

By. Raya Omar

1- Intermolecular forces 3-12

2- State of matter من سلايدر
13

States of Matter

Dr Nizar Al-Zoubi

Binding forces between molecules

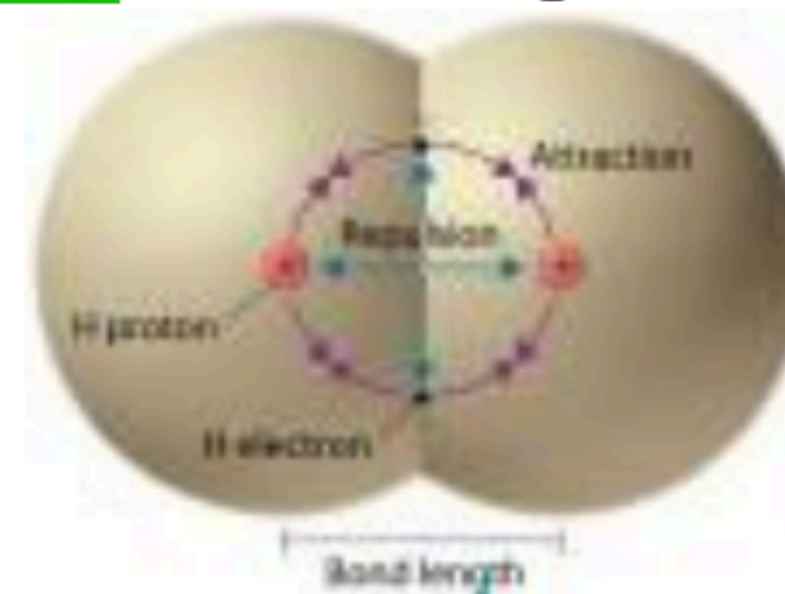
- For molecules to exist as aggregates in gases, liquids, and solids, **intermolecular forces** must exist.
- These *intermolecular forces* involve **both attractive and repulsive** forces.
- These forces must be **balanced** in an energetically favored arrangement for the molecules to interact.

* التوازن مهم ← من حيث الطاقة

أقل طاقة = أكثر ثبات

Repulsive and Attractive Forces

- When two atoms or molecules are brought closer together, the opposite charges and binding forces in the two molecules are closer together than the similar charges and forces, causing the molecules to attract one another.
- When the molecules are brought so close that the similar charges touch, they repel each other like rigid elastic bodies.
- At a certain equilibrium distance, (about $3-4 \text{ \AA}$), the repulsive and attractive forces are equal. At this position, the potential energy of the two molecules is a minimum and the system is most stable.

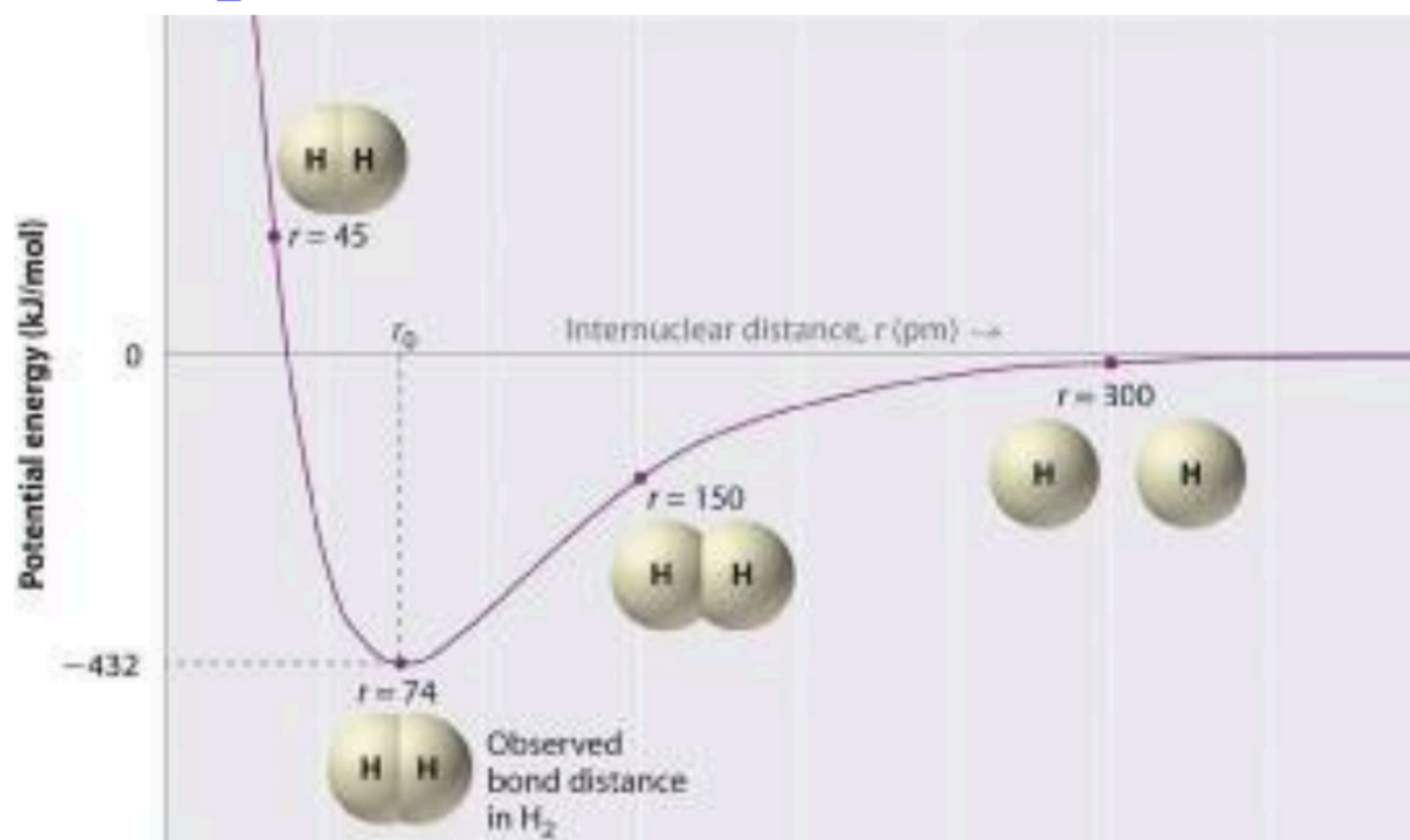


سبب التجاذب
هو اقتراب
opposite
charges

$3-4 \text{ \AA}$

* Attraction = Repulsion
* Potential energy = minimum
* Stability = maximum

Repulsive and Attractive Forces



Intermolecular forces

Intermolecular forces can be divided into:

- 1 • **Van der Waals** forces
- 2 • Ion-dipole interaction
- 3 • Ion-induced dipole interaction
- 4 • Ion-ion interaction
- 5 • **Hydrogen** bonds

Van der Waals forces

توزيع الشحنة عبر الجزيء

- Van der Waal interactions are **weak** forces that involve the dispersion of charge across a molecule called a **dipole**. تمايز الشحنة
- Van der Waal interactions can be classified into:
 - A. Dipole-dipole interaction, orientation effect, or **Keesom force**
 - B. Dipole-induced dipole interaction, induction effect, or **Debye force**
 - C. Induced dipole-induced dipole interaction, dispersion effect, or **London force**

Polar + Polar HCl + HCl

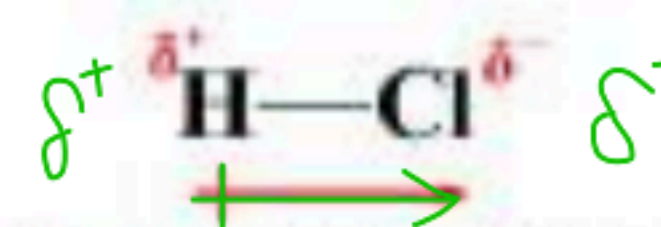
Polar + Non Polar O₂ + H₂O

Non polar + Non polar
He, Ne,
Hydrocarbon

Van der Waals forces

• **Keesom forces** occur between **polar** molecules in which the **permanent dipoles** interact with one another (**dipole-dipole interactions**) or (**orientation effect**).

- Polar molecules have polar **covalent bonds** which are **unevenly** distributed in space due to the **difference in the electronegativity of the atoms forming the bond** e.g. HCl.
- The nucleus of the **chlorine atom** pulls the **electron pair** involved in the **chlorine-hydrogen bond** **closer** to itself and creates a **permanent partial positive charge** on the hydrogen and a **permanent partial negative charge** on the chlorine (**Permanent dipole**),



Dipole Moment has a Magnitude and a Direction

لها مقدار واتجاه

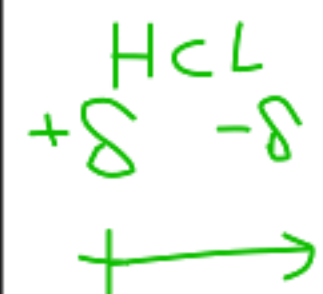
Permanent diopke
(partial opposite charge)

لجذب عندما تجذب
نواة الذرة الأعلى
electronegativity

زوج الإلكترونات
الرابطة.

سحب
جذب دالة

توزيع الشحنات
غير متساوي
بسبب اختلاف
الكهرسالية
للذرات داخل
الجزيء.



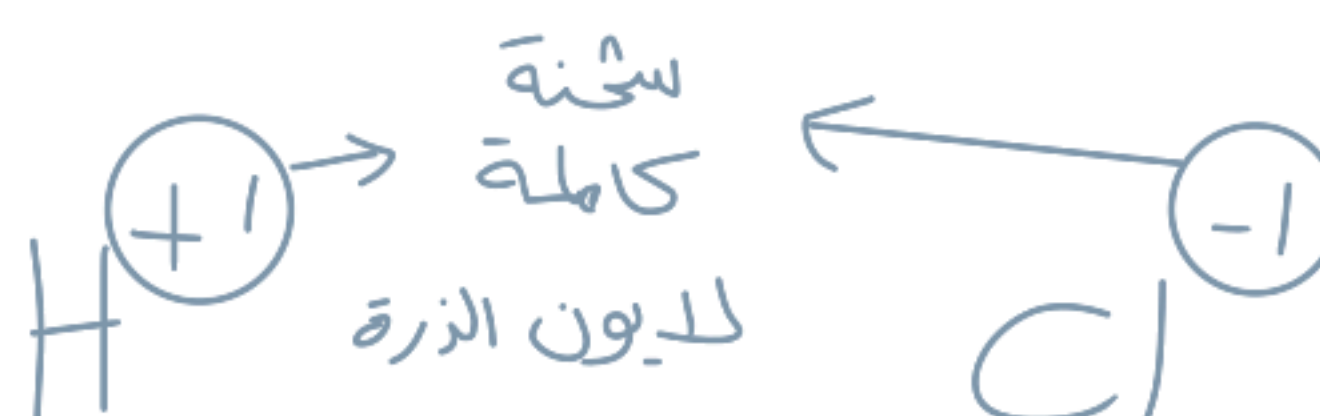
Van der Waals forces

- The **Partial opposite charges** (**permanent dipoles**) attract one another (**dipole-dipole interactions**)
- The **dipole-dipole forces** increases as the **polarity** of the molecule increases.
- **Keesom forces** are **much weaker** than ionic bonds **because the charges involved in bonding are partial**.



لحظة
جذب
داخل جزيء

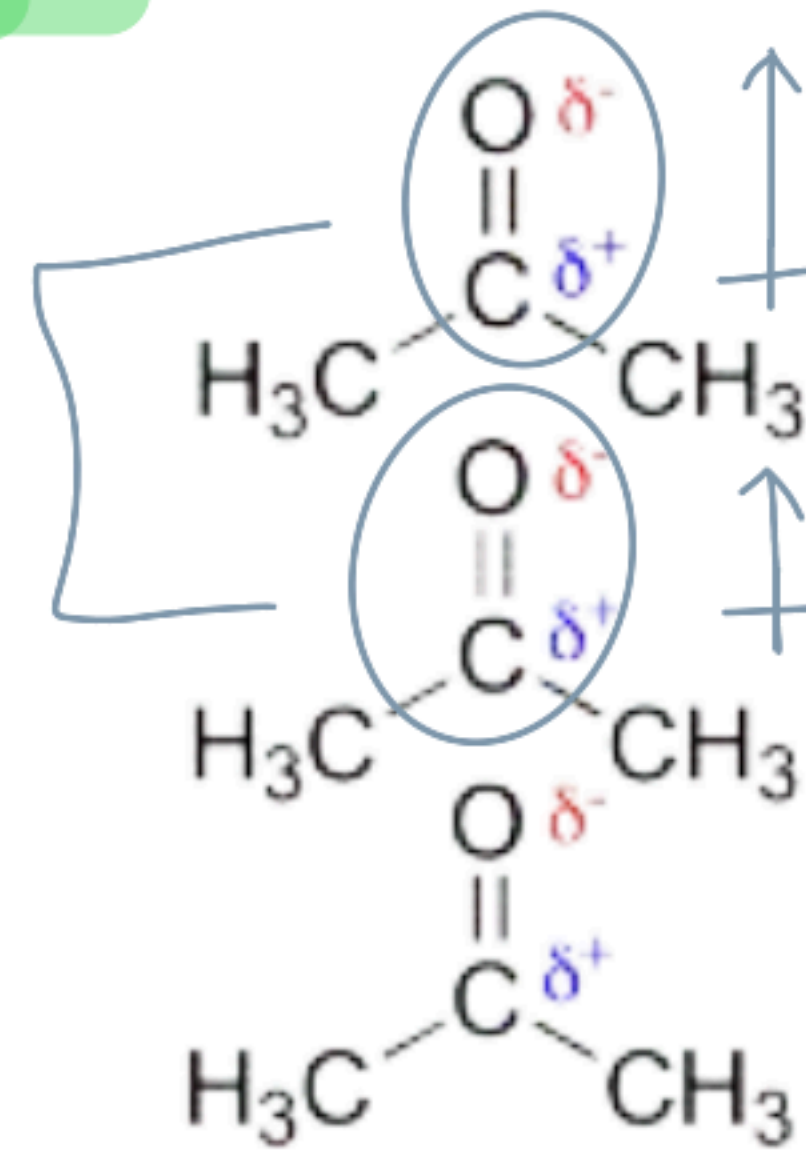
↑ polarity
↑ dipole-dipole
↑ Keesom



Van der Waals forces

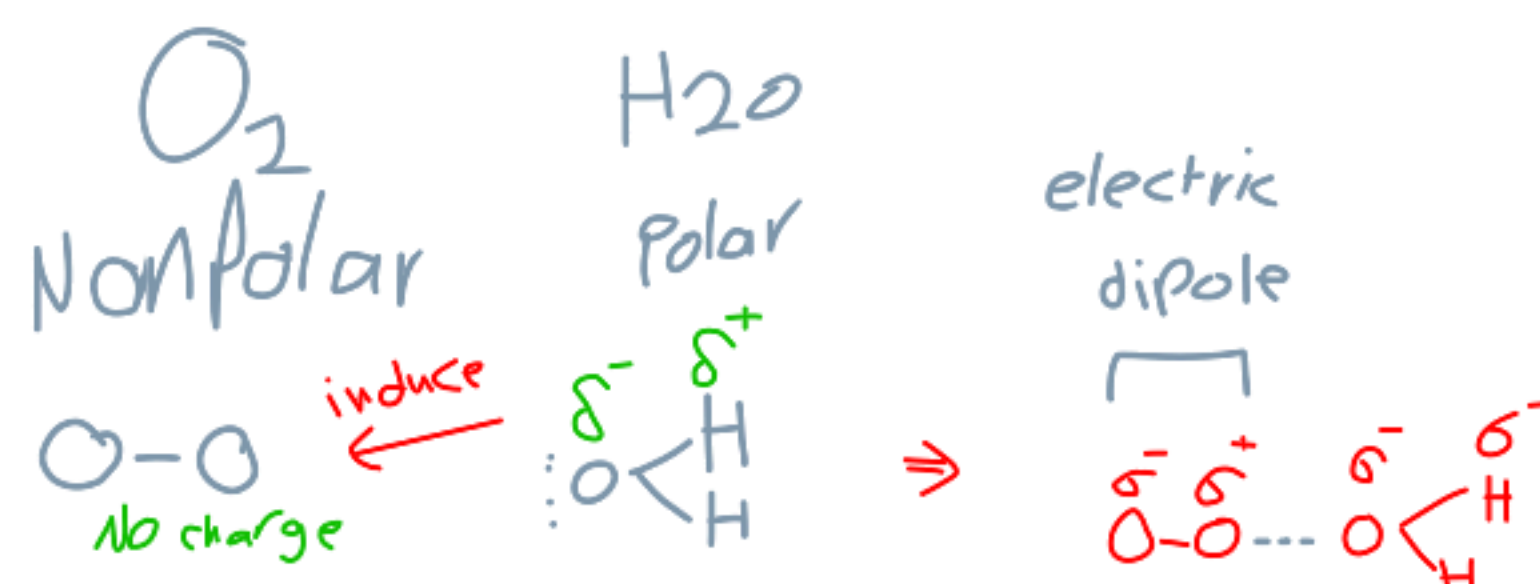
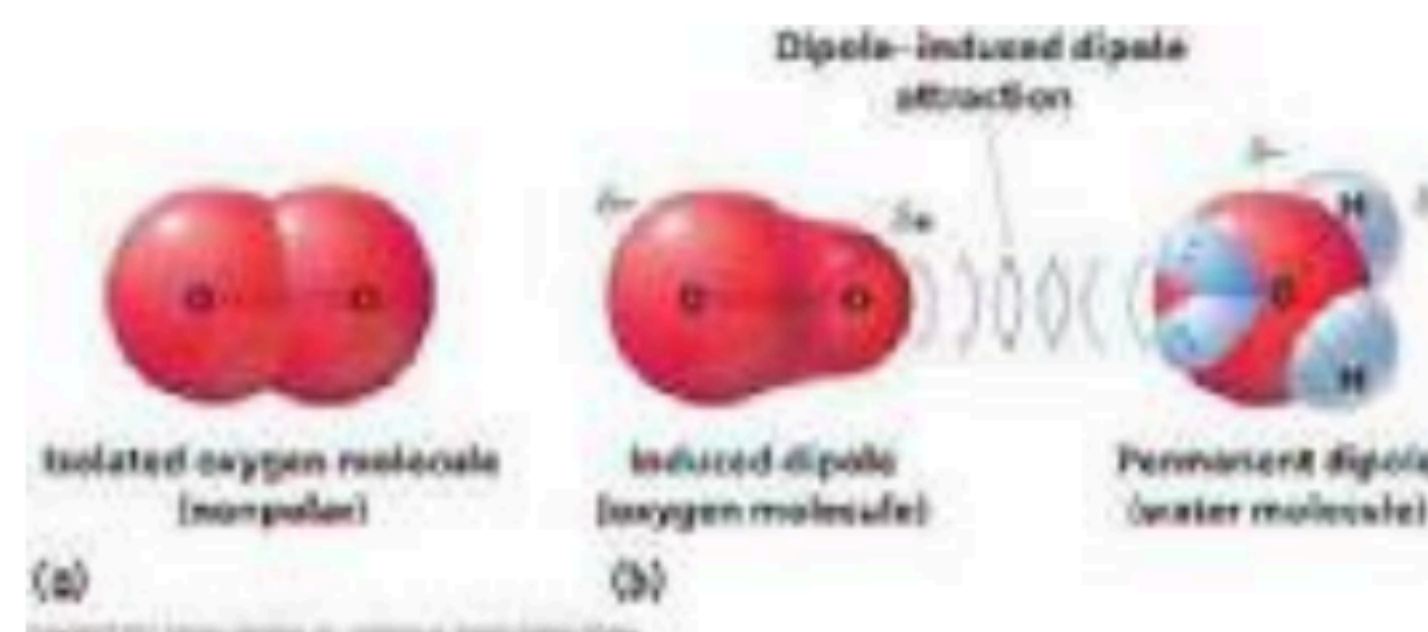
- Example of Keesom forces

- Acetone



Van der Waals forces

- **Debye** forces occur between a **polar** and a **nonpolar** molecule in which the permanent dipole in the polar molecule induce an electric dipole in the non polar one (dipole-induced dipole interactions) or (induction effect) e.g. **water and oxygen**.



الجزئي القطبي
يملك

Permanent
Dipole.

أما الجزئي غير
القطبي فلا
يملك قطبية،
لكن عندما

يقترّب من

الجزئي القطبي
تتشوّه سحابتّه

الإلكترونية

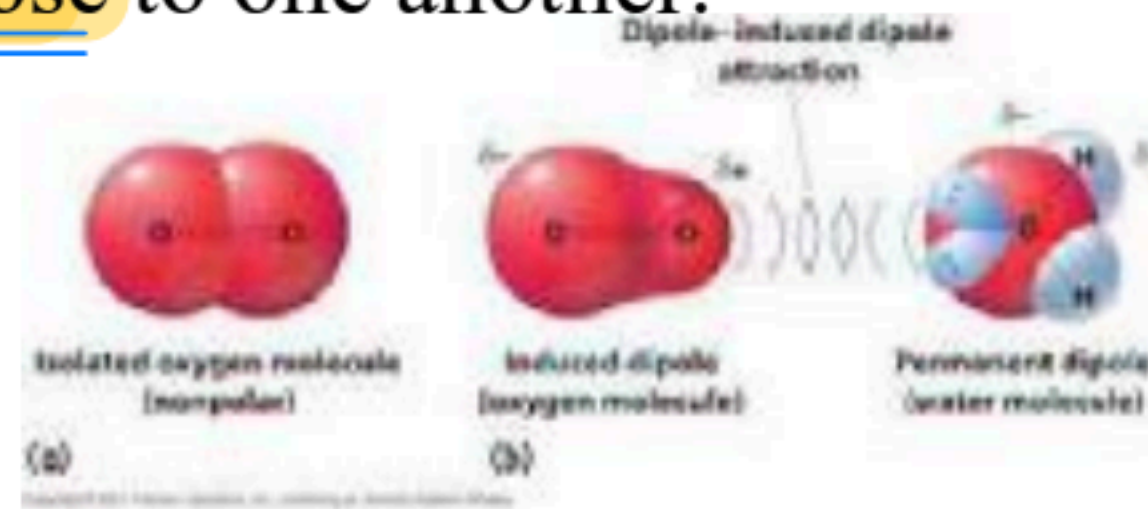
ويتكوّن فيه

Induced
Dipole.

Van der Waals forces

- The oxygen molecule is nonpolar. However, when it comes close to the oxygen atom in a water molecule, the partial negative charge on the oxygen atom repels the electrons in the oxygen molecule. This causes (induces) a temporary partial positive charge in the end closest to the water molecule and a buildup of a partial negative charge in the end furthest away. This induced dipole is temporary and forms only when the two molecules are extremely close to one another.

في H_2O
في O_2
مؤقتة
مؤقت
اقتراب
شديد



:إذا كان الجزيء غير القطبي سهل الاستقطاب

→ بسهولة Dipole تتكون

→ أقوى Debye تصبح

Van der Waals forces

- The strength of Debye forces increases with the ease of distortion of the electron cloud of the nonpolar molecule (i.e. polarizability of the molecule).
- Debye forces is weaker than Keesom forces because the dipole in the nonpolar molecule is temporary (induced) and forms only when the two molecules are extremely close to each other.

كلما زادت
قابلية الجزيء
غير القطبي
للاستقطاب
(سهولة تغير
توزيع السحابة
الالكترونية في
جزيء Nonpolar)
يعني تكون
dipole

↑ polarizability
↑ debye
↑ dipole-induced
dipole

London < Debye < Keesom < ionic
Weakest induced dipole partial charge

Van der Waals forces

- **London forces** occur between two nonpolar (neutral) molecules in which molecules can induce polarity on each other (induced dipole-induced dipole interactions) or (dispersion effect). e.g. Helium, Neon, hydrocarbons...

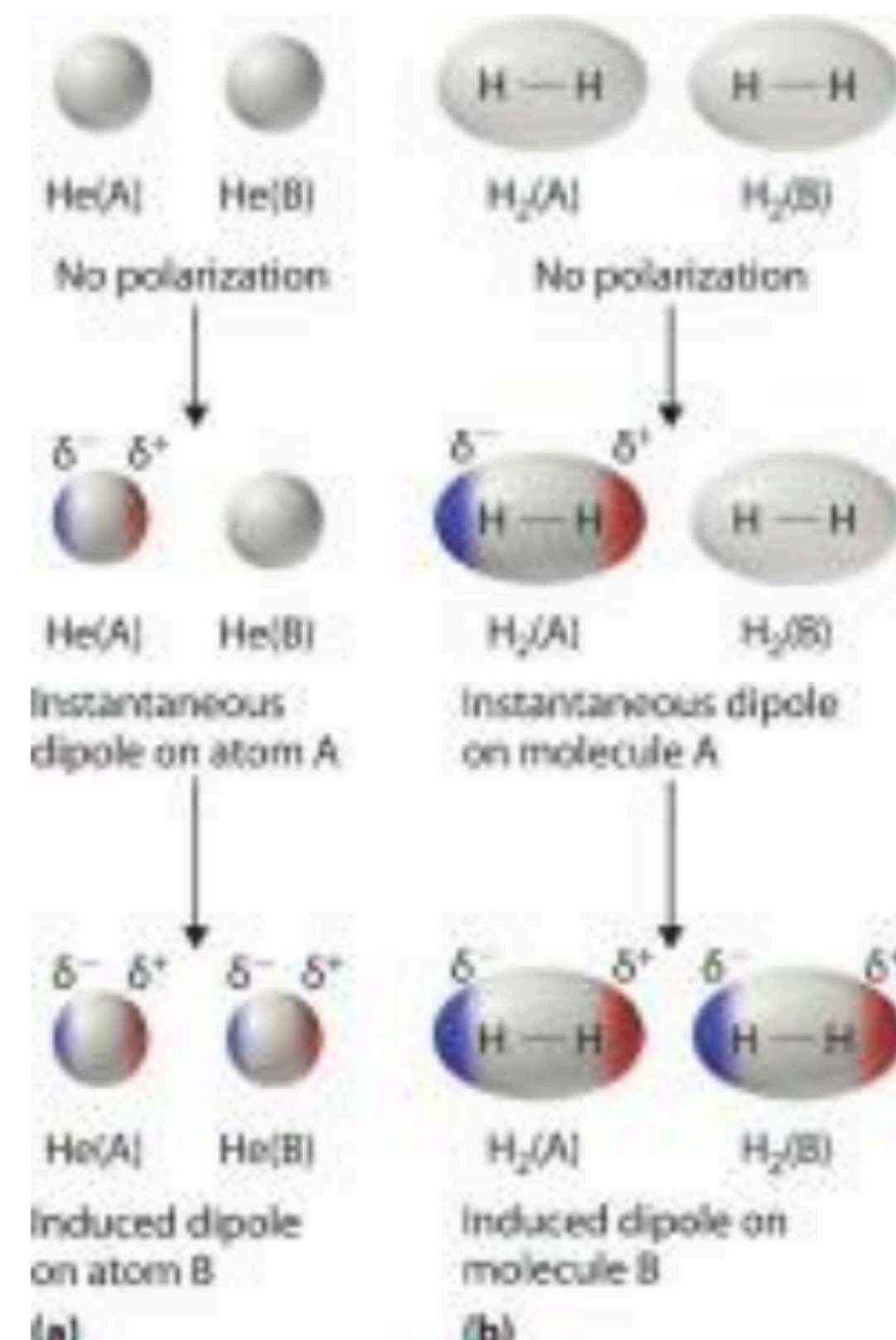


آثار الجذب

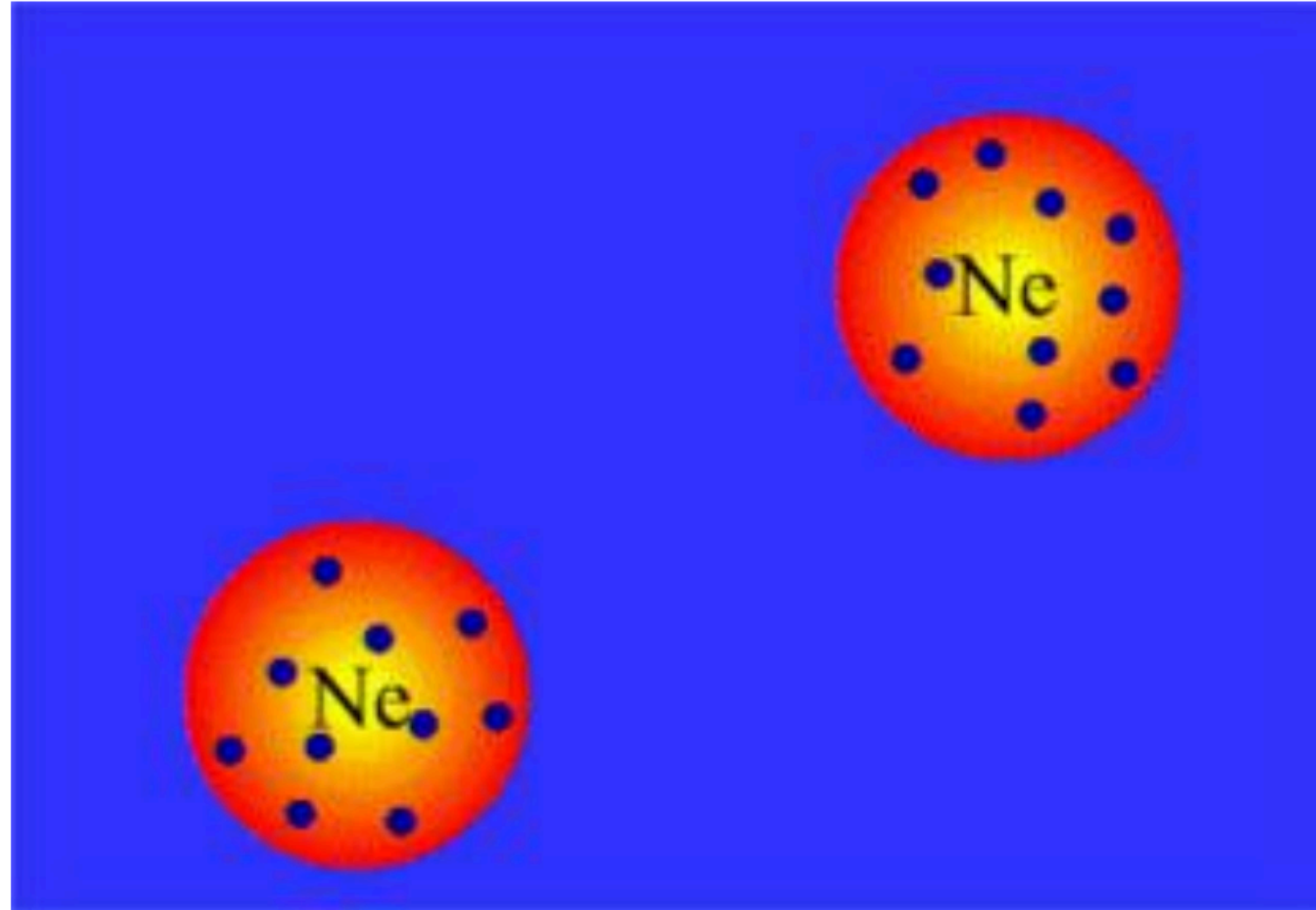
Van der Waals forces

- This attraction is produced by temporary asymmetry in the distribution of the electrons around the nucleus.

عدم تماثل مؤقت (لحظي) في توزيع الإلكترونات



Van der Waals forces



Van der Waals forces

- **London forces** occur between all atoms and molecules (between polar/polar and polar/nonpolar molecules as well)
- The larger the atom or molecule, the greater its polarizability (easier to induce a momentary dipole) and the stronger the dispersion forces become.
- This is because:
 1. The electrons are farther from the positive nucleus and so are held less strongly
 2. The number of electrons is greater
- London Force is the weakest of all the intermolecular forces.

London
موجودة في كل
الجزيئات

two Neutral
molecules
(Nonpolar)
تكون London
القوى الوحيدة بينهم

↑ size
↑ more further
↑ less held
↑ number e^-
↑ Neutral
↑ induced-induced
↑ London

لحظي

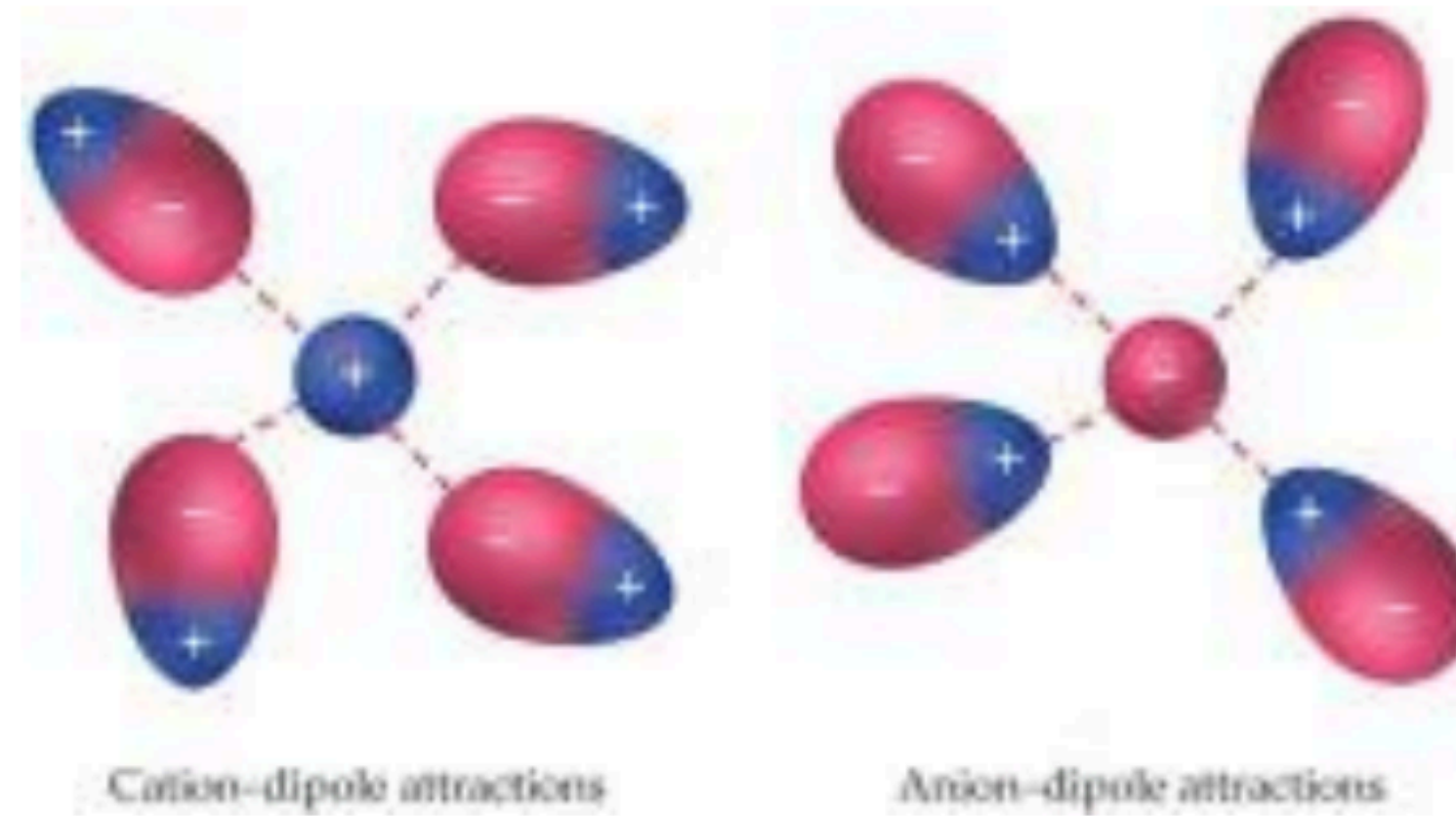
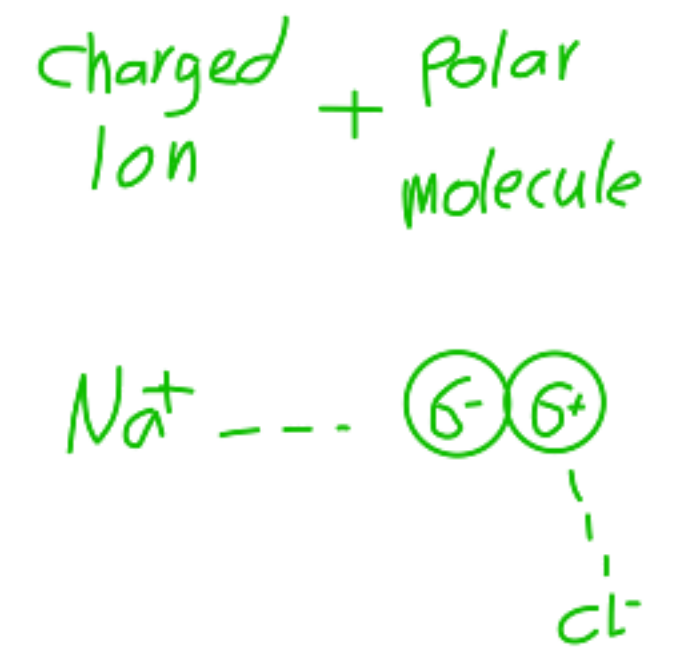
أبعد

أخذ ترتيبهم بالنزول

2

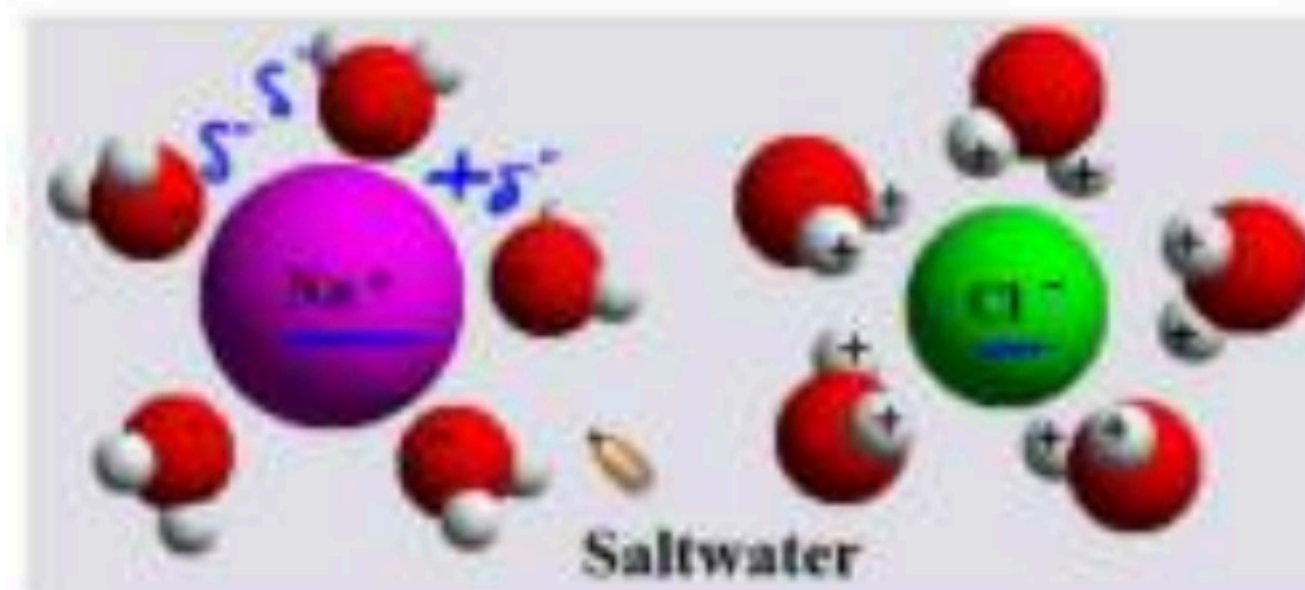
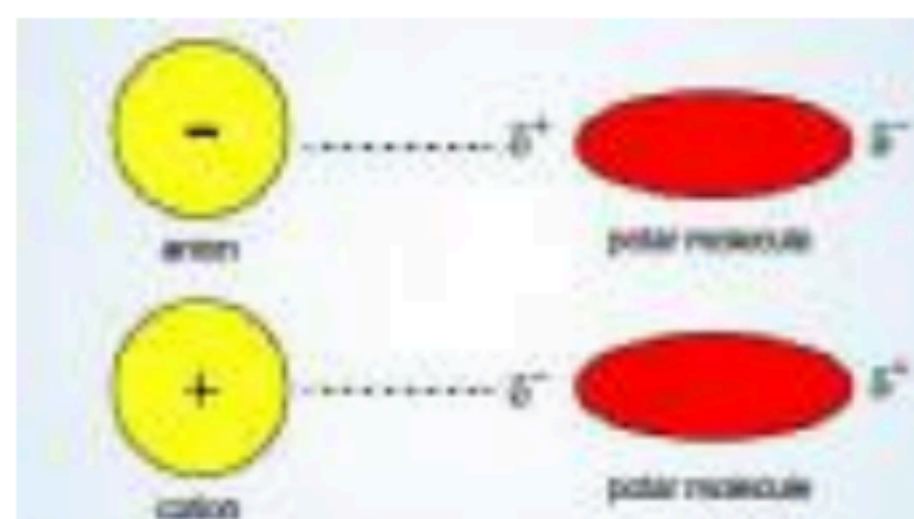
Ion-dipole forces

- Ion-dipole forces occur between a **charged ion** and a **polar molecule** (i.e. a molecule with a dipole). Cations are attracted to the negative end of a dipole, while anions are attracted to the positive end of a dipole.



Ion-dipole forces

- These types of interactions account in part for the **solubility of ionic crystalline substances in water**; the cation, for example, attracts the relatively negative oxygen atom of water and the anion attracts the hydrogen atoms of the dipolar water molecules.



Ion-dipole * قوی

لهي سبب ذوبان

الاملاح في الماء

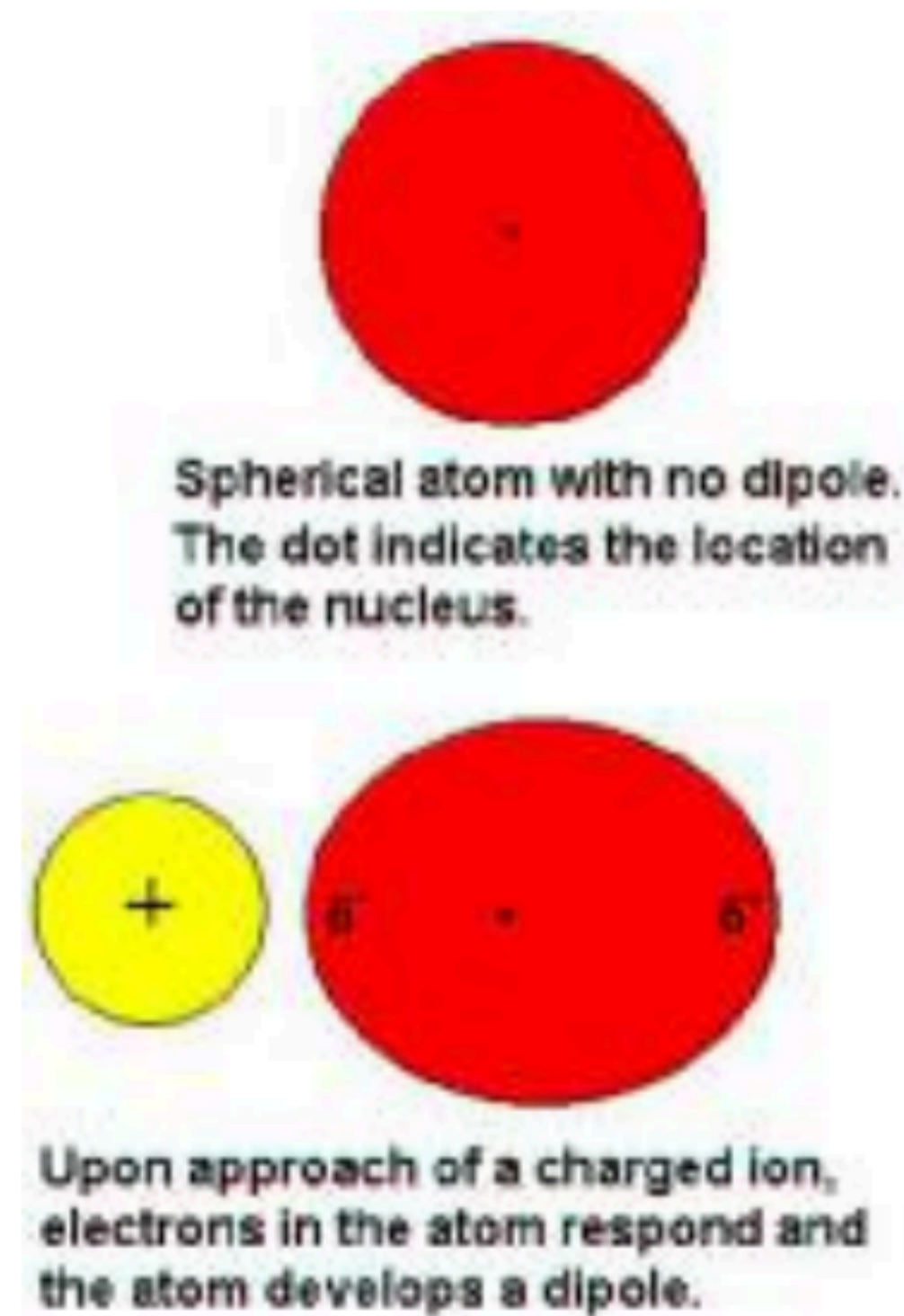
3

تنشأ هذه القوى
عندما يؤدي
اقتراب الأيون
إلى استحثاث
ثنائي قطب في
ذرة أو في
جزيء غير
قطبي عن طريق
إحداث اضطراب
في ترتيب
الإلكترونات.

Ion-Induced dipole

- **Ion-Induced dipole forces occur between a charged ion and a nonpolar molecule.**
- These forces result when the approach of an ion induces a dipole in an atom or in a nonpolar molecule by disturbing the arrangement of electrons
- Ion-induced dipole forces are presumably involved in the formation of the iodide complex
- $I_2 + K + I^- = K + I_3^-$

Nonpolar ion



4

Ion-ion interactions

- A cation on one compound will interact with an anion of another compound.
- Ion-ion interactions may be intermolecular (e.g. a hydrochloride salt of a drug) or intramolecular (e.g., a salt bridge interaction between counter ions in proteins).

intermolecular
HCl-HCl

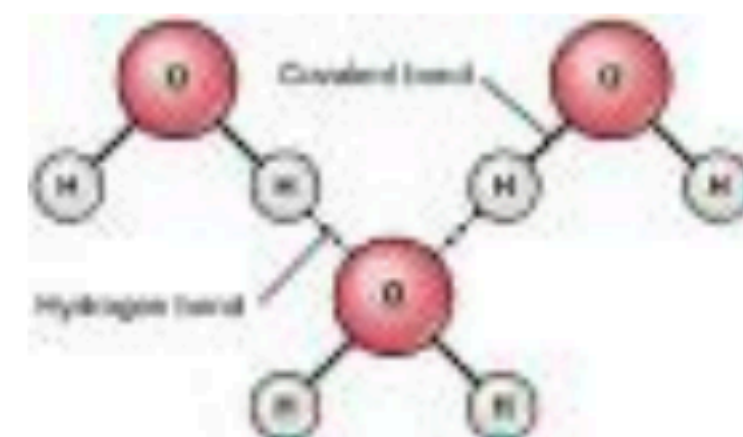
بين جزيئين

Intra molecular
داخل نفس الجزيء



Hydrogen bond

- Hydrogen bond is a **strong type** of **dipole-dipole** interaction that occurs between a **molecule** containing a **hydrogen** atom and a **strongly electronegative** atom such as **fluorine**, **oxygen**, or **nitrogen**.
- In order to create the bond, the **hydrogen atom** must be **covalently attached to another electronegative atom**.
- A perfect example of hydrogen bond is **water**.
- Hydrogen bonds can also exist **between alcohol** molecules, **carboxylic acids**, **aldehydes**, and **DNA** and **polypeptides**.



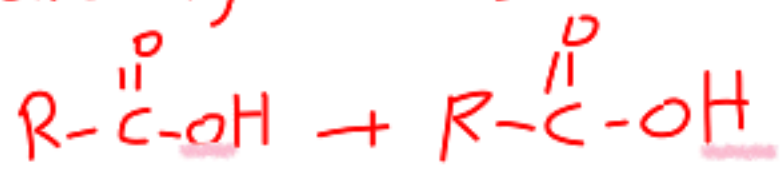
alcohol



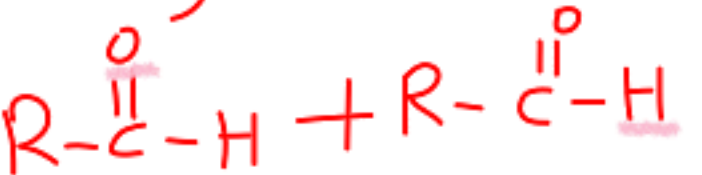
* Alcohols



* carboxylic acids



* Aldehydes

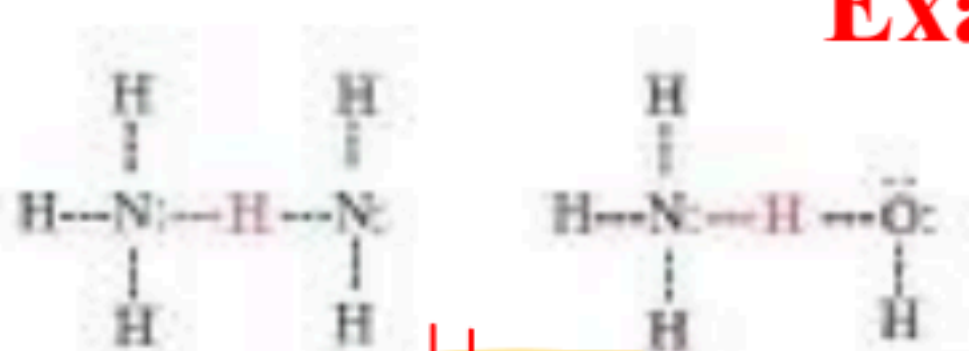


* water

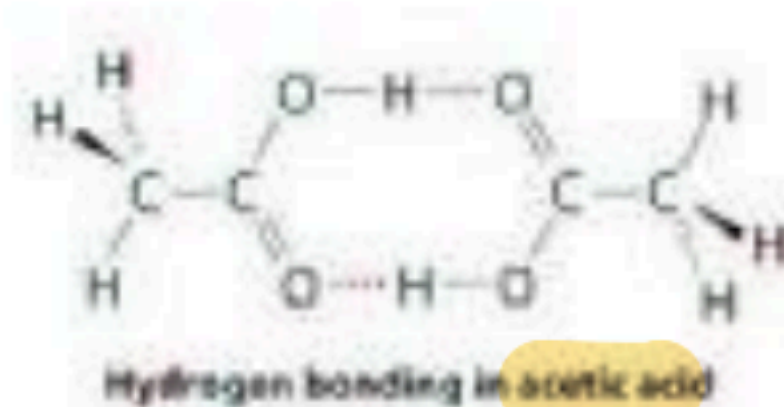


Hydrogen bond

Examples

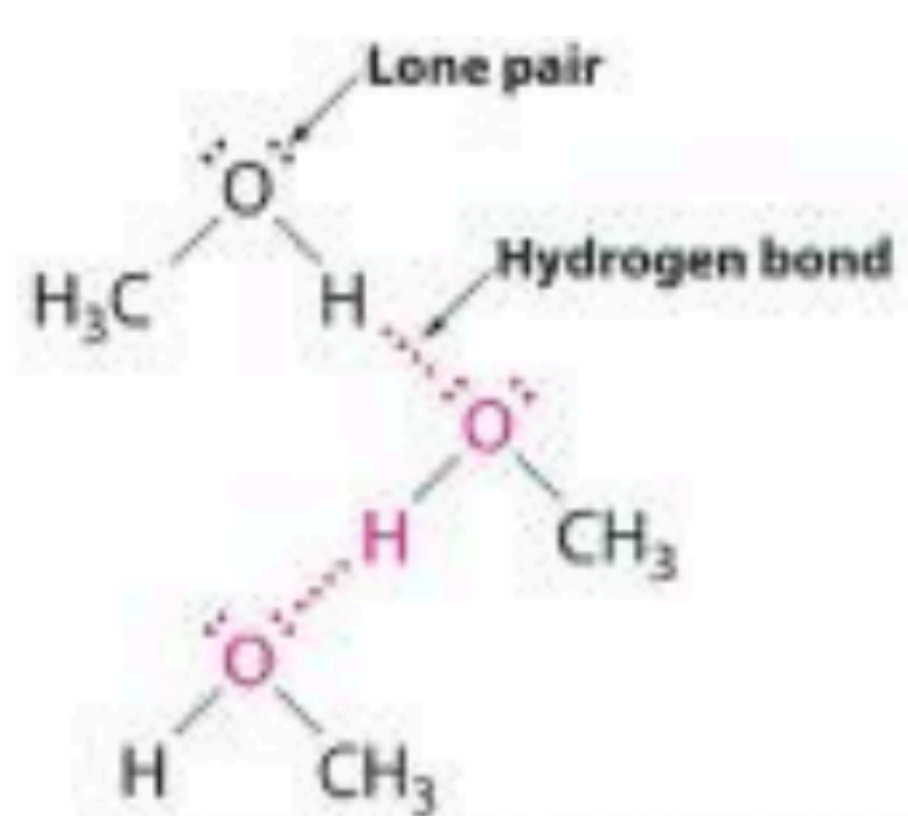


H₂O



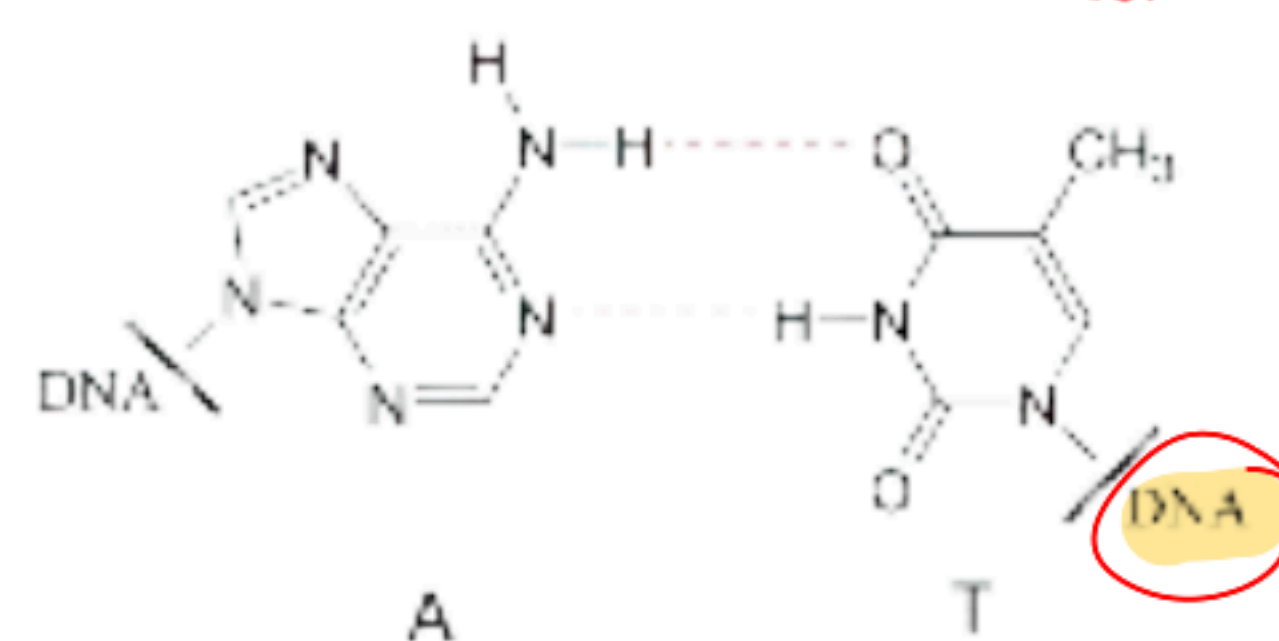
Hydrogen bonding in acetic acid

carboxylic acid



Hydrogen bonding in methanol

alcohol



تكون الروابط
الهيدروجينية
مسؤولة عن
العديد من
الخواص
الفيزيائية غير
الاعتيادية للماء،
ومنها انخفاض
ضغط بخاره
بشكل غير
طبيعي، وارتفاع
درجة غليانه،
وزيادة حجم
الجليد مقارنة
بالماء.

Liquid

Hydrogen bond

- Hydrogen bonds are responsible for many unusual physical properties of water including its abnormally low vapor pressure, high boiling point, and the greater volume of ice water.
- Hydrogen bonding is stronger than all Van der Waals intermolecular forces (they are given their own classification), but are still weaker than ionic and covalent bonds.

$\text{Ionic} > \text{Covalent} > \text{H-Bond} > \text{Keesom} > \text{Debye} > \text{London}$

Bond energies

- Bond energy is a measure of the strength of bond.

1-Intramolecular forces:

$\text{Ionic} > \text{covalent} > \text{metallic}$

2-Intemolecular forces:

- $\text{Ion-dipole} > \text{ion-induced dipole} > \text{hydrogen bond} > \text{keesom} > \text{Debye} > \text{London}$

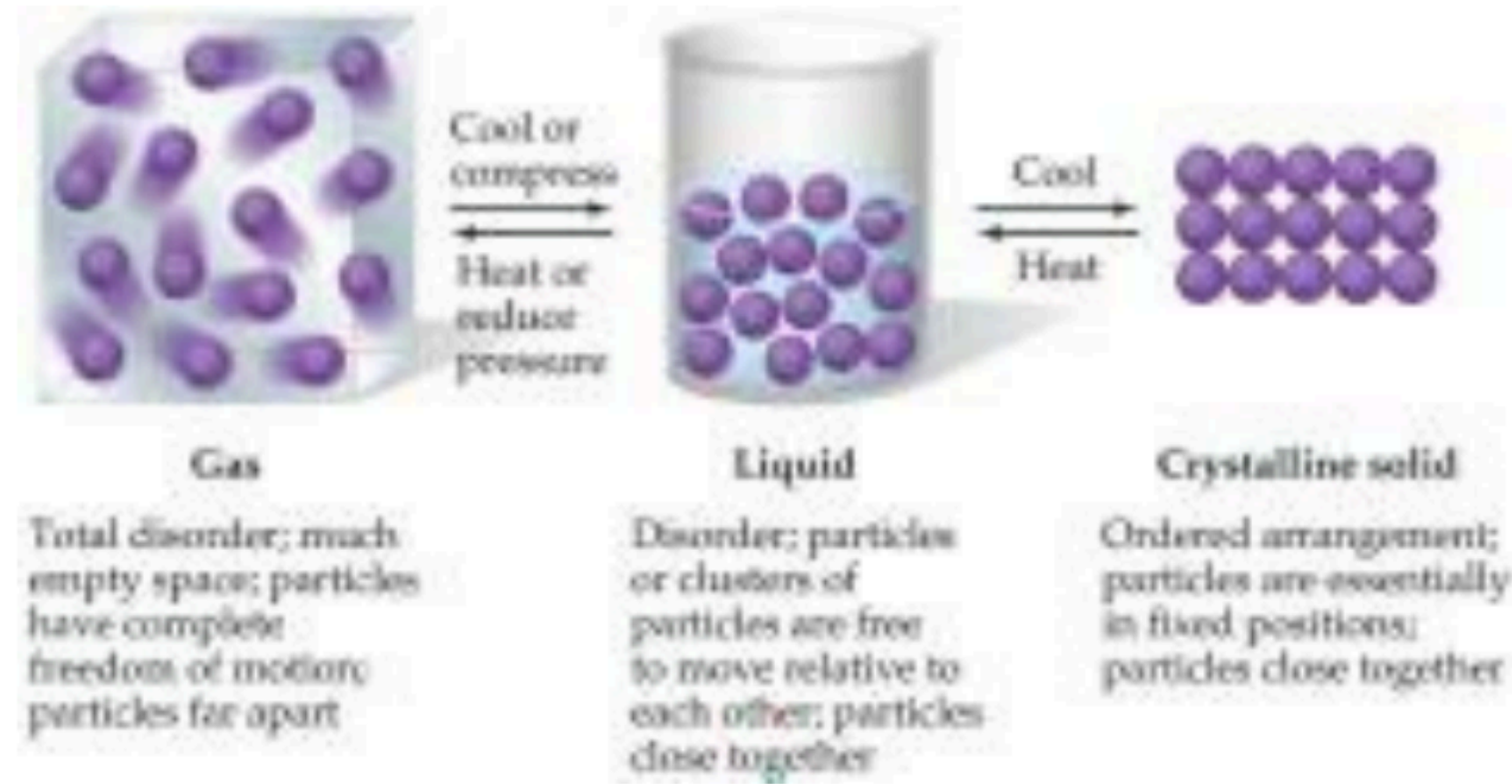
داخل الجزيء

تقسم المادة إلى ثلاث حالات رئيسية حسب ترتيب الجزيئات وقوة الترابط بينها
 Gas: الجزيئات متباعدة جدًا وحركتها سريعة.
 Liquid: الجزيئات متقاربة لكن تستطيع الانزلاق والحركة.
 Solid: الجزيئات مترابطة وتهتز في أماكنها.

States of Matter

- Three primary state of matter

1) Gaseous state 2) Liquid state 3) Solid state

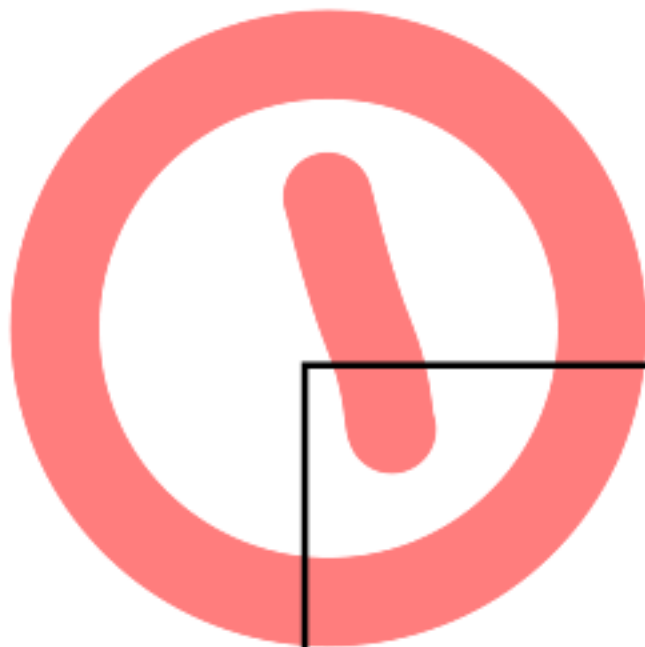


- Other mesophases: حالات وسيطة

Liquid crystals, Supercritical fluids

بلورات سائلة
liquid-solid

موائل فوق حرجية
gas-liquid



The gaseous state

- Gases are described as molecules that have high kinetic energy → rapid motion of molecules.
- Gas molecules exert relatively small forces on each other (molecules try to act independently of one another).

General properties

- A gas mixes rapidly and completely with any other gas.
- A gas uniformly fills any container and assumes its shape (volume).
- Gas is the only state that is compressible.
- The vigorous motion produces a pressure called vapor pressure.

Pressure units

International State

- The SI unit is the Pascal (Pa) where:

$$1 \text{ Pa} = 1 \text{ N m}^{-2}$$

- The relationship of other commonly used pressure units to the Pascal is as follows:

$$\square 1 \text{ bar} = 10^5 \text{ Pa}$$

$$\square 1 \text{ mmHg} = 1 \text{ torr} = 133.32 \text{ Pa}$$

$$\square 1 \text{ atm} = 1.013 \times 10^5 \text{ Pa}$$

$$\square 1 \text{ psi} = 6894.76 \text{ Pa}$$

- Standard atmospheric pressure is $760 \text{ mmHg} = 760 \text{ torr} = 1.013 \text{ bar} = 1.013 \times 10^5 \text{ Pa}$ $= 1 \text{ atm}$

Ideal gas

- Ideal gas is a gas where no intermolecular interactions exist and collisions are perfectly elastic, and thus no energy is exchanged during collision.

- The properties of the ideal gas can be described by the general ideal gas law, which is derived from Boyle, Charles and Gay-Lussac laws

Ideal gas

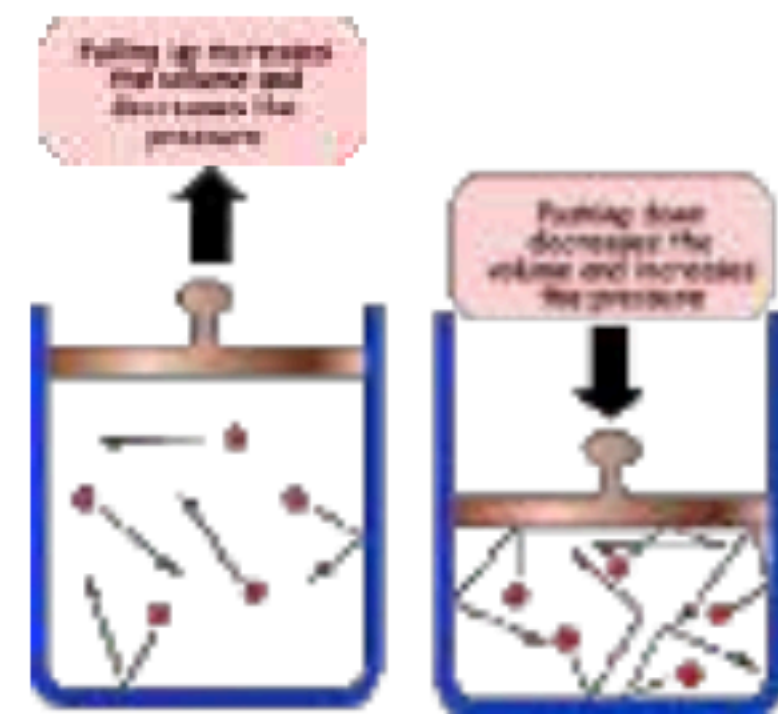
- **Boyle's law** states that the volume and pressure of a given mass of gas is **inversely** proportional (i.e. when the pressure of a gas **increases**, its volume **decreases**).

$$P \propto \frac{1}{V} \text{ or } PV = k$$

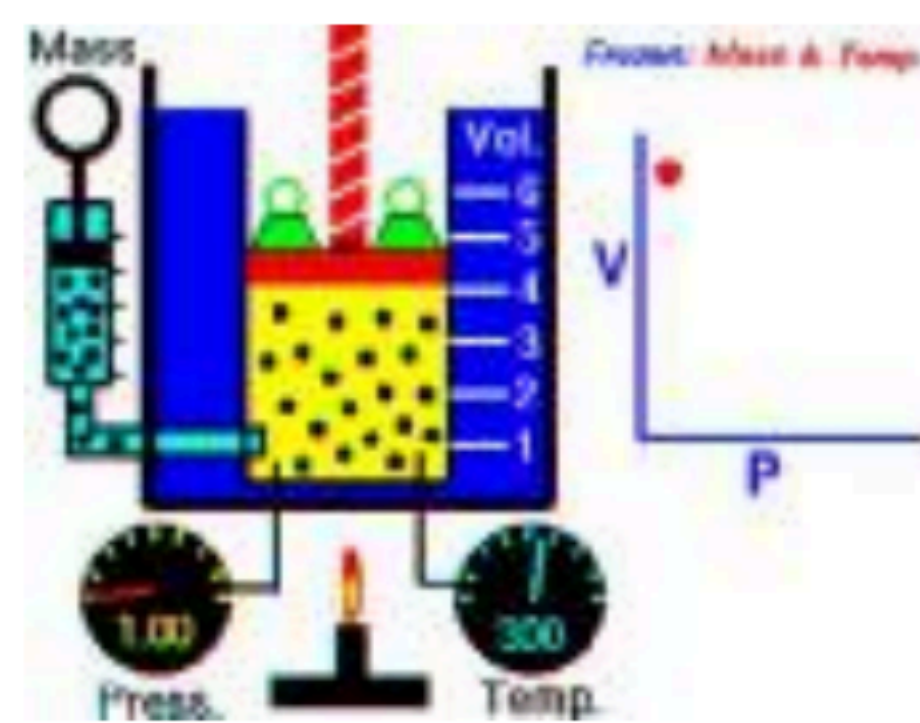
$$P_1 V_1 = P_2 V_2$$

P: pressure, K: constant,

V: volume



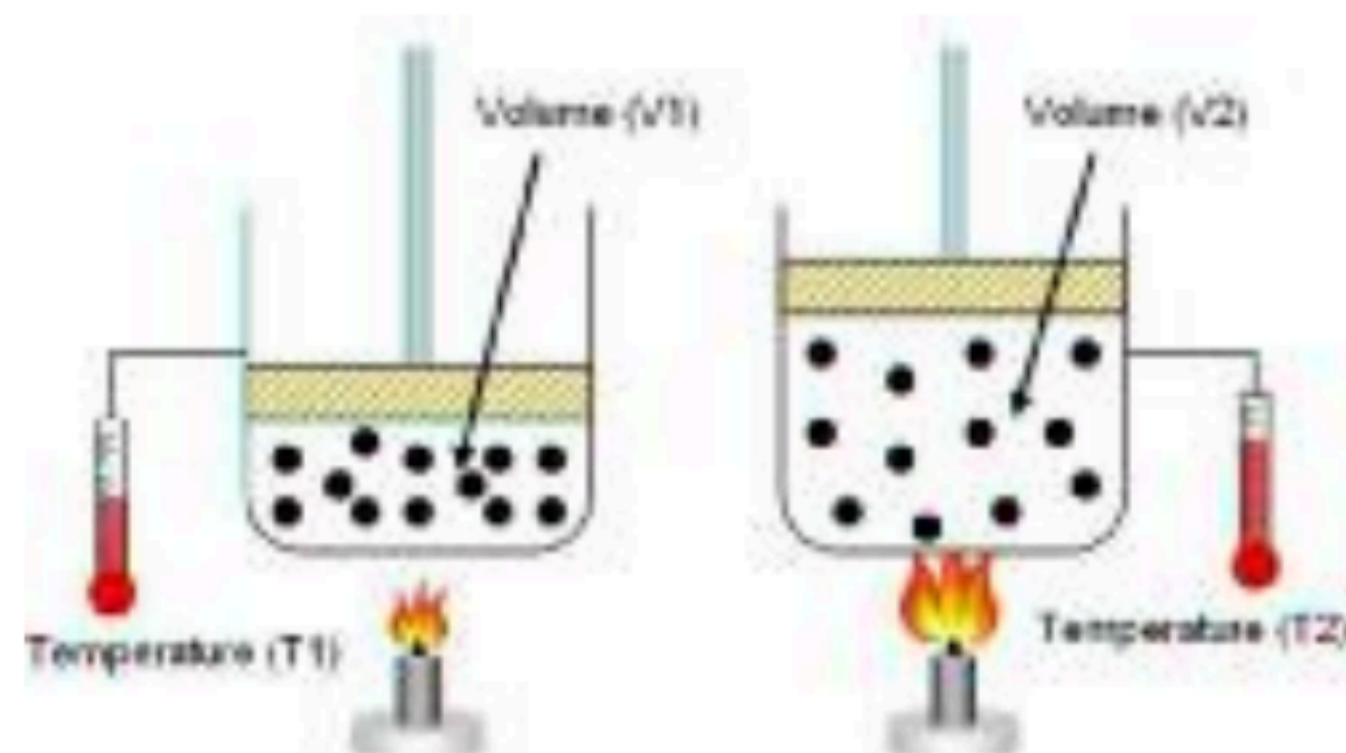
The molecules exert a pressure on the walls of the cylinder. This pressure is what we measure as 'pressure exerted by the gas'.



Ideal gas

- The **Charles** law states that the volume and **absolute** temperature of a given mass at **constant pressure** are directly proportional: $V \propto T$

$$V \propto T \text{ or } V = kT$$



$\uparrow T, \uparrow V$

Ideal gas

- **Gay-Lussac's law** states that the pressure of a given mass of gas varies directly with the absolute temperature of the gas, when the volume is kept constant:

$$P/T = k$$

Ideal gas

- Boyle, Gay-Lussac and Charles law can be combined to obtain the familiar relationship:

$$\frac{P_1 V_1}{T_1} = \frac{P_2 V_2}{T_2}$$

Ideal gas

Example

- In the assay of ethylnitrite spirit, the nitric oxide that is liberated from a definite quantity of spirit and collected in a gas burette occupies a volume of 30.0 ml , at a temperature of 20°C and a pressure of 740 mm Hg . Assuming the gas is ideal, what is the volume at 0°C and 760 mm Hg ?

$$\frac{740 \times 30.0}{273 + 20} = \frac{760 \times V_2}{273}$$

$$V_2 = 27.2 \text{ mL}$$

General ideal gas law

- General ideal gas law (also called equation of state) relates the pressure, volume, and temperature of a given mass of gas.

$$\frac{P_1 V_1}{T_1} = \frac{P_2 V_2}{T_2} \Rightarrow \frac{P V}{T} = R$$

- R**: the molar gas constant value for the PV/T ratio of an ideal gas.
- For n moles the equation becomes:

$$PV = nRT$$

(معادله)
(حالت)

General ideal gas law

- The volume of 1 mole of an ideal gas under standard conditions of temperature and pressure (i.e., at 0° C and 1 atm) has been found by experiment to be 22.414 liters.

- Substituting this value in general ideal gas law:

$$R = \frac{PV}{T} = \frac{1 \times 22.414}{273.16} = 0.08205 \text{ atm L/mole K}$$

- The molar gas constant can also be expressed by energy units:

- $R = 8.314 \text{ Joules/mole K}$ or

- $R = 1.987 \text{ cal/mole deg}$

$$1 \text{ atm} = 1.0133 \times 10^6 \text{ dynes/cm}^2$$

$$1 \text{ Joule} = 1 \text{ N.m} = 1 \text{ Pa.m}^3$$

$$1 \text{ cal} = 4.184 \text{ Joule}$$

General ideal gas law

Example: Calculation of volume using the ideal gas law

- What is the volume of 2 moles of an ideal gas at 25°C and 780 mm Hg? $1.02 \times V = 2 \times 0.082 \times 298$

- $\frac{780 \text{ mm Hg}}{760 \text{ mm Hg}} = 1.0263 \text{ atm}$

- $25^\circ\text{C} + 273 = 298 \text{ K}$

- $PV = nRT \rightarrow V = \frac{nRT}{P} = \frac{2 \times 0.08205 \times 298}{1.026} = 47.65 \text{ L}$

$1 \text{ atm} \rightarrow 760$
 $X \rightarrow 780$

$$\frac{780}{760} = 1.0263 \text{ atm}$$

دواء
غاز دافع

concentrate
+
propellant

$$V_{\text{tot}} = V_{\text{gas}} + V_{\text{concentrate}}$$

ملاحظة

Aerosols and ideal gas law



- **Pressure Calculation:** The ideal gas law ($PV = nRT$) is critical for determining the pressure inside aerosol containers, when compressed (not liquefied) gases (e.g., nitrogen, carbon dioxide) are used as propellants.
- **Key Assumption:** The law assumes ideal behavior (no intermolecular forces, negligible molecular volume), simplifying pressure predictions for aerosol systems.
- **Practical Use:**
 - Calculate the pressure exerted by a known amount of gas (moles) at a given temperature and container volume.
 - Ensure safe and effective product performance by maintaining optimal pressure.

فكر
الأسئلة

n
u
T

P = ??

لضمان أداء آمن وفعال للمنتج عن طريق المحافظة على الضغط المناسب

General ideal gas law

Example: Calculation of pressure using the ideal gas law

Calculate the pressure at 25°C within an aerosol container of internal volume 250 cm³ containing 160 cm³ of concentrate above which has been introduced 0.04 mol of nitrogen gas. Assume ideal behavior.

Answer

$$PV = nRT$$

$$P = \frac{0.04 \times 8.314 \times 298}{(250 - 160) \times 10^{-6}}$$

$$P = 1.01 \times 10^6 \text{ N m}^{-2} \text{ (or Pa)}$$

كبر

نوع الدواء

$$\text{Gas Volume} = 250 - 160 = 90 \text{ cm}^3$$

$$1 \text{ L} \rightarrow 1000 \text{ cm}^3 \quad \frac{90}{1000} = 0.090 \text{ L} \quad 1000 \text{ cm}^3 = 1 \text{ L}$$

General ideal gas law: Molecular weight of gas

الوزن الجزيئي التقريبي

The approximate molecular weight of a gas can be determined by use of the ideal gas law:

$$PV = nRT$$

since $n = g/M$ then:

✓

$$= \frac{\text{mass}}{\text{molar mass}} = \frac{m}{M} \quad PV = \frac{g}{M} RT$$

$$M = \frac{gRT}{PV}$$

$$M = \frac{mRT}{PV}$$

General ideal gas law: Molecular weight of gas

Example: Molecular weight determination using the ideal gas law

If 0.30 g of ethyl alcohol in the vapor state occupies 200 mL at a pressure of 1 atm and a temperature of 100°C , what is the molecular weight of ethyl alcohol?

$$100^\circ\text{C} + 273 = 373 \text{ K}$$

$$200 \text{ mL} \div 1000 \text{ mL} = 0.2 \text{ L}$$

$V = 0.2 \text{ L}$
 $T = 373$
 $\rightarrow$ ideal gas law

$$M = \frac{gRT}{PV} = \frac{0.3 \times 0.082 \times 373}{1 \times 0.2} = 46 \frac{\text{g}}{\text{mole}}$$

فرضية الحركة الجزيئية Ideal gas

Kinetic Molecular Theory

Kinetic molecular theory explains the behavior of gases according to the ideal gas law:

- Gases are composed of particles called atoms or molecules, the total volume of which is so small (negligible) in relation to the volume of the space in which the molecules are confined.
- Gas molecules exert neither attractive nor repulsive forces on one another
- The particles exhibit continuous random motion. The average kinetic energy, E , is directly proportional to the absolute temperature of the gas, or $E = (3/2)RT$.
- The molecules exhibit perfect elasticity; there is no net loss of speed or transfer of energy after they collide with one another and with the walls of the confining vessel.

$T \uparrow$
 $\uparrow$ سرعة حركة الغاز
 $\uparrow E$

تصادم

عندما تصطدم الجزيئات

لا تفقد طاقة

لا تفقد سرعة

تستمر بالحركة مباشرة

ولهذا يسمى التصادم

Perfectly Elastic Collision

Real gas

- Real gases do not interact without energy exchange, and therefore do not follow the laws of Boyle, Charles, and Gay-Lussac.
- Real gases are not composed of infinitely small and perfectly elastic non-attracting spheres.
- They are composed of molecules of a finite volume that tend to attract one another.
- The significant molecular volume and the intermolecular attractions between gas molecules affect both the volume and the pressure of a real gas respectively.

حجم حقيقي

- 1 حجم الجزيئات مهمل مقارنة بحجم الوعاء
- 2 لا توجد قوى تجاذب أو تنافر بين الجزيئات
- 3 الجزيئات تتحرك حركة عشوائية مستمرة
- 4 الطاقة الحركية تتناسب طرديًا مع درجة الحرارة المطلقة
- 5 التصادمات مرنة تمامًا ولا يحدث فقد للطاقة

الحجم المتاح لحركة الجزيئات ليس
بل: V
 $V-nb$

إذا كانت قوى التجاذب قوية، فإن الضغط
المقاس يكون أقل من الضغط الحقيقي، لذلك
نضيف هذا التصحيح إلى الضغط

Real gas: van der Waals equation

- The van der Waals equation is a modified ideal gas equation that takes into account the factors that affect the volume and pressure of a real gas.

For n mole of gas: $\left(P + \frac{an^2}{V^2}\right)(V - nb) = nRT$

- where a and b are constants for a particular gas.
- Around each molecule of a gas is a particular volume from which other molecules are excluded for purely physical reasons. The bulk molar volume, V , of the gas is consequently an overestimation of the true molar volume.

لا يمكن لجزيئين أن يشغلا المكان نفسه في الوقت نفسه.

(حجم مستبعد) Excluded Volume لذلك يوجد لكل جزيء

b . وهذا هو سبب استخدام الثابت

الحجم الحقيقي المتاح للغاز أقل من حجم الوعاء لأن جزءاً منه مشغول بالجزيئات نفسها.

Real gas: van der Waals equation

- The influence of non-ideality is greater when the gas is compressed (At high pressure and low temperature).

- When the volume of a gas is large (At low pressure and high temperature), the molecules are well dispersed and far apart. Under these conditions, a/V^2 and b become insignificant with respect to P and V , respectively, and the van der Waals equation for the real gas reduces to the ideal gas equation: $PV = nRT$

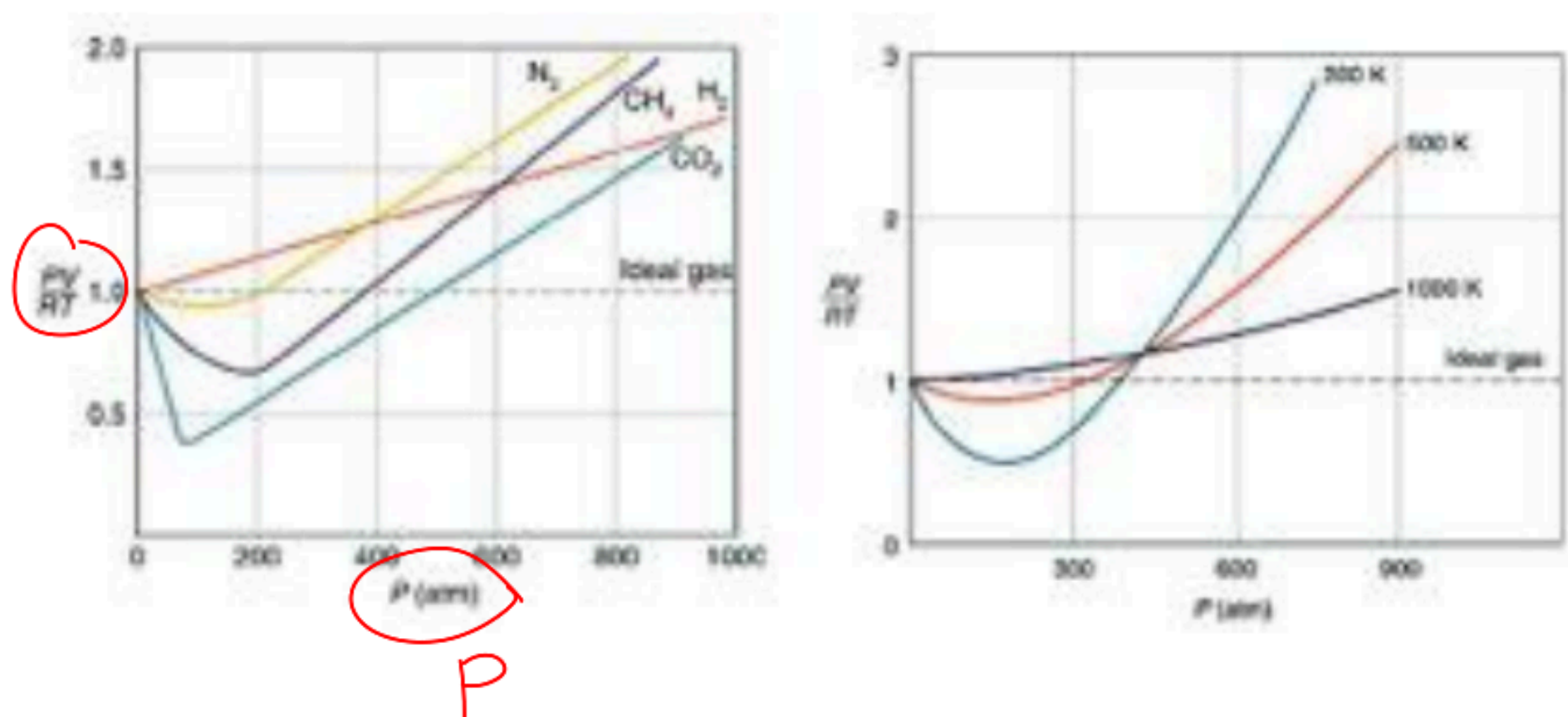
- At these conditions, real gases behave in an ideal manner.
- A convenient means of expressing departure from ideality is by a plot of PV/RT as a function of pressure for 1 mole of each gas

$$\frac{PV}{RT} = 1 \Rightarrow \text{ideal gas}$$

موزع ومتباعد
Small
Large

سرعة الحركة
يزداد التجاذب

$$\frac{PV}{RT}$$



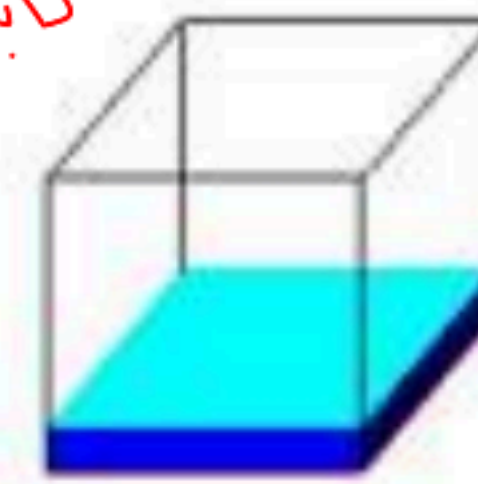
The liquid state

- The transitions from a gas to a liquid and from a liquid to a solid depend on both temperature and pressure.
- When a gas is cooled, it loses some of its kinetic energy in and the velocity of the molecules decreases.
- If pressure is applied to the gas, the molecules are brought within the range of the van der Waals forces and pass into the liquid state.

The liquid state

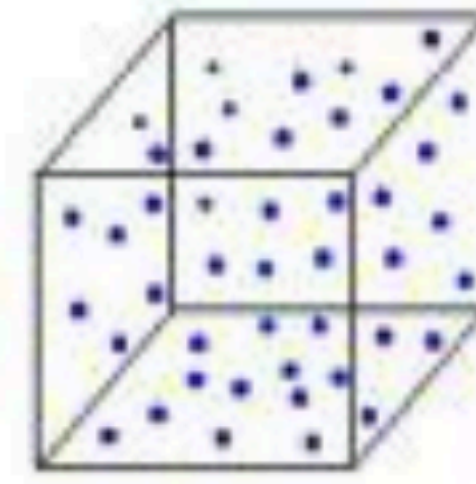
تقارب الجزيئات

- Liquids are **denser** than **gases** and **occupy a definite volume** and **density** due to the presence of van der Waals forces.
- Liquids are relatively incompressible.
- Liquids are **fluids** (have **no definite shape**) like gases.



Liquid

Shape of Container
Free Surface
Fixed Volume



Gas

Shape of Container
Volume of Container

غير قابلة للانضغاط

لا تملك شكل ثابت

fluid $\left\{ \begin{array}{l} \text{Liquid} \\ \text{gas} \end{array} \right.$

Vapor pressure of liquids

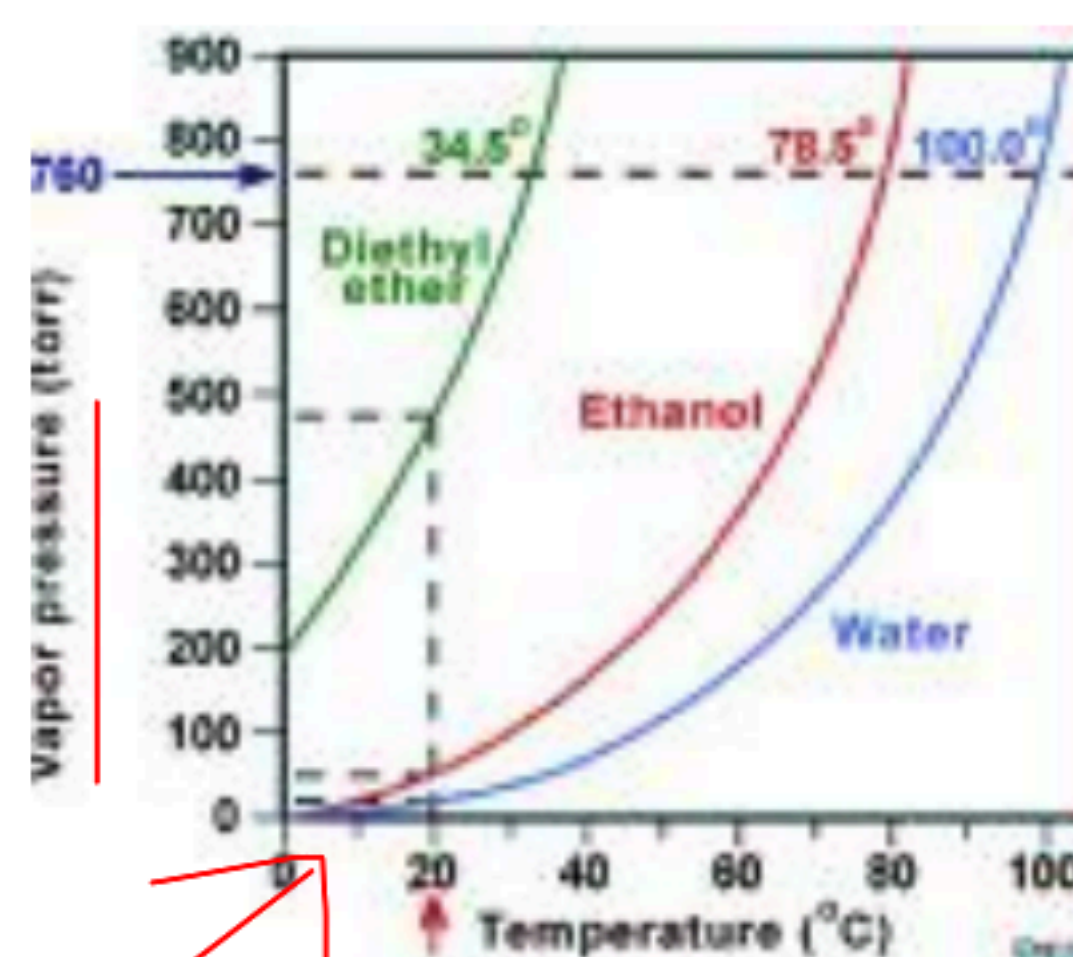
وعاء مفرغ

- When a liquid is placed in an evacuated container at a constant temperature, the molecules with the **highest energies** break away from the surface of the liquid and pass into the gaseous state (evaporate), and some of the molecules subsequently return to the liquid state (condense).
- When the rate of condensation equals the rate of vaporization at a definite temperature, the vapor becomes saturated and a dynamic equilibrium is established.
- The pressure of the saturated vapor above the liquid is then known as the equilibrium vapor pressure.

تساوي

Vapor pressure of liquids

- As the temperature of the liquid is elevated, more molecule approach the velocity necessary for escape and pass into the gaseous state.
- As a result the vapor pressure increases with rising temperature.
- Any point on one of the curves represents a condition in which the liquid and the vapor exist together in equilibrium.



Vapor pressure of liquids

- Clausius–Clapeyron equation** expresses the relationship between the vapor pressure and the absolute temperature of a liquid:

$$\ln \frac{P_2}{P_1} = \frac{\Delta H_v (T_2 - T_1)}{RT_1 T_2}$$

- P_1 and P_2 : vapor pressures at absolute temperatures T_1 and T_2 .
- ΔH_v : the molar heat of vaporization (the heat absorbed by 1 mole of liquid when it passes into the vapor state).
- R : molar gas constant

زيادة الجزيئات التي
تقترب سرعتها
للتحول إلى غاز

$$P_1 = ?$$

$$P_2 = 1 \text{ atm}$$

$$\ln\left(\frac{P_2}{P_1}\right) = \frac{\Delta H_v (T_2 - T_1)}{RT_1 T_2} = \frac{9720(393 - 373)}{1.987 \times 373 \times 393} = 0.6676 \Rightarrow \ln\left(\frac{1}{P_1}\right) = 0.6676$$

$$e^{\ln(1/P_1)} = e^{0.6676} \Rightarrow \frac{1}{P_1} = 1.9496$$

$$\Rightarrow \frac{1}{P_1} = e^{0.6676}$$

$$\frac{1}{P_1} = 1.9496$$

$$P_1 = \frac{1}{1.9496}$$

$$P_1 = 0.513 \text{ atm}$$

المعطيات :

$$P_2 = 1 \text{ atm}$$

$$T_1 = 373 \text{ K } (100^\circ\text{C})$$

$$T_2 = 393 \text{ K } (120^\circ\text{C})$$

$$\Delta H_v = 9720 \text{ cal/mol}$$

$$R = 1.987 \text{ cal/mol}\cdot\text{K}$$

Vapor pressure of liquids

Example: Application of Clausius–Clapeyron equation

- Compute the vapor pressure of water at 120°C . The vapor pressure of water at 100°C is 1 atm, and ΔH_v is 9720 cal/mole.

$$\ln \frac{P_2}{P_1} = \frac{\Delta H_v (T_2 - T_1)}{RT_1 T_2}$$

$$\ln \frac{P_2}{1} = \frac{9720(393 - 373)}{1.987 \times 393 \times 373}$$

$$P_2 = 1.95 \text{ atm}$$

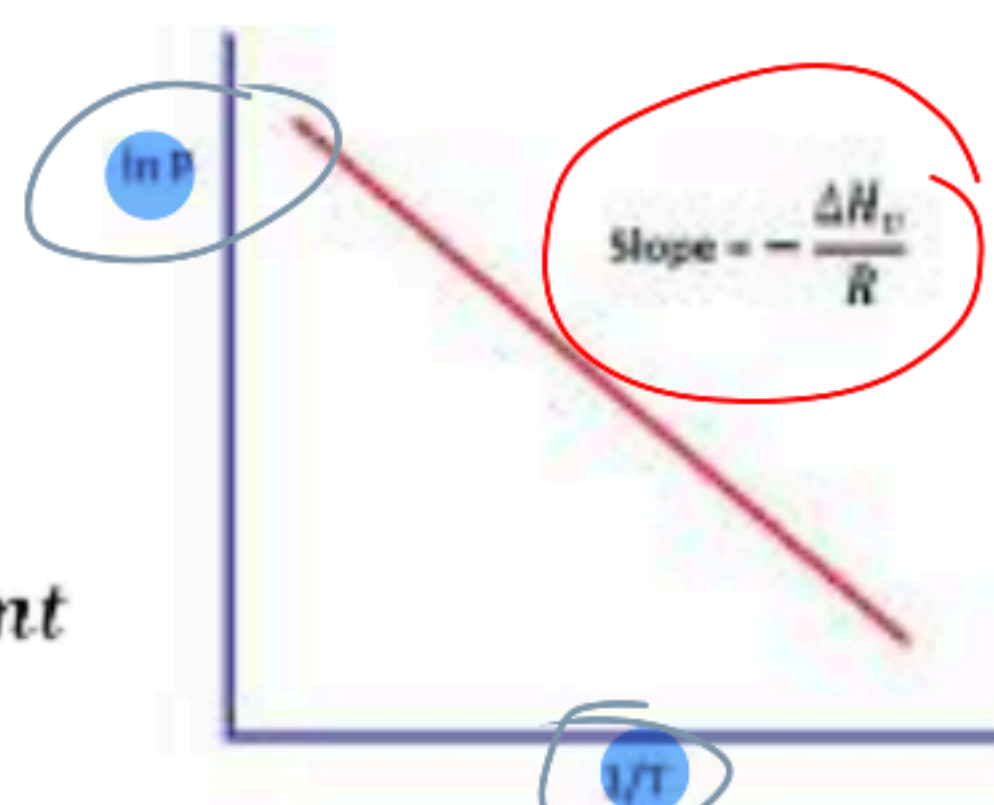
Vapor pressure of liquids

- The Clausius–Clapeyron equation can be written in a more general form:

$$\ln P = -\frac{\Delta H_v}{R} \frac{1}{T} + \text{Constant}$$

or

$$\log P = -\frac{\Delta H_v}{2.303 R} \frac{1}{T} + \text{Constant}$$

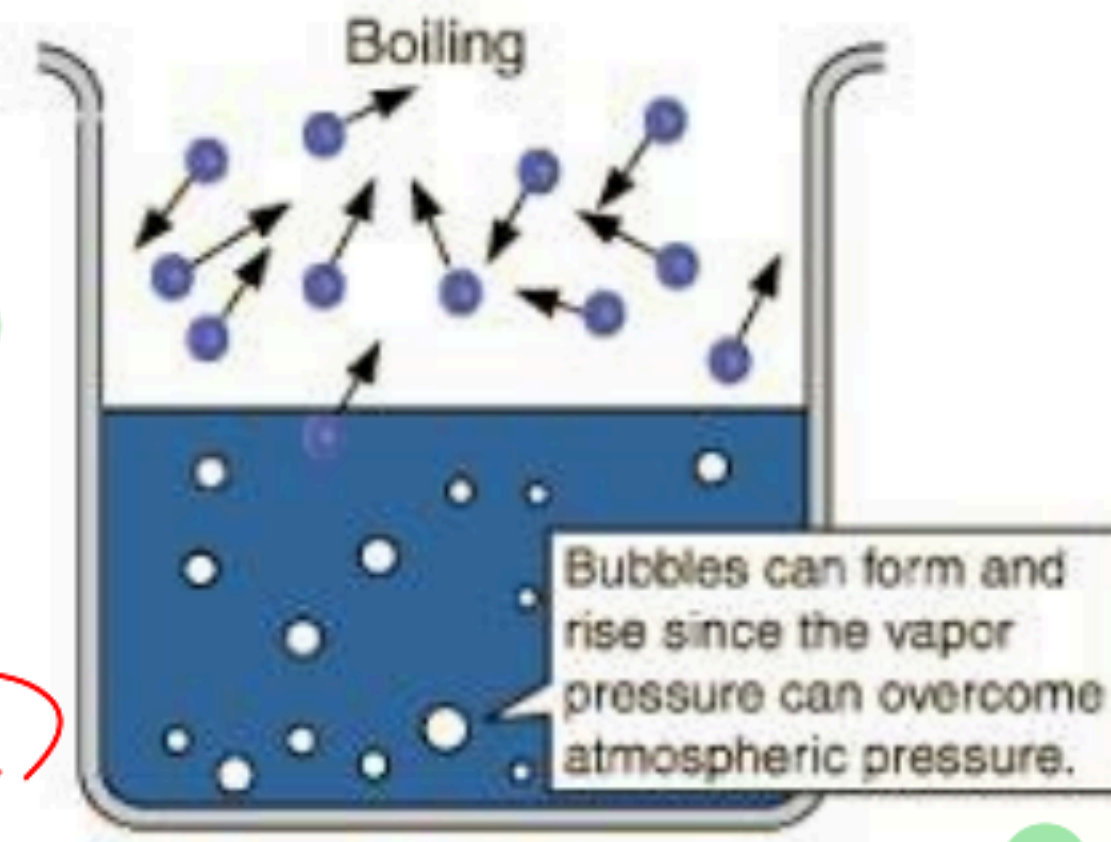


- A plot of $\ln P$ (or $\log P$) against $1/T$ results in a straight line. The heat of vaporization of the liquid can be calculated from the slope of the line.

ΔH_v

Boiling point

- If a liquid is placed in an open container and heated until the vapor pressure equals the atmospheric pressure, the liquid starts to boil and escape into the gaseous state.
- The temperature at which the vapor pressure of the liquid equals the external or atmospheric pressure is known as the boiling point.
- The absorbed heat used to change the liquid to vapor is called the latent heat of vaporization.



كيفية
تأثير زيادة الضغط
على نقطة الغليان
Liquid $\rightarrow$ vapor

Boiling point

- The temperature at which the vapor pressure of the liquid equals an atmospheric pressure of 1 atm is called normal boiling point.
- At higher elevations, the atmospheric pressure decreases and the boiling point is lowered.
- At a pressure of 700 mm Hg, water boils at 97.7°C; at 17.5 mmHg, it boils at 20°C.
- The change in boiling point with pressure can be computed by using the Clausius–Clapeyron equation.

DRP

على قمم الجبال
الضغط الجوي أقل
لذلك لا يحتاج
السائل للوصول إلى
ضغط بخاري كبير
فيغلي عند درجة
حرارة أقل.

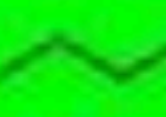
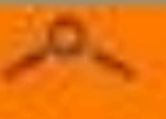
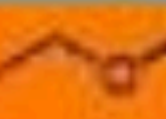
الدرجة الحرارية

Boiling point

- The boiling point can be considered the temperature at which thermal agitation can overcome the attractive forces between the molecules of a liquid.
- The boiling point of a compound, like the heat of vaporization and the vapor pressure, depends on the magnitude of the attractive forces.
- Nonpolar substances have low boiling points and low heats of vaporization because the molecules are held together predominantly by the weak London forces.
- Polar molecules (e.g. water) exhibit high boiling points and high heats of vaporization because they are associated through hydrogen bonds.

Boiling point

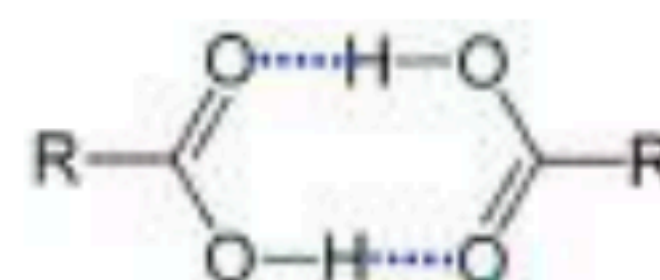
- The boiling points of normal hydrocarbons, simple alcohols, and carboxylic acids increase with molecular weight because van der Waals forces become greater with increasing numbers of atoms.

ALKANES				
Boiling point	-42 °C	0 °C	36 °C	69 °C
ALCOHOLS				
Boiling point	97 °C	117 °C	138 °C	158 °C
CARBOXYLIC ACIDS				
Boiling point	141 °C	164 °C	186 °C	202 °C
ETHERS				
Boiling point	-24 °C	35 °C	80 °C	

Carboxylic acid > alcohol > Ethers > Alkane

Boiling point

- Alcohols boil at a much higher temperature than saturated hydrocarbons of the same molecular weight because of association of the alcohol molecules through hydrogen bonding.
- The boiling points of carboxylic acids are higher than that of alcohols because the acids form dimers through hydrogen bonding. That can persist even in the vapor state.



شماره ۱
جوابی و تپنی د نمون (H)

تپنی

Boiling point

- Branching of the chain produces a less compact molecule with reduced intermolecular attraction, and a decrease in the boiling point.

Branching
↓
Vol =
↓
BP ↓

Name	Formula	Boiling point (°C) (at 1 atm)
Methanol	CH_3OH	-78.5
Ethanol	$\text{CH}_3\text{CH}_2\text{OH}$	-78.5
Propanol	$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$	-78.5
Isopropanol	$\text{CH}_3\text{CH}(\text{CH}_3)\text{OH}$	-78.5
Butanol	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	-78.5
Isobutanol	$\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}$	-78.5
tert-Butanol	$(\text{CH}_3)_3\text{COH}$	-78.5

3

Solid state

- Solid particles are made up of **molecules**, **atoms** or **ions** that are held in **close proximity** to each other.
- They are **much denser** than both gases and liquids due to the presence of **very strong forces** between molecules, atoms or ions.
- Solids are **unique** because their **physical form** (the **packing** of molecules and the **size** and **shape** of **particles**) can have an **influence** on the way the material will behave.
- Solids may be **crystalline** or **amorphous** (or a combination of both).

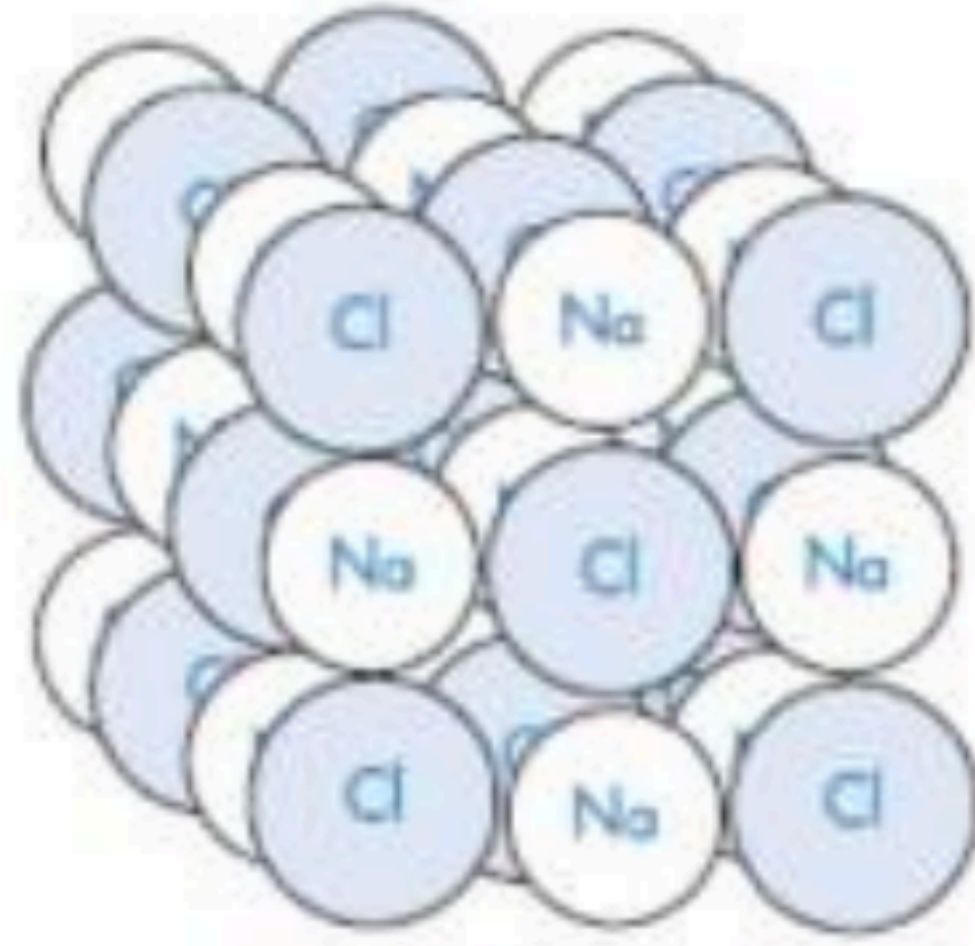
عبر بلورية

1

Solid state

- **Crystalline** materials are those in which the **units** (i.e. molecules, ions or atom) are packed in a **defined order**, and this same order **repeats** over and over again throughout the particle.
- The **forces** of interaction between units include:
 - 1- **metallic bonds**
 - 2- **covalent bonds** (e.g. **Diamond**)
 - 3- **ionic bonds** (between ions in salts such as NaCl crystals)
 - 4- **hydrogen bonds** (between molecules),
 - 5- **van der Waal's forces**

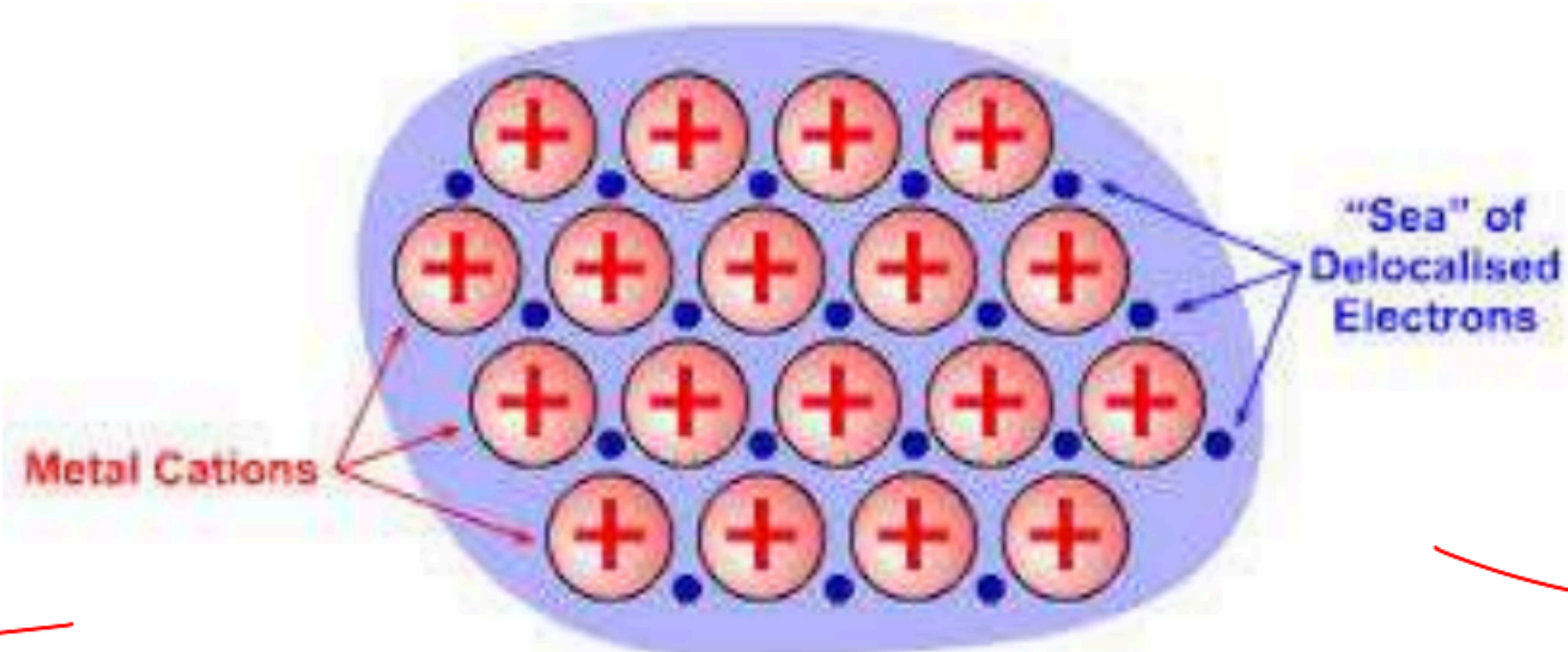
Ionic bonds



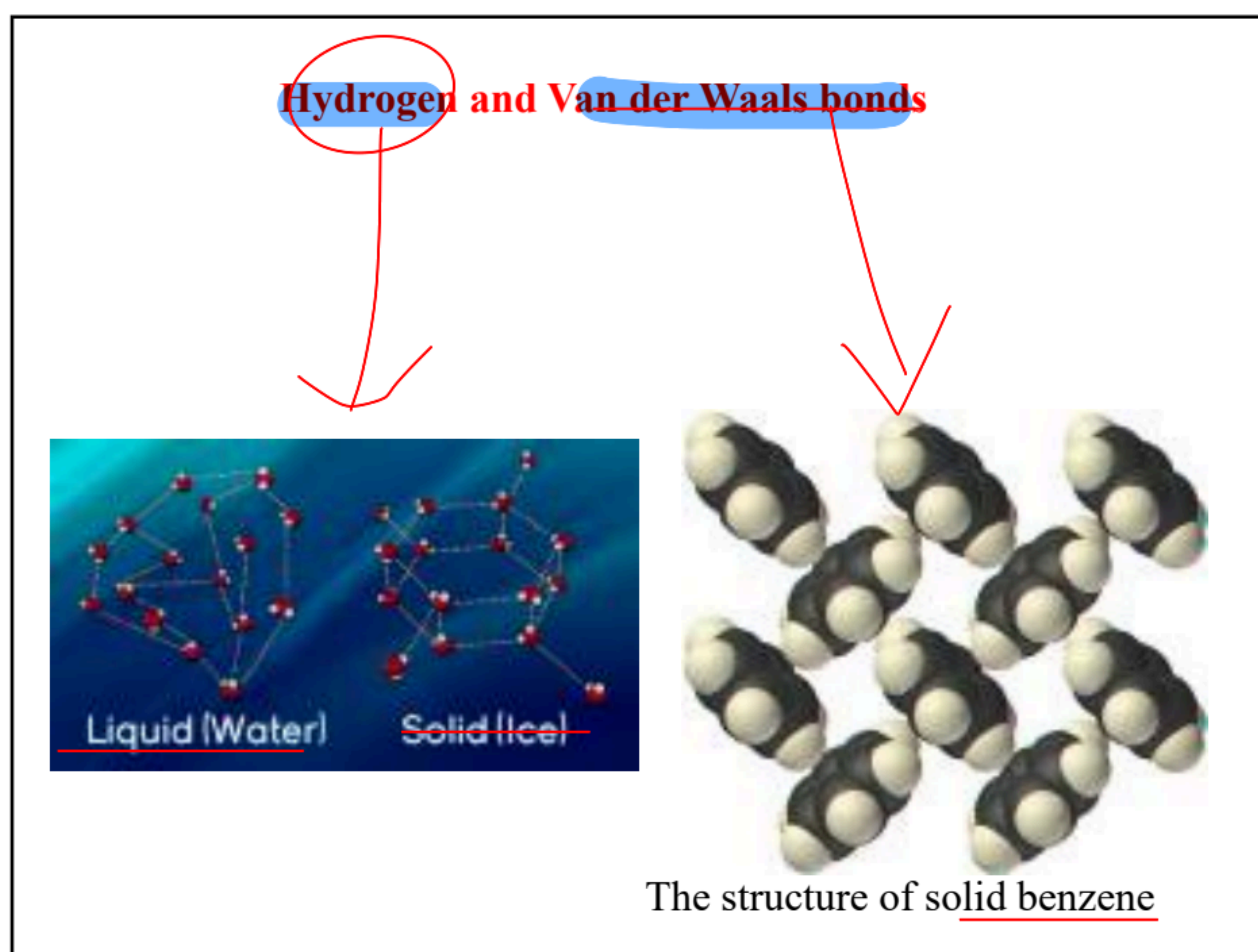
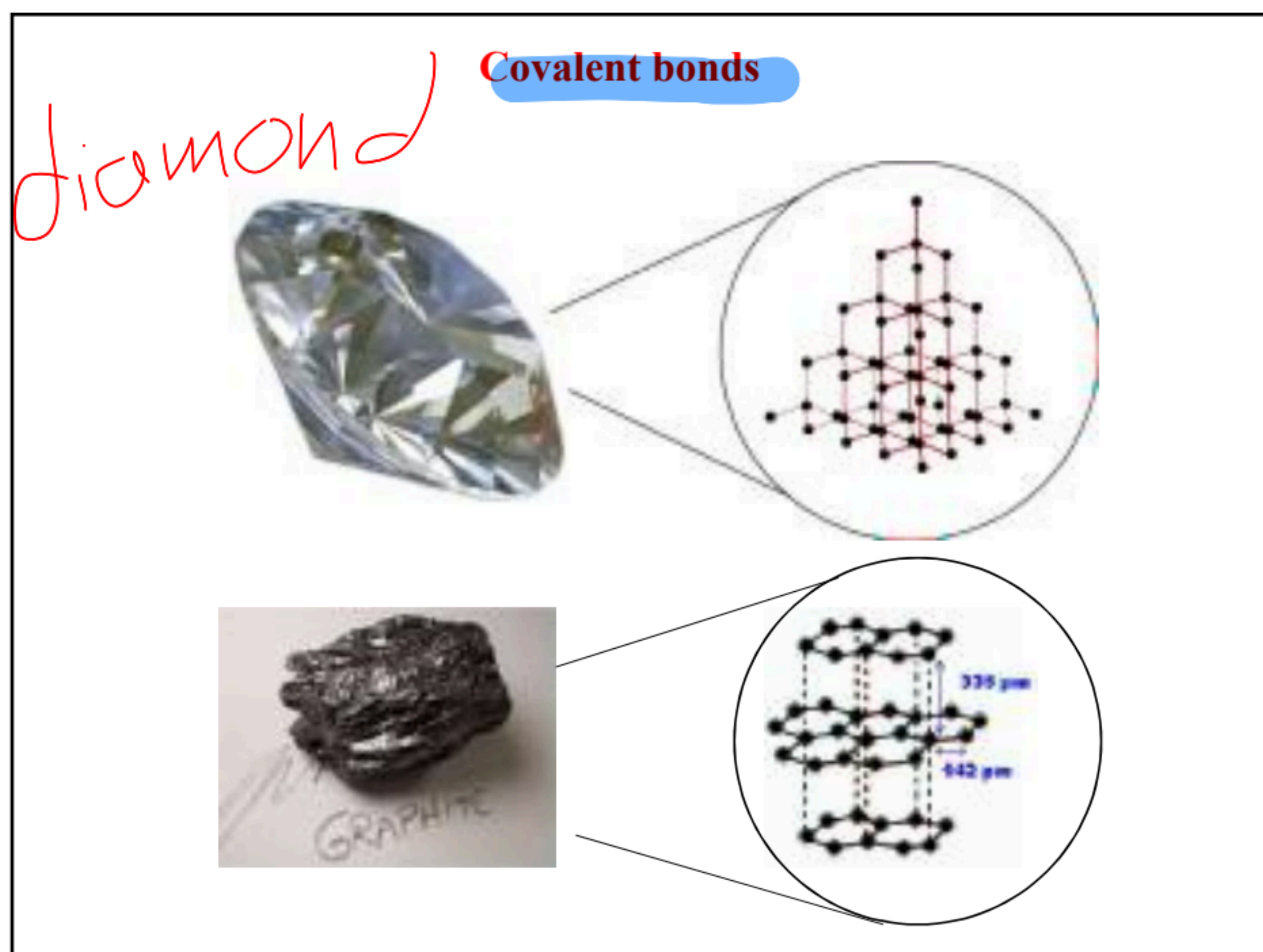
Space lattice of sodium chloride crystal. Each sodium ion is ~~8~~ octahedrally surrounded by ~~six~~ ~~6~~ chloride ions and each chloride ion is octahedrally surrounded by six sodium ions.

*Octahedral
arrangement*

Metallic bonds



Electrons are not bonded to any particular atom and are free to move about in the solid



HydroCarbon

Solid state

- Crystalline solids have a **melting point** which is the temperature at which crystal lattice breaks down.
- Crystals with weak forces holding the molecules together will have low melting points, whereas crystals with strong attractive forces will have high melting point.

Substance	Bonding	MP
CH ₄	van der Waal's	-182°C
CH ₃ F	dipole-dipole	-141°C
CH ₃ OH	hydrogen bonds	-93°C
Al	metallic	660°C
AlF ₃	ionic	1291°C
C	covalent	3550°C

Increasing Strength

Crystallization

- Crystals are produced by inducing a change from the liquid or gas state to the solid state by either:

1 Crystallization from melt

- Cooling of a molten sample to below its melting point.

2 Crystallization from solution

- To make a supersaturated solution by: فوق المشبع
 - Removing the liquid by evaporation
 - Cooling the solution, as most materials become less soluble as temperature is decreased. تقل الذوبانية
 - Adding antisolvent (another liquid which will mix with the solution, but in which the solute has low solubility)

3 Crystallization from vapor

elixir في

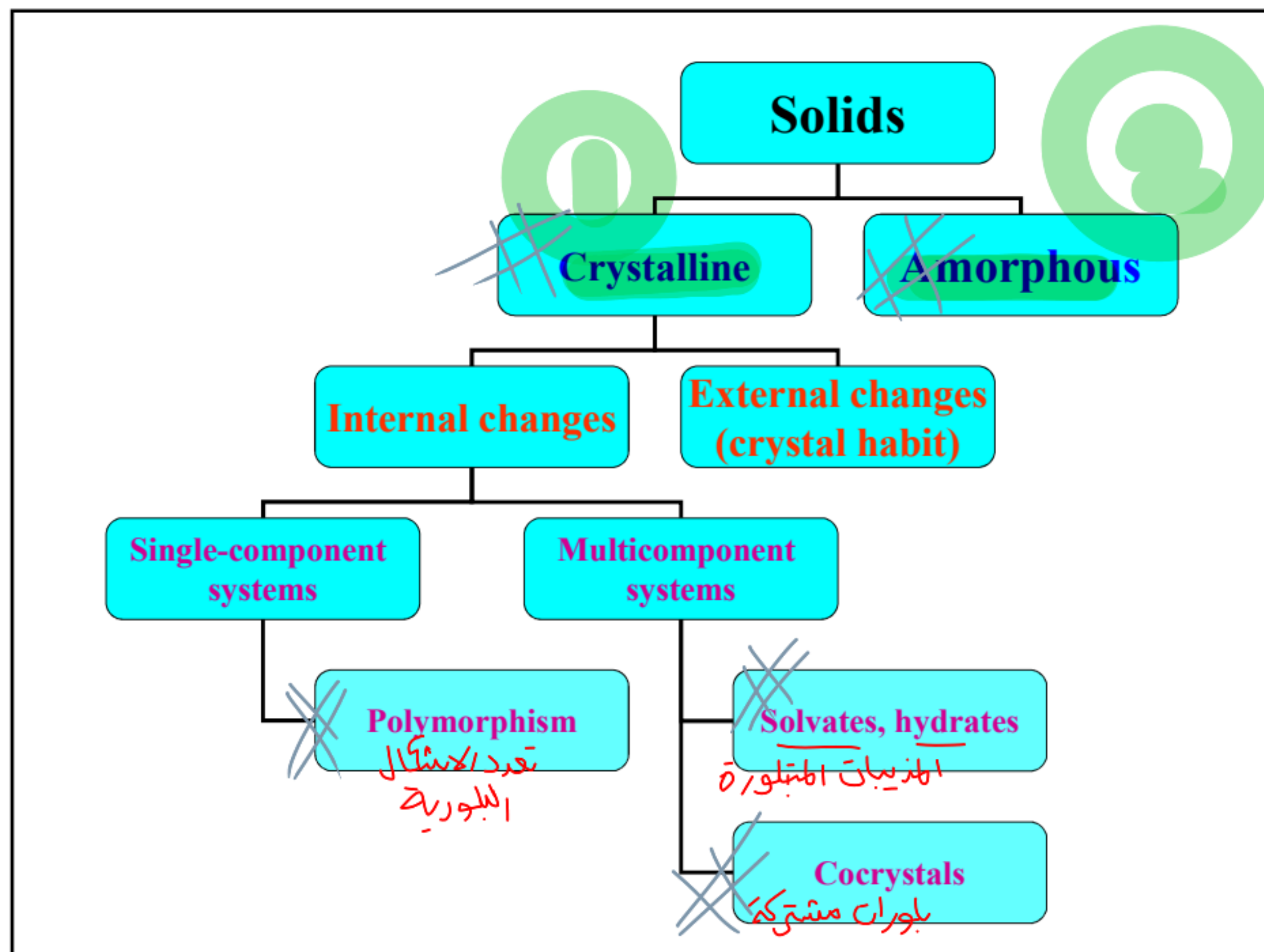
في alcohol و water ✓

Co solvent
المذيبات المشتركة

ex
alcohol
propylene glycol

Crystallization

- The processes by which a crystal forms are called nucleation and growth.
تنوية ونمو
- Nucleation is the formation of a small mass on to which a crystal can grow.
Nucleus formation
- Growth is the addition of more solute molecules to the nucleation site.
- In order to achieve nucleation and growth it is necessary to have a supersaturated solution.
*

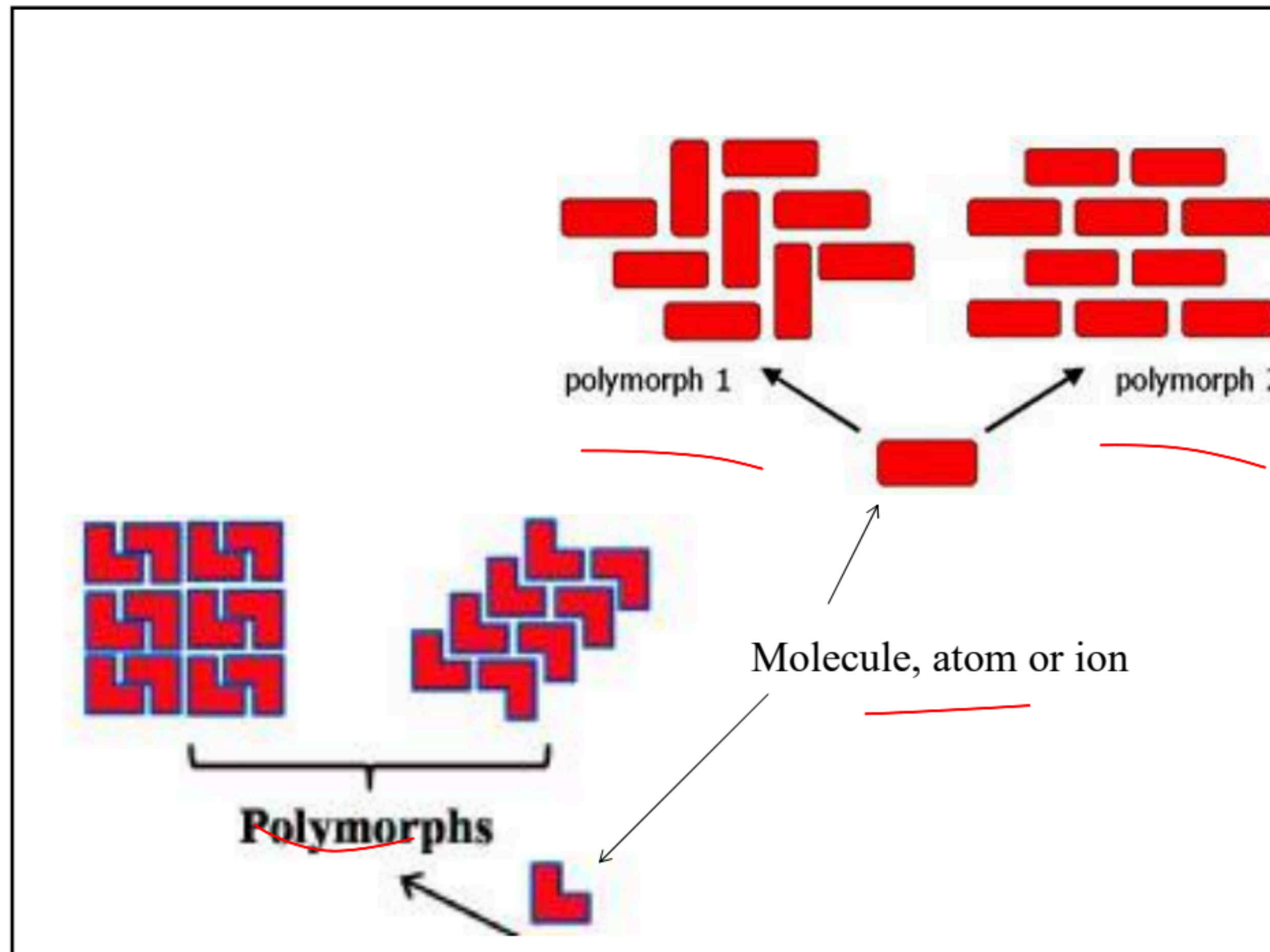


التركيب الكيميائي ثابت

Polymorphism

نظام ترتيب

- The ability of material to exist in more than one packing pattern (leading to crystals with different internal structure = different crystal lattice) is termed polymorphism
- Number of polymorphs ≥ 2
- If the crystallization conditions are changed, it is possible that the molecules may start to form crystals with a different packing pattern from that which occurred with the original conditions.
- The change in condition could be :
 - A different solvent
 - Change in the stirring
 - Different cooling conditions
 - Different impurities in the crystallization liquid



Polymorphism

- Many drugs and excipients exhibit polymorphism.
- Different polymorphs have different physical properties such as: true density, melting point, apparent solubility, dissolution rate, hardness, hygroscopicity
- For a compound that exhibits polymorphism, only one of the forms will be the most thermodynamically favorable (stable) at room temperature and the other(s) is/are termed metastable.
- Transformation of the metastable polymorph(s) to the stable one may occur and may be catalyzed by:
 - Energy (heating, milling)
 - Presence of solvent

MP → solid
BP → Liquids

Physical properties of pharmaceutical significance that may be affected by polymorphism

Physical property	Examples on pharmaceutical importance
Melting point	Suppository base (Theobroma oil)
Apparent solubility	Poorly soluble drugs
Dissolution rate	Poorly soluble drugs
Hardness	Milling, Tableting (paracetamol)
Hygroscopicity	Chemical stability
Rates of solid state reactions	Chemical stability
Habit (i.e., shape)	Powder flow, mixing

Polymorphism

الانفصاف العلامة

- In general there will be the following correlation between the melting point of different polymorphs and their dissolution rate:

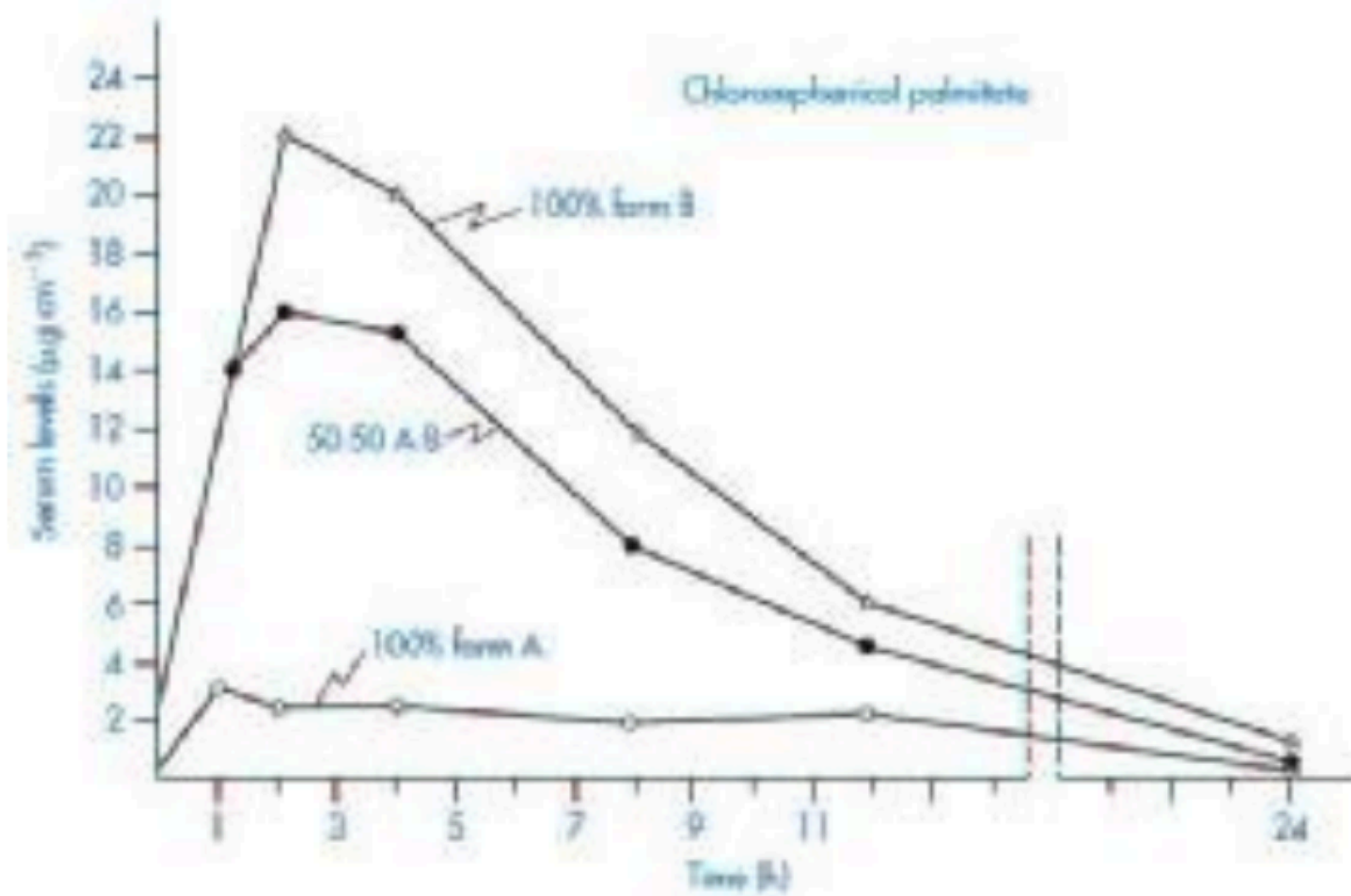
الذوبان

High melting point = strong lattice = hard to remove molecules = low dissolution rate (and vice versa)

- The stable form has the highest melting point → slowest dissolution.
- When a metastable polymorphic form is dissolved it can give a greater amount of material in solution than the saturated solution. These supersaturated solutions will eventually return to the equilibrium solubility due to the precipitation of stable crystal form.

Polymorphism and bioavailability

- Many drugs are hydrophobic and have limited aqueous solubility resulting in only a small percentage of the administered drug actually being available to the patient (low bioavailability).
- Importance of polymorphism in bioavailability is related to different solubility and dissolution rate for different polymorphs, which might be significant (e.g. chloramphenicol palmitate).



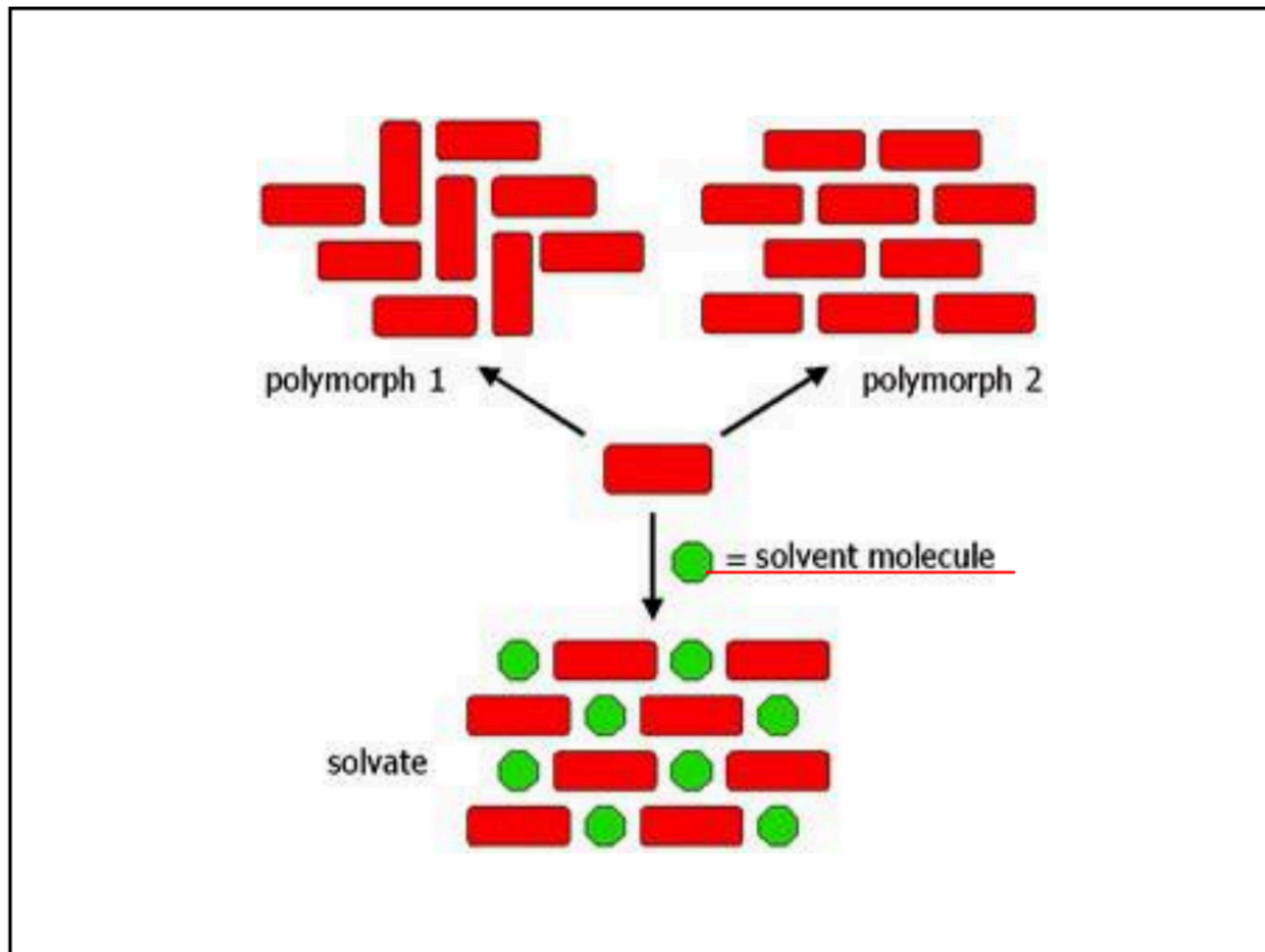
Comparison of serum levels ($\mu\text{g cm}^{-3}$) obtained with suspensions of chloramphenicol palmitate after oral administration of a dose equivalent to 1.5 g of chloramphenicol.

ملاحظة: تسمى
Pseudopolymorphs
أشياء تعدد
لأنها (الأشكال
تختلف بسبب وجود
جزيئات المذيب
داخل البلورة، وليس
بسبب اختلاف
ترتيب الجزيئات
فقط.

Hydrates and solvates (pseudopolymorphs)

- Entrapment of molecules of the solvent within the crystal lattice in a stoichiometric ratio leads to solvates. If the solvent is water they are termed hydrates.
احتجاز نسبة متكررة الأشكال البلورية
- It is possible for a material to have many different levels of hydrate. *Mono / Di / Tri*
نسبة جزيء مذيب
- In general it is undesirable to use solvates for pharmaceuticals because the presence of retained organic solvents would be regarded as unnecessary impurity in the product.

يُعتبر المذيب الباقي داخل البلورة impurity



Hydrates and solvates (pseudopolymorphs)

- Hydrates often have very different properties from the anhydrous form in the same way as two different polymorphs have different properties from each other. *Melting | dissolution rate*
- It is possible that the hydrates have either faster or slower dissolution rate than anhydrous form. The most common situation is that hydrates have slower dissolution than anhydrous.

↓
slow

Table 1.4 Intrinsic dissolution rates of the crystal forms of oxyphenbutazone^a

Sample	Intrinsic dissolution rate ^b ($\mu\text{g min}^{-1} \text{cm}^{-2}$)
Solvate C	21.05 $\pm$ 0.02
Solvate B	18.54 $\pm$ 0.47
Anhydrate	14.91 $\pm$ 0.47
Hemihydrate	17.01 $\pm$ 0.78
Monohydrate	9.13 $\pm$ 0.23

^a Reproduced from A. P. Lotter and J. G. van der Walt, *J. Pharm. Sci.*, 77, 1047 (1988).
^b Mean $\pm$ range of uncertainty of two determinations.

کی چیز درای
مقایسه 2 و 1

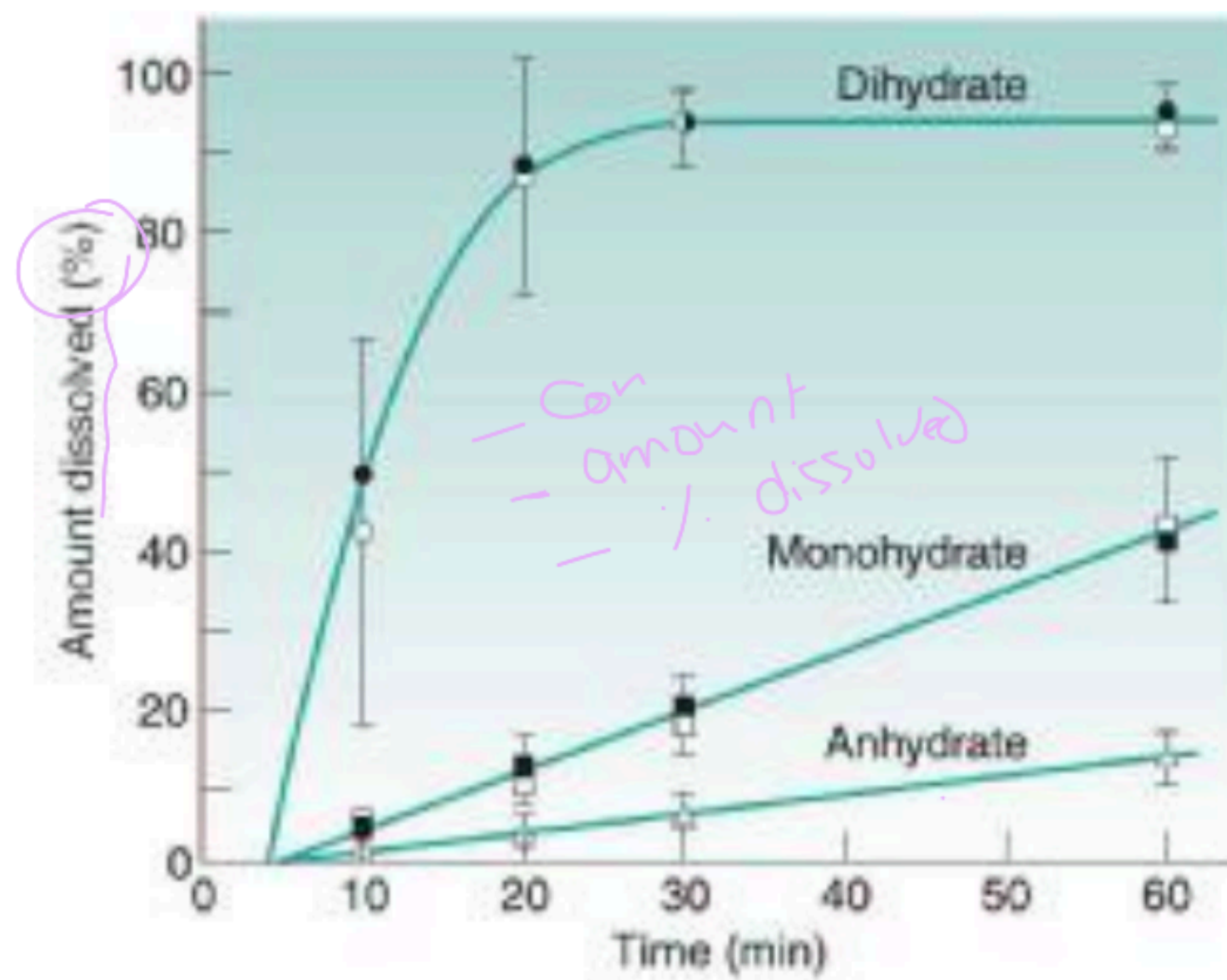
20H₂O

کد جزئی

در مقابل جزئی



Serum levels ($\mu\text{g cm}^{-3}$) obtained after oral administration of a suspension containing 250 mg ampicillin as the anhydrate and as the trihydrate.



The dissolution behaviour for erythromycin as the anhydrate, monohydrate and dihydrate, showing a progressively faster dissolution rate as the level of hydrate is increased. Adapted from Allen et al., 1978

Dehydration/Desolvation

- Hydrates and solvates are less stable at higher temperatures.
- Indeed, heating has been routinely applied to remove crystallization solvents that are incorporated into the lattice, i.e., desolvation.

حالة
لإزالة المذيب

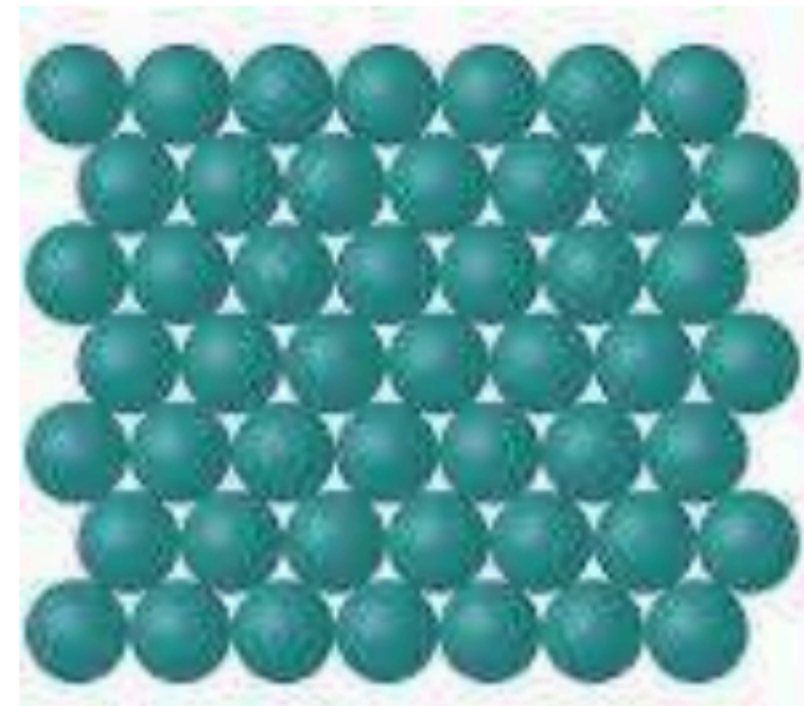
intermolecular forces ←
قوى الجذب المتبادلة

2

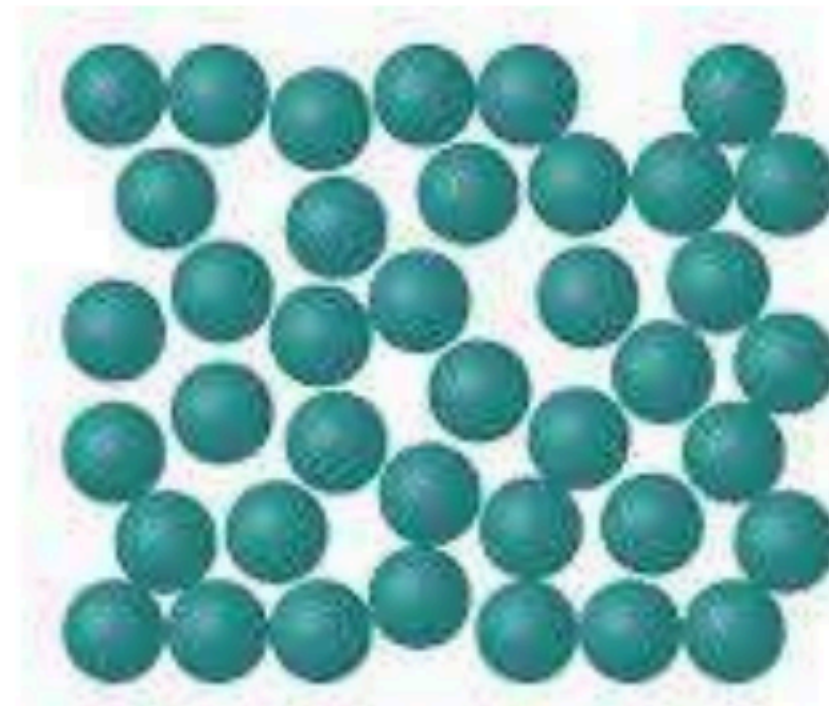
The amorphous state

غير بلورية
غير منتظمة
الترتيب

- When a material is in the solid state but the molecules are not packed in a repeating long-range ordered fashion, it is said to be amorphous.
- Amorphous state may exhibit some degree of molecular arrangement, but no long-range ordered molecules.



Crystalline



Amorphous

هنا
سأحي
بأن
الأمورفوس

Cocrystals

- Co-crystals can be defined as crystalline complexes of two or more neutral molecular constituents bound together in the crystal lattice through noncovalent interactions (primarily hydrogen bonding).
- The distinction between cocrystals and crystalline solvates is that a cocrystal comprises an API plus a pharmaceutically acceptable cocrystal former that is a solid at room temperature, rather than a liquid (as in a solvate)

Cocrystal	Solvate
API + مادة صلبة	API + مذيب سائل
Solid + Solid	Solid + Liquid
لا يحتوي مذيب عضوي محتجز	يحتوي مذيب داخل البلورة
أكثر قبولاً دوائياً	أقل تفضيلاً

Pharmaceutical cocrystals

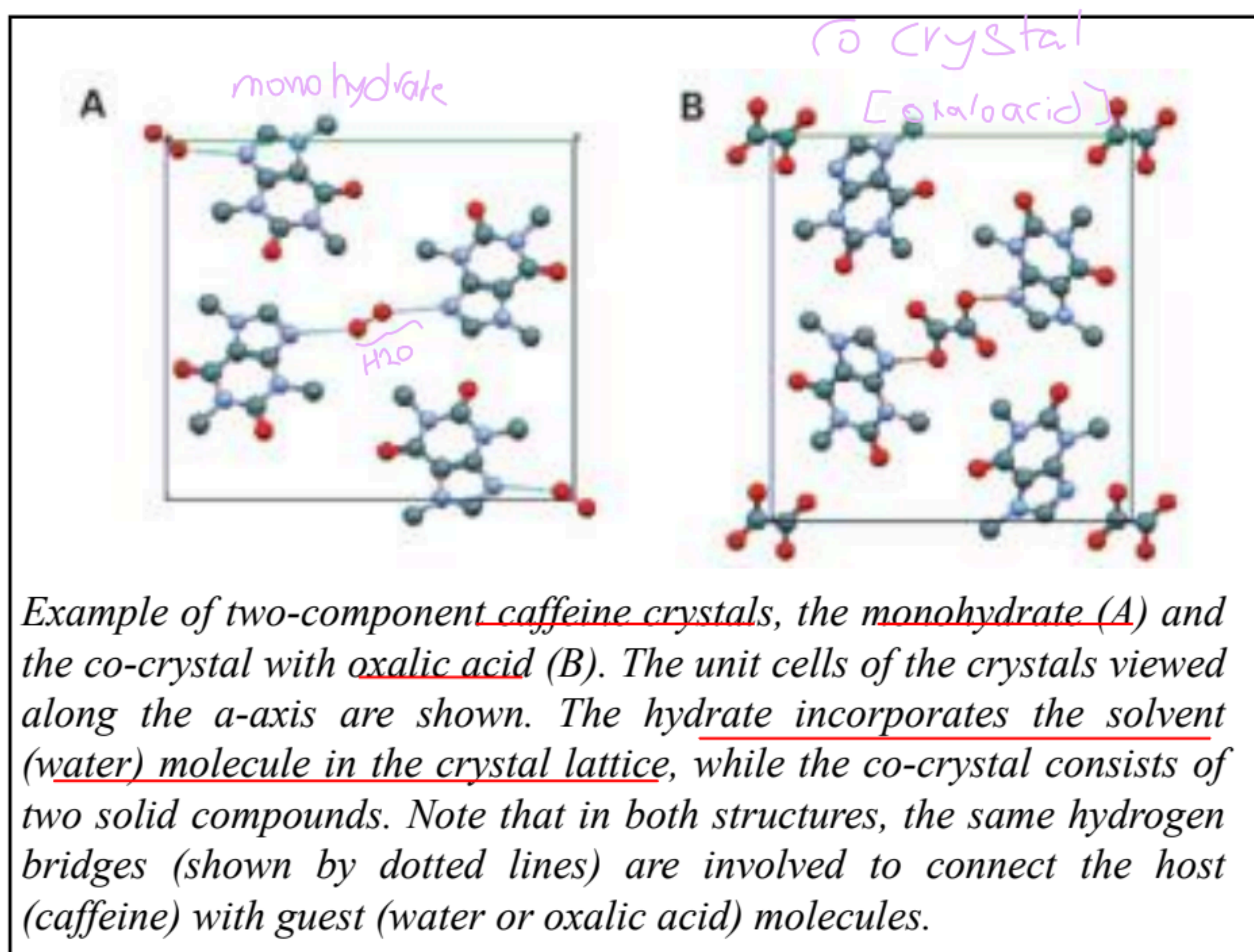
- The formation of pharmaceutical co-crystals involves incorporation of a given API with another pharmaceutically acceptable molecule (pharmaceutical excipients or other APIs) in the crystal lattice.
- The resulting multi-component crystalline phase will maintain the intrinsic activity of the parent API while possessing a distinct physicochemical profile.

دواء
API

مادة مساعدة

co crystal

بنشاط الدواء محفوظ



Pharmaceutical cocrystals

- Properties that relate to pharmaceutical performance and that can be controlled by cocrystal formation include

- ← melting point, -solubility,
- dissolution, -chemical stability,
- hygroscopicity, -mechanical properties,
- Bioavailability

Potential advantages of cocrystals:

- Improved solubility, dissolution rate and bioavailability
- Improved chemical and physical stability

↓ MP
للإجراءات والمراقبة
يأتي بتعليق ذوبان



Pharmaceutical cocrystals

Potential advantages of cocrystals:

Improved physical stability (inhibit moisture-induced phase-transformations)

The caffeine/oxalic acid co-crystals have been demonstrated to be superior to caffeine anhydrate in terms of physical stability to humidity

أكثر مقاومة للرطوبة

Improved chemical stability

Carbamazepine cocrystal formation inhibits photodegradation of carbamazepine by altering the molecular arrangements in the solid state and by preventing hydrate formation.

Changing the melting point of an API

Changing the melting point of an API provides advantages in pharmaceutical processes; for example when a melted state of a thermally labile API is desired during some processes such as hot melt extrusion

• صنع كوكالان
الافوار بسبب
الرطوبة

Hydrate	Solvate	Cocrystal
يحتوي ماء داخل البلورة	يحتوي مذيب عضوي داخل البلورة	API + مادة صلبة أخرى
Water	Organic solvent	Solid cofomer
Anhydrous	غير مفضل دوائيا	يحسن خواص الدواء
قد يتعرض لـ Dehydration	قد يتعرض لـ Desolvation	يزيد الدوائية والبيات والوافر الحيوي

حالة غير بلورية

The amorphous state

- Polymeric materials have molecules that are so large and flexible that it is not possible for them to align perfectly to form crystals.
- For these materials it will be usual to have ordered regions within the structure surrounded by disorder, so they are described as semicrystalline.
- Amorphous form in low molecular weight material may be produced by:

- Rapid solidification of the melt
- Spray or Freeze drying
- Milling of crystalline material

Amorphous: طرق تكوين

التبريد السريع للمصهور

التجفيف بالرش

التجفيف بالتجميد

طحن البلورات

The amorphous state

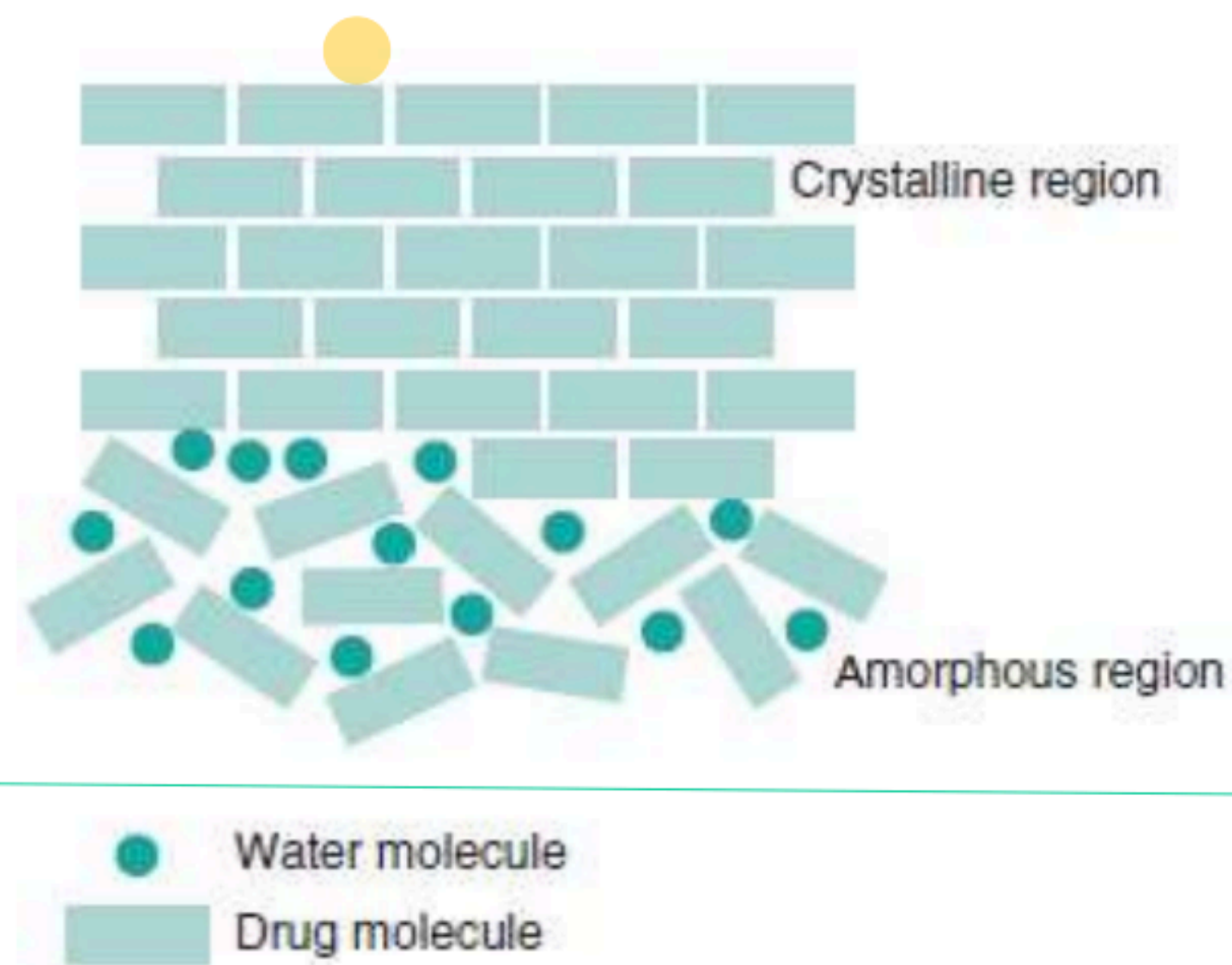
- Amorphous solids have different properties from the crystalline form of the same material:
 - They tend to flow when subjected to sufficient pressure over a period of time
 - They do not have definite melting point.
 - They have a characteristic temperature called glass transition temperature (T_g). If the sample is stored below the T_g the amorphous form will be brittle and is described as the glassy state. If the sample is above its T_g it becomes rubbery.
 - They have higher solubility and bioavailability.
 - They have the ability to absorb water in much larger quantities than crystalline materials.
 - They have low chemical and physical stability (overtime, amorphous solid may transform to the more stable crystalline state).

Important

القوى
الضعف

تفكيك

و بالتالي تحول تفكك



The disruption of a crystal giving the possibility for water vapor absorption in the amorphous region

Degree of crystallinity

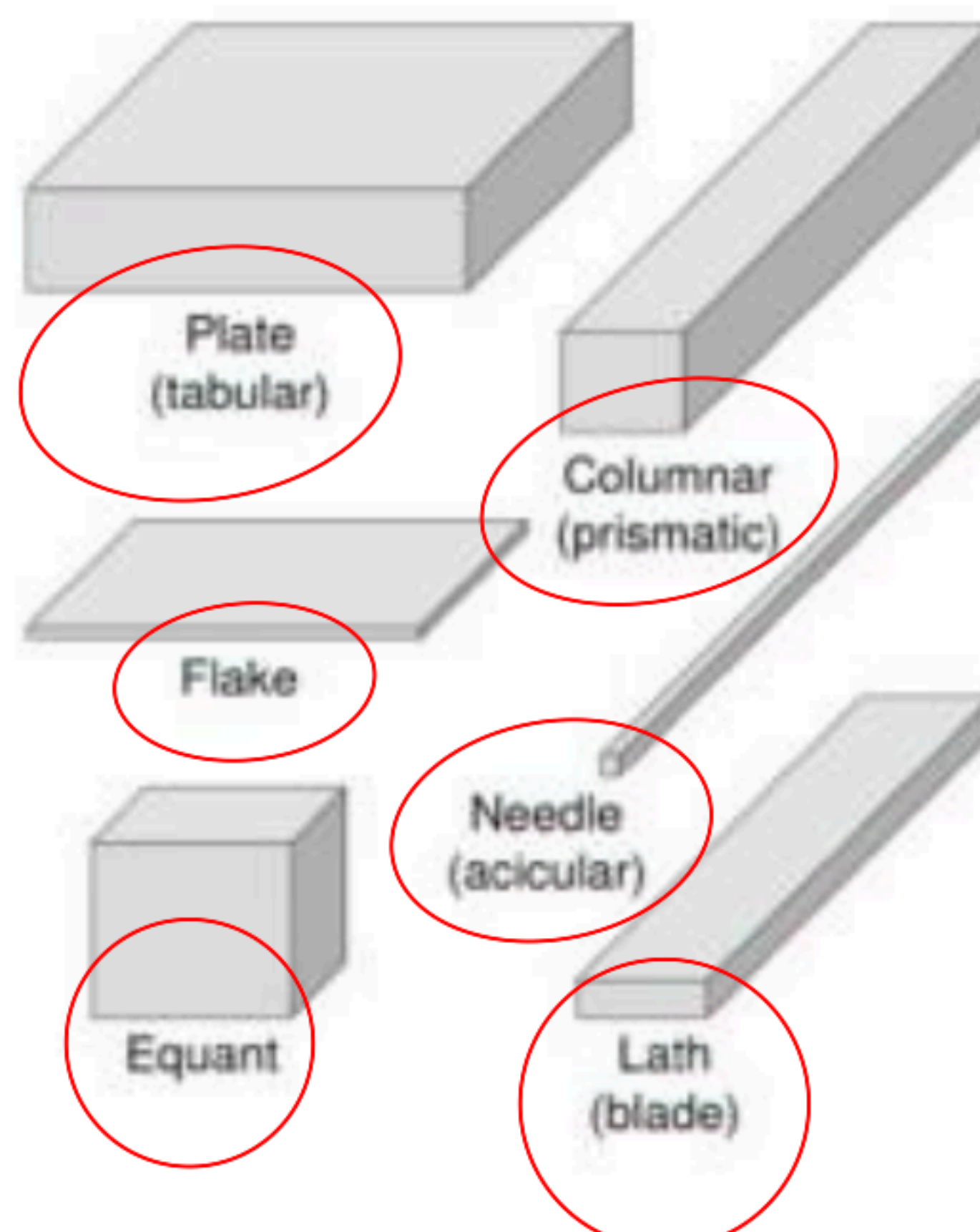
- The crystalline state characterized by perfectly ordered crystal lattice and amorphous state characterized by a disordered lattice represent two extremes and intermediate states are possible.
- The term *degree of crystallinity* is useful in attempts to quantify these intermediate states of lattice order
- The *degree of crystallinity* has a big influence on physical properties of materials like hardness, density...

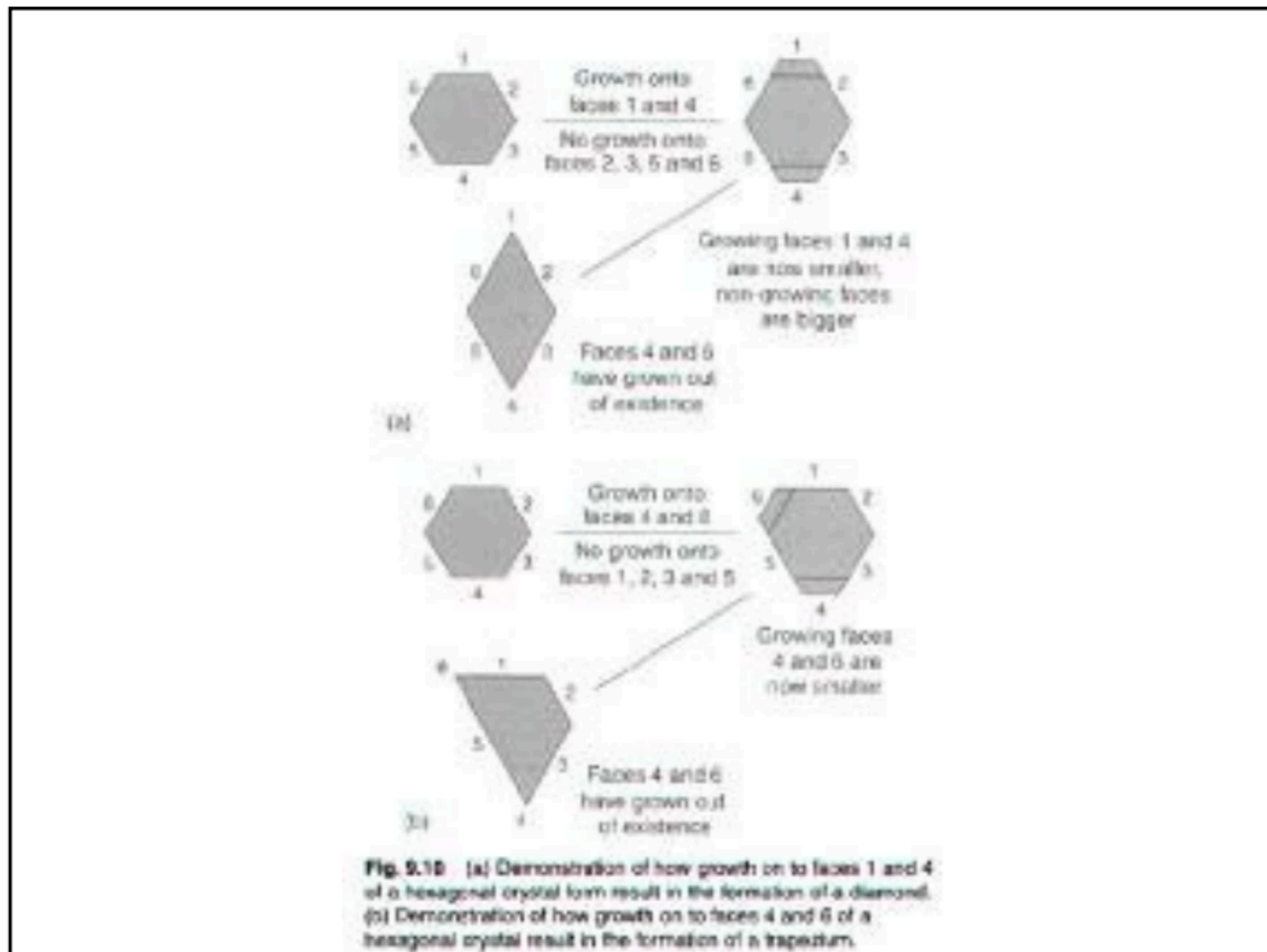
قد تكون المادة
بلورية بالكامل
غير بلورية بالكامل
أو بينهما

Crystal habit

- The external shape of crystal is termed crystal habit.
- Different crystal habits result from different growth rates of different crystal faces.
- The largest face is always the slowest growing.

The six basic crystal shapes

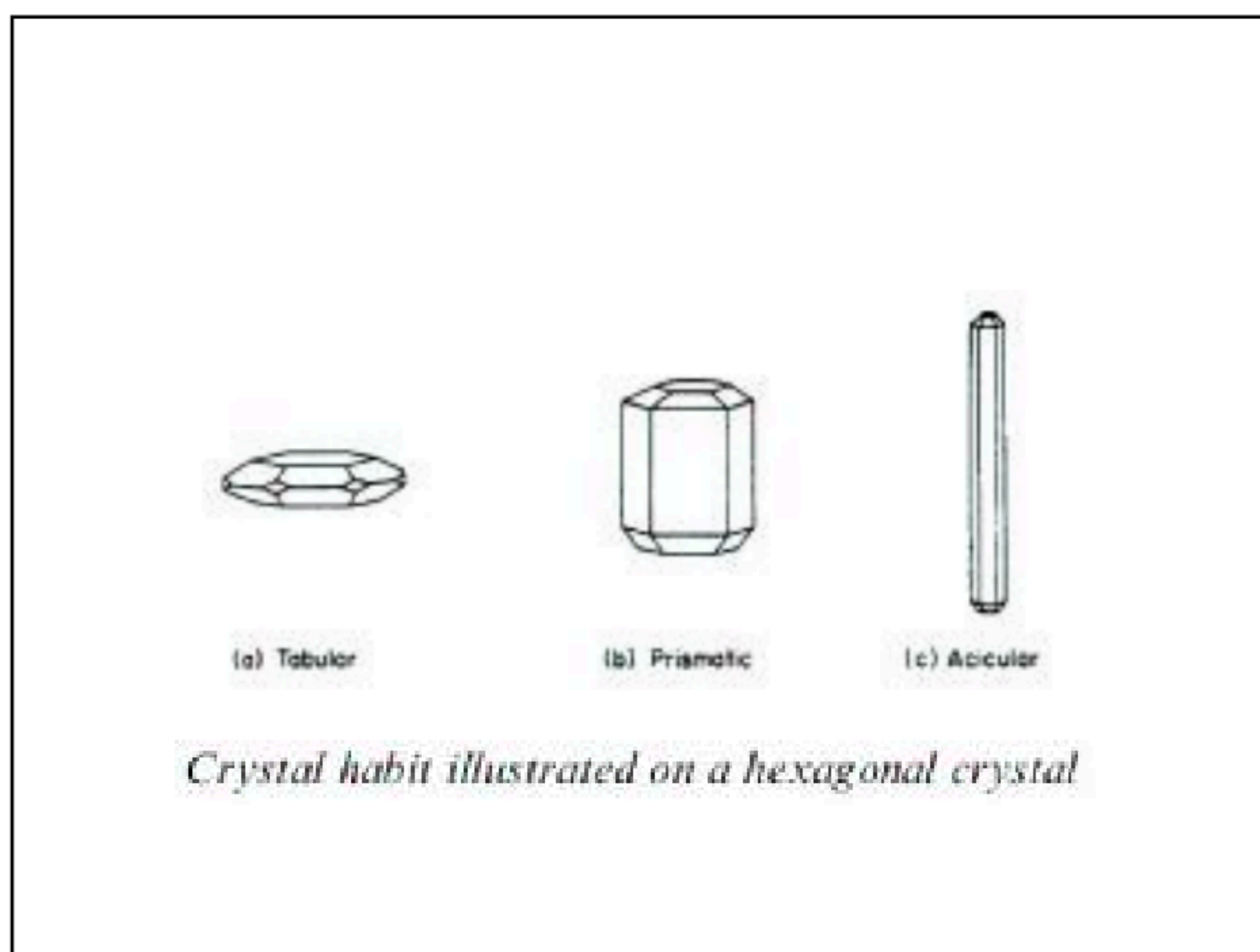
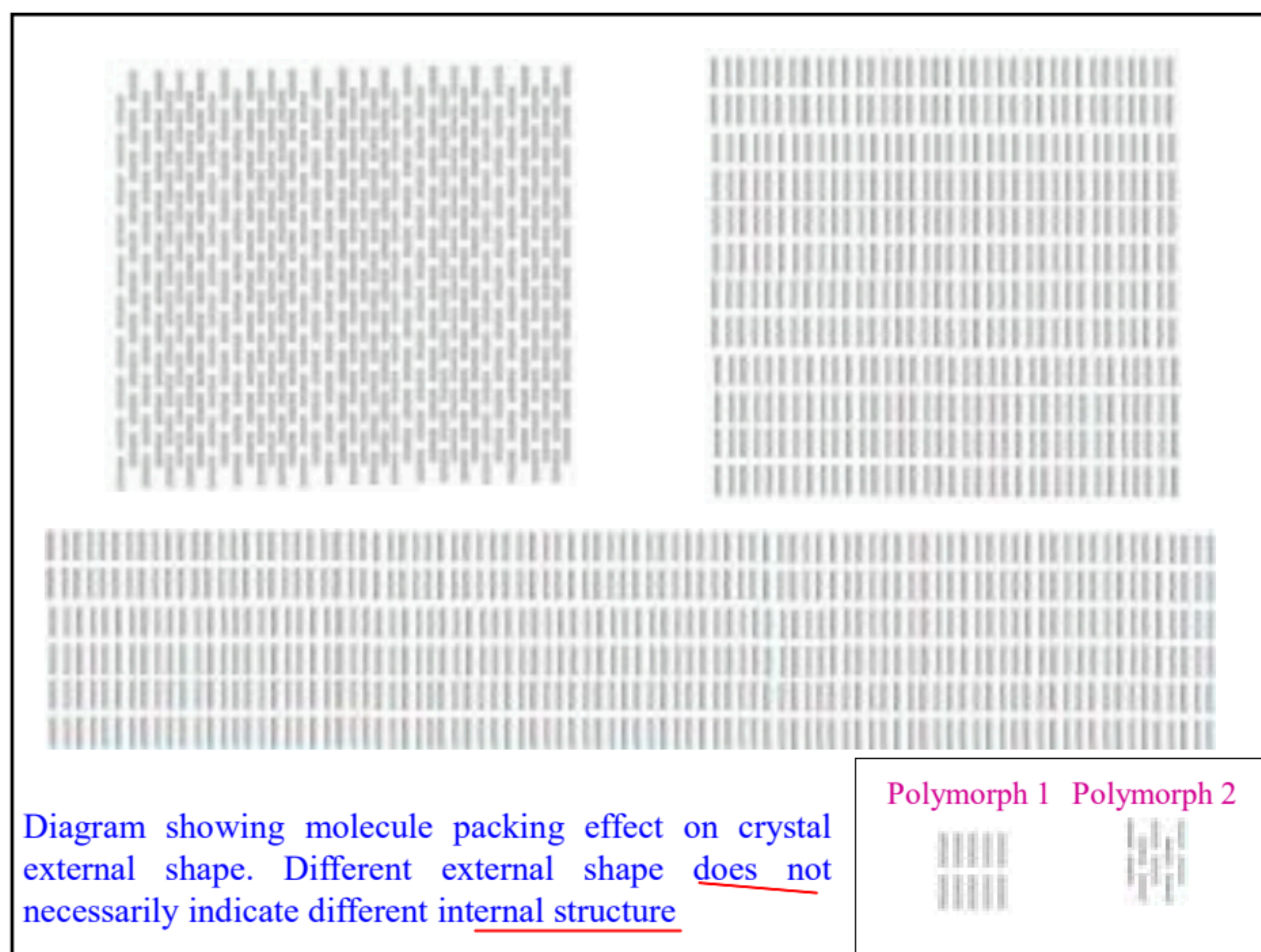




Crystal habit

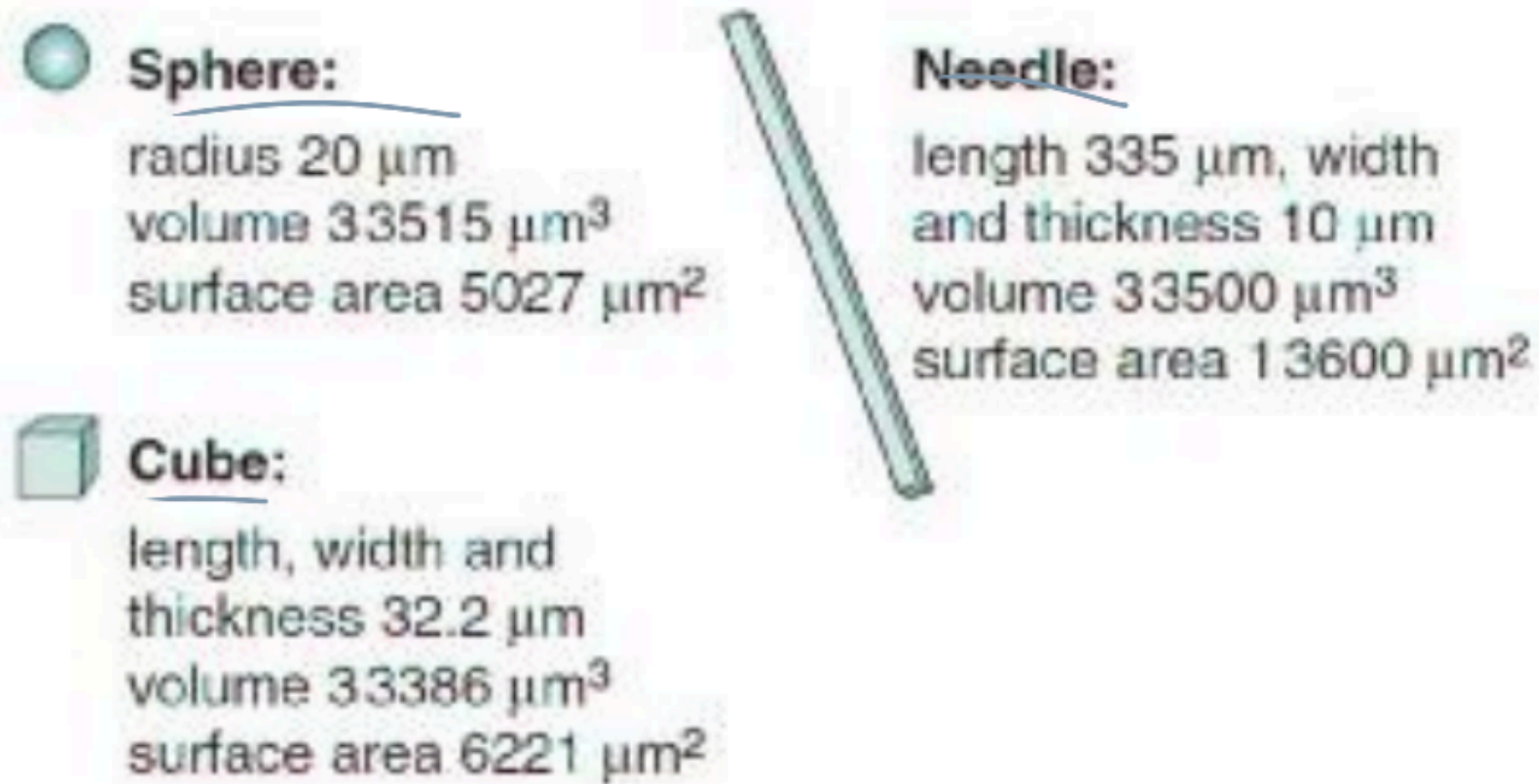
- Changes in internal structure usually give different habits.
- However, it is also possible to change the external shape for the same crystal packing by changing the crystallization conditions.

Solvent
Temp.
Rate of cooling

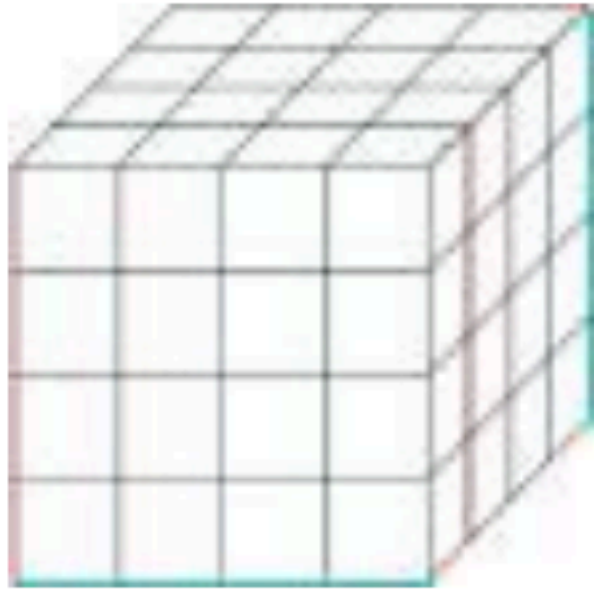


Crystal habit

- Crystal habit can alter the properties of drug and excipients such as:
 - Powder flow
 - Compression behavior
 - Specific surface area (total surface area of a material per unit of mass or volume)
 - Dissolution rate
 - Sedimentation and caking of suspension
- Crystal engineering: Crystal habits may be changed by manipulating the growth of different faces to obtain crystals with suitable properties.



The relative surface areas of a sphere, cube and needle that have similar volumes of material



Volume = $4 \times 4 \times 4 = 64 \mu\text{m}^3$
Area = $4 \times 4 \times 6 = 96 \mu\text{m}^2$
Specific surface area = $1.5 \mu\text{m}^{-1}$



Volume = $2 \times 2 \times 16 = 64 \mu\text{m}^3$
Area = $(2 \times 16 \times 4) + (2 \times 2 \times 2) = 136 \mu\text{m}^2$
Specific surface area = $2.125 \mu\text{m}^{-1}$

1- Adsorption
(الامتزاز)
تلتصق جزيئات البخار على سطح الجسيمات فقط.

لا تدخل إلى داخل المادة فقط.  Surface

2- Absorption
(الامتصاص)
تدخل جزيئات البخار إلى داخل المادة نفسها.

 Inside the bulk.

3- Hydrate / Solvate Formation

تدخل جزيئات الماء أو المذيب داخل الشبكة البلورية.

يتكون Hydrate أو Solvate كما درسنا سابقًا.

4- Deliquescence (التميع)

تمتص المادة كمية كبيرة من بخار الماء تذوب تدريجيًا في الماء الذي امتصته.

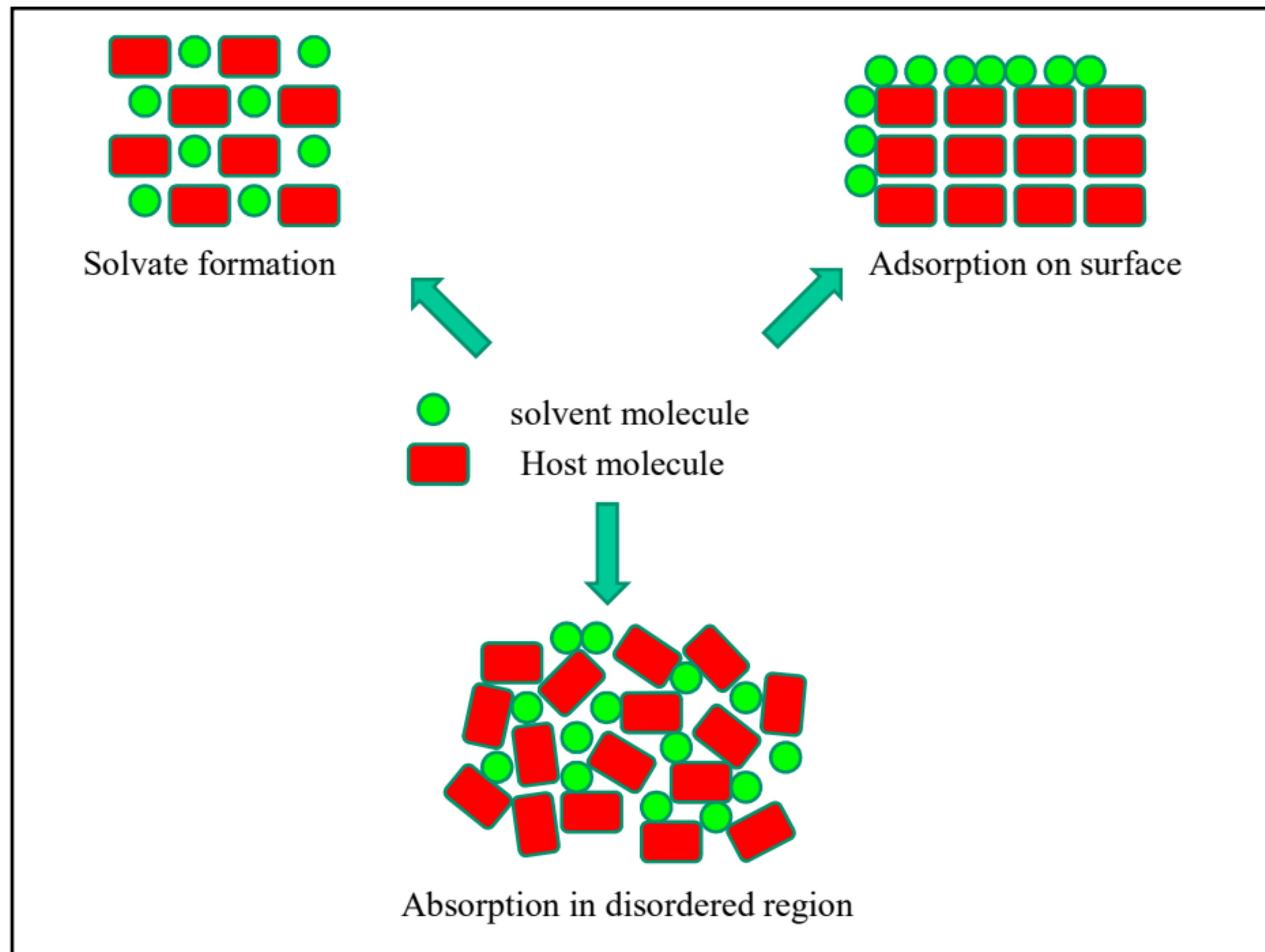
تتحول إلى محلول سائل.

(امتصاص الأبخرة بواسطة المواد الصلبة)

Vapor sorption by solids

- When a powder is exposed to a vapor or gas, the interaction will take one of the following forms:
 - Adsorption of vapor to the powder surface
 - Absorption into the bulk
 - Hydrate / solvate formation
 - Deliquescence
- Absorption into the bulk can occur if the sample is amorphous, whereas the interaction will be limited to adsorption if the powder is crystalline.

امتزاز
امتصاص
تميع



Importance of particle size

Particle size influence

- Drug dissolution

Important for poorly-soluble drugs (e.g. griseofulvin, tolbutamide, spironolactone, indomethacin and nifedipine)

- Mixing of powders (content uniformity for potent drugs, segregation)

- Hygroscopicity

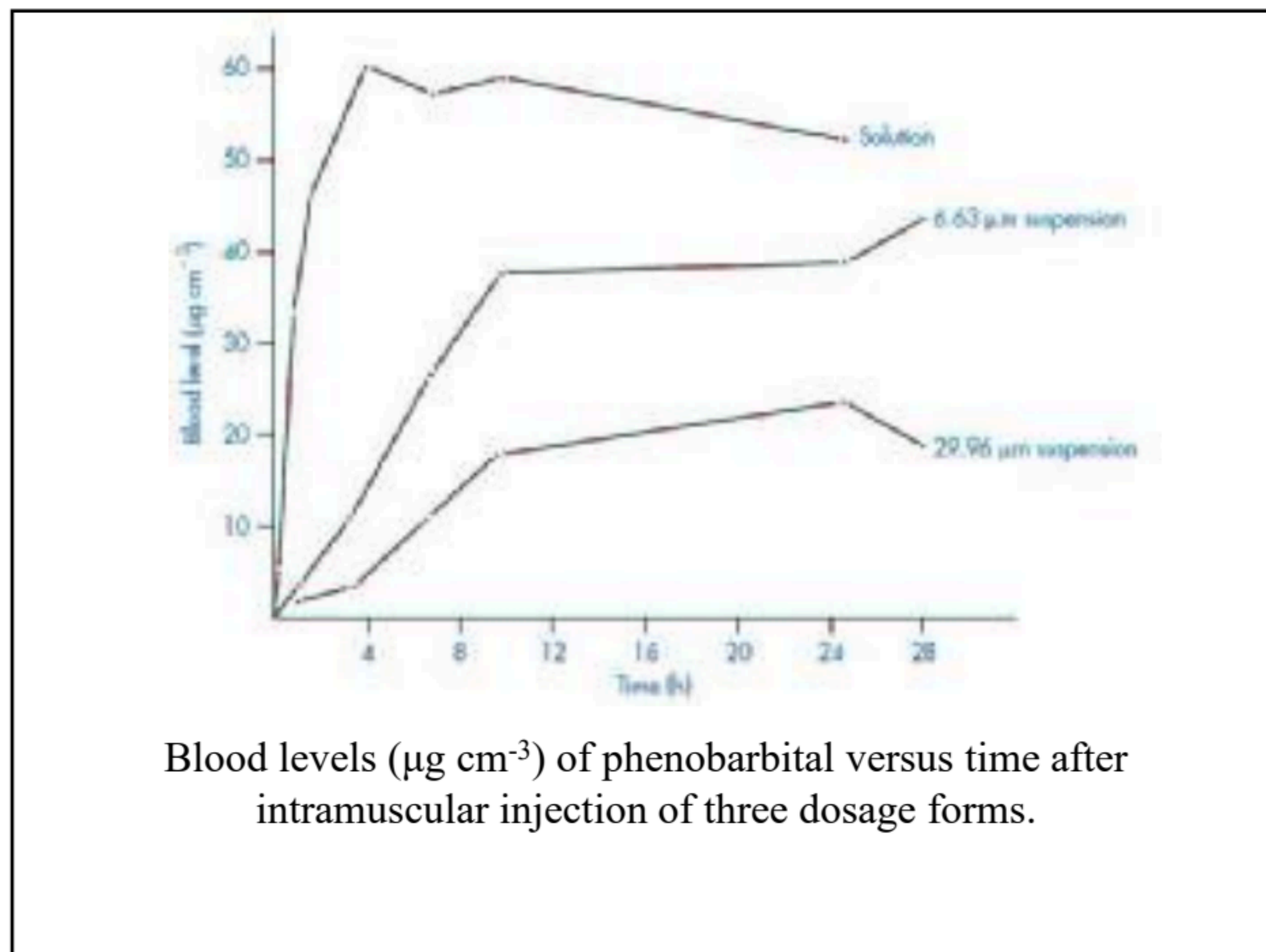
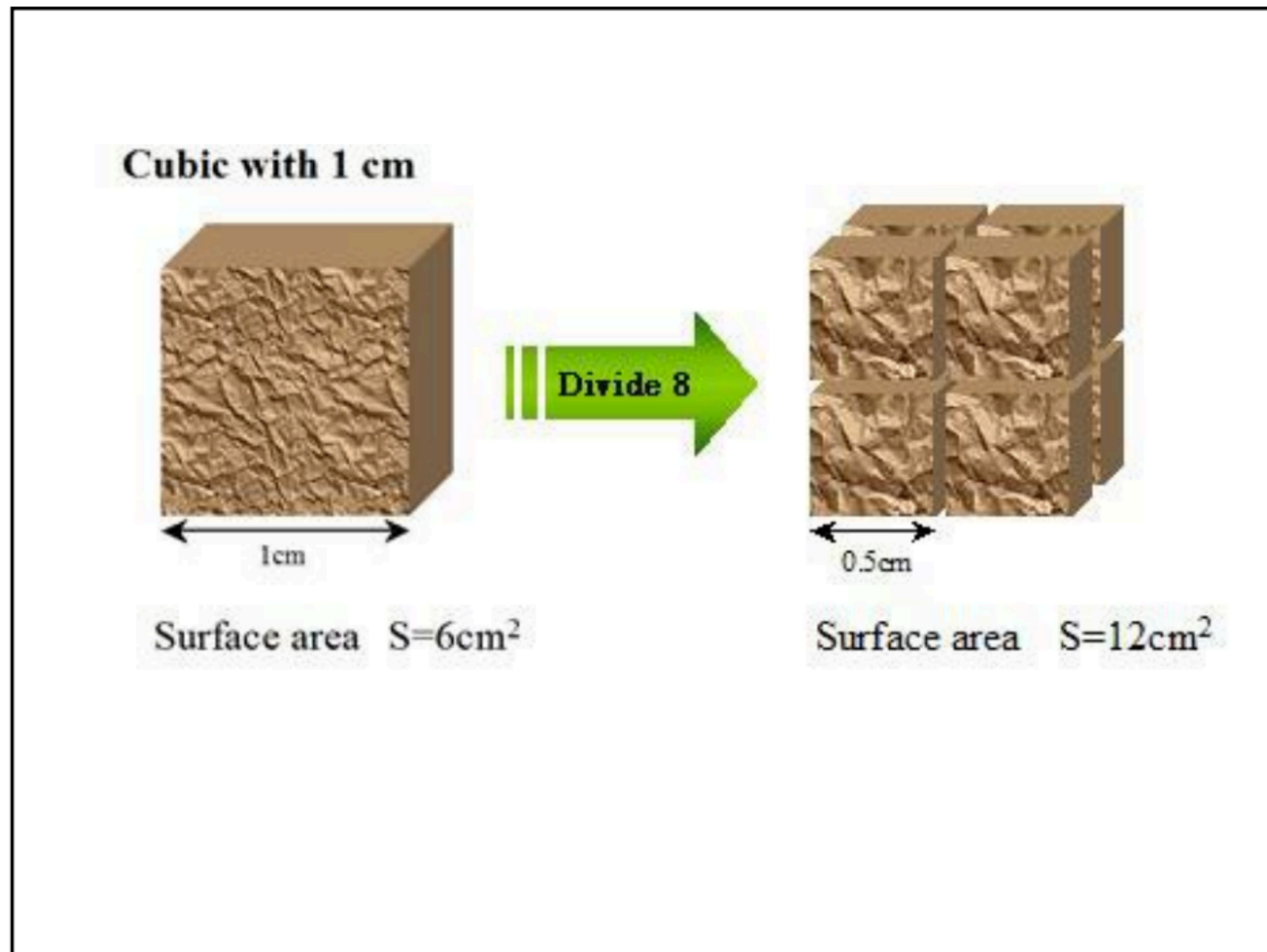
↓ PS ↑ Hygroscopicity

القوة
الدوية
كانس

انقسام
الجسيمات

↓ PS

↑ Dissolution



1- معدل الترسيب، القوام، الطعم، والخواص الانسيابية (Rheology).

2 — سهولة السحب بالحقنة، سهولة الحقن، والتحرر

Importance of particle size

Particle size influence

- The properties and behavior of various dosage forms:

- 1 - suspensions: sedimentation rate, texture, taste, rheology
- 2 - parenteral suspensions: syringeability, injectability and sustained release.
- 3 - ophthalmic suspensions: irritation of the eye surface (small particle size is used)
- 4 - Dry powder inhalers: The position and retention of particles in the bronchopulmonary tract
- 5 - topical formulation: grittiness (powder must be impalpable)

غير محسوس

حسونة

معدل ترسيب