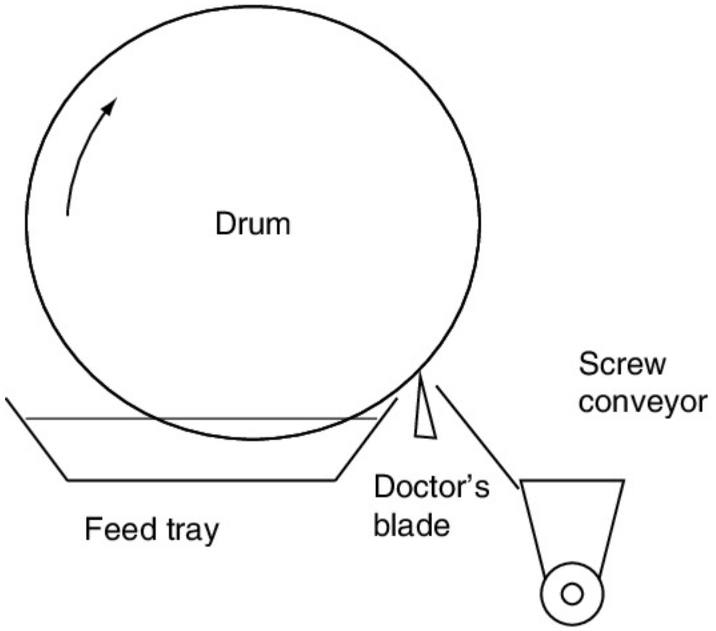
Drying Part II

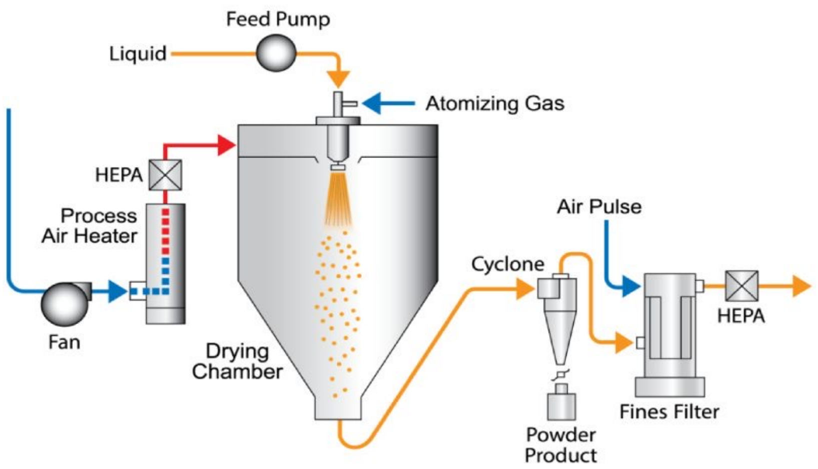
Dryer for solution and suspensions
Drum Dryer

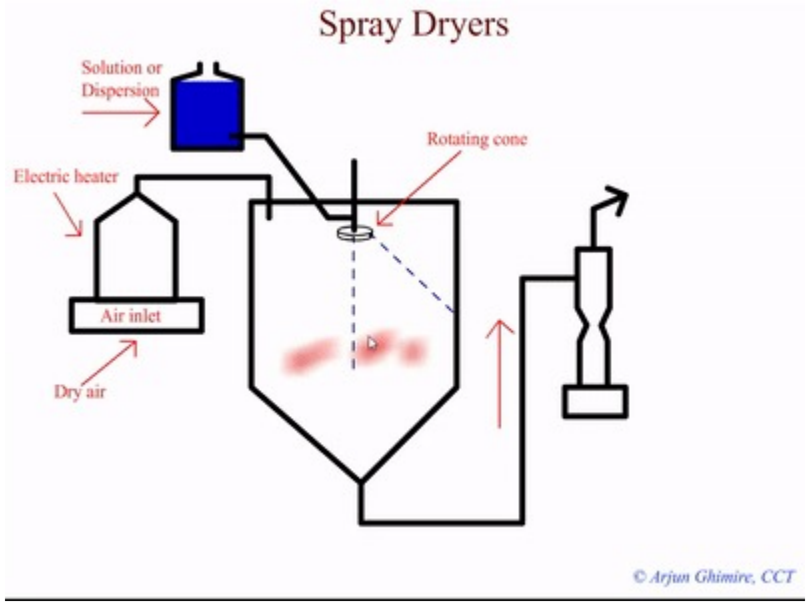
- Consist of **one or two slowly rotating** steam heated cylinders, coated with solution of slurry by means of a **dip feed**.
- The lower portion of the drum is **immersed** in an agitated trough of feed materials.
- Drying takes place by **simple evaporation** rather than by boiling.
- The dried material is scraped from the drum at a suitable point by a scraper.
- **Advantage**:
- Due to short contact time with heat, it is used for thermolabile materials.



Dryer for solution and suspensions
Spray Dryer

- The objective of these dryers is to **generate a large surface area in** the liquid for heat and mass transfer and to provide an effective means of collecting the dry solid.
- The spray dryer provides a large surface area for heat and mass transfer **by atomizing the liquid into small droplets**.
- These are sprayed into a stream of circulating hot air, so that each droplet dries to an individual solid particle.
- **Thus, particle formation and drying occur in the one process**.



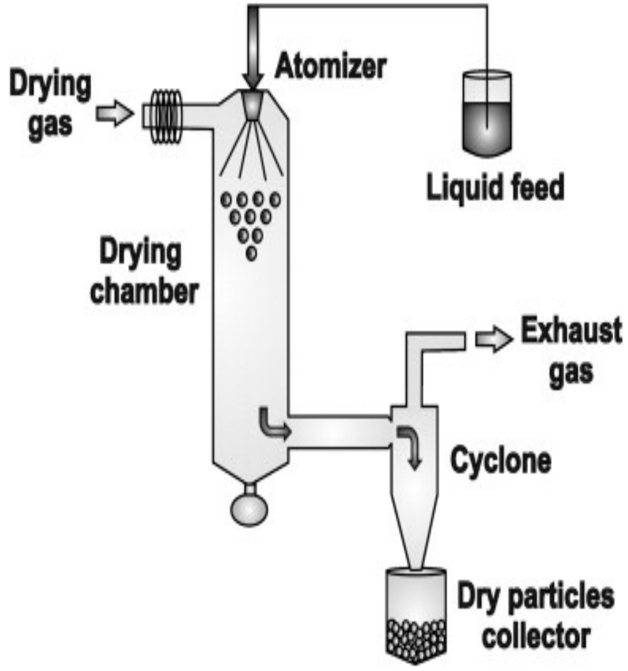


- The drying chamber resembles a cyclone. This ensures:

1. Good circulation of air.
2. Facilitates heat and mass transfer.
3. Encourages the separation of dried particles from the moving air by the centrifugal action.

Spray Dryer
Principle

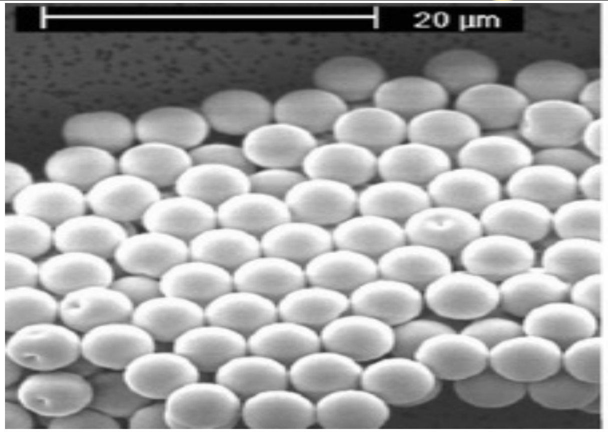
- When the **liquid droplet** come into contact with the **hot gas**, they quickly reach a high temperature and the water at the **surface will evaporate**.
- When the drying continues, the liquid in **the interior** of the droplet must **diffuse** through this shell.
- The diffusion of the liquid occurs a a much slower rate than does the transfer of heat from outside to inside of the droplet.
- Heat transfer will cause that the liquid inside the droplet to **evaporate faster** than it can diffuse to the surface.
- This internal pressure caused the **droplet to swell**, the shell becomes thinner which will allow faster diffusion.

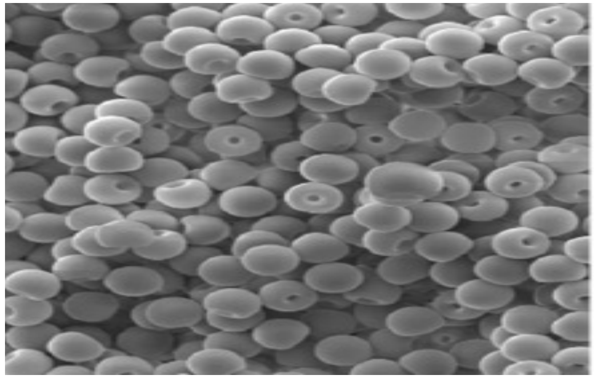


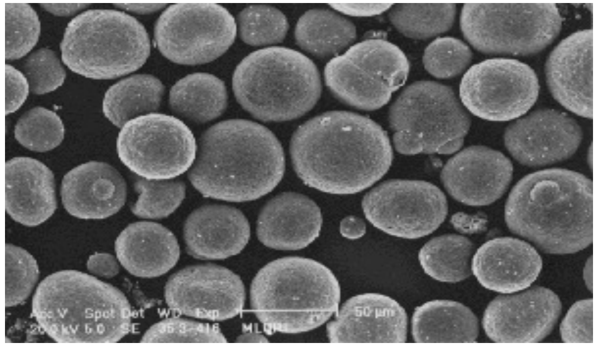
Advantages

- Spray drying will generate millions of small particles that dry fast and at lower temperature this will ensure several advantages:

1. The actual drying time of a droplet is only a fraction of a second, and the overall time in the dryer only a few seconds.
2. Because evaporation is very rapid, the droplets **do not attain a high temperature**. Most of the heat is used as latent heat of vaporization and the temperature of the particles is kept low by **evaporative cooling**.
3. The characteristic particle form allows efficient particle packing and thus gives the product a **high bulk density**.
4. Rapid dissolution because of the large surface area. It may also increase drug bioavailability of poorly water soluble drugs.







Advantages continue

5. Provided that a suitable atomizer is used, the resulting powder will have a **uniform and controllable particle size**.
6. The product is **free- flowing, with almost spherical particles**, and is especially convenient for tablet manufacture as it has excellent ow and compaction properties.
7. **Labor costs are low**, the process yielding a dry particles in a single operation with no handling.
8. It can be used as a **continuous process** if required.
9. Used in production of inhaled particles because it is capable of producing particles with size range of 1-7 um.
10. Used in drying of some antibiotic formulation where only water is removed and all other constituent are dried including the color and flavor.

Disadvantages

1. The equipment is **very bulky** and, with the ancillary equipment, is **expensive**.
2. **The overall thermal efficiency** is rather low since the air must still be hot enough when it leaves the dryer to avoid condensation of moisture. Also, large volumes of heated air pass through the chamber without contacting a particle and thus not contributing directly to the drying process. This will consume energy.

Freeze Drying

- Freeze drying is a process used to dry **extremely heat-sensitive materials**.
- The process is also called **lyophilization**.
- It can allow the drying, without excessive damage, of proteins, blood products and even microorganisms which retain a small but significant viability.
- **In this process**, the initial liquid solution or suspension is **frozen**, the **pressure** above the frozen state is **reduced** and the **water removed by sublimation**.
- overall liquid-to-vapor transition takes place, as with all the previous dryers discussed, **but all three states of matter are involved: liquid to solid, then solid to vapor.**
- The dried product is called **lyophilized** and can be redissolved by adding water prior to their use by a process called **reconstitution**.

Liquid of susp is frozen

↓

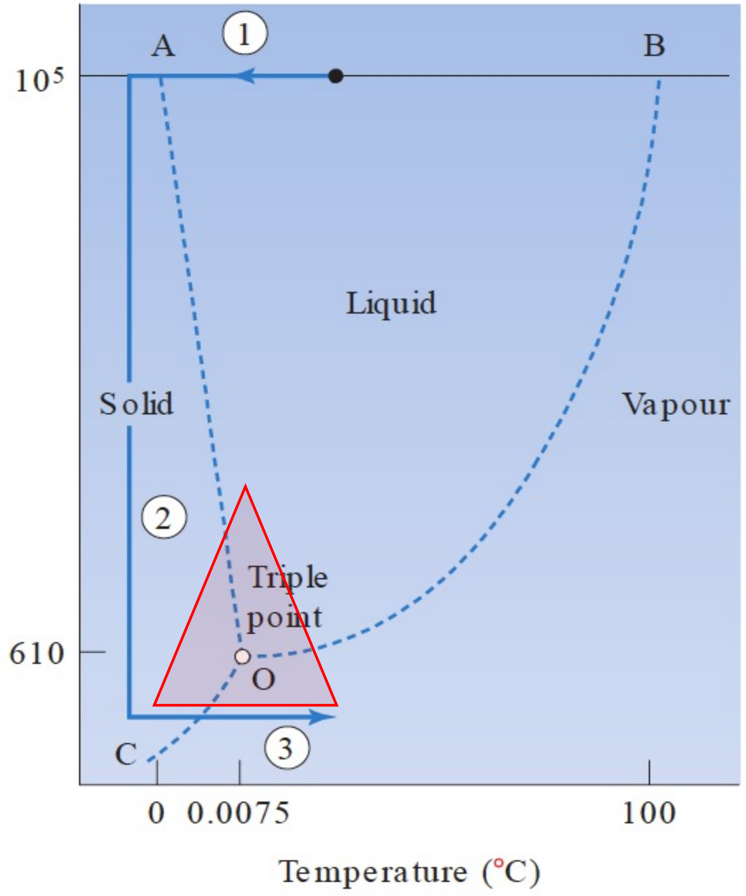
Decrease the pressure by vacuum

↓

Water sublimate

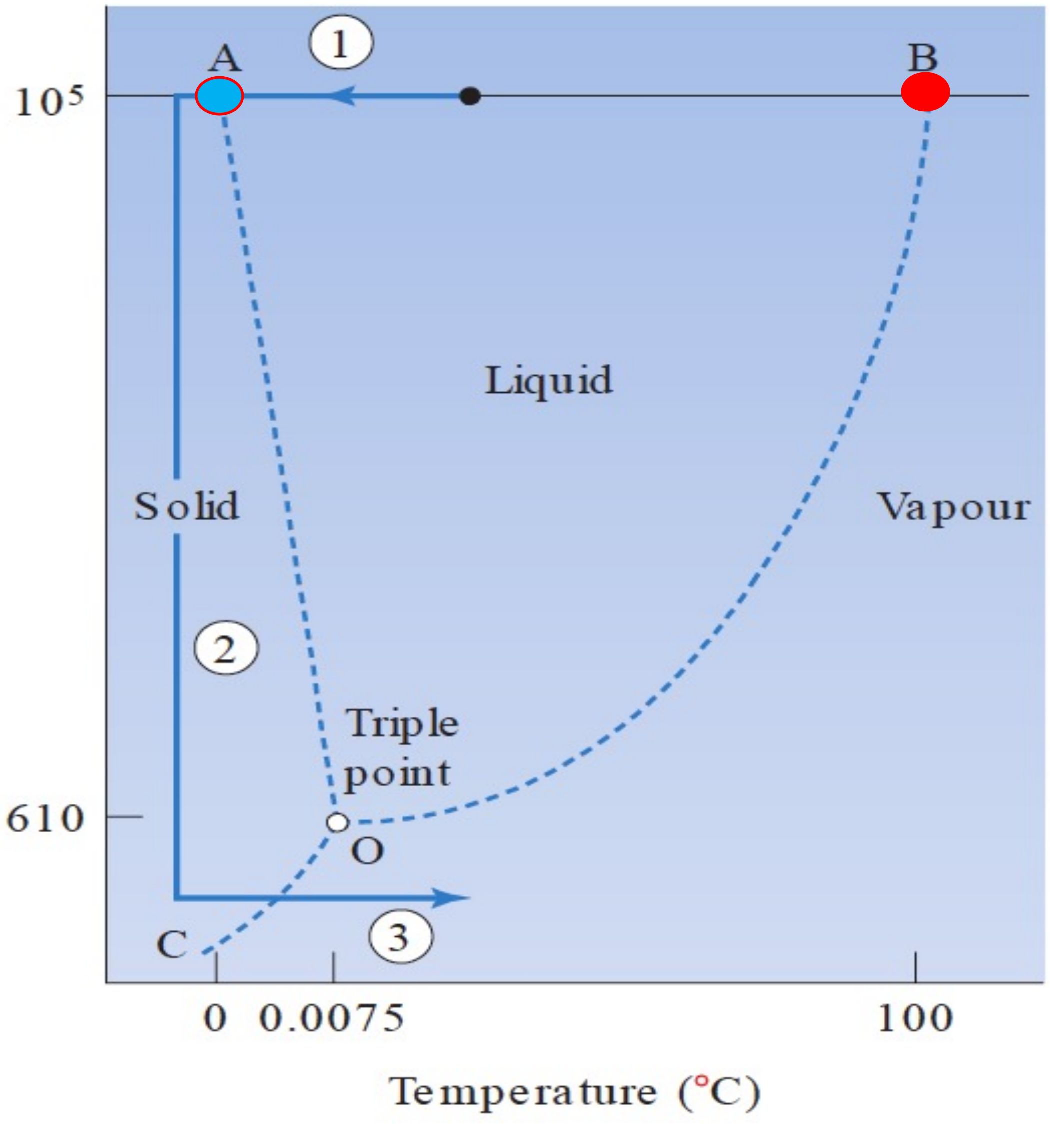
Freeze Drying

- The theory and practice of freeze drying are based on an understanding and application of the **phase diagram** for the water system.
- The phase diagram for the water system consists of **three separate** areas. Each area represents a single phase of water vapor, liquid or solid.
- **Two phases can <u>coexist</u> along** a line under the conditions of **temperature** and **pressure** defined by any point on the line.
- The point **O** is the one unique point where all **three phases can coexist** and is known as the **triple point**.
- Its coordinates for **pure water** are a **pressure** of 610 Pa (as a comparison, atmospheric pressure is approximately 10^5 Pa) and a **temperature** of 0.0075 °C.



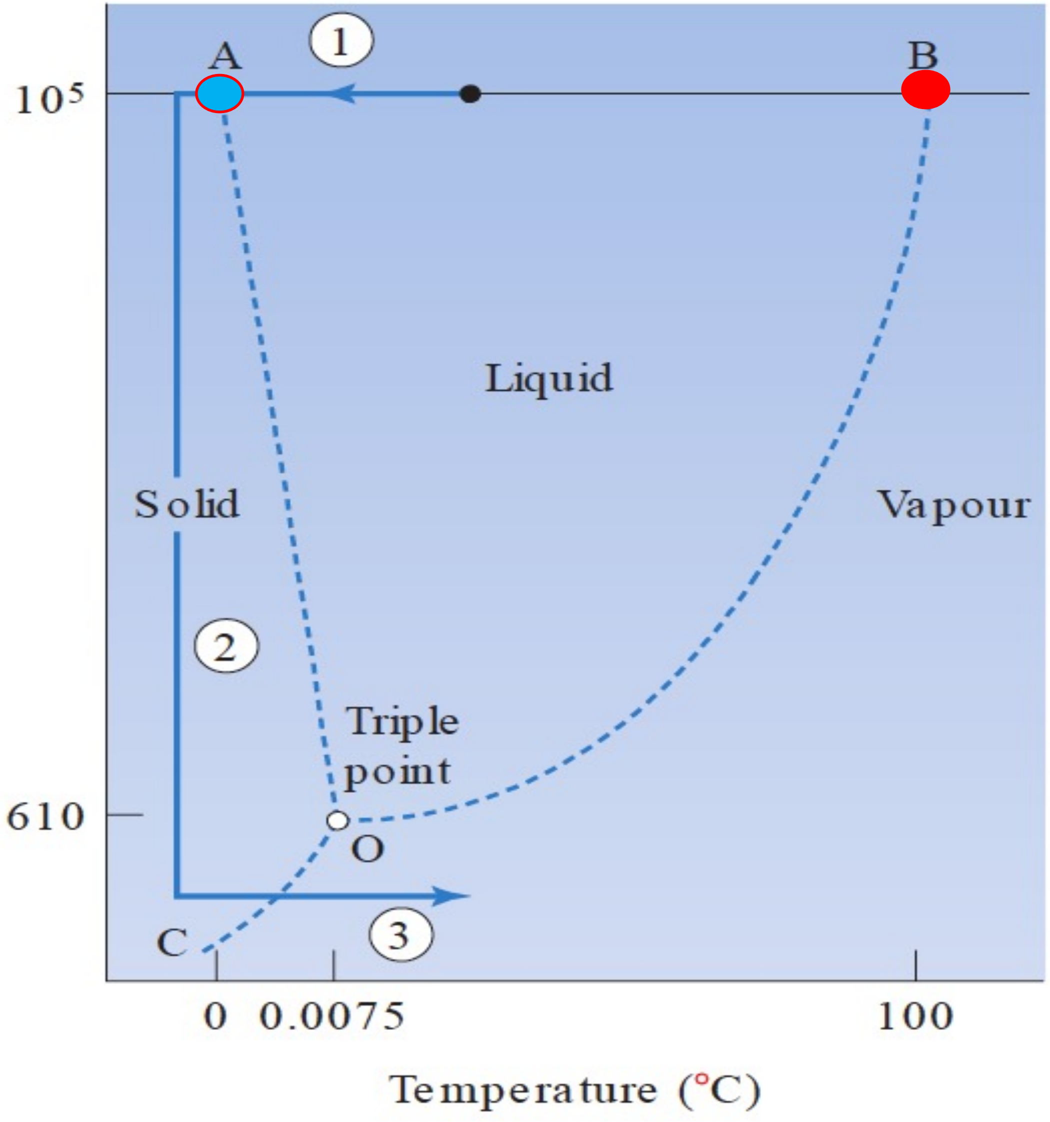
Phase Diagram

- The **lines** on the phase diagram **represent the interphase** equilibrium lines which show:
- The **boiling point** of water as it is **lowered** by reduction of the external pressure above the water (**BO**).
- The **variation of the melting** point of ice on reduction of the external pressure above it. There is a very slight rise in the melting point (**AO**).
- The **reduction** of the **vapor pressure** exerted by ice as the temperature is reduced (CO).



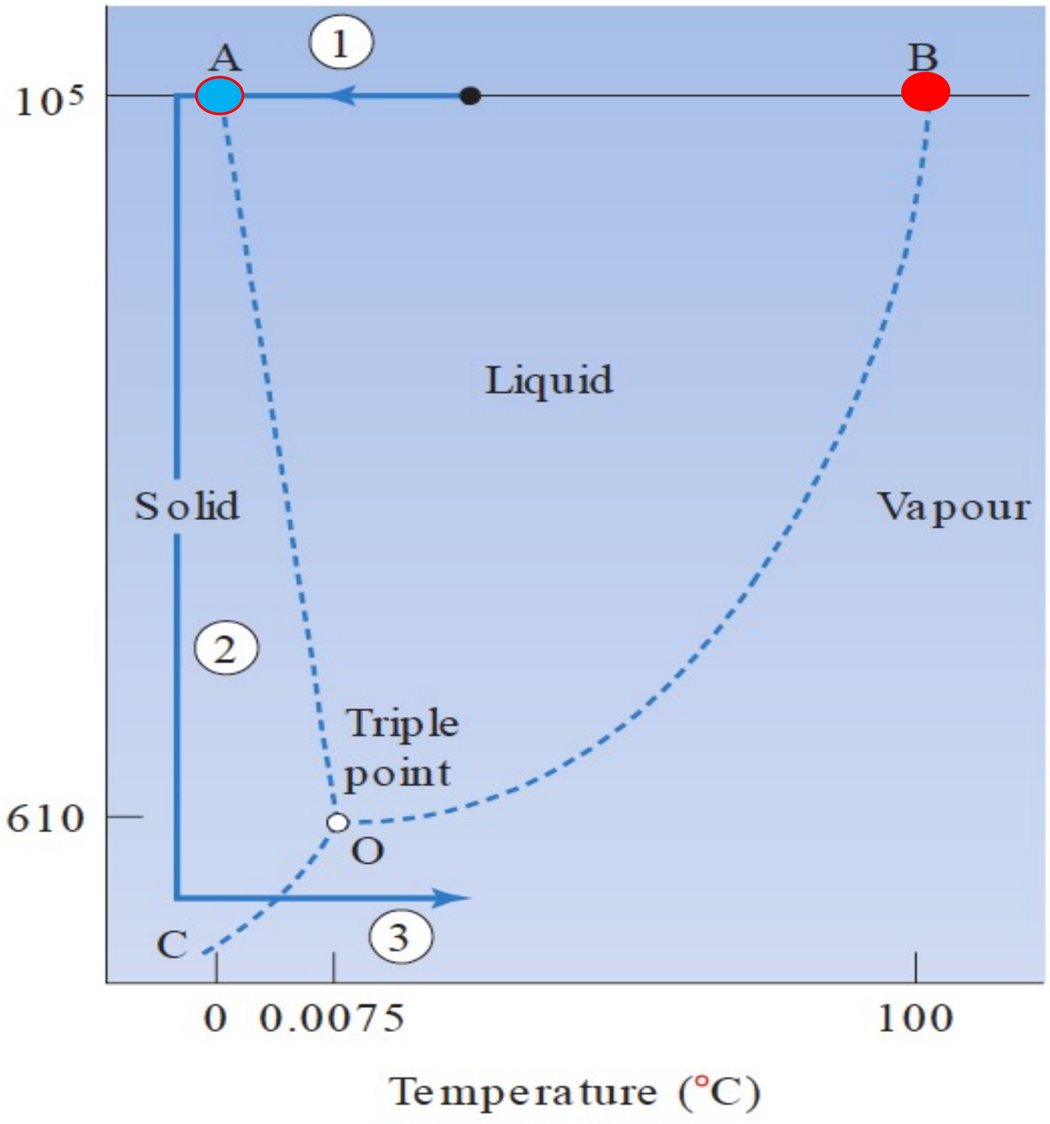
Phase diagram

- On heating ice at atmospheric pressure, it will **melt** when the temperature rises to **0˚C**, i.e. at this temperature the ice will change to liquid water.
- Continued heating at atmospheric pressure will raise the temperature of the water to **100˚C**.
- If heating is continued, the liquid water will be converted into water vapor at 100˚C.
- If **solid ice** is maintained at a **pressure below** the triple point then **on heating**, the ice will **sublime** and pass **directly** to water vapor **without** passing through the liquid phase.



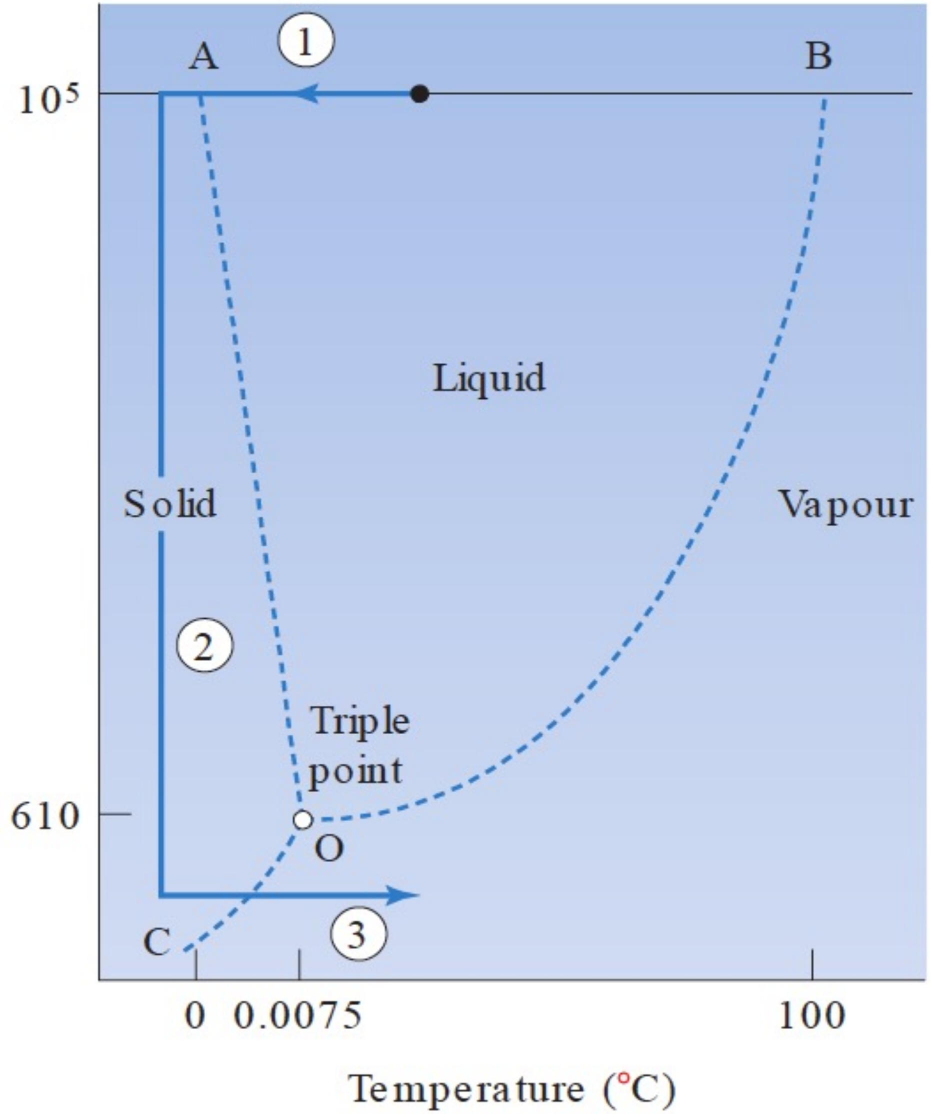
Phase Diagram

- The **sublimation**, and therefore **drying**, will only **occur at a temperature below** that of the triple point.
- It will only happen **if the pressure** is prevented from rising above the triple point pressure during the process.
- To ensure that the pressure is low enough, the vapor evolved must be removed as fast as it is formed. This is done by using an efficient **vacuum pump.**



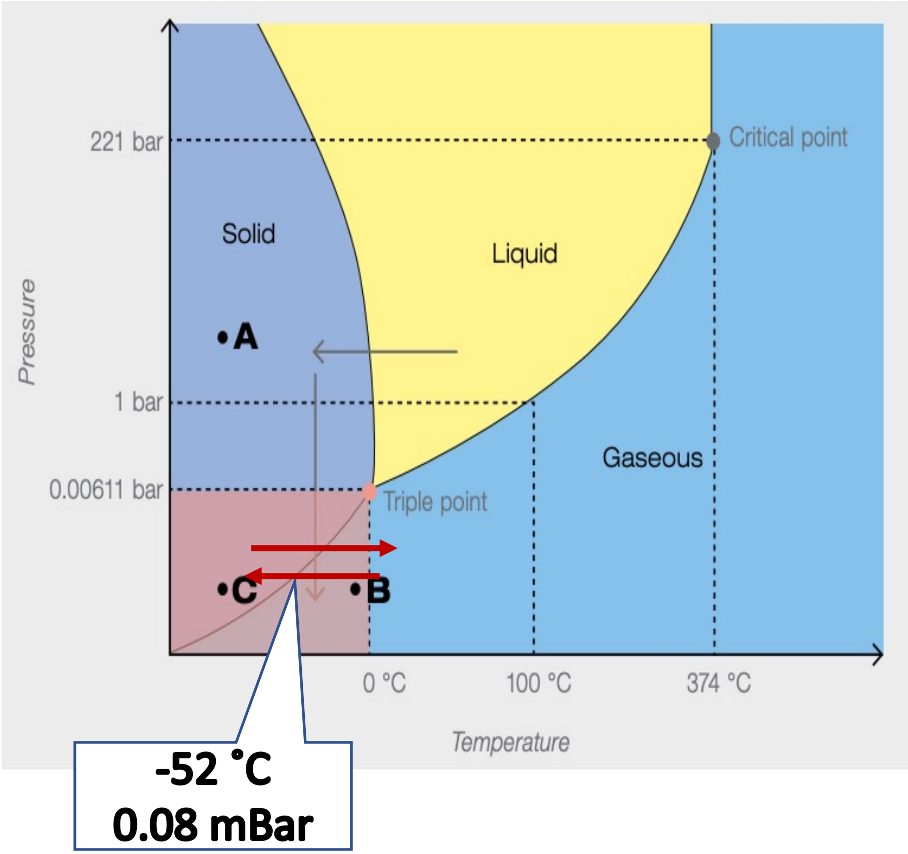
Freeze Drying

- Freeze drying comprises three steps:
- Freezing the solution.
- Reducing the atmospheric pressure above the ice to below that of the triple point of the product.
- Adding heat to the system to raise the temperature to the sublimation curve (CO) to provide the latent heat of sublimation.



Freezing Stages

- The liquid material is frozen **before** the application of a vacuum to avoid frothing.
- **Liquid is cooled** well below the normal freezing temperature for pure water and it is usual to work in the range –10 to –30˚C or even less.
- **Vacuum Stage**:
- A vacuum pump is used to drop the pressure **below the triple point**.
- It will also use to remove the formed water vapor during sublimation.
- Low pressure will cause **water to boil** at much lower temperature.
- Usually, the vacuum is able to reduce the pressure well below that of triple point to ensure that enough vacuuming is available at all times.

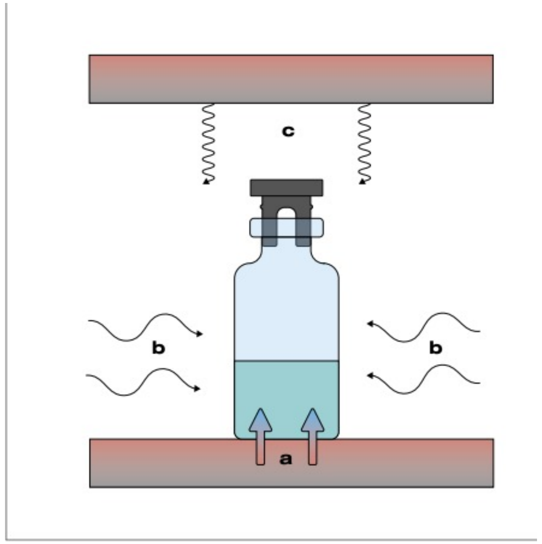


Freezing Stages

- **Sublimation stage**:
- **Heat** of sublimation must be supplied. As the process takes place at a low temperature, the additional heat needed to sublime the ice will be small.
- Since the **sublimation stage is slow** (about 1 mm thickness of ice per hour) and required solid surface, we need to make sure that we have large solid surface to speed up the process.
- The surface area can also be increased by freezing the containers in **angled position**.
- This stage will result in a **powder with very low moisture** content (less than 0.5%).
- **Secondary Drying**:
- The **removal of the final amounts** of residual moisture at the end of primary drying is performed by raising the temperature of the solid to as high as 50 or 60°C.

Packaging

- Attention must be paid to packaging freeze-dried products to ensure protection from moisture during storage.
- Containers should be closed **without contacting the atmosphere**, if possible, and vials, for example, are closed while still under vacuum.

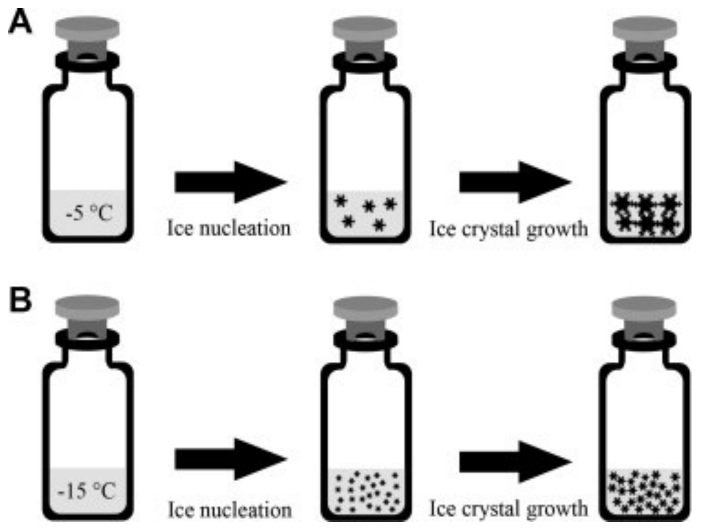


Advantages

1. Drying takes place at very low temperatures, so that **enzyme action is inhibited** and chemical decomposition, particularly **hydrolysis, is minimized**.
2. The solution is frozen such that the final dry product is a network of solid occupying the same volume as the original solution. Thus, the **product is light and porous**.
3. The porous form of the product **gives ready solubility** of the freeze-dried product.
4. There is **no concentration of the solution prior to drying**. Hence, salts do not concentrate in the wet state and denature proteins, as occurs with other drying methods.
5. Since the process takes place under high vacuum, there is little contact with air and **oxidation is minimized**.

Disadvantages

1. Ice **crystal will form during freezing** which may destroy the product such as blood cells and **reduce the viability** of microbial cultures.
2. The porosity, ready solubility and complete dryness of the product result in one with a **very hygroscopic nature**. Unless dried in the final container and sealed in situ, packaging requires special consideration.
3. The **process is very slow and** uses complicated plant that is **very expensive**. It is not a general method of drying, but is limited to certain types of valuable products that, because of their heat sensitivity, cannot be dried by any other means.



Solute migration

- **Solute migration** is the phenomenon that can occur during drying which results from the **movement of a solution** within a wet system.
- The **solvent** moves towards the surface of a solid (from where it evaporates), **taking** any dissolved solute with it.
- Many **drugs** and **binding agents** are soluble in granulating fluid and during the drying of granulates these solutes can move towards the surface of the drying bed or granule and be deposited there when the solvent evaporates.
- Migration associated with drying granules can be of **two types**:

1. **Intergranular** migration (between granules).
2. **Intragranular** migration (within individual granules).

Solute Migration

1. **<u>Intergranular Migration</u>**

- Intergranular migration, where the solutes **move:**

a) From **granule to granule**, may result in **gross maldistribution** of active drug.

b) From **granule to granule towards the top surface** of the bed where evaporation takes place.

- When the granules are compressed, the tablets **may have a deficiency** or an **excess of drug**.
- This type of migration mostly occur in fixed bed dryers such as tray dryer.

2. **<u>Intragranular migration</u>**

- Drying methods based on fluidization and vacuum tumbling keep the granules separate during drying and so prevent the intergranular migration.
- In this case the **solutes move** towards the **periphery of each granule**.

Consequences of Solute Migration

- **Loss of active drug**:
- May happen **during fluidized bed** drying when the fine drug-rich dust will be **eluted in the air** and carried to the **filter bag or lost**.
- This is why we need to be careful in collecting fines during drying and to regularly evaluates the drying process.

- **Migration of solute binders**:
- Intragranular migration may deposit a soluble **binder at the periphery** of the granules and so confer a '**hoop stress' resistance**, making the granules harder and more resistant to abrasion

Consequences of Solute Migration

- **Mottling of colored tablets**:
- Intragranular migration of the color may give rise to dry granules with a highly **colored outer zone** and a **colorless interior**.
- During compaction granule fracture takes place and the colorless interior is exposed. The eye then sees the colored fragments against a colorless background and the tablets **appear mottled**.
- This problem **can be reduced** by:

1. using **lake color** and/or;
2. Formulation **smaller granules** that do not fracture.