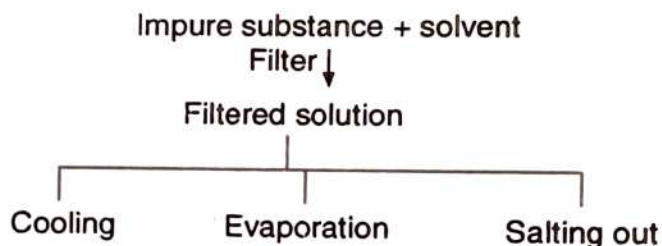


Crystallization

In some solutions, under certain conditions, the solutes, separate-out, in the form of crystals. This process is called 'Crystallization'. This is one of the unit operations, mainly used in chemical industry to purify the substances. The process involves the addition of a diluent solvent to the impure substance to form a solution. It is filtered to remove the insoluble impurity matters, if present. Then the process of Crystallization is effected by any one of the following unit operations :

1. Making the solution to supersaturation by cooling directly or indirectly.
2. Making solution to supersaturation by evaporating the solvent partially.
3. Converting or changing the solution to supersaturation by adiabatic evaporation, that is cooling with evaporation.
4. Salting out the substance (solute) by adding another electrolyte substance that reduces the solubility of the solute in question. This is known as common ion effect.



[Note: Substances obtained by the process of sublimation, *i.e.*, solid to vapour and sublimates as crystalline form, bypassing the state of liquid form, has not been studied under this unit operation Crystallization. Only crystals obtained from liquid state are dealt here.]

18.1. DEFINITION

A crystal may be defined as "a homogenous particle of solid which is formed by solidification under favourable conditions, of a chemical element or a compound, whose boundary surfaces are planes symmetrically arranged at definite angles to one another in a definite geometric form".

18.2. MARKET DEMAND

The requirements of industry in crystallization are

- (i) Highest yield.
- (ii) Purest, i.e., high purity with minimum impurities.
- (iii) Crystal size and shape.
- (iv) Low cost.

18.3. ROLE OF HEAT

Heat transfer plays a major part in the crystallization process. The heat includes sensible heat, latent heat and the heat of Crystallization. With substances whose solubility increases with increase in temperature, there is an absorption of heat, when the substance dissolves. In substances with decreasing solubility, as the temperature increases, there is an evolution of heat when solution occurs. When there is no change in solubility with change in temperature, there is no heat effect.

Examples of substances whose solubility decreases in water with increase in temperature are—Calcium acetate, Calcium hydroxide, chlorine, bromine, hydrobromic acid, carbon dioxide, sulphur dioxide, nitric oxide and nitrous oxide.

At equilibrium, the heat of Crystallization is equal and opposite in sign to the heat of solution. (Heat of solution can be exothermic or endothermic). Using the heat of solution at infinite dilution as equal, but opposite in sign to the heat of Crystallization is equivalent to neglecting the heat of dilution. With many materials the heat of dilution is small in comparison with the heat of solution and hence the approximation is justified; However, there are some exceptions. Relatively large heat effects are usually found in the crystallization of hydrated salts. In such cases, the total heat released by this effect may be a substantial portion of the total heat effects in a cooling type crystallizer. In evaporative type crystallizers, the heat of crystallization is usually negligible when compared with the heat of vapourising the solvent.

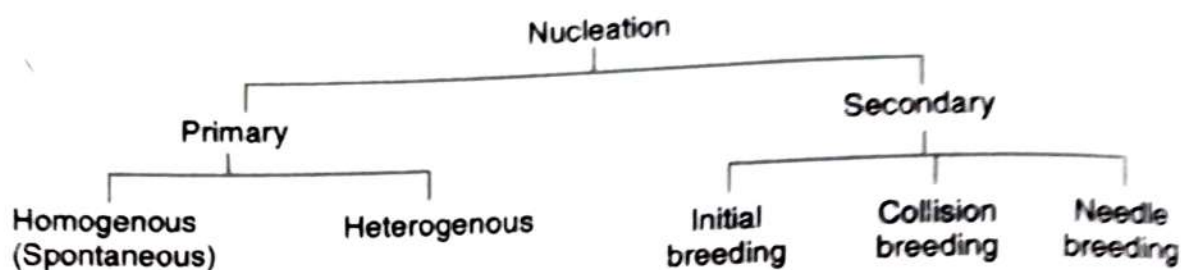
18.4.1 Miers Theory of Supersaturation

Mier's theory states that *"in a solution completely free from any foreign particles, spontaneous nucleation occurs at supersaturation and not near the saturation concentration"*. But this has several limitations and hence of no significant use in actual practice.

Crystal growth is a layer by layer process. First a nucleus forms which then grows to bigger size.

The mechanism of crystallization of substances from the solution involves three steps:

- (a) Supersaturation—cooling/evaporation.
- (b) Nucleus formation—Nucleation may occur spontaneously or it may be induced artificially. Nucleation is classified as primary nucleation and secondary nucleation. *Primary nucleation* is the nucleation in the systems that do not contain any crystalline matter. *Secondary nucleation* represents the condition where nuclei are generated in the vicinity of crystals present in a supersaturated solution.



(c) Crystal growth is a diffusion process and surface phenomenon. This takes place at super saturated concentration level.

Solution \longrightarrow Supersaturated solution \longrightarrow Loose Aggregates \longrightarrow
 Nuclei Nucleation \longrightarrow $\xrightarrow[\text{and Deposition}]{\text{Diffusion}}$ Crystal growth

In the science of Crystallography, the crystals are classified according to the angles between faces — as Cubic, Tetragonal, Orthorhombic, Hexagonal, Monoclinic and Triclinic.

18.4.2. Conditions of Mier's Theory

In a solution ions or molecules can interact to form short lived cluster which develops into embryos or sub-nuclei, many of which failed to achieve maturity. They redissolve due to their extreme unstability. When these aggregates attain the size at which cohesive lattice forces exceed the force which tend to return them into the solution a stable or critical nucleus is formed. Thus Mier's theory points out that the greater the degree of supersaturation, the more chance there is of nuclei forming. Also if the supersaturation passes a certain range of values, nucleus formation is apt to be extremely rapid,

18.4.3. Limitations of Mier's Theory

- (i) The solution must be free from foreign particles, but in practice it is difficult to avoid contamination, especially from the atmosphere.
- (ii) Mier's Theory postulated with experiments of smaller volume of solution, whereas with large volume of batches in industrial practice nucleation takes place spontaneously at lower degree of saturation. This may be attributed to the contamination taking place in handling large volumes, which increases the chances of collisions.
- (iii) Likewise, when the solution of lower degree of supersaturation kept for longer period, due to more chances of contamination leading to collisions effecting spontaneous nucleation.
- (iv) Due to above, the nucleation takes place not at a particular supersaturation concentration, but at a zone of supersaturation in the system. Thus a specific concentration cannot be fixed for individual systems.
- (v) Apart which from the above factors, the system is subjected to external stimulus like mechanical shock, vibration etc., which changes the ideal conditions of Mier's theory of nucleation.

18.5. CRYSTAL HABIT

Crystal is a polyhedral solid with a number of planar surfaces. The arrangement of these faces is termed as habit. In other words, the term crystal habit is used to denote the relative development of the different types of faces. For example, sodium chloride crystallizes from aqueous solutions with cubic faces only. On the other hand, if sodium chloride is crystallized from an aqueous solution containing a small quantity of urea, the crystals obtained will have octahedral faces. Both types of crystals belong to the cubic system but differs in habit. The question of whether a material crystallizes in symmetrical crystal, in plates or needles or prisms is usually an accident resulting from the condition under which it is grown and has no relation either to its crystallographic classification or its habit. The word habit is sometimes wrongly used to designate these features of external form, but when properly used, it refers to the type of faces developed and not to the shape of the resulting crystals. (This much knowledge is enough for a pharmacist, as Crystallography in itself is a separate study and dealt in detail by chemical engineers.)

18.6. FACTORS OF CRYSTAL GROWTH

The factors that effect the rate of crystal growth are :

- (i) Rate of diffusion of the solute from the mass of solution to the interface.
- (ii) Magma density—which is the ratio of solid to mother liquor in the circulating material. Heavier magma will produce larger crystal surface.
- (iii) Rate of circulation.
- (iv) Amount of vacuum in the system.
- (v) Operating temperature.

18.8. CLASSIFICATION OF CRYSTALLIZERS

Equipments used to obtain crystals by the unit operation crystallization are called crystallizers. They are classified based on the type of other unit operation involved in the process, which are stated in the beginning above.

I. Supersaturation by cooling alone.

(a) Batch processes

1. Static tank crystallizers
2. Agitated batch crystallizers

(b) Continuous processes

1. Swenson-Walker crystallizer.
2. Others.

II. Supersaturations by evaporation of the solvent.

(a) Salting evaporators—Swenson crystallizer.

- #### (b)
1. Krystal crystallizer
 2. Swenson circulating magma crystallizer.

III. Supersaturation by adiabatic evaporation (*i.e.*, cooling plus evaporation) Vacuum crystallizers.

(a) With external classifying seed bed.

(b) Without external classifying seed bed.

IV. Supersaturation by salting out.

18.8.1. Static Tank Crystallizer

Hot and nearly saturated solution is made, filtered and transferred to open rectangular tanks made up of materials which are resistant to the corrosive effect of the solution. Cooling of solution is effected by natural convection and radiation. Glass enamelled or S.S. vessel of 0.5 m is generally used. No agitation inside the tank. Insulation may be used to the tank in order to reduce the rate of cooling in the initial phase of the cycle and prevent the formation of too many nuclei. Surface cooling may be increased by a jacket outside the tank in which chilled water circulated in the later phase. The empty jacket will act as insulation in the first phase. (See Fig. 18.1)

Crystals grow slowly and form in large size and considerably interlocked. This interlocking results in the occlusion of mother liquor, thus introducing impurities in it. When the tanks had cooled sufficiently which is normally a matter of several days, any mother liquor remaining is drained off and crystals removed by hand or with blunt shovel. A battery of such vessels is used in practice. Large floor space is required and the process takes long time. More labour required but still preferred because of its inexpensiveness in some places. No running cost on electricity. Though better crystallizers are available, this is still used in the production of Glauber's salt

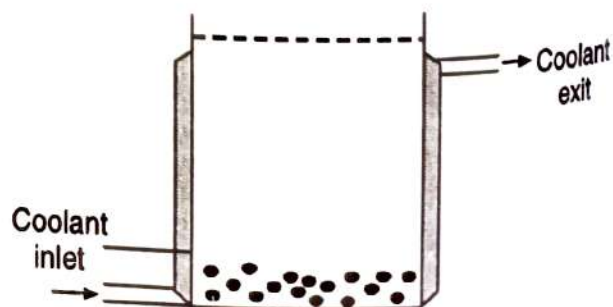


Fig. 18.1. Tank crystallizer.

(Na_2SO_4) and for small scale operations. This method is adopted in under-developed areas, where the labour cost is extremely low and no skill required. Rods or strings can be hung in the tanks to give the crystals additional surface on which to grow.

18.8.2 Agitated Tank Crystallizer

Saturated solution is made to supersaturation by cooling. To hasten-up the Crystallization process, artificial cooling coils as well as jacketted coverings are adopted. Agitation by slow moving propellers with paddles attached is used (no cutting sharp edged blades). (Fig. 18.2) This slow agitation performs two functions—*first*, it increases the rate of heat transfer and keeps the temperature of the solution more uniform; *second*, by keeping the fine crystals in suspension, it provides them more opportunity to grow uniformly instead of forming large crystals or aggregates. The product obtained by this is not only more uniform but also very much finer than that from the older static tanks.

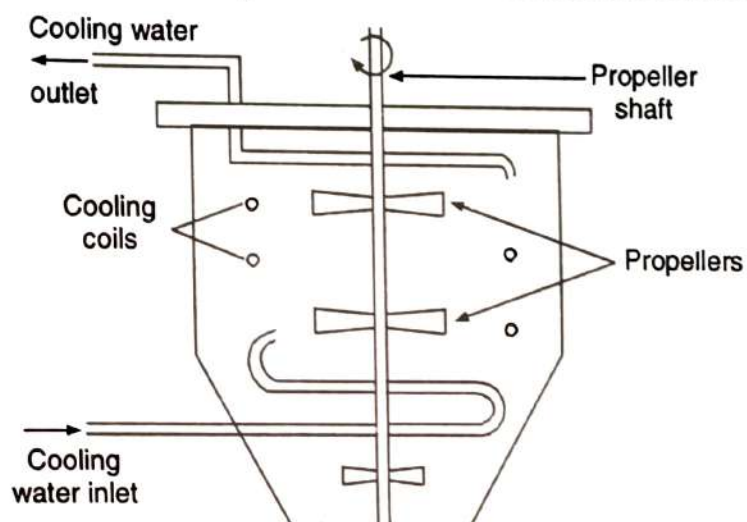


Fig. 18.2. Agitated batch crystallizer.

Drawbacks of agitated Tank Crystallizer

- (a) It is a batch operation and not continuous.
- (b) The solubility is least at the surface of the cooling coils. Consequently the growth is more rapid at these points and the coils build-up with a mass of crystals very fast, that decreases the rate of heat transfer.

It is recommended that the temperature difference between the tube wall and the solution shall not exceed 10°C so as to prevent crystal deposition. This is the best choice for fine chemicals and some pharmaceuticals, where fine crystals are preferred and the rate of production is comparatively low.

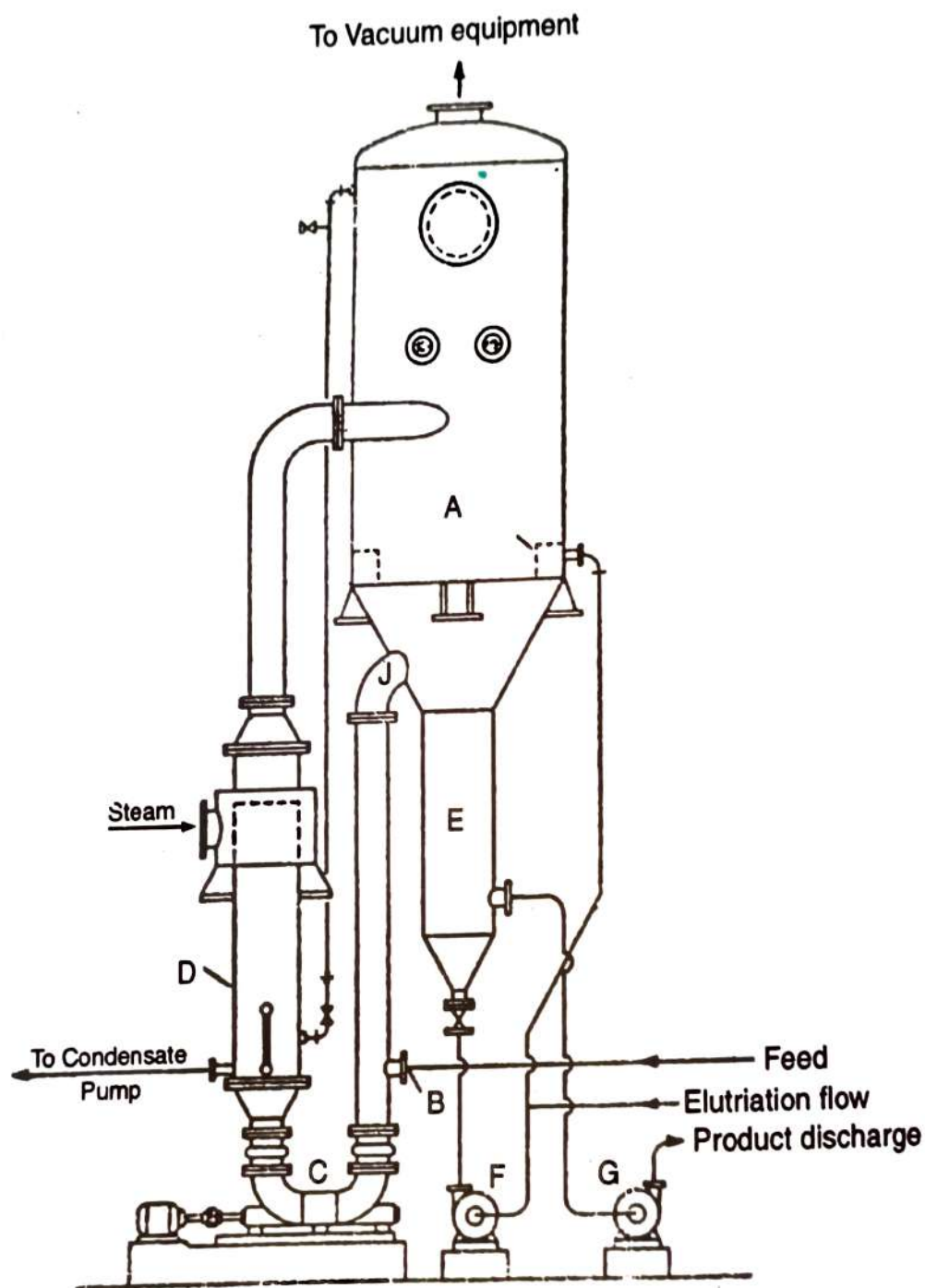
18.8.3 Swenson Walker Crystallizer

Swenson Walker Crystallizer is a continuous operation crystallizer based on supersaturation by cooling. It consists of an open trough two feet wide and ten feet long with a semi-cylindrical bottom, a water jacket welded to the outside of the trough and a slow speed, long pitch spiral agitator running at about seven rpm and set very close to the

18.8.6 Circulating Magma Crystallizer

(Magma is the term used for solutions suspended with crystals).

This is a modification of vacuum crystallizer in which growing crystals are brought intentionally to the zone of the crystallizer where supersaturation is being created. The zone of generation of supersaturation is the boiling surface. The presence of growing crystals in the zone where supersaturation is created immediately utilizes this driving force, and the real supersaturation level is therefore considerably lower than other types refer (Fig. 18.5).



A-Crystalliser body; B-Feed connection; C-Circulating pump;
D-heating or cooling element; E-Elutriation; F-Elutriation pump;
G-Product discharge pump; H-Baffles

Fig. 18.5. Circulating magma crystallizer.

18.9. FACTORS THAT EFFECT THE RATE OF CRYSTAL GROWTH

1. Rate of diffusion of the solute from the mass of the solution to the interface.
2. Magma density, which is the ratio of solid to mother liquor in the circulating material. Heavier magma will produce larger crystal surface.
3. Rate of circulation
4. Amount of vacuum
5. Cooperating temperatures.

In all forced circulation crystallizers, the size of the crystalline material produced varies with the operating parameters and the characteristics of the material being handled. With sodium chloride, urea, citric acid and many similar inorganic and organic chemicals, the crystalline product is in the range of 20 to 150 mesh sizes.

18.10. CAKING OF CRYSTALS

Caking of crystalline substances is the tendency of the crystals to cake or bind together. This is troublesome in bulk storage and in large containers, as it will be difficult to remove the material or to transfer into other containers. It may not be so serious in small packings. The extent of caking may vary from formation of loose aggregates that fall apart between the fingers to that of solid lumps that have to be crushed with considerable force. Consumers will not like this and hence demand a free flowing material. Thus prevention of caking is a serious problem to the bulk manufacturer.

If a crystal of soluble salt is in contact with air that contains less water than would be in equilibrium with the saturated solution of the salt, the crystal will remain dry since if the crystal were to be surrounded with a film of its solution, that solution necessarily evaporates. On the other hand, if the crystal is brought into contact with air containing more moisture that would be in equilibrium with its saturated solution, then the crystal will become damp and in time will absorb water until it is first completely dissolved and finally until the solution becomes so dilute that it is in equilibrium with the air.

Following steps are adopted to prevent the caking crystals :

1. Maximum critical humidity of the substance obtained by removing impurities to the maximum extent. The critical humidity of a solid salt is the humidity above which it will always remain dry. If the salt is coated with impurities derived from the mother liquor during Crystallization and subsequent separation, this may result in a critical humidity higher or lower than that of the pure salt depending on whether the impurities give the solutions greater or lesser vapour pressure than that of the salt in question.
2. Producing a more uniform mixture of crystal size thus increasing the percent of voids. For a given crystal form and for absolutely uniform sized crystals, the percent of voids is the same irrespective of the crystal size. Non-uniformity of particle size rapidly decreases the percent voids. On the other hand a fine product has more points of contact per unit volume than a coarse one and hence a greater tendency to cake.

3. Coating with a powdery material that can absorb moisture and protect the crystal. This method will not be possible with active medicaments, even if the coating material is inert, as the potency will come down considerably. Examples in other fields are:
 - (a) dusting of table salt with magnesia or Tricalcium phosphate, and
 - (b) the coating of flake calcium chloride with 25% H_2O with anhydrous calcium chloride.

18.11. APPLICATION OF CRYSTALS/CRYSTALLIZATION IN PHARMACY

1. Purification of drug—recrystallization technique.
2. Change in micromeritics—free flowing, compressibility, wettability, prolonged and improved bio-availability.
3. Ease of handling in transport and storage.
4. Better chemical stability.
5. Physical stability—improvement in suspension and in tablet hardness.