PHAR1822 Notes

Pharmaceutical calculations

$d = \frac{m}{v}$	$density\ (g/mL) = \frac{mass\ (g)}{volume\ (mL)}$
$c = \frac{n}{v}$	$concentration\ (mol/L) = \frac{moles\ (mol)}{volume\ (L)}$
$n = \frac{m}{MM}$	$no.moles = \frac{mass\ (g)}{molecular\ mass\ (g/mol)}$
$c_1v_1 = c_2v_2$	$use\ for\ dilutions$

	Drug/mixture
w/w	grams/100g
w/v	grams/100mL
v/v	mL/100mL
v/w	mL/100g

- dL = decilitre = 100mL
- If a mixture is made up of water and drug, add x grams of drug, and then (100 – x) mL of water to make the mixture a *total* amount of 100mL (or 100g)
    - I.e. add water to make the volume up to 100mL
- Dilution ≈ paediatric sample – use $C_1V_1=C_2V_2$
- If working with a liquid drug or solvent other than water (e.g. ethanol) – density formula

Liquids and Solutions

Solution	Mixture of two or more components that form a single phase which is homogeneous down to the molecular level
Phase	Part of a system separated by one or more boundaries/interfaces, which can be separated physically (e.g. filtration, centrifuge)
Dissolution	Transfer of molecules or ions from the solid state into solution
Miscibility	Combination of two solvents that mix completely to form a homogenous solution

<u>Solubility</u>

- Limit to which a solute can be dissolved in a solvent under a particular set of conditions
- Determined at 20°C
- Based on amount of solvent in mL or grams ("parts"), required to dissolve 1g of drug/excipient
    - Soluble – 10-30 parts solvent
    - Insoluble – >10000 parts solvent
- Water solubility – depends on polarity and functional groups – H-bonds and ion-dipole bonds
    - -NH, -OH or C=O functional groups will H-bond with water
    - Ion-dipole bonds are even stronger than hydrogen bonds

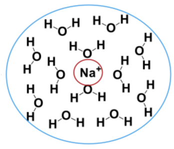
<u>Salt form of drugs</u>

- Salt form of drugs are more water soluble than neutral form
- They form more, and stronger, hydrogen bonds with water
- However:
    - Samples can be hygroscopic (draw in moisture from air)
    - Can change pH of solution (important for injection and oral solutions)
    - Reactions with packaging (glass and basic solutions)
    - Different salts of a drug can work differently
    - Salts interact with each other and precipitate out of solution
- Most common salt forms of drugs:
    - Acidic drugs – Na^+, K^+, Ca^{2+}, Zn^{2+}
    - Basic drugs – Cl^-, SO_4^{2-}, PO_4^{3-}

<u>Salting out</u>

- Precipitation of peptides and proteins from solution at high salt concentrations
- At high [salt], water molecules bind to the salt instead of the protein (not enough free water available) – causes precipitation of protein molecules (less soluble solute)
- Some drugs based on proteins and peptides – must ensure drugs do not precipitate

- Van der Waals radius – imaginary radius of an atom or molecule
    - Physical space the drug/particle takes up
- Hydrodynamic radius – imaginary radius of drug/particle and any bound subparticles (e.g. water) that travel through the solution with the drug particle
- Brownian motion – random movement of particles suspended in a liquid or gas
    - Caused by collisions with molecules of the surrounding medium
    - Rate of drug/particle movement through solution is directly related to size



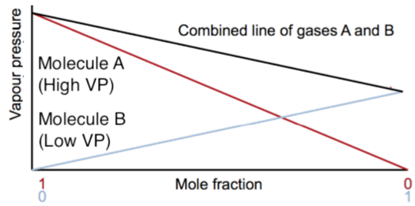
Stokes – Einstein equation

- Rate at which drug diffuses through solution is largely dependent on hydrodynamic radius and solvent viscosity
- $D = \frac{KT}{6\pi\eta r}$
    - D = diffusion coefficient (m^2s^{-1})
    - K = Boltzmann constant ($1.38*10^{-23}JK^{-1}$)
    - T = temperature (K)
    - η = solvent viscosity (water: $1.232*10^{-3}$Pa S)
    - r = hydrodynamic radius (metres)

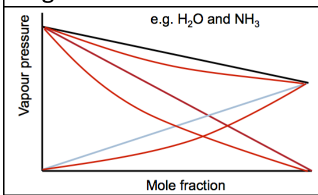
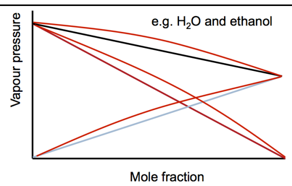
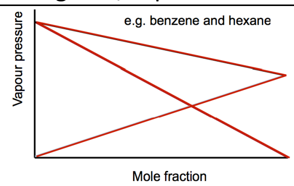
Change	**Rate of drug diffusion**
Increase temperature	Faster
Change form water to oil	Slower
Change from neutral drug to salt form	Slower
Make a nanoparticle formulation of the drug	Slower

Vapour pressure

- Pressure of vapour above liquid when liquid and vapour are at equilibrium
- Amount of vapour about liquid depends on intermolecular forces
    - More bonding between molecules – less vapour formed – lower vapour pressure
- Lower vapour pressure – boils at higher temperature
- Higher vapour pressure – boils at lower temperature
- 50/50 mixture of ethanol and water
    - Does NOT mean mixture of vapour is also 50/50
    - More ethanol molecules in air than water since ethanol has a higher vapour pressure



- $P_{total} = X_A P_A + X_B P_B$
    - P_{total} = total pressure from all molecules in the gas/vapour phase
    - X_A = mole fraction of gas A
        - Total of mole fractions ($X_A + X_B$) must equal 1
    - P_A = vapour pressure of gas A
    - Raoult's Law

2 polar molecules	**1 polar 1 non-polar**	**2 non-polar**
H-bonding – keeps in liquid phase	Repulsion – more molecules in gas/vapour phase	Ideal conditions Hydrophobic forces very weak; no repulsion
Lower vapour pressure for both Higher BP	Higher VP Lower BP	No effect on partial pressures of the gases/vapours
		

Freezing point depression

- Dissolution of polar solute into a solvent results in drop in the freezing point of the solvent
    - Salt + water – lowers freezing point, so water doesn't freeze as easily
    - Blood contains many polar molecules (proteins, salts) – lowers freezing point of blood
- Size of FPD depends on solvent and amount of solute (no. molecules, not no. moles)
- Any solution injected into vein, or eye drops – must have FDP of 0.52°C