Liquid	Liquid	Carbonated beverages (CO_2 in H_2O) Swimming pool (Cl_2 in H_2O)
Liquid	Liquid	Liquid	Wine (ethanol in H_2O) Vinegar (acetic acid in H_2O)
Liquid	Solid	Solid	Dental amalgam for fillings (liquid mercury in solid silver)
Solid	Liquid	Liquid	Saline (NaCl in H_2O) Sugar in water
Solid	Solid	Solid	14-karat gold (Ag in Au) Steel (carbon in iron)

Solutions

- **Non-electrolytes:** do not yield ions when dissolved in water; therefore, do not increase electrical conductivity of solution (e.g. sugar, some polymers, some drugs).
- **Electrolytes:** form ions in solution; therefore, increase electrical conductivity (e.g. NaCl).



Electrolyte solution Nonelectrolyte solution

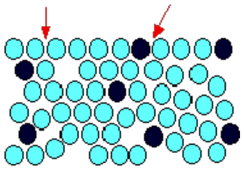
Solutions

Concentration expressions

- **Molarity(M):** no. of moles of solute in 1 litre of solution.
- **Molality (m):** no. of moles of solute in 1 kg of solvent.
- **Normality(N):** no. of equivalents in 1 liter of solution.
- **Mole fraction (X):** ratio of number of moles of one component to total moles of all constituents (solute and solvent).
- **Percent by weight (w/w):** no. of grams of solute in 100 g of solution.
- **Percent by volume (v/v):** no. of milliliters of solute in 100 ml of solution.
- **Percent weight in volume (w/v):** no. of grams of solute in 100 ml of solution.

Ideal solutions

- Solutions in which there is no change in the properties of the components when they are mixed.
- For a mix of molecules of A and B, the interactions between unlike neighbors (U_{AB}) and like neighbors U_{AA} and U_{BB} must be of the same average strength, i.e., $2U_{AB} = U_{AA} + U_{BB}$
- No heat is evolved or absorbed, the final volume is the sum of the volume of the individual components.



In an ideal solution, the forces between the solvent molecules . . .

. . . are exactly the same as those between solvent and solute.

That means that it takes the same amount of energy for solvent molecules to break away from the surface in either case.

Ideal solutions

Ideal solution:

- E.g.100 ml of ethanol + 100 ml of methanol = 200 ml solution.
- No heat is evolved or absorbed.

Real solution:

- E.g.100 ml of sulfuric acid + 100 ml of water = 180 ml solution.
- Heat is evolved (exothermic).

Ideal solutions

Raoult's Law

- Cohesive interactions in liquid prevent all molecules from escaping as a vapor. Disrupting the cohesion (by increasing T) will increase the tendency of molecules to escape from the liquid as a vapor.
- When the vapor pressure equals the external pressure, the system is said to be in equilibrium, and the vapor pressure is known as the *equilibrium vapor pressure (P)*
- A substance with a high vapor pressure at normal temperatures is often referred to as volatile.

Ideal solutions

Raoult's Law:

- The partial vapor pressure of each component in an ideal solution is equal to the vapor pressure of the pure component multiplied by its mole fraction in the mixture.

Ideal solutions

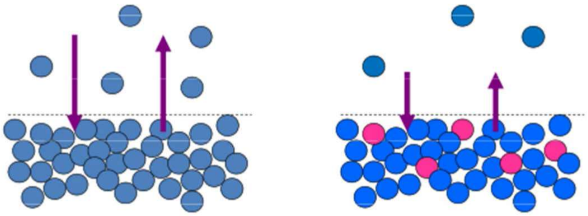
Raoult's Law

- For a non-volatile solute, the total vapor pressure (P_{total}) is equal to the vapor pressure of the solvent ($P_{solvent}$) only: $P_{total} = P_{solvent}$

$$P_1 = X P°_1$$

X: mole fraction of solvent

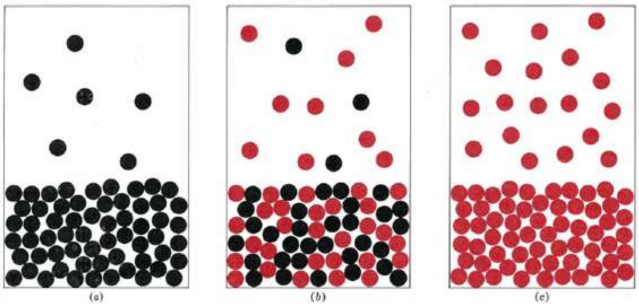
$P°_1$: vapor pressure of pure solvent



Ideal solutions

Raoult's Law

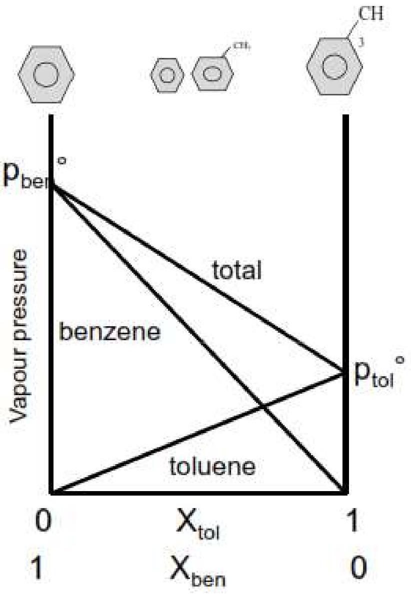
- If components constituting a solution are volatile, each will produce a partial pressure above the solution, which can be calculated from **Ideal Solutions Raoult's Law**
- The total pressure is the sum of the partial pressures of all the constituents.



Ideal solutions

Raoult's Law

- For two constituents, toluene and benzene:
- $P_{tol} = P_{tol°} X_{tol}$
- $P_{ben} = P_{ben°} X_{ben}$
- $P_{total} = P_{tol} + P_{ben}$
- P_{tol}, P_{ben}: partial vapor pressures
- $P_{tol°}$, $P_{ben°}$: vapor pressures of pure components.
- X_{tol}, X_{ben}: mole fractions



Ideal solutions

Aerosols and Raoult's law

- Raoult's law is important because it allows the calculation of vapour pressure from a knowledge of the composition of the solution.
- The requirement of the Montreal Protocol in 1989 for the replacement of chlorofluorocarbon (CFC) propellants in pressurised metered-dose inhalers with hydrofluoroalkanes (HFAs), because of the ozone-depleting properties of CFCs, led to a substantial review of the formulation of these devices as a consequence of major differences in physical and chemical properties of these propellants.
- The two most widely used HFAs are HFA 227 and HFA 134a.
- The vapour pressure of metered dose inhalers determines the aerosol droplet size and consequently has an important influence on the efficiency of deposition in the lungs

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Ideal solutions

Example:

- Calculate the vapour pressure (in Pa) at 20°C above an aerosol mixture consisting of 30% w/w of HFA 134a (tetrafluoroethane, molecular weight 102) with a vapour pressure of 68.4 psig and 70% w/w of HFA 227 (heptafluoropropane, molecular weight 170) with a vapour pressure of 56.0 psig. Assume ideal behaviour.

Answer

No. of moles of HFA 134a in 100 g mixture = 30/102 = 0.2941 moles

No. of moles of HFA 227 in 100 g mixture = 70/170 = 0.4118 moles

$x_{134} = 0.2941/0.7059 = 0.4166$

$x_{227} = 0.4118/0.7059 = 0.5834$

$P = p^{o}_{134}x_{134} + p^{o}_{227}x_{227}$

$P = (68.4 \times 0.4166) + (56.0 \times 0.5834)$

$P = 61.17$ psig $= 5.23 \times 10^{5}$ Pa

Real solutions

- In real solutions, the attractive forces are not uniform.
- The adhesive attraction of A for B might be less or exceed the cohesive attraction between A and A or B and B.
- This can happen even if the liquids are completely miscible.
- The more dissimilar the nature of A and B, the more strongly the solution is expected to deviate from ideality.
- These real solutions may not obey Raoult’s law. There can be negative or positive deviations.

Real solutions

Partial pressures of components less than in ideal solution.

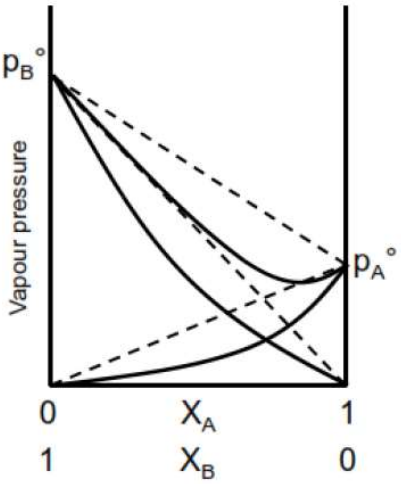
Adhesive attractions (AB) greater than cohesive attractions (AA and BB).

A holds B back and B holds A back.

Total vapor pressure may show a minimum.

E.g. chloroform and acetone form hydrogen bonds

$CHCl_3$ - - - $O=C(CH_3)_2$



Real solutions

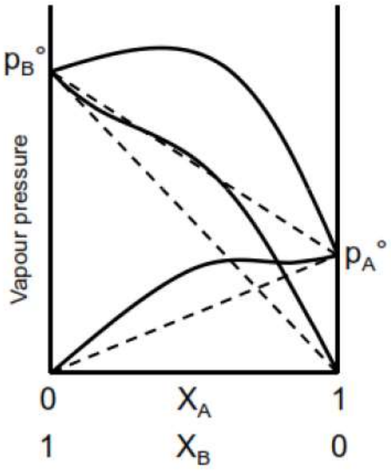
Partial pressures greater than in ideal solution.

Cohesive attractions (AA and BB) greater than adhesive attractions (AB).

A disrupts B cohesion so easier for B to escape and vice-versa

Total vapor pressure may show a maximum

E.g. CCl4 - MeOH



Colligative Properties of Solutions

- Colligative properties are properties of solutions that depend upon the ratio of the number of solute particles to the number of solvent molecules in a solution, and not on the type of chemical species present.

- Colligative properties of solution include:
  1. Lowering of vapor pressure
  2. Elevation of boiling point
  3. Depression of freezing point
  4. Osmotic pressure

Colligative Properties of Solutions

Lowering of vapor pressure

- When a non-volatile solute is dissolved in a volatile solvent, the vapor above the solution is provided by the solvent only. The solute particles (atoms, molecules or ions) at the surface reduce the escaping tendency of the solvent
- Therefore, the tendency of the solvent molecules to exert vapor pressure is lowered in the presence of the solute.

Colligative Properties of Solutions

Lowering of vapor pressure

- Vapor pressure lowering of a solution depends on the number of solute molecules (mole fraction) present in the solution.
- The higher the solute fraction, the lower the vapor pressure above the solution.
- Vapor pressure lowering is the key to all four of the colligative properties.

Colligative Properties of Solutions

Lowering of vapor pressure

- The change of vapour pressure following the addition of a nonvolatile solute to a solvent may be determined by application of Raoult's law.

$$p = p_1 = p^o_1 x_1 = p^o_1\,(1 - x_2)$$

$$(p^o_1 - p_1)/\,p^o_1 = x_2 = n_2/(n_1+n_2)$$

- p_1: the vapor pressure of the solvent (with solute), p^o_1 : vapor pressure of the pure solvent x_1: mole fraction of solvent, x_2 = mole fraction of solute,

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Colligative Properties of Solutions

Lowering of vapor pressure: Example

What is the relative vapor pressure lowering for a solution containing 171.2 g of sucrose (MW = 342.3) in 1000 g of water (MW = 18.02)?

$\Delta P/\,P_1{}^{\circ} = n_2\,/\,(n_1 + n_2)$

$n = m/MW$

Moles of water = $n_1 = m_1/MWt_1 = 1000/18.02 = 55.5$

Moles of sucrose = $n_2 = m_2/MWt_2 = 171.2/342.3 = 0.5$

$\Delta P/\,P_1{}^{\circ} = n_2\,/\,(n_1 + n_2) = 0.5/(55.5 + 0.5) = 0.0089$

The vapor pressure of this solution has been lowered 0.89% by sucrose

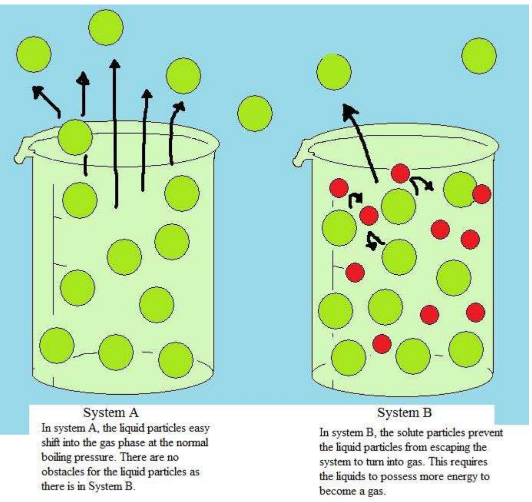
Colligative Properties of Solutions

Boiling Point Elevation

- **Normal Boiling Point:** is the temperature at which the vapor pressure (P) of the liquid becomes equal to the atmospheric pressure.
- Presence of solute particles lower the vapor pressure of the solution (we need to increase temperature to increase p to make it boil).
- The boiling point of a solution (T) is higher than that of the pure solvent alone (T°)

Colligative Properties of Solutions

Boiling Point Elevation

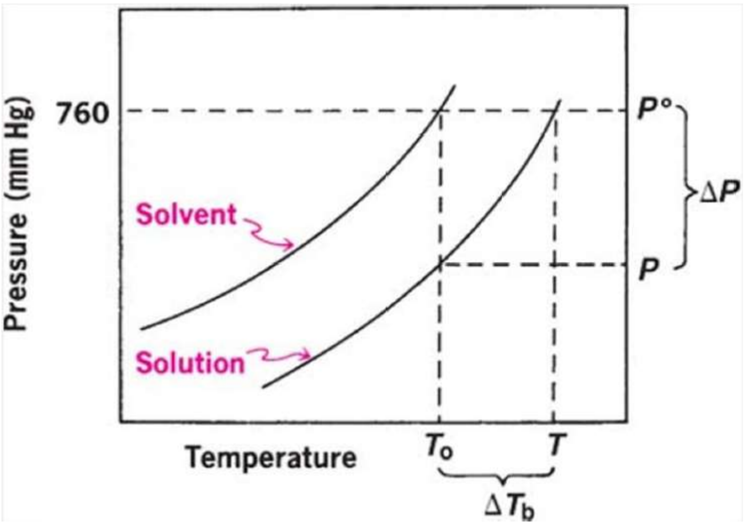


System A

In system A, the liquid particles easy shift into the gas phase at the normal boiling pressure. There are no obstacles for the liquid particles as there is in System B.

System B

In system B, the solute particles prevent the liquid particles from escaping the system to turn into gas. This requires the liquids to possess more energy to become a gas.



Boiling point elevation of solvent due to the addition of a solute

Colligative Properties of Solutions

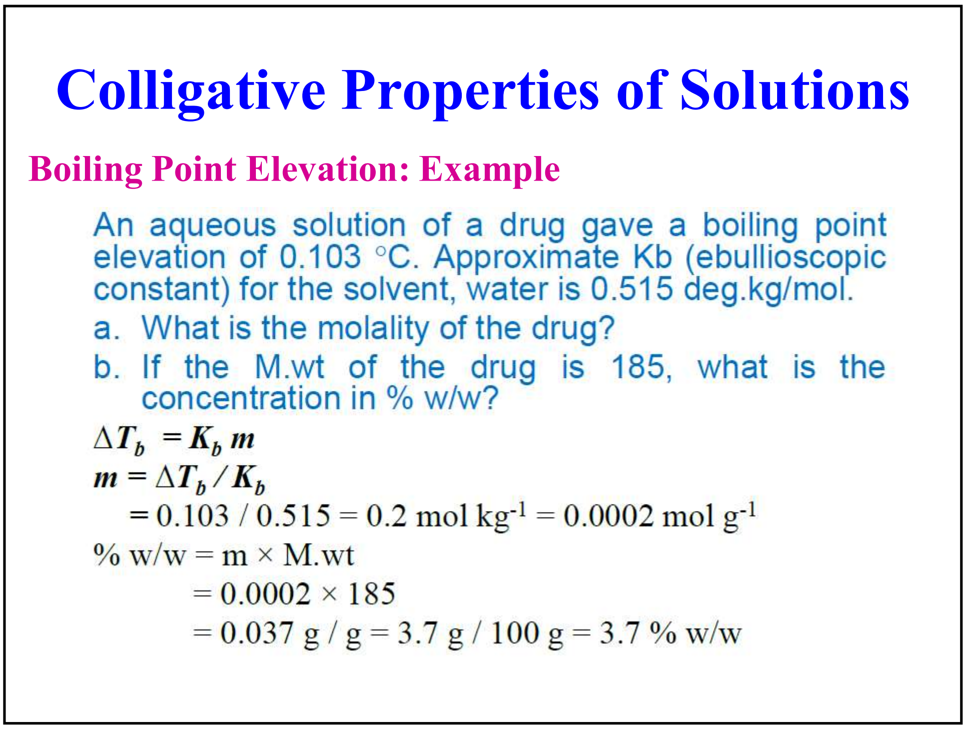
Boiling Point Elevation

- The boiling point elevation, ΔT_b is estimated by this equation.

$$\Delta T_b = K_b m$$

$$T - T_0 = \Delta T_b$$

- **K_b**: molal elevation constant (ebullioscopic constant)
- **m**: molality



Colligative Properties of Solutions

Boiling Point Elevation: Example

An aqueous solution of a drug gave a boiling point elevation of 0.103 °C. Approximate Kb (ebullioscopic constant) for the solvent, water is 0.515 deg.kg/mol.

a. What is the molality of the drug?

b. If the M.wt of the drug is 185, what is the concentration in % w/w?

$\Delta T_b = K_b\, m$

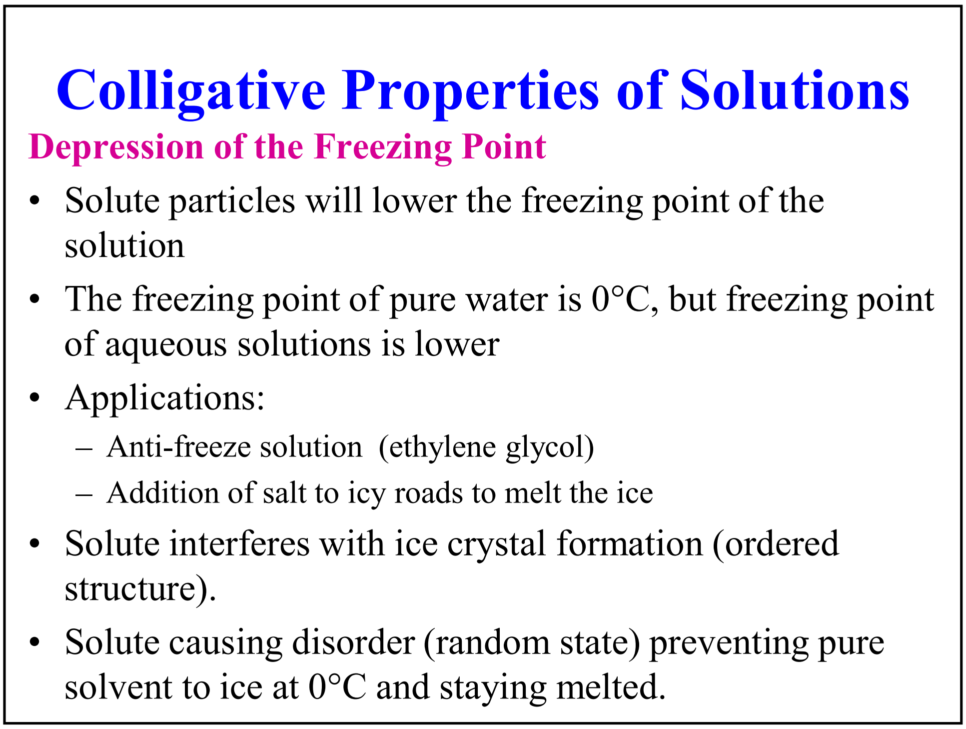
$m = \Delta T_b / K_b$

$= 0.103 / 0.515 = 0.2 \text{ mol kg}^{-1} = 0.0002 \text{ mol g}^{-1}$

$\%\ w/w = m \times M.wt$

$= 0.0002 \times 185$

$= 0.037 \text{ g / g} = 3.7 \text{ g / 100 g} = 3.7\ \%\ w/w$



Colligative Properties of Solutions

Depression of the Freezing Point

- Solute particles will lower the freezing point of the solution
- The freezing point of pure water is 0°C, but freezing point of aqueous solutions is lower
- Applications:
  - Anti-freeze solution (ethylene glycol)
  - Addition of salt to icy roads to melt the ice
- Solute interferes with ice crystal formation (ordered structure).
- Solute causing disorder (random state) preventing pure solvent to ice at 0°C and staying melted.

Colligative Properties of Solutions

Depression of the Freezing Point

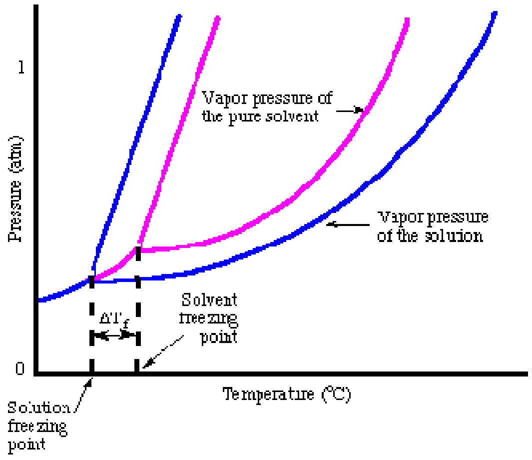
- The lowering of the freezing point of a solution is directly proportional to the molar concentraton of the solute (i.e. number of particles in solution, (molecules or ions).

$$\Delta T_f = K_f m$$

- ΔT_f: Freezing point depression
- K_f: Cryoscopic constant
- m: molality of solution

Colligative Properties of Solutions

Depression of the Freezing Point



Colligative Properties of Solutions

Depression of the Freezing Point: Example

What is the freezing point of a solution comprising 3.42 g of sucrose (MW = 342) and 500 g of water? Take kf to be 1.86 (°C kg mol-1)

$\Delta T_f = K_f\, m$

m = molality of sucrose

$$= \frac{\text{no. of mole}}{\text{Wt}_{\text{solvent}}} = \frac{\text{Wt/MW}}{\text{Wt}_{\text{solvent}}} = \frac{3.42/342}{0.5} = 0.02 \text{ mol kg}^{-1}$$

$\Delta T_f = K_f\, m$ = 1.86 × 0.02 = 0.037 °C (i.e. ΔT_f, freezing point depression)

Hence, the freezing point of this solution is –0.037 °C as (pure water $T_f = 0$ °C)

This solution will stay melted at temp of 0 °C

Colligative Properties of Solutions

Osmotic pressure

- Whenever a solution is separated from a solvent by a membrane that is permeable only to solvent molecules (referred to as a *semipermeable membrane*), there is a passage of solvent across the membrane into the solution.
- This is the phenomenon of *osmosis.*
- If the solution is totally confined by a semipermeable membrane and immersed in the solvent, then a pressure differential develops across the membrane, which is referred to as the *osmotic pressure.*

Colligative Properties of Solutions

Osmotic pressure

- Osmotic pressure is determined by the total number of particles in the solution, regardless of chemical nature
- Van’t Hoff recognized a proportionality between osmotic pressure concentration and temperature and suggested a relationship that corresponds to an ideal gas:

$\pi v = n\ R\ T \quad \Rightarrow$ **Van’t Hoff equation:** $\pi = c\ R\ T$

π: Osmotic pressure in atmospheres

c: molarity of solution

R: Gas constsant (0.082 L.atm/mol.deg)

T: Absolute temperature

Colligative Properties of Solutions

Osmotic pressure

- Morse and others have shown that when the concetration is expressed in molality rather than in molarity, the results compare more nearly with the experimental findings:

Morse equation: $\pi = m\ R\ T$

π: Osmotic pressure in atmospheres

m: molality of solution

R: Gas constsant (0.082 L.atm/mol.deg)

T: Absolute temperature

Colligative Properties of Solutions

Osmotic pressure: Example

One gram of sucrose, molecular weight 342, is dissolved in 1000 gm of solution at 25° C. What is the osmotic pressure in the solution?

Answer

Number of moles of sucrose = Wt/M.wt = 1/342 = 0.0029

Molality = number of moles/kg = 0.0029/1kg =2.9×10^{-3} m

$\pi = mRT$

$T = 273+25 = 298$ K

$\pi = 2.9\times10^{-3}\times0.082\times298 = 7.08\times10^{-2}$ atm

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Molecular weight determination

- The colligative properties can be used to calculate molecular weights of non-electrolytes present as solutes.

Determination of molecular weight by boiling point elevation

$$\begin{tikzcd}
\Delta T_b = K_b m \arrow[r] & m = \dfrac{w_2/M_2}{w_1} \times 1000 = \dfrac{1000 w_2}{w_1 M_2} \arrow[d] \\
M_2 = K_b \dfrac{1000 w_2}{w_1 \Delta T_b} & \Delta T_b = K_b \dfrac{1000 w_2}{w_1 M_2} \arrow[l]
\end{tikzcd}$$

W_2 = weight of solute, W_1 = weight of solvent, M_2 = molecular weight of solute

Molecular weight determination

EXAMPLE 5-15

Determination of the Molecular Weight of Sucrose by Boiling Point Elevation

A solution containing 10.0 g of sucrose dissolved in 100 g of water has a boiling point of 100.149°C. What is the molecular weight of sucrose? We write

$$\begin{aligned} M_2 &= 0.51 \times \frac{1000 \times 10.0}{100 \times 0.149} \\ &= 342 \text{ g/mole} \end{aligned}$$

Molecular weight determination

- Determination of molecular weight by freezing point depression

$$M_2 = K_f \frac{1000 w_2}{\Delta T_f w_1}$$

EXAMPLE 5-16

Calculating Molecular Weight Using Freezing Point Depression

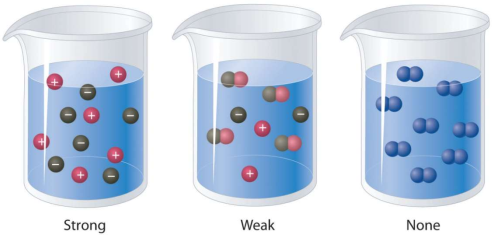
The freezing point depression of a solution of 2.000 g of 1,3-dinitrobenzene in 100.0 g of benzene was determined by the equilibrium method and was found to be 0.6095°C. Calculate the molecular weight of 1,3-dinitrobenzene. We write

$$M_2 = 5.12 \times \frac{1000 \times 2.000}{0.6095 \times 100.0} = 168.0 \text{ g/mole}$$

Solutions of electrolytes

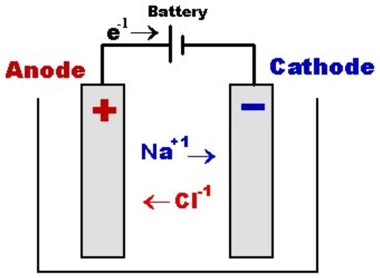
Solutions of electrolytes

- 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%).



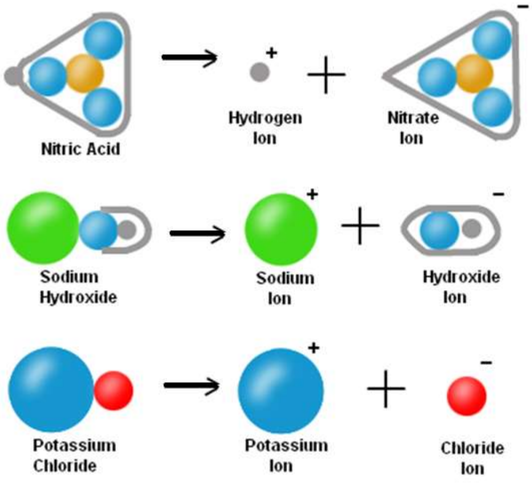
Solutions of electrolytes

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



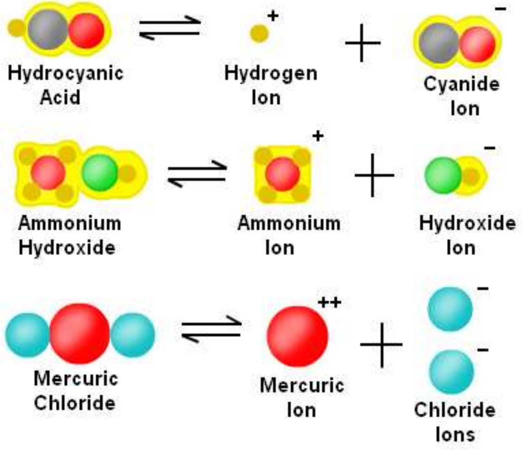
Solutions of electrolytes

- 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

- 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 $FeCl_3$).

Colligative properties

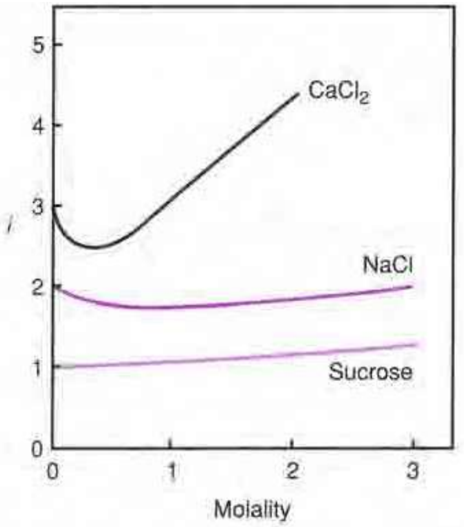


Fig. 6–5. van't Hoff *i* factor of representative compounds.

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.

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

$$\Delta T_f = i K_f m$$

$$\Delta T_b = i K_b m$$

$$\pi = iRTm$$

- The first equation applies only to dilute aqueous solutions

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

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

- The van’t Hoff factor **i** can be connected with the degree of dissociation α in the following way:

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

where **v** is the number of ions produced from the electrolyte ionization e.g. for NaCl v=2, for $CaCl_2$ v=3

- The cryoscopic method is used to determine i from the expression

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

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:

$$\mathbf{a = m}$$

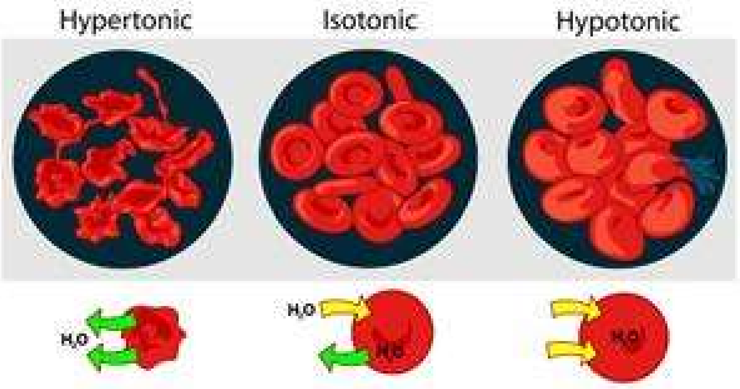
- As the concentration of the solution is increased, the ratio becomes less than unity because the effective concentration or activity of ions becomes less than the molal concentration. This ratio is known as the practical activity coefficient (γ), thus:

$$\mathbf{a = \gamma m}$$

Isotonic Solutions

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.



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

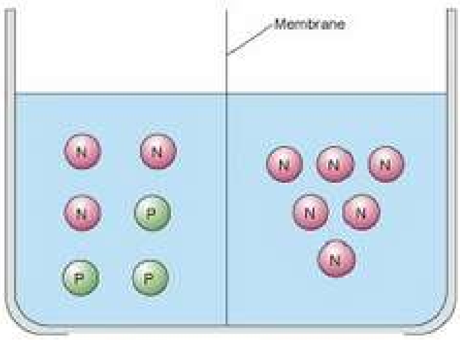
- Where n is the number of species into which the solute is dissolved

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

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

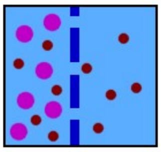
Isosmotic Solutions

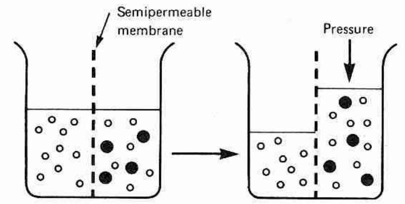
- When two solutions are separated by a perfect semipermeable membrane and there is no net movement of solvent molecules across the membrane, the solutions are isosmotic (i.e. have equal osmotic pressure or osmolarity).
- Perfect semipermeable membrane is permeable only to solvent molecules.



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

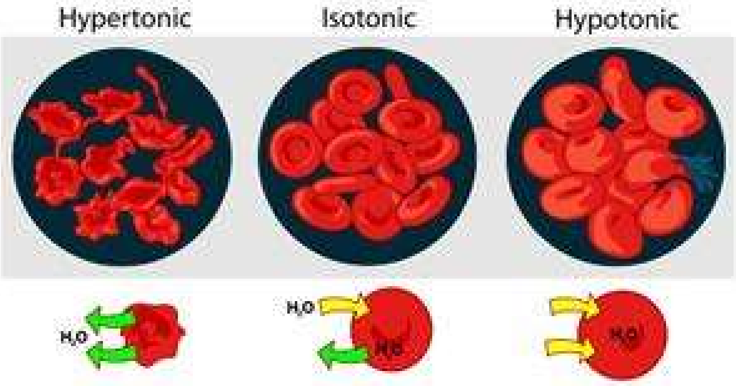




Measurement of Tonicity

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

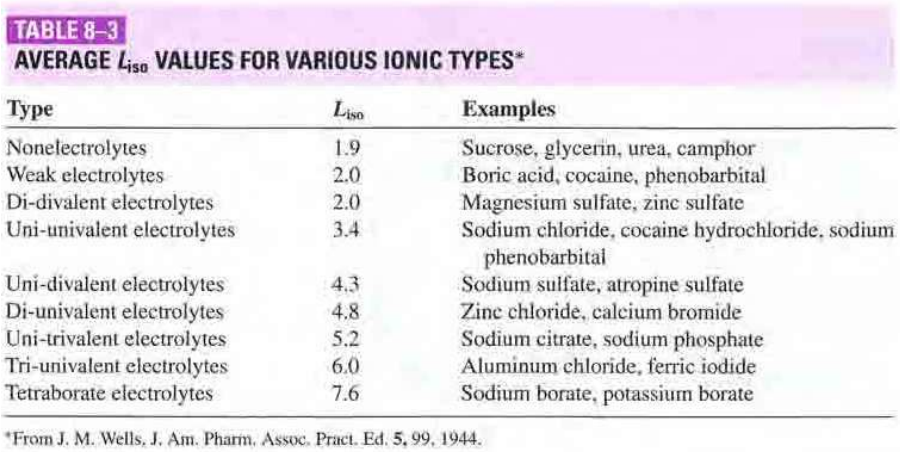


TABLE 8–3

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.

Methods of Adjusting Tonicity

NaCl equivalent method

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

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

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

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

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

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.

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

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

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:

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

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.

$$\boldsymbol{V} = \boldsymbol{w} \times \boldsymbol{E} \times \mathbf{111.1}$$

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

$$\boldsymbol{V} = \boldsymbol{w} \times \boldsymbol{E} \times \mathbf{111.1}$$

$$\boldsymbol{V} = 0.3 \times 0.21 \times 111.1 = 7 \text{ ml}$$

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.