تفريغ فيزيكال

اسم الموضوع: Solubility and distribution phenomena (part 1)

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Soul Academy

لجان الدُفعات

Solubility and distribution phenomena

Introduction

- A *solution can be defined as a system in which* molecules of a solute are dissolved in a solvent vehicle.
- Solubility is defined as the maximum solute (1.) concentration in a certain solvent (2.) at a certain temperature (3.).

* لازم اذكر ال ٣
لما احكي عن ال Solubility
وهما الاشياء الي بأثروا بذائبية
أي مادة .

Solute concentration < solubility → undersaturated solution

Solute concentration = solubility → saturated solution

Solute concentration > solubility → supersaturated solution

الي حكينا كيف بنحضرهم
بمادة الفيرست .
إما بتبخر ال solvent
أو تغيير ال temp
معظم المواد ذائبيتها بتزيد في
التسخين .

- ممكن اعرّف الذائبية بانها :
concentration of saturated solution

Expressions of solubility

- The solubility of a drug can be expressed in terms of concentration such as:
  - Molarity
  - Normality
  - Molality
  - Mole fraction
  - percentage (% w/w, % w/v, % v/v).

الذائبية وحدتها وحدة concentration
أي وحدة ممكن أعبّر فيها

Expressions of solubility

- The pharmacopeias used the following less specific way to denote to solubility

Descriptive term	Approximate volume of solvent in milliliters per gram of solute
very soluble	less than 1
freely soluble	from 1 to 10
soluble	from 10 to 30
sparingly soluble	from 30 to 100
slightly soluble	from 100 to 1000
very slightly soluble	from 1000 to 10 000
practically insoluble	more than 10 000

Prediction of solubility

hydrophilic solvent ال
بذوب ال hydrophilic solute
وال lipophilic solvent
يذوب ال lipophilic solute

- Solubility depends on chemical, electrical & structural effects that lead to mutual interactions between the solute and the solvent.
- "like dissolves like".
- **A solute dissolves best in a solvent** with similar chemical properties. i.e.
  - Polar solutes dissolve in polar solvents. e.g **salts & sugar dissolve in water** .
  - Non polar solutes dissolve in non polar solvents. Eg. **naphtalene dissolves in benzene.**

Prediction of solubility

- If the solvent is **A** and the solute B and the forces of attraction are represented by $\underbrace{A—A, B—B}_{\text{cohesive}}$ and A—B, one of three conditions will arise: ↳ Adhesive

1. If A—A >> A—B, i.e. the affinity of a solvent molecule for its own kind is markedly greater than its affinity for a solute molecule, the solvent molecules will be attracted to each other and form aggregations from which the solute is excluded (e.g. benzene in water). → ذائبية قليلة
2. If B—B >> A—B, the solvent will not be able to break the binding forces between solute molecules and disperse them (e.g. sodium chloride in benzene).
3. If A—B > A—A or B—B, or the three forces are of the same order, the solute will disperse and form a solution.

Factors influencing solubility

Polar solvents

- Polar solvents dissolve ionic solutes and polar substances.
- The solubility of a drug in polar solvent depends on:

1. **The polarity of the solvent (measured by dielectric constant)**
2. **The ability of the solute to form hydrogen bonds.**
   - Water dissolves Phenols, alcohols. aldehydes, ketones, amines, and other oxygen- and nitrogen-containing compounds that can form hydrogen bonds with water
3. **The ratio of polar to nonpolar groups of the molecule**
   - As the length of a nonpolar chain of an aliphatic alcohol increases, the solubility in water decreases (e.g. Straight chain monohydroxy alcohols, aldehydes, and acids with more than 4 carbons cannot enter into the hydrogen- bonded structure of water and hence are only slightly soluble).

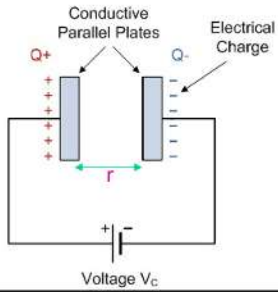
Dielectric constant

- A molecule can maintain a separation of electric charge either through induction by an external electric field or by a permanent charge separation within a polar molecule.
- Dielectric constant (relative permittivity) of a material is its (absolute) permittivity expressed as a ratio relative to the permittivity of vacuum.

Dielectric constant

إذا قربتهم على بعض مسافة معينة
التيار ممكن ينتقل مو بالضروري
يتلامسوا . لكن قابلية التيار حتى
ينتقل بتعتمد على طبيعة المادة

- Consider two parallel conducting plates, such as the plates of an electric condenser, which are separated by some medium across a distance r and apply a potential across the plates.
- Electricity will flow from the left plate to the right plate through the battery until the potential difference of the plates equals that of the battery supplying the initial potential difference.



Dielectric constant

- The *capacitance, C* (in farads), is equal to the quantity of electric charge, *q* (in coulombs), stored on the plates, divided by the potential difference, *V* (in volts), between the plates:

$$C = q/V \qquad C = \frac{q}{V}$$

- The capacitance of the condenser depends on the type of medium separating the plates as well as on the thickness *r*.

كل ما اقتربوا على بعض بصير في فرصة أكبر لانتقال الشحنات الكهربائية

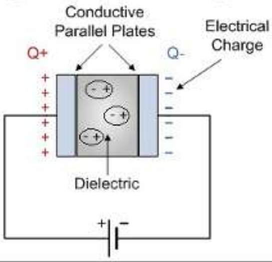
- When a vacuum fills the space between the plates, the capacitance is C_0.

كل ما كان بين ال plates 2 مادة مستقطبة، بصير عندها قدرة انها تنقل الشحنات

- This value is used as a reference to compare capacitances when other substances fill the space.

Dielectric constant

- If water fills the space, the capacitance is increased, since the water molecule can orientate itself so that its negative end lies nearest the positive condenser plate and its positive end lies nearest the negative plate.
- This alignment provides additional movement of charge because of the increased ease with which electrons can flow between the plates.
- Thus, additional charge can be placed on the plates per unit of applied voltage.



Dielectric constant

- The capacitance of the condenser filled with some material, C_x, divided by the reference standard C_0, is referred to as the *dielectric constant*, $1/\varepsilon$:

$$\varepsilon = C_x / C_0$$

- The dielectric constant ordinarily has no dimensions, since it is the ratio of two capacitances.

Vacuum فراغ	1.0 (by definition)
Metals	Infinite قيمتها إلى ما لا نهاية
Gases	1.00xx (at one atmosphere) تقريبا نفس الفراغ
Water	87.9 (0°C) to 55.5 (100°C)
Hexane	1.8865 (20°C)
Cyclohexane	2.0243 (20°C)
Benzene	2.285 (20°C)
Hydrocarbon lubrication oils	2.1 to 2.4 (room temperature)

Table 1. Dielectric Constant of Common Materials

ال dielectric constant بزيد كل ما زادت ال polarity لل solvent

وهي مقياس لل solvents polarity of

Dielectric constant

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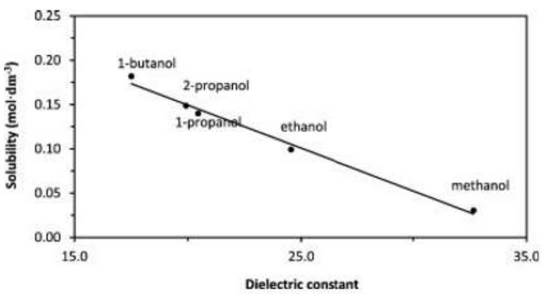
Table 1. Dielectric Constant of Common Materials

Dielectric constant

- The dielectric constants *of* solvent mixtures can be related to drug solubility:



علاقة عكسية
∴ ال flavonoid هو hydrophobic
لو كان hydrophilic
بتكون العلاقة طردية

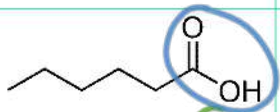
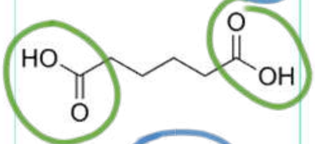
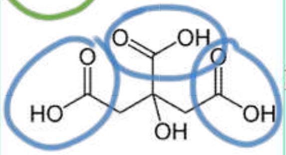
Solubility of morin flavonoid in alcohols (Journal of Molecular Liquids, Volume 233, 2017)

ال dielectric constant بزيد يعني بكون عنا polarity أعلى
ولا dielectric قليل ∴ عنا non polar

Factors influencing solubility

Polar solvents

- When additional polar groups are present in the molecule, water solubility increases greatly.

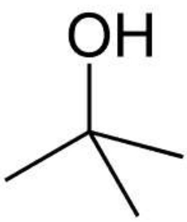
Name	Chemical formula	structure	Solubility الذائبية في الماء
Hexanoic acid	$C_6H_{12}O_2$		1 g/100 ml
Adipic acid	$C_6H_{10}O_4$		24 g/100 ml
Citric acid	$C_6H_8O_7$		148 g/100 ml very soluble in water

Factors influencing solubility

Polar solvents

- Branching of the carbon chain reduces the nonpolar effect and leads to increased water solubility (e.g. Tertiary butyl alcohol is miscible in all proportions with water, whereas n-butyl alcohol dissolves to the extent of about 8 g/l00 mL of water at 20°C).

n-butanol



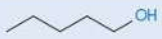
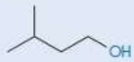
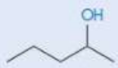
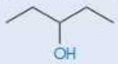
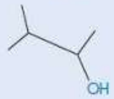
tert-butanol

Factors influencing solubility

Polar solvents

Table 5.2 Solubilities of pentanol isomers in water[a]

كلهم عندهم خمس كربونات

Compound	Solubility (molality, m)	Surface area (nm^2)	Boiling point (°C)	Structure
n-Pentanol	2.6×10^{-1}	3.039	137.8 أعلى b.p قوة الترابط بين الجزيئات عالية	
3-Methyl-1-butanol	3.11×10^{-1}	2.914	131.2	
2-Methyl-1-butanol	3.47×10^{-1}	2.894	128.7	
2-Pentanol	5.3×10^{-1}	2.959	119.0	
3-Pentanol	6.15×10^{-1}	2.935	115.3	
3-Methyl-2-butanol	6.67×10^{-1}	2.843	111.5	
2-Methyl-2-butanol	1.403	2.825	102.0 أقل b.p	

أكثر تفرع له أعلى ذائبية

علاقة عكسية بين ال solubility
وال boiling point
كل ما ال b.p أعلى معناها قوى
الارتباط ما بين الجزيئات في ال liquid state
أعلى وهذا يعني ذائبية في الماء أقل

Factors influencing solubility

Nonpolar solvents

- Non polar solvents are unable to reduce the attraction between the ions due to their *low dielectric constants.*
- They are unable to form hydrogen bonds with non electrolytes.
- Non polar solvents can dissolve non polar solutes through weak van derWaals forces
- Example: solutions of oils & fats in carbon tetrachloride or benzene.

Factors influencing solubility

Semipolar solvents

- Semipolar solvents, such as ketones can induce a certain degree of polarity in non polar solvent molecules.
- They can act as intermediate solvents to bring about miscibility of polar & non polar liquids.
- Example: acetone increases solubility of ether in water.

Solubility of gases in liquids

غاز لونه يميل للاصفر المخضر
يذوب في الماء
CO_2 يستخدم في المياه الغازية

- Examples of pharmaceutical solutions of gases include: HCl, ammonia water & effervescent preparations containing CO_2 maintained in solution under pressure.
- The solubility of a gas in a liquid *is the concentration of dissolved gas when it is in equilibrium with some of the pure gas above the solution.*
- The solubility depends on:
  - molecular weight of gas
  - the pressure
  - temperature
  - presence of salts
  - chemical reactions that sometimes the gas undergoes with the solvent

Solubility of gases in liquids

Effect of molecular weight of gas

- بشكل عام ذائبية الغازات بتزيد بزيادة الـ Molecular weight لأنه بصير عندي ← stronger London & Debye forces.

- The solubility of gas molecules typically increases with $\boxed{\text{increasing}}$ molecular weight of gas due to stronger London and Debye forces between gas and solvent molecules. مثل O_2 مع H_2O

Effect of pressure

- بتزيد ذائبية الغازات بزيادة ضغط الغاز فوق السائل.

- The effect of the pressure on the solubility of a gas is expressed by *Henry's law*, which, states that in a very dilute solution at constant temperature, the concentration of dissolved gas is proportional to the partial pressure of the gas above the solution at equilibrium.

Solubility of gases in liquids

Effect of temperature

- As the temperature increases, the solubility of most gases decreases, owing to the greater tendency of the gas to expand, increased kinetic energy of gas molecules, leading to breaking of intermolecular forces.

Presence of salts

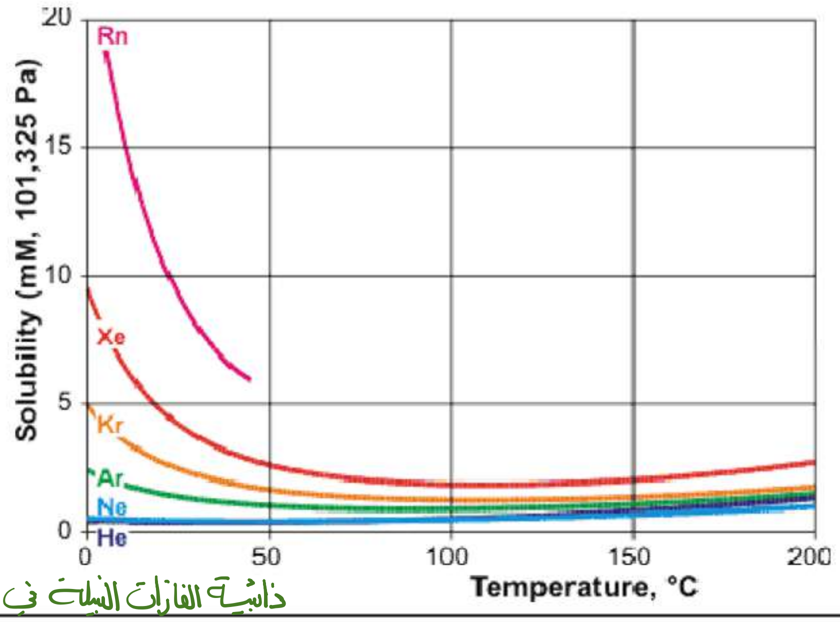
- Gases are often liberated from solutions in which they are dissolved by the introduction of an electrolyte such as sodium chloride and sometimes by a nonelectrolyte such as sucrose. This phenomenon is known as *salting out*.

- فعليًا الملح رح يتفاعل مع المي ويبطل في كمية كافية من المي للتفاعل مع الغازات

ومصطلح الـ Salting out بطلعوه على أي ذائبية بتقل وليس فقط الغازات

Solubility of gases in liquids

الها علاقة بال
atomic weight



ذائبية الغازات النبيلة في الماء

Solubility of gases in liquids

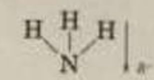
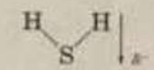
Effect of chemical reactions

- Henry's law applies strictly to *gases* that are only slightly soluble in solution and that do not react in any way in the solvent.
- Gases such as hydrogen chloride, ammonia, and carbon dioxide show deviations as a result of chemical reaction between the gas and solvent, usually with a resultant increase in solubility.
- Accordingly, hydrogen chloride is about 10,000 times more soluble in water than is oxygen.

⇐ هسك بتكون ذائبيتهم أعلى من المتوقع وهاد بعود لل chemical reactions الي بتصير

Solubility of gases in liquids

Table 4–3 Solubilities of some gases in water

Gas	Structure*	Polarity	Solubility in water (g/L)	Temperature (°C)
Nitrogen	N≡N	Nonpolar	0.018	40
Oxygen	O=O	Nonpolar	0.035	50
Carbon dioxide	O=C=O	Nonpolar	0.97	45
Ammonia		Polar	900	10
Hydrogen sulfide		Polar	1,860	40

Solubility of liquids in liquids

➢ Liquid-liquid systems may be divided into 2 categories:

1) Systems showing *complete miscibility such as alcohol & water, glycerin* & alcohol, benzene & carbon tetrachloride.

- *Complete miscibility occurs when the adhesive forces between different molecules* (A-B) >>cohesive forces between like molecules (A-A or B-B).

2) Systems showing *Partial miscibility as phenol and water;* two liquid layers are formed each containing some of the other liquid in the dissolved state.

الي بتكون بمعظم الأدوية

Solubility of solids in liquids

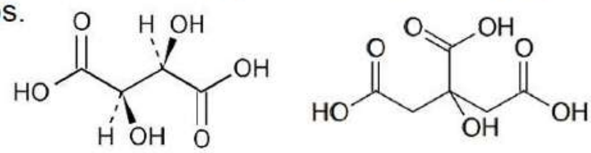
Effects of substituents

Substituents can influence solubility by affecting the solute molecular cohesion and its interaction with water molecules.

Polar groups such as –OH are capable of hydrogen bonding (high solubility).

2 OH & 2 carboxylic

E.g. Hydroxy acids, such as tartaric and citric acids, are quite soluble in water because they are solvated through their hydroxyl groups.



Non-polar groups such as $-CH_3$ and –Cl are hydrophobic (low solubility).

Factors influencing solubility

Table 5.4 Substituent group classification

Substituent	Classification
$-CH_3$	Hydrophobic
$-CH_2-$	Hydrophobic
—Cl, —Br, —F	Hydrophobic
$-N(CH_3)_2$	Hydrophobic
$-SCH_3$	Hydrophobic
$-OCH_2CH_3$	Hydrophobic
$-OCH_3$	Slightly hydrophilic
$-NO_2$	Slightly hydrophilic
—CHO	Hydrophilic
—COOH	Slightly hydrophilic
$-COO^-$	Very hydrophilic
$-NH_2$	Hydrophilic
$-NH_3^+$	Very hydrophilic
—OH	Very hydrophilic

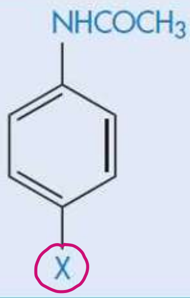
مع الـ N ← hydrophilic لكن وجود الكربونتين خلاها كمركب كامل hydrophobic

—CHO → aldehyde group

- من خلال معرفة هاي المجموعات على الجزيئات بإمكاننا نتنبأ كيف ذائبية الجزيء رح تكون بالمي

Factors influencing solubility

Table 5.5 The effect of substituents on solubility of acetanilide derivatives in water



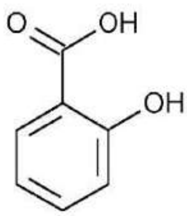
Derivative	X	Solubility ($mg\ dm^{-3}$)
	H	6.38
	Methyl	1.05
	Ethoxyl	0.93
	Hydroxyl	13.9
	Nitro	15.98
	Aceto	9.87

Solubility of solids in liquids

Effects of substituents

The position of the substituent on the molecule can affect the solute molecular cohesion and its interaction with water molecules, and hence its solubility.

E.g. the OH group of salicyclic acid cannot contribute to the solubility because it is involved in an intramolecular hydrogen bond.



هون عنا OH و carboxylic جنب بعض
التنين hydrophilic فالمعروض ذائبية هاد
المركب عالية ، لكن فعليا هي منخفضة
والسبب انه في intramolecular hydrogen
bonding

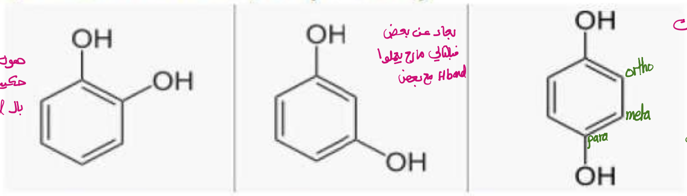
فال OH بدل ما تعمل H-bonding مع المي
وال COOH مع المي
هما بعملوا مع بعض ، بسبب قربهم من بعض
وبالتالي بتقل ال interaction مع ال Solvent
فعشان هيك بتكون ذائبية قليلة.

Solubility of solids in liquids

Effects of substituents

E.g. the aqueous solubility of o-, m- and p-dihydroxybenzenes are 4, 9 and 0.6 mol/L, respectively.

صون نفس الي
حكيناعنه فوق
بال Salicylic acid



صون بعاد عن بعض مع ذلك
الذائبية قليلة
لانه هاد الشكل بعطيني
compact crystal
وبامكانهم يصطفوا جنب بعض
في حالة ال meta كان في
فراغ

Symmetric particles (p-dihydroxybenzenes) can be less soluble than unsymmetric ones (m-dihydroxybenzenes) because they form a compact crystals (which require more work to separate the particles), while the unsymmetric particles pack less efficiently in crystals.

Solubility of solids in liquids

Effects of solid state

- The less stable solid state (e.g. metastable polymorph, amorphous or anhydrous state) will be more soluble than the stable state.

Particle size

اذا جبت سكر ناعم وسكر خشن رح
يختلف معدّل الذوبان (الوقت الي
لا يختلف) ، هاد الحكي صحيح
ضمن الرينج الخشن والناعم.
لكن على مستوى ال micro وال submicro
ممكن الذائبية تزيد لانه لما يصير
كثير ناعم في الغالب بكون بخرّب
البناء البلوري فبتكون أقرب لل
amorphous

- Above a certain size, solubility is not influenced by the particle size of the solid solute. However, the reduction in the size of particles to micron or sub-micron size can influence solubility.

  نانوميتر

- A micronized drug may have an increase in solubility if the micronization process breaks down the crystal lattice of the solid.

Solubility of solids in liquids

Effects of salt form

ذائبية الدواء ممكن تعتمد على نوع ال salt الي استخدمته للدواء .

- The solubility of the drug in aqueous media may be markedly dependent on the salt form.

$cm^3 = 1 mL$
$cm^3 = 10^{-3}$ Liter

Table 5.13 Solubilities of salts of an antimalarial drug (**XIX**)[a]

Salt	Melting point (°C)[b]	Solubility (mg cm^{-3})
Free base	215	7–8
Hydrochloride	331	32–15
dl-Lactate	172 (dec)	1800
l-Lactate	193 (dec)	900
2-Hydroxy-1-sulfonate	250 (dec)	620
Methanesulfonate	290 (dec)	300
Sulfate	270 (dec)	20

[a] Reproduced from S. Agharkar, S. Lindenbaum and T. Higuchi, *J. Pharm. Sci.*, 65, 747 (1976).
[b] (dec) – with decomposition.

- نستنتج :

ال free base أقل ذائبية
والذائبية بتختلف، ممكن أكثر من ٢٠٠ ضعف
وفي بعض الاملاح ٣ أو ٤ أضعاف فقط

- العلاقة بين زيادة الذائبية وال melting point هي علاقة عكسية .

أقل m.p أعطى أعلى ذائبية

ال m.p هي قوة الروابط الموجودة بالبلورة .

Solubility of solids in liquids

$dm^3 = 1$ Liter
$dm^3 = 1000 mL$

Table 5.3 Correlation between melting points of sulfonamide derivatives and aqueous solubility

Compound	Melting point (°C)	Solubility
Sulfadiazine	253	1 g in 13 dm^3 (0.077 g dm^{-3})
Sulfamerazine	236	1 g in 5 dm^3 (0.20 g dm^{-3})
Sulfapyridine	192	1 g in 3.5 dm^3 (0.29 g dm^{-3})
Sulfathiazole	174	1 g in 1.7 dm^3 (0.59 g dm^{-3})

أعلى m.p أقل ذائبية [حجم الماء إلي بحتاجها بكون أكثر]

Solubility of solids in liquids

Effect of temperature

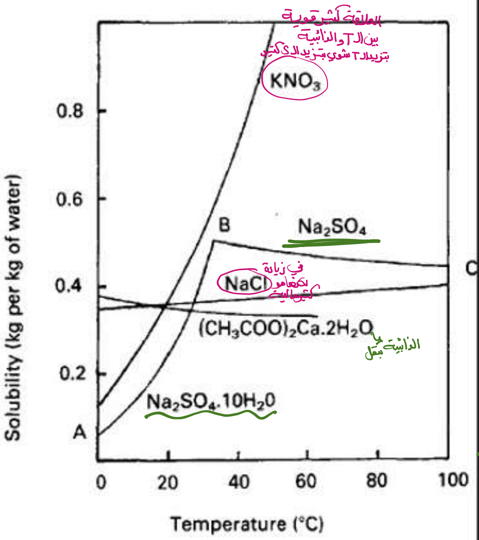
الغالبية

- A rise in temperature will lead to an increase in the solubility of a solid with an endothermic dissolution. يعني ذوبانه بحتاج إلى طاقة
- Conversely, in the case of the less commonly occurring systems that exhibit exothermic dissolution, an increase in temperature will give rise to a decrease in solubility. بعطي طاقة
- Plots of solubility versus temperature, which are referred to as *solubility curves*, are often used to describe the effect of temperature on a given system.
- Most of the curves are continuous; however, abrupt changes in slope may be observed with some systems if a change in the nature of the dissolving solid occurs at a specific transition temperature.

Solubility of solids in liquids

Effect of temperature

- Sodium sulphate exist as the decahydrate $Na_2SO_4,10H_2O$ up to 32.5°C, and its dissolution in water is an endothermic process.
- Its solubility therefore increases with rise in temperature until 32.5°C is reached.
- Above this temperature the solid is converted into the anhydrous form Na_2SO_4, and the dissolution of this compound is an exothermic process.
- The solubility therefore exhibits a change from a positive to a negative slope as the temperature exceeds the transition value.



$Na_2SO_4 . 10H_2O$
العلاقة طردية في البداية ، وبعدها تنزل .
السبب : انه عند temp معينة رح يفقد المي الي موجودة في البلورة ويصير لها اله ، فبتقل ذائبيته .

* اذا كانت الـ solubility بتزيد بزيادة الـ temperature هاد طبيعي .
* اذا كانت الـ solubility بتقل بزيادة الـ temperature هاد طبيعي .
* اذا كانت الـ solubility تزيد وبعدها قلّت معناها صار في تغيير على تكوينه .

Solubility of solids in liquids

Influence of pH on solubility of weak electrolytes

weak acid
weak base

Systems of solids in liquids include the most frequent and important type of pharmaceutical solutions.

5% → neutral

≃25% ≃70%

Most drugs belong to the class of weak acids and bases. They react with strong acids or bases to form water soluble salts.

Acidic drugs (e.g. NSAIDs), are more soluble in alkaline solutions where the ionized form is the predominant.

$$pH - pK_a = log\frac{[Ionized]}{[Unionized]}$$

Basic drugs (e.g. ranitidine), are more soluble in acidic solutions where the ionized form of the drug is predominant.

$$pH - pK_a = log\frac{[Unionized]}{[Ionized]}$$

Solubility of solids in liquids

Influence of pH on solubility of weak acids

- If we represent the drug as HA and the total saturation solubility of the drug as *S, and if S_0* is the solubility of the undissociated species HA then:

$$pH - pK_a = \log(\frac{S - S_0}{S_0})$$

شو بستفيد منها؟

* اذا بعرف قيمة ال S_0
وال pKa و pH بإمكاني أحدد
قيمة ال solubility عندي أي pH ببياياه

S_0 is termed intrinsic solubility

ذائبية ال HA

ذائبية ال HA قيمة
ثابتة ما بتتغير بتغير ال pH
* طيب كيف بتزيد ذائبية
العامة؟ نتيجة زيادة نسبة
ال A^- ، وليست تغير ذائبية
ال HA

$HA \rightleftharpoons H^+ + A^-$

$S = [HA] + [A^-]$

$S_0 = [HA]$

Ionized = $S - S_0 \rightsquigarrow [A^-]$

Unionized = S_0

تركيز ال A^- بعتمد على ال pH
وتركيز ال HA برضه بعتمد على ال pH

* ممكن أقيس الـ intrinsic solubility عن طريق انه أقيس الـ solubility في point one normal HCl (strong acid solution) ، لأنه كلها رح تكون على شكل HA (unionized) لأنه الـ weakly acidic drug بتكون ionized في الـ high pH وبتكون unionized في الـ low pH ، وبالتالي بعرف أعلى قيمة لتركيز الـ HA

Solubility of solids in liquids

- **Example**

  What is the pH below which sulfadiazine ($pK_a = 6.48$) will begin to precipitate in an infusion fluid, when the initial molar concentration of sulfadiazine sodium is 4×10^{-2} mol dm^{-3} and the solubility of sulfadiazine is 3.07×10^{-4} mol dm^{-3}?

- ***Answer***

  The pH below which the drug will precipitate is calculated using equation (5.11):

$$pH = 6.48 + \log \frac{(4.00 \times 10^{-2}) - (3.07 \times 10^{-4})}{3.07 \times 10^{-4}}$$

$$= 8.60$$

intrinsic solubility

رح أعرف قيمة الـ pH إلي عندها بكون وصلت للـ solubility ، تحتها رح يكون supersaturation وبالتالي ممكن تتبلور .

Solubility of solids in liquids

Influence of pH on solubility of weak bases

- If we represent the basic drug as B and BH+ and the total saturation solubility of the drug as S, *and if* S_0 is the solubility of the unprotonated species B then:

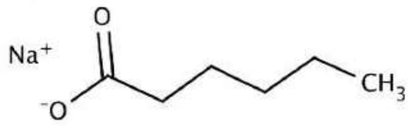
$$pH - pK_a = \log\left(\frac{S_0}{S - S_0}\right)$$

Solubility of solids in liquids

Influence of pH on solubility of weak electrolytes

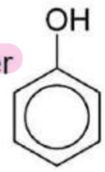
زي ال fatty acids

Carboxylic acids containing more than 5 carbons are relatively insoluble in water; however, they react with dilute NaOH, carbonates, and bicarbonates to form soluble salts.



The fatty acids (> 10 carbon) form soluble soaps with the alkali metals and insoluble soaps with other metal ions.

Phenol is weakly acidic and only slightly soluble in water but is quite soluble in dilute sodium hydroxide.



Solubility of solids in liquids

Boiling point and melting point

In general, aqueous solubility decreases with increasing boiling and melting point.

This is because the higher the boiling point of liquids and melting point of solids, the stronger the interactions between the molecules in the pure liquid or the solid state.

Solubility increases with decreasing particle size, due to the increased particle surface area; meaning more of the solid is in contact with the solvent.