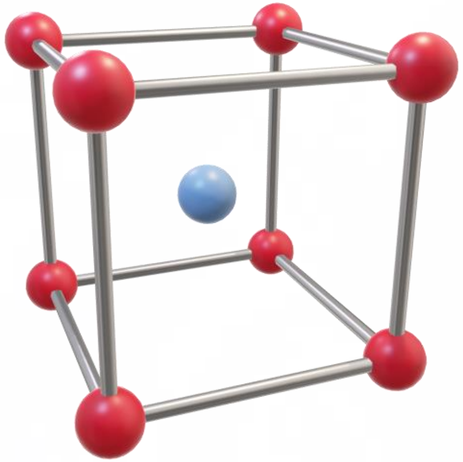
Physical Pharmacy

The Solid State



Contents

In this lecture you will learn:

- Solids and their Characteristics

- Types of Solids
  A. Amorphous solids
  B. Crystalline solids

- Crystalline Solids
  A. Structure
  B. Shape
  C. Polymorphism :Definition-Types-Factors affecting polymorphism-Application in Pharmacy
  D. Psueodopolymrophism

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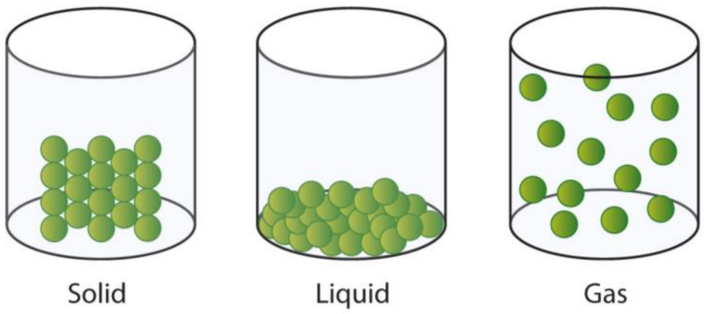
Solids and their Characteristics

- The solid state represents the state of matter in which the constituent particles (**atoms, ions or molecules**) are closely packed and are held together by strong intermolecular forces of attraction.

- The arrangement of the constituents particles of solids may be regular or irregular.



- The strong forces of attraction in the structural units of solids do not allow any type of motion except that particles only vibrate about their mean positions.

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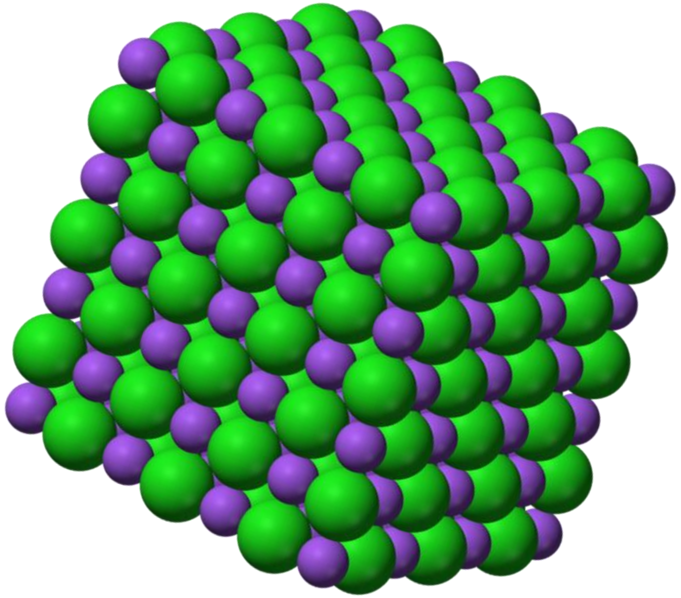
Solids and their Characteristics

The main characteristics of the solids are:

- **Rigidity and definite shape:**

A. Solids are rigid and have definite shape and volume, and will not deform or flow without limit like a liquid or gas.

B. Atoms in a solid are not mobile; although the atom is not stationary but instead oscillates rapidly about a fixed point (the higher the temperature, the faster it oscillates).



- **Low compressibility:**

A. Solids have strong intermolecular forces and very little kinetic energy.

B. They have extremely low compressibility due to non-availability of vacant spaces.

Solids and their Characteristics

The main characteristics of the solids are:

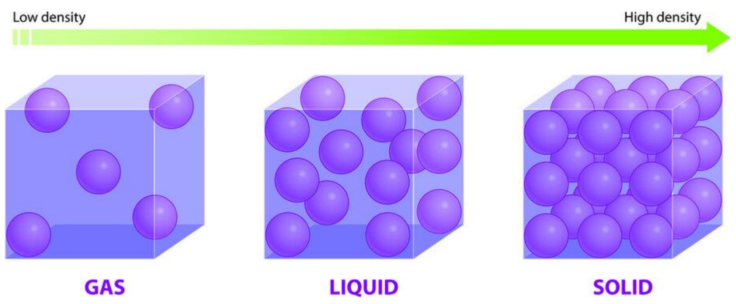
- **High density:**

A. They generally have high density due to close packing of the structural units.

- **Melting point:**

A. Generally, solids have definite melting points which depend on the magnitude of attractive forces between the particles.

B. On supplying sufficient energy to solids, the particles move away from their fixed positions,resulting into formation of liquid state.



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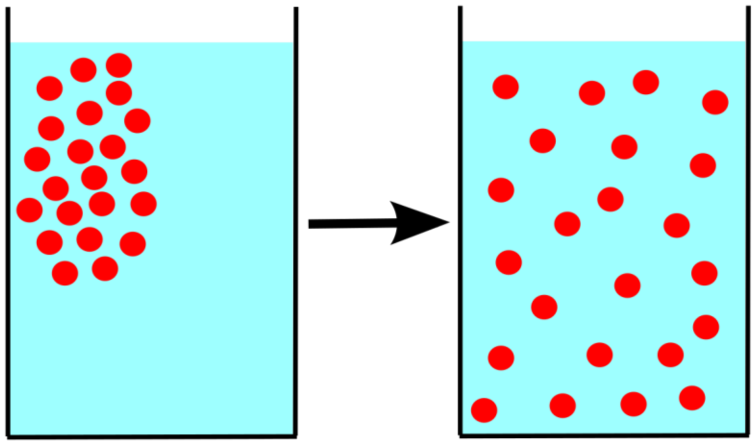
Solids and their Characteristics

The main characteristics of the solids are:

- **Diffusion:**

A. In solids, the particles either diffuse slowly or do not diffuse at all.



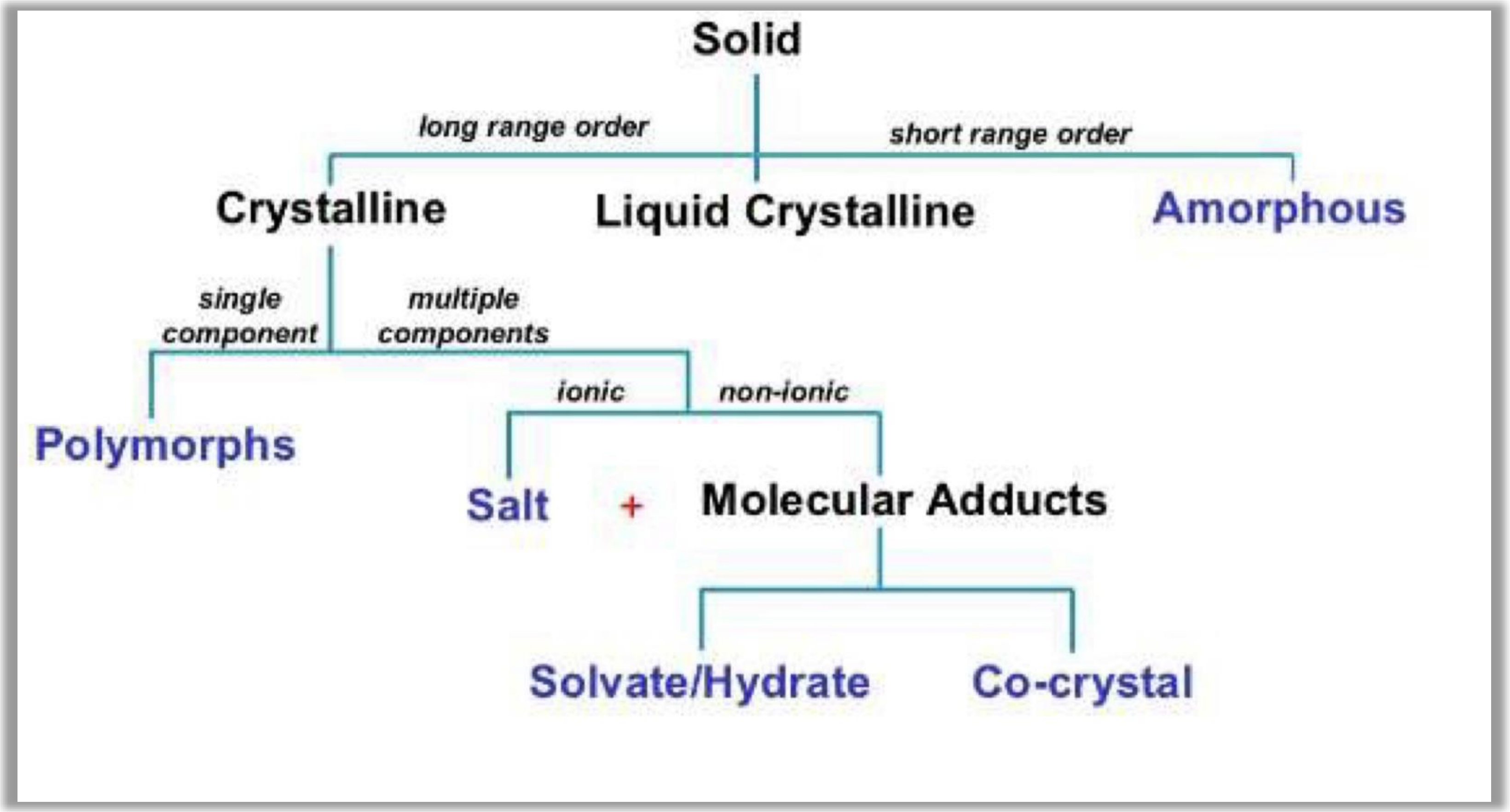
- **Vapour pressure:**

A. Vapour pressure of solids is much less than that of liquids at a given temperature.

B. Some particles near the solid surface may acquire sufficient energy to get converted into vapour state.

Solids and their Characteristics

Types of Solid Forms



Amorphous Solids

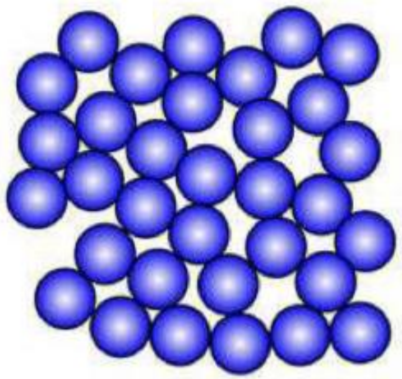
- **(Greek: a =without, morphe´ = shape) = non crystalline solids**

- Amorphous solids are solids in which the particles are arranged in completely random manner and are not organized in a definite lattice pattern.

- **Examples**: glass, rubber, plastics, wax, cotton candy, etc.

- Amorphous materials are “high-energy materials”.

Particles



Example: cotton candy

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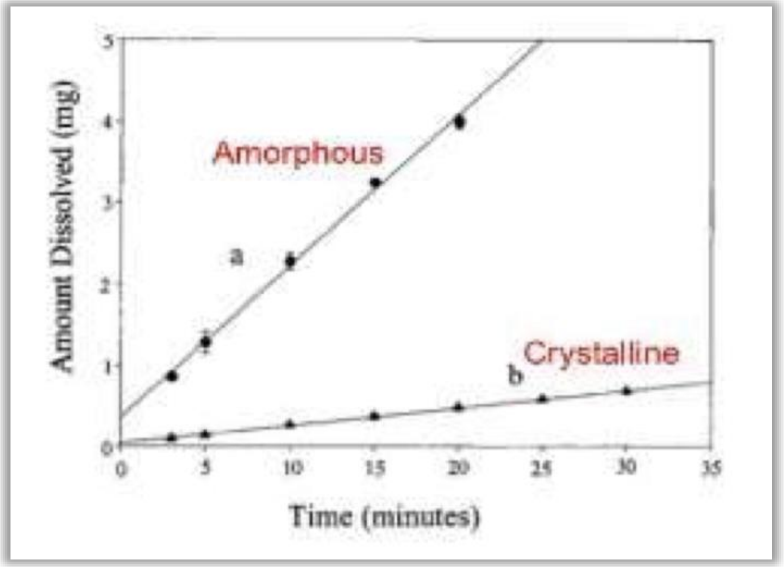
Amorphous Solids

- Therefore, they usually have appreciably higher solubilities and faster dissolution rates than their crystalline equivalents.

- Being in a “**thermodynamically** unstable state”, amorphous materials will change structure with time, first by relaxation and ultimately by crystallization.

- The benefits of formulating in an amorphous form must be set against the risk of change (**and hence reduction in performance**) upon storage.



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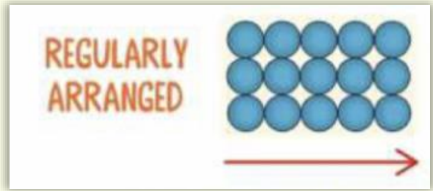
Amorphous Solids

Crystalline solids

- Regular arrangement of particles.



- Long order in arrangement of particles.
- They are called **True Solids.**

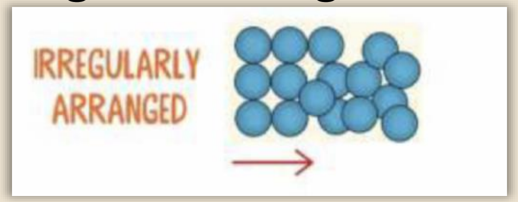
PERFECT SOLIDS

TRUE PROPERTIES
- Regular Arrangement
- Long Order

- Sharp Melting Point. < 5 °C

Amorphous solids

- Irregular arrangement

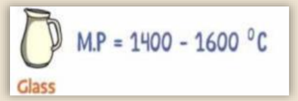


- Short order in arrangement of particles.
- **Pseudo Solids / Super Cooled Liquids**

IMPERFECT SOLIDS

FAKE PROPERTIESNO / ABILITY TO FLOW
- Arrangement No Long Order
- Over Time If Temperature Changes No Long Order

- Ranged Melting Point. > 5 °C



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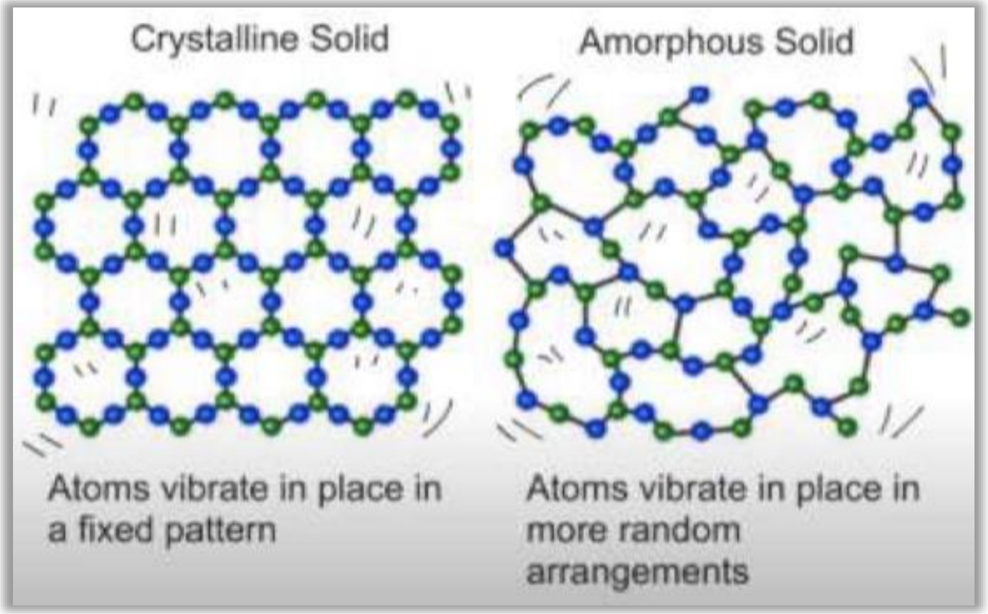
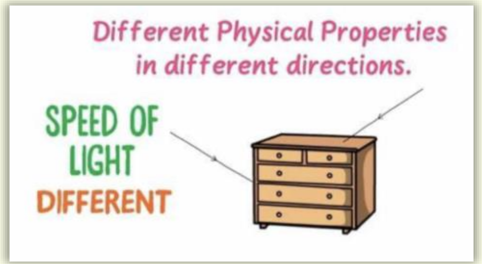
Amorphous Solids



Amorphous Solids

Crystalline solids

- Anisotropic in nature.



physical properties such as refractive index, electrical or thermal conductivity are different in different directions, within the crystal

- Have definite symmetry in shape such as cubic, tetragonal or hexagonal

Amorphous solids

- Isotropic in nature

- Do not have symmetry; hence, they do not have any definite geometrical shape

Amorphous Solids

Crystalline solids	Amorphous solids
Rigid and their shape is not distorted by mild deforming forces	Not rigid and their shape is distorted by compression forces
They give a clean cut	They give irregular cut
They have definite value of heat of fusion	They have no definite value of heat of fusion
Cooling curves have two wo breaks 'a' and 'b' which correspond to the beginning and end of process of crystallization.	Cooling curve for an amorphous substance is smooth

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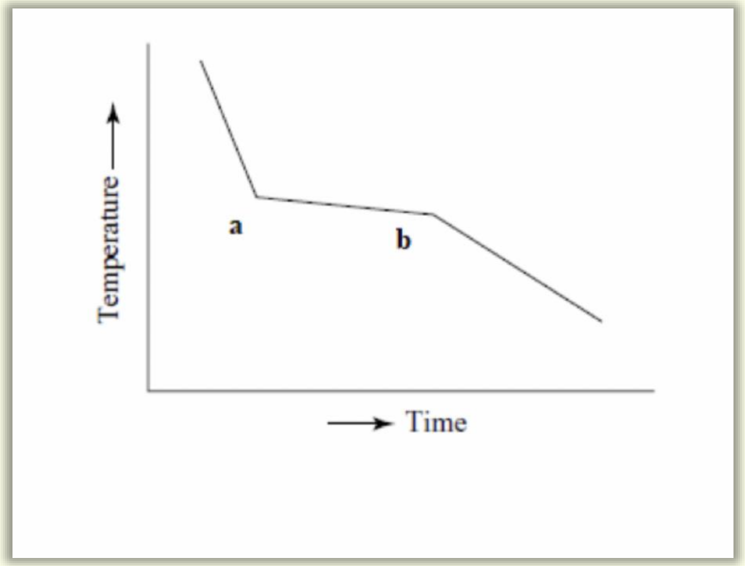
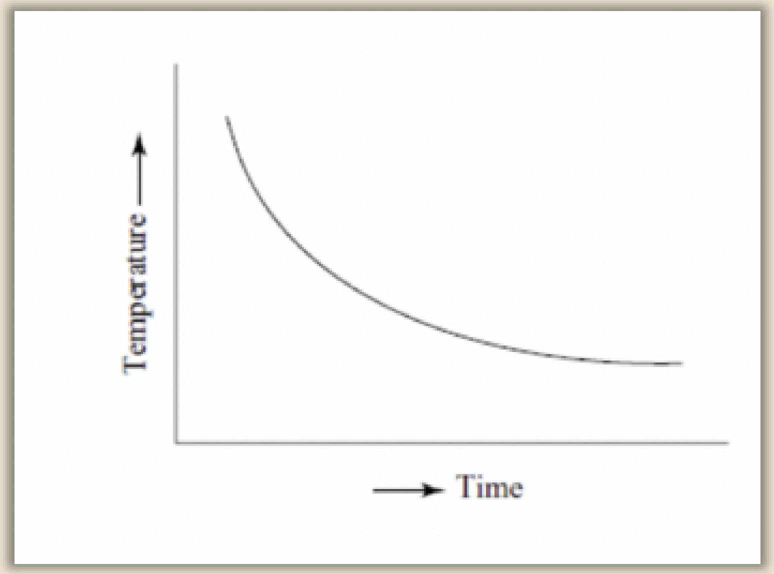
Amorphous Solids

Crystalline solids



Amorphous solids

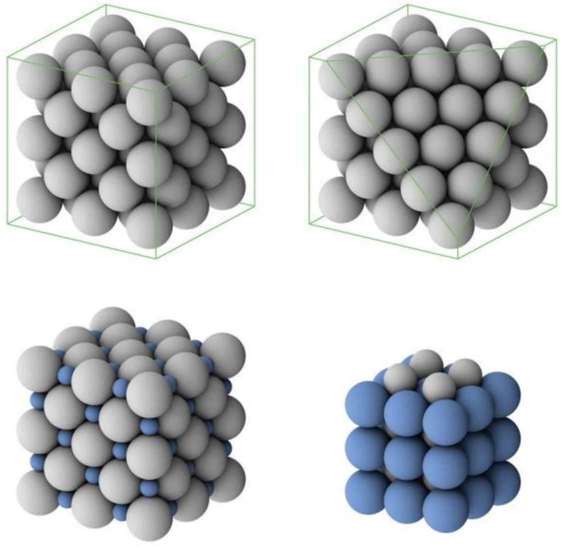


Crystalline solids

1. Crystal Structure

- Crystalline solids are substances which is composed of particles (**atoms, ions or molecules**) arranged in highly ordered repetitive way (three dimensional pattern), held together by non-covalent interactions.

- The regular, periodic arrays which describes the **three-dimensional** arrangement of particles in a crystal structure is known as the "crystal lattice" (or space lattice)

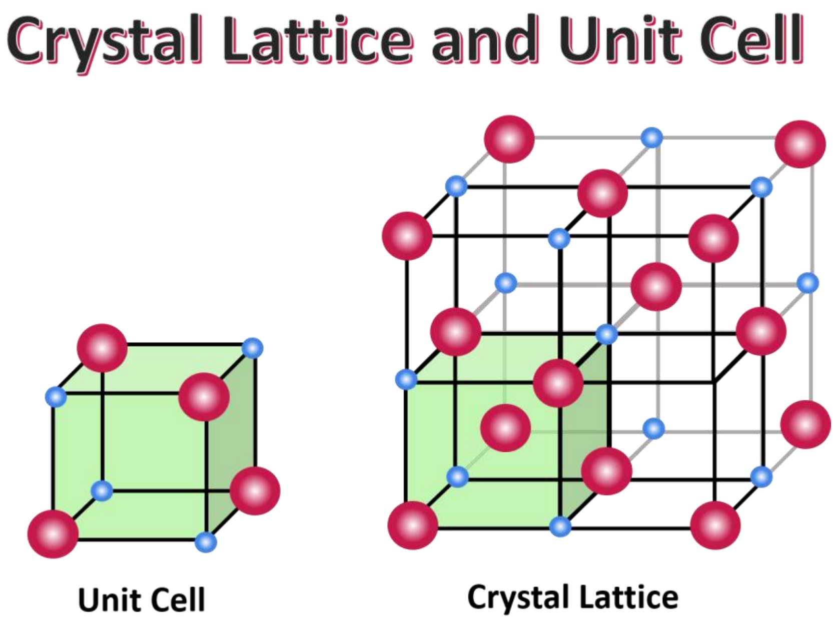


Crystalline solids

1. Crystal Structure

- The crystal lattice is constructed from repeating units called "unit cells." The unit cell is the basic repeating structure of the crystal, it represents the smallest group of atoms that form the basic building blocks of the crystal.

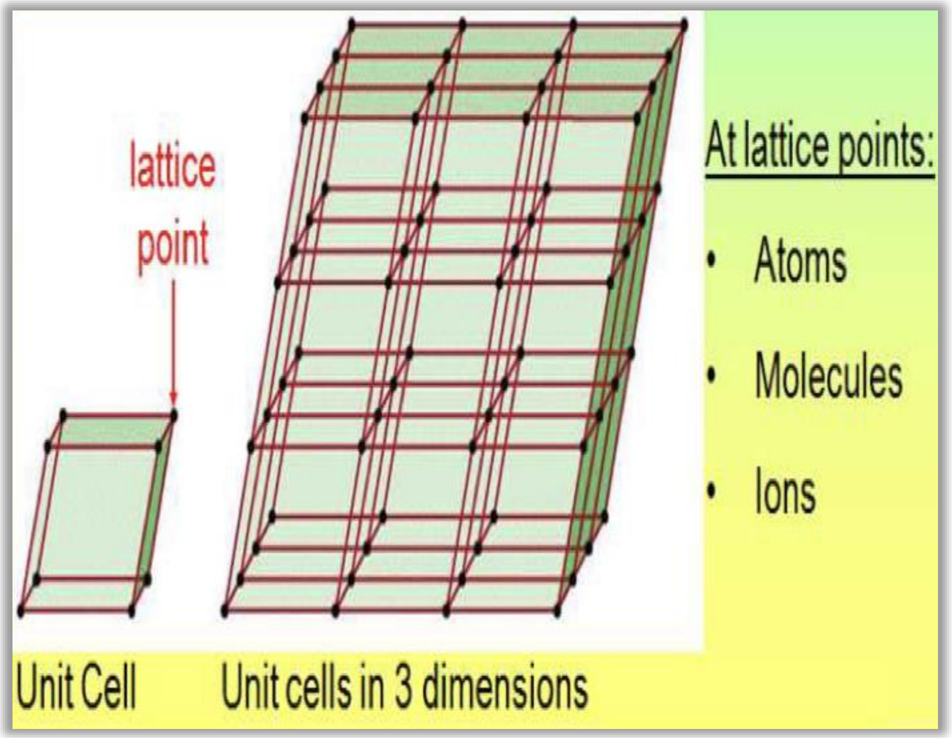
- All unit cells in a specific crystal are the same size and contain the same number of molecules or ions arranged in the same way.



Crystalline solids

1. Crystal Structure

- The nature of the unit cell is very important because different unit cells have different properties such as solubility, stability, and compressibility; these properties are very important for drug delivery and pharmaceutical manufacturing.



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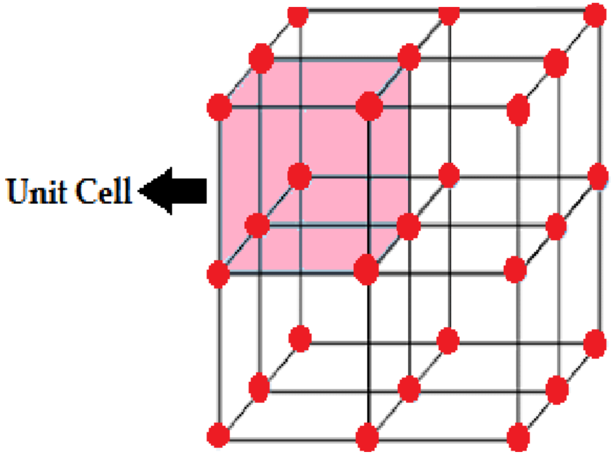
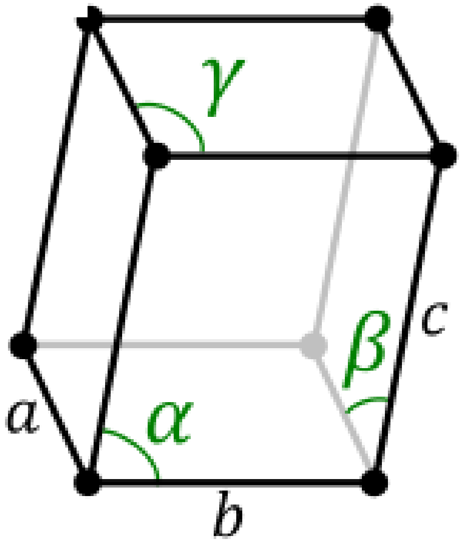
Crystalline solids

1. Crystal Structure

- In order to describe a unit cell, we ought to know that the particles represents the corners of the unit cell, the distances (i.e., **the lengths of the axes of unit cell:** known as "**lattice constants"**) are designated as a, b, c and and the angles between the three imaginary axes are named by **(α, β, γ)** which may or may not be equal to **90°**





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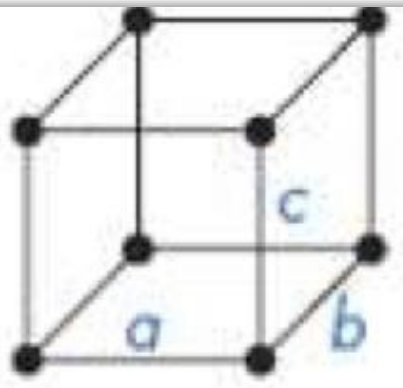
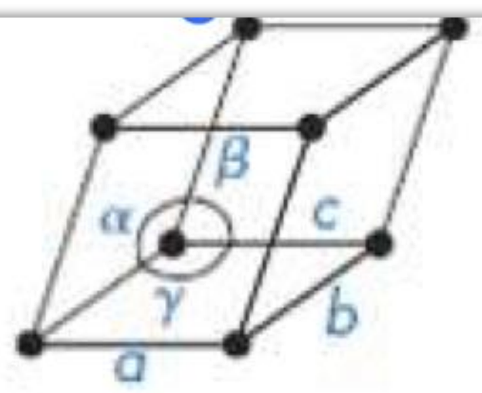
Crystalline solids

1. Crystal Structure

(between sides *b* and *c*)
(between sides *a* and *c*)
(between sides *a* and *b*)





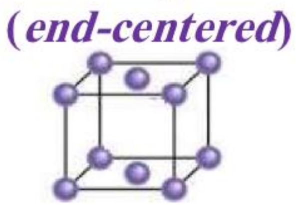
Crystalline solids

1. Crystal Structure : Variations of unit cells

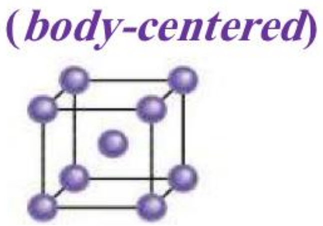
- the center of the unit cell does not contain any internal atom, the unit cell is called **“Primitive unit cell”**

- It is possible to find unit cells with atoms or molecules not located only on the corners, and will therefore have centered units cells” **with the following varieties:**

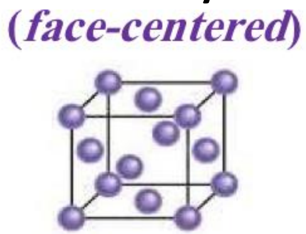
the center of the top or bottom faces



a single atom in the center of the cell



the center of every face



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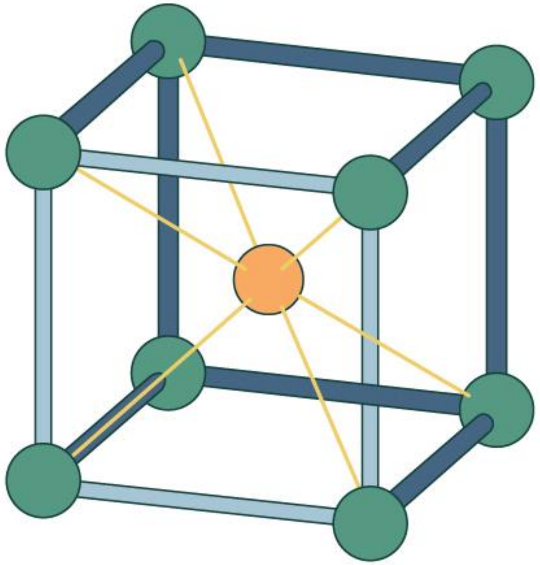
Crystalline solids

1. Crystal Structure : Unit cell arrangements

- Since certain primitive unit cells may have different variations (note that variations do not occur with every type of unit cell :

1. **End centered (monoclinic and orthorhombic)**
2. **Body-centered (cubic, tetragonal and orthorhombic)**
3. **Face-centered (cubic and orthorhombic)**



- Therefore, there will be a total of 14 possible unit cells called **“Bravais lattices”**

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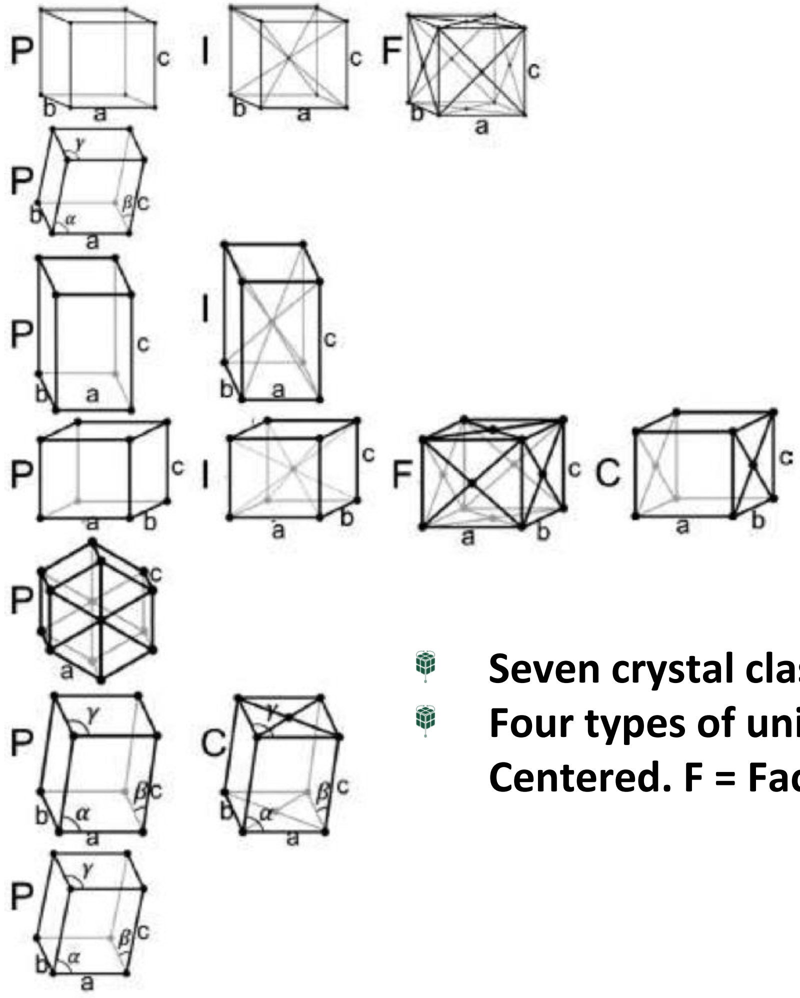
Crystalline solids

1. Crystal Structure : Unit cell arrangements

- Cubic
  - a = b = c
  - $\alpha = \beta = \gamma = 90^\circ$
- Trigonal (rhombohedral)
  - a = b = c
  - $\alpha = \beta = \gamma \neq 90^\circ$
- Tetragonal
  - a = b ≠ c
  - $\alpha = \beta = \gamma = 90^\circ$
- Orthorhombic
  - a ≠ b ≠ c
  - $\alpha = \beta = \gamma = 90^\circ$
- Hexagonal
  - a = b ≠ c
  - $\alpha = \beta = 90^\circ$
  - $\gamma = 120^\circ$
- Monoclinic
  - a ≠ b ≠ c
  - $a = \gamma = 90^\circ$
  - $\beta \neq 90^\circ$
- Triclinic
  - a ≠ b ≠ c
  - $\alpha \neq \beta \neq \gamma \neq 90^\circ$



- For drugs there are three common types of unit cell: triclinic, monoclinic and orthorhombic.

- Seven crystal classes - 14 Bravais Lattices
- Four types of unit cells - P = Primitive. I = Body Centered. F = Face Centered. C = Side Centered

Crystalline solids

Crystal Morphology (crystal habit)

- The external shape of a crystal is termed the "crystal habit", and a variety of shapes have been defined

Habit	Description
Acicular	Elongated prism, needlelike
Angular	Sharp edged, roughly polyhedral
Bladed	Flattened acicular
Crystalline	Geometric shape fully developed in fluid
Dendritic	Branched crystalline
Fibrous	Regular or irregular threadlike
Flaky/Platy	Plate or saltlike

Habit	Description
Granular	Equidimensional irregular shape
Irregular	Lacking any symmetry
Nodular	Rounded irregular shape
Prismatic	Columnar prism
Spherical	Global shape
Tabular	Rectangular with a pair of parallel faces

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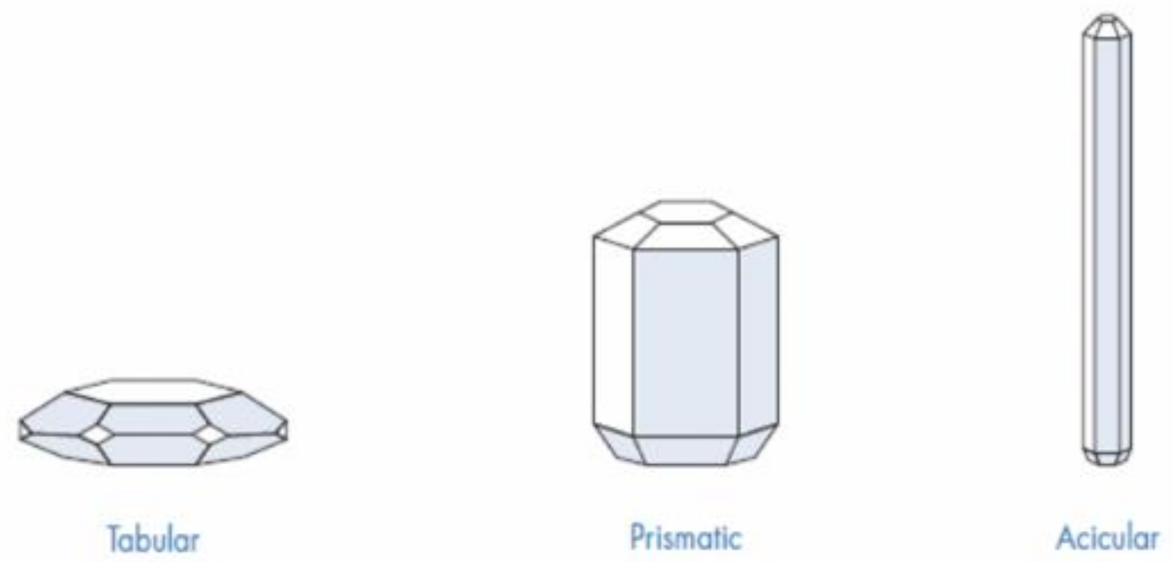
Crystalline solids

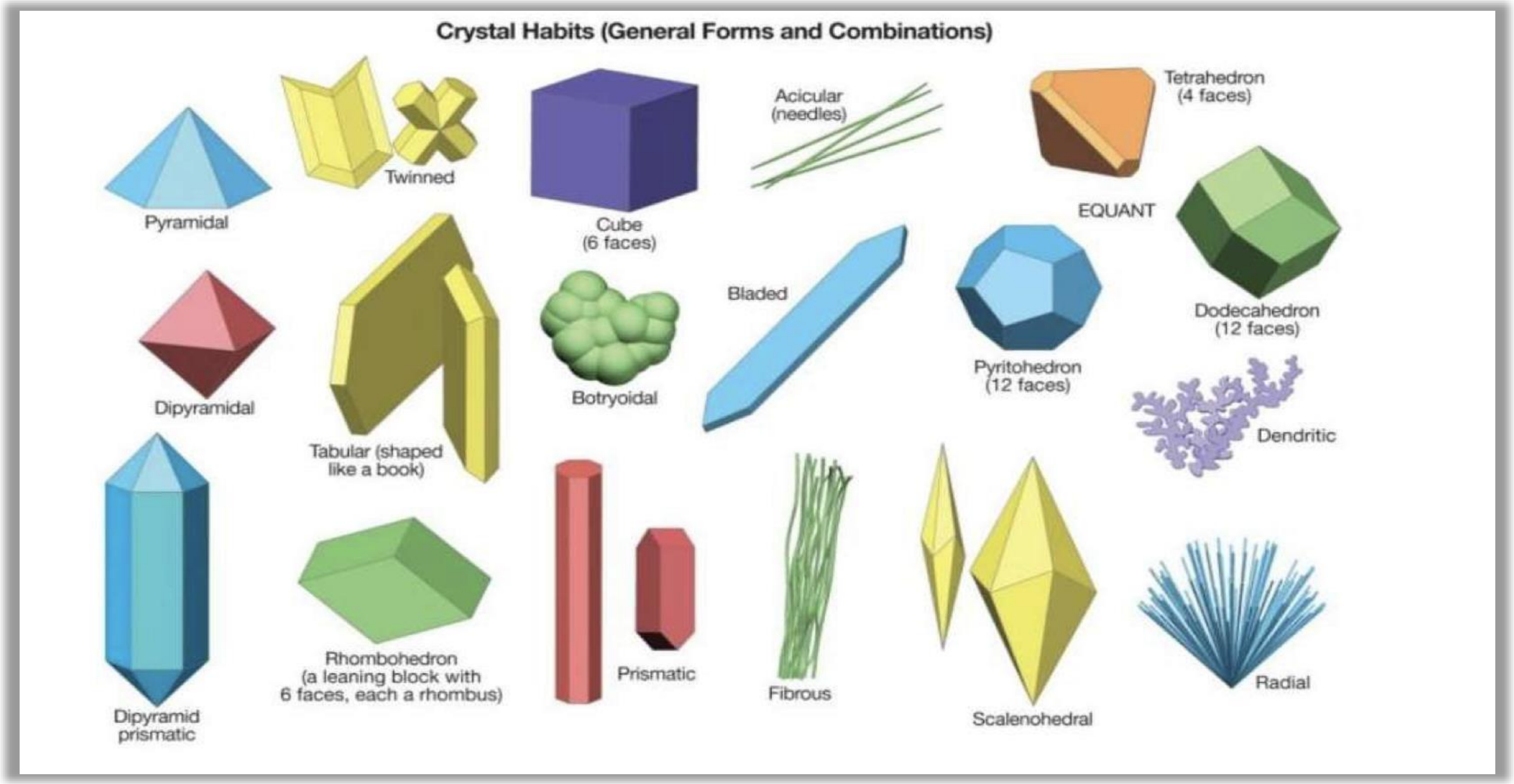
Crystal Morphology (crystal habit)



Crystal habits of a hexagonal crystal.

Crystalline solids

Crystal Morphology (crystal habit)



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Crystalline solids

Crystal Morphology (crystal habit) :The crystal habit depends on:

- **Conditions of crystallization** (such as solvent used, the temperature, and the concentration and presence of impurities)

- **For example**: Ibuprofen is usually crystallized from hexane as elongated needle-like crystals, which have been found to have poor flow properties; crystallization from methanol produces equidimensional crystals with better flow properties and compaction characteristics, making them more suitable for tableting.

- **Conditions of crystal growth**:Surfactants in the solvent medium used for crystal growth can alter crystal form by adsorbing onto growing faces during crystal growth.

Crystalline solids

Crystal Morphology (crystal habit) :The crystal habit affects on:

- Ability to inject a suspension containing a drug in crystal form – platelike crystals are easier to inject through a fine needle than needle-like crystals

- Flow properties of the drug in the solid state – equidimensional crystals have better flow properties and compactioncharacteristics than needle-like crystals, making them more suitable for tableting.

- Strength and disintegration time of tablets –crystal morphology of the excipients (such as powdered cellulose)included in tablet formulations can have a significant influence on the disintegration strength and time of tablets.

- **Dissolution rate** – compounds with different crystal habits can also exhibit differences in dissolution rate.

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Crystalline solids

Supplementary material

- Crystallization It is the slow precipitation (separation) of crystals from a saturated solution.

- For crystallization to occur the solution at hand ought to be supersaturated.

- During crystallization process, the supersaturated solution is warmed in an open container, allowing the solvent to evaporate, that atoms gather to make tightly bonded or connected groups known as crystals

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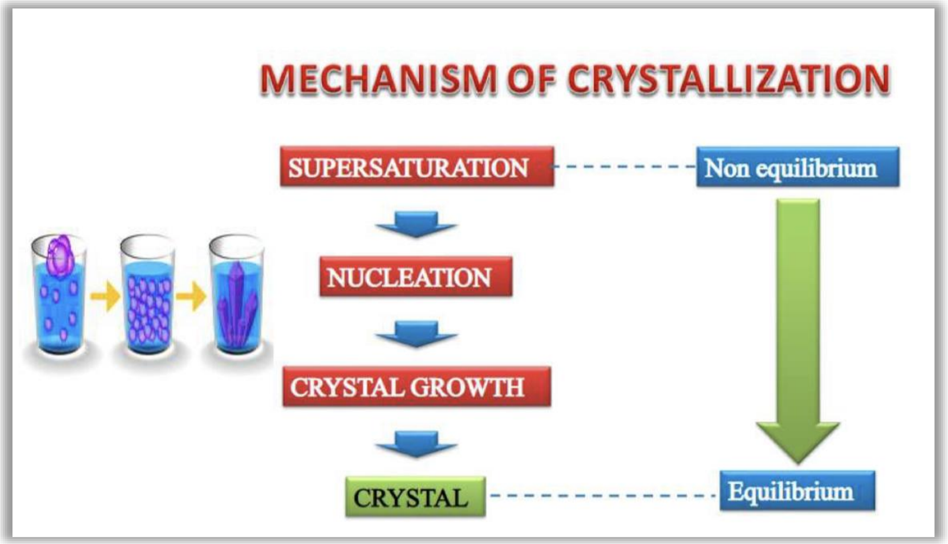
Crystalline solids

Supplementary material



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Thank You !

https://t.me/Dr_Cube