# تفريغ فيزيكال

اسم الموضوع: Solubility and distribution part .2

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# Solubility products

- For poorly soluble materials such as silver chloride and barium sulfate the concept of the solubility product can be used.
- The following equilibrium exists in solution between crystalline silver chloride $AgCl_c$ and ions in solution:

$$AgCl_c \rightarrow Ag^+ + Cl^-$$

- An equilibrium constant $K$ can be defined as:

$$K = \frac{[Ag^+][Cl^-]}{[AgCl_c]}$$

- At saturation the concentration of the crystalline silver chloride $[AgCl_c]$ is essentially constant and the solubility product, $K_{sp}$, may therefore be written:

$$K_{sp} = [Ag+][Cl-]$$

# Solubility of slightly soluble electrolytes

**Table 5.7** Solubility products of some inorganic salts

| Compound | $K_{sp}$ (mol$^2$ dm$^{-6}$) |
|---|---|
| AgCl | $1.25 \times 10^{-10}$ |
| $Al(OH)_3$ | $7.7 \times 10^{-13}$ |
| $BaSO_4$ | $1.0 \times 10^{-10}$ |

- The solubility product equation is not applicable to freely soluble salts (such as NaCl) and losses accuracy for sparingly soluble (1 part in 30-100 parts) or if other salts are present.
- When other salts are present activity rather than concentration should be used

# Solubility products

- As in the case of other equilibrium expressions the concentration of each ion is raised to a power equal to the number of ions appearing.
- Thus, for $Al(OH)_3$

$$Al(OH)_{3\ solid} \rightarrow Al^{+3} + 3OH^-$$

$$K_{sp} = [Al^{+3}][OH^-]^3$$

# Solubility products

- Example: Calculate the solubility of AgBr in water in grams per liter if $K_{sp} = 5.0 \times 10^{-13}$
- We start with the balanced equation for the equilibrium.

$$AgBr(s) \Leftrightarrow 1\ Ag^+(aq) + 1\ Br^-(aq)$$

We then write the solubility product expression for this reaction.

$$Ksp = [Ag+][Br-] = 5.0 \times 10^{-13}$$

- Because there is no other source of either ion in this solution, the concentrations of these ions at equilibrium must be the same.

$$[Ag^+] = [Br^-]$$

- Substituting this equation into the $K_{sp}$ expression gives the following result. $[Ag^+]^2 = 5.0 \times 10^{-13}$
- Taking the square root of both sides of this equation gives the equilibrium concentrations of the $Ag^+$ and $Br^-$ ions.

$$[Ag^+] = [Br^-] = 7.1 \times 10^{-7} M$$

# Solubility products: common ion effect

- The presence of other sources of the same ions like Cl- or Ag+ reduces the solubility of AgCl.
- Because

$$[Ag^+][Cl^-] > K_{sp}$$

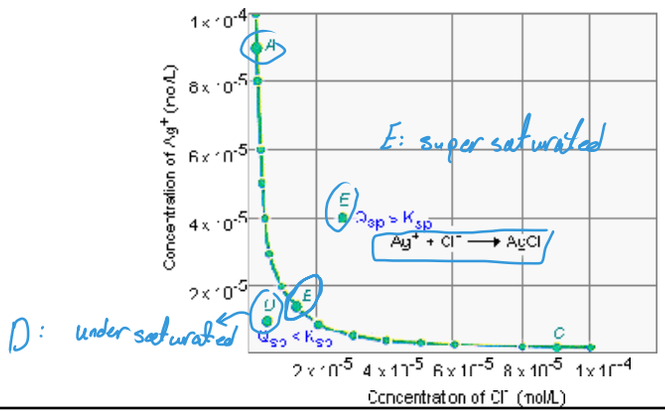
AgCl precipitates until $[Ag^+][Cl^-] = K_{sp}$

- In some cases the solubility increases when a common ion is added this is due to the formation of complexes with the compound that are soluble.

# Solubility products: common ion effect

**Saturated solution of AgCl to which NaCl has been added:**

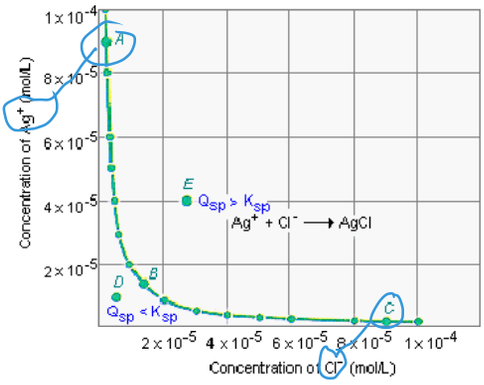
- The figure below shows a small portion of the possible combinations of the Ag+ and Cl- ion concentrations in an aqueous solution. Any point along the curved line in this graph corresponds to a system at equilibrium, because the product of the Ag+ and Cl- ion concentrations for these solutions is equal to Ksp for AgCl.



# Solubility products: common ion effect

**Saturated solution of AgCl to which NaCl has been added:**

- Point A represents a solution at equilibrium that could be produced by dissolving two sources of the Ag+ ion such as AgNO3 and AgCl in water.
- Point B represents a saturated solution of AgCl in pure water, in which the [Ag+] and [Cl-] terms are equal.
- Point C describes a solution at equilibrium that was prepared by dissolving two sources of the Cl- ion in water, such as NaCl and AgCl.




# Solubility problems in formulation

**Mixtures of acidic and basic compounds** form salt but with low solubility then form ppt

**e.g. Septrin infusion**

- Sulfamethoxazole is a weakly acidic substance and trimethoprim is a weakly basic one.
- In consequence, in an ordinary aqueous solution sulfamethoxazole and trimethoprim demonstrate a high degree of incompatibility and mutual precipitation occurs on mixing. عدم تجانس
- To optimize mutual dissolution, an aqueous solution which includes 40% propylene glycol is utilized in the formulation of the infusion. as cosolvent Concentrated → لا يعطوه للمريض بل يخففوه
- On dilution, the infusion becomes less stable and at the recommended 1 in 25 dilution stability is about 7 hours. with normal saline 1:25

# Partition coefficient

## Pharmaceutical applications

The movement of molecules from one phase to another is called partitioning. Examples of the process include:

- The absorption and distribution of drug in the body is affected by partitioning between aqueous phases and lipid biophases
- Preservative molecules in emulsions partitioning between the aqueous and oil phases
- Antibiotics partitioning into microorganisms
- Drugs and preservative molecules partitioning into the plastic of containers or giving sets
- Extraction from crude drugs.

# Partition coefficient

- If a substance (liquid or solid) is added to a mixture of two immiscible liquids, it will distribute itself between the two phases in a definite concentration ratio.
- The distribution of the solute between the two phases is represented by the partition coefficient or distribution coefficient, P, defined as the ratio of the solubility in the nonaqueous (oily) phase, $C_o$, to that in the aqueous phase, $C_w$, i.e.

$$P = C_o / C_w$$

# Partition coefficient

**Example**

When boric acid is distributed between water and amyl alcohol at 250 C', the concentration in water was found to be 0.0510 mole/liter and in amyl alcohol it was found to be 0.0155 Mole/liter. What is the distribution coefficient?

$$K_{w/o} = C_{H2O}/C_{alc} = 0.0510/0.0155 = 3.29$$

No convention has been established with regard to whether the concentration in the water phase or in the organic phase should be placed in the numerator. Therefore, the result may also be expressed as

$$K_{o/w} = C_{alc}/C_{H2O} = 0.0155/0.0510 = 0.304$$

One should always specify in which of these two ways the distribution constant is being expressed.

# Partition coefficient

**Octanol as a nonaqueous phase**

- Octanol is often used as the nonaqueous phase in experiments to measure the partition coefficient of drugs.
- It most closely simulates the properties of biological fluids. Its polarity means that water is solubilised to some extent in the octanol phase (biological membranes are also not simple anhydrous lipid phases).

$$P = C_o/C_w$$

- It is usual to express the partitioning as log *P*. The greater the value of log *P*, the higher the lipid solubility of the solute.

higher log P = greater lipid solubility

log p

log H+ زي فكرة بدل ما نتعامل مع الشمس فبجيبلنا p pH pOH ...

# Partition coefficient

$-\log_{10} 1 = 0$

P > 1 or Log P > 0 implies that the drug has affinity for lipid or hydrophobic membranes.

P = 1 or Log P = 0 there is equal distribution between the water and oil layer.

P < 1 or Log P < 0 the drug has affinity for water or hydrophilic layer.

Structure affect the value of partition coefficient P e.g. substituent that increase P value are -alkyl, -aryl, -halogens and substituent that decrease P decrease are -OH, -COOH, -NH2, -O, -CO.

أي حرف hydrophobic رح تزيد P

وأي حروف hydrophilic رح تقلل P

# Apparent partition coefficient ($P_{app}$)

When association and dissociation of drugs occur, the situation becomes more complicated, e.g. benzoic acid associates in the oil phase and dissociates in the aqueous phase.

hydrophobic للطبقة الدهنية رح يروح

benzoic acid رح يفل

hydrophilic للطبقة المائية رح يروح

Drugs that are weak acids or weak bases ionize in water, depending on their $pk_a$s and on the pH of the aqueous phase.

هاد تركيز بيكون مهم

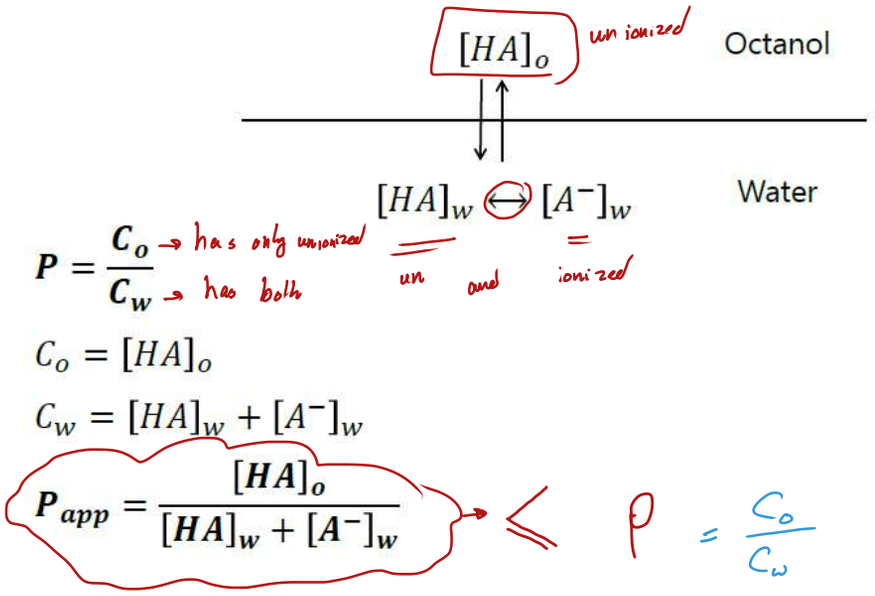
In general, **ionized structures cannot partition in octanol** or other hydrophobic solvents.

P value cannot be used to assess the true distribution of the ionizable drug in the two immiscible phases, simply because its value is dependent on the ionic state of the drug (which in turn depends on pH).

octanol has: un ionized

water has: unionized + ionized

# Apparent partition coefficient ($P_{app}$)




$$P = \frac{C_o}{C_w}$$ → has only unionized / has both

$$C_o = [HA]_o$$

$$C_w = [HA]_w + [A^-]_w$$

$$P_{app} = \frac{[HA]_o}{[HA]_w + [A^-]_w}$$ < $P = \frac{C_o}{C_w}$

نهاية المادة

اللهم اغفر لي ولوالدي وللمسلمين والمسلمات
والمؤمنين والمؤمنات الاحياء والاموات

اللهم اني اسالك توبة قبل الموت وشهادة عند الموت ومغفرة بعد الموت
وأمانا من المار ونصيبًا من الجنة آمين آمين