INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION

国际创新药学院

Drying

Course BSc (Pharm) or BSc (ATT)

Year 2024-2025 II

Module Medicines: Pharmaceutics 2 (MP2)

Lecturer Dr. Shi Du

Learning Outcomes

1. Review the states of matter and heat transfer in relation to the process of drying
2. Describe the concepts of moisture content, humidity and their relationship to drying processes
3. List and describe the principal types of equipment used to dry wet solids
4. Describe two specialised drying processes: spray drying and freeze drying
5. Explain the concept of solute migration and list methods to reduce its occurrence in tabletting

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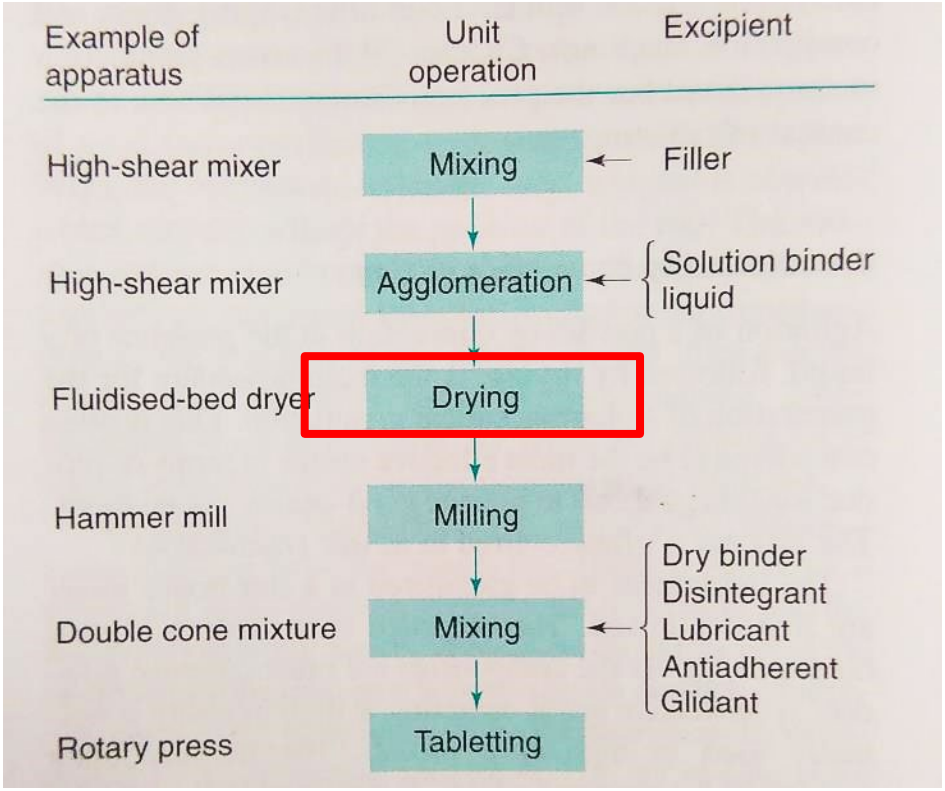
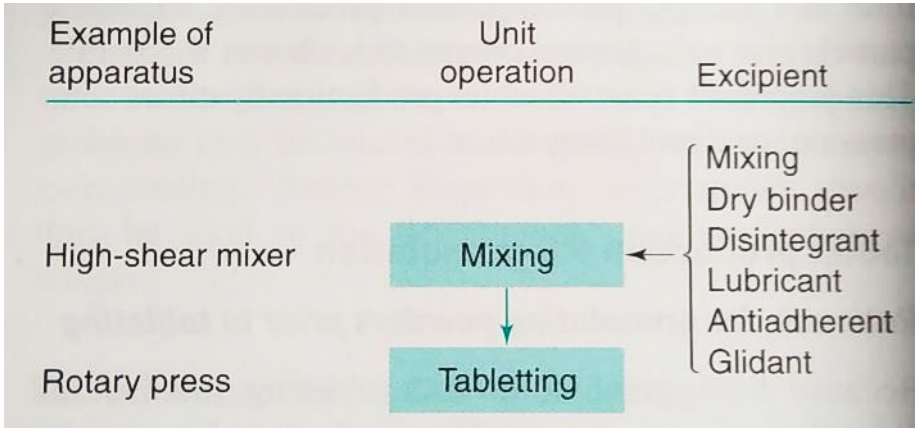
Unit Operations in Tabletting

Tablet Production with Granulation



Tablet Production with Direct Compression



Drying is the process in which all or most of the liquid associated with a wet pharmaceutical product is removed.

- Drying is important for stability, flow properties and compaction in tabletting processes
- Drying processes in pharmaceutical manufacturing involves evaporation or sublimation with removal of liquid vapour-> Importance of latent heat
- Drying processes reflect the three main methods of heat transfer

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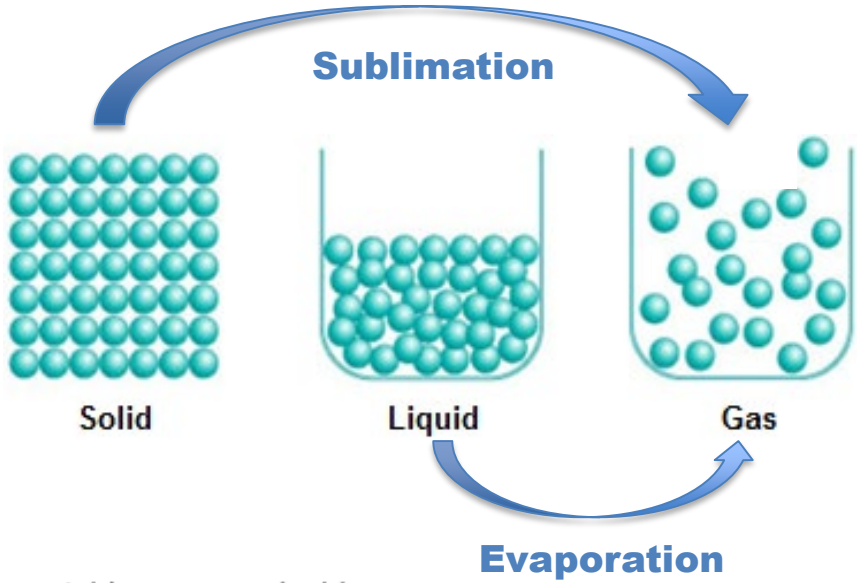
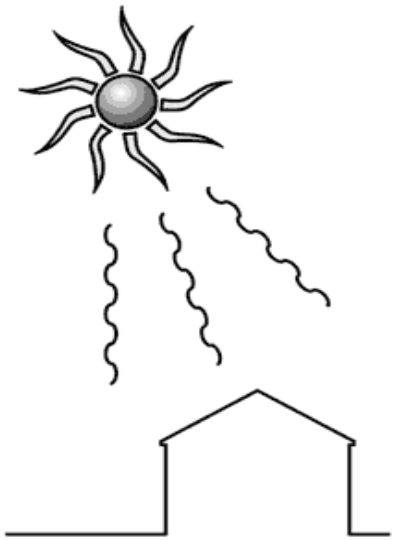
Drying: States of Matter and Heat Transfer

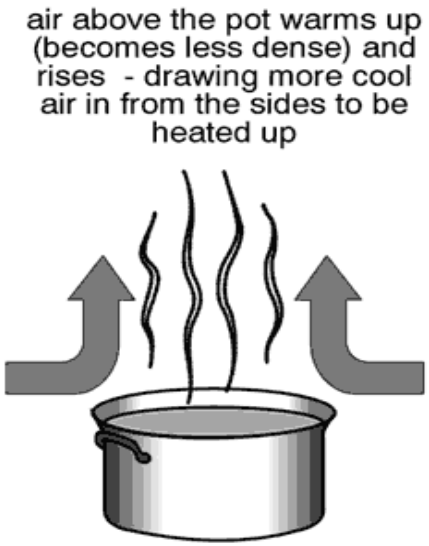


Methods of heat transfer



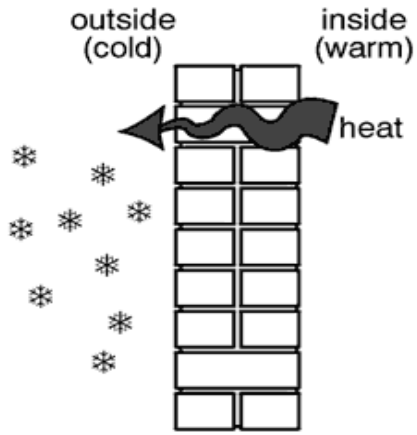
radiation

heat transferred through electromagnetic waves e.g. thermal infrared energy (sunlight)



convection

heat transfer within a gas or liquid



conduction

heat transfer through a solid material

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Drying: Essential Concepts

- Drying processes are related to the moisture content of the wet solid, the moisture content of air and relative humidity of the air
  - The moisture content of a solid is often expressed as a percentage of the completely dry mass
  - The **total moisture content** of a wet solid mass is composed of easily **unbound water** (easily removable) and **bound water** (harder to remove)
  - **Free moisture content**: The unbound water existing in the mass as a liquid that is easily evaporated to give an **air dry** solid
  - **Equilibrium moisture content:** The water within a solid that is a result of the equilibrium between the solid and air moisture

- Moisture content of air vs relative humidity of air
  - Ambient air is a solution of water in a mixture of gases
  - Water solubility depends in air on the temperature
  - Relative humidity refers to the percentage of saturation at a certain temperature

- In drying processes, the temperature and moisture content of air can change
  - Importance of vapour removal in process

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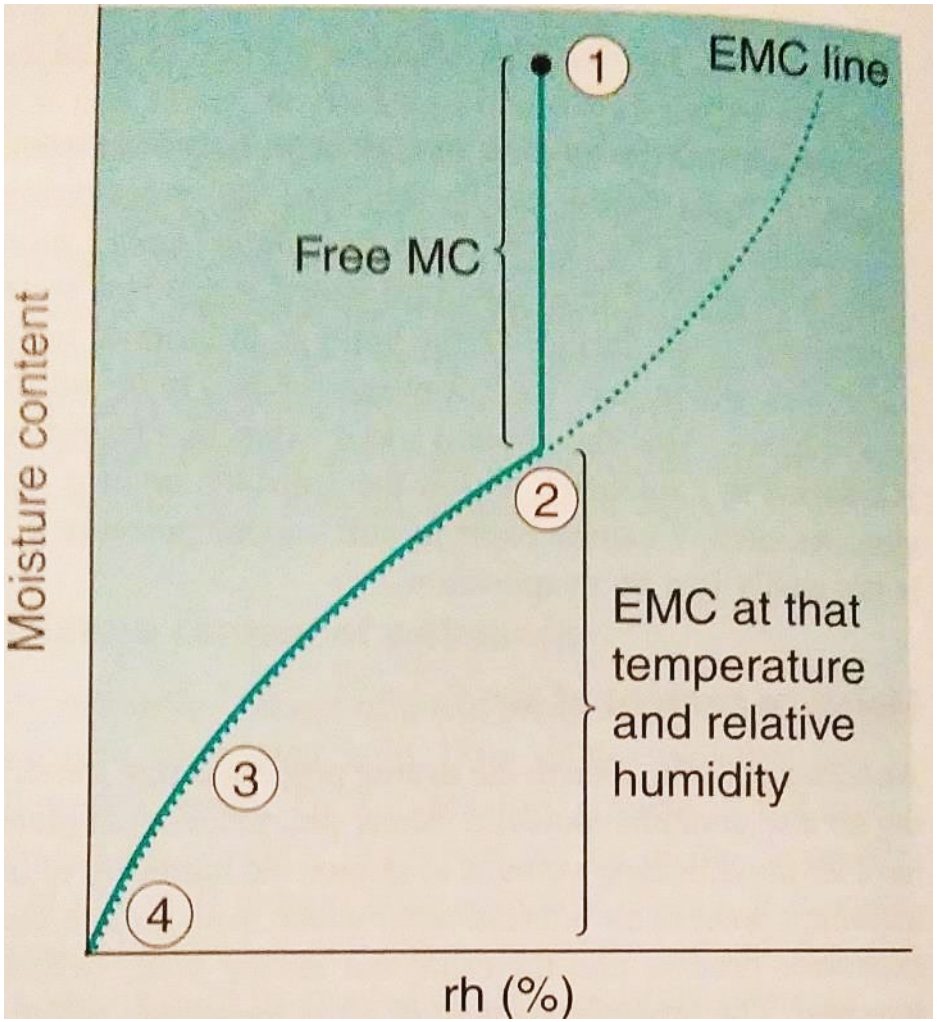
Drying: Essential Concepts



1. Wet solid before drying
2. Solid after evaporation (EMC)
3. Lower rh to reduce EMC
4. Lower rh to reduce EMC

EMC = Equilibrium moisture content
rh = Relative humidity

Relative humidity influences the drying process!

- EMC and bound water
- Moisture regained after drying
- Most materials have more favourable properties when they contain small amounts of residual water (e.g. granules 1-2%)

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Drying Equipment

- Factors to consider when choosing a drying method for tablets
  1. Heat sensitivity of materials
  2. Physical characteristics of materials
  3. Nature of liquid to be removed
  4. Scale

- Dryers use convective, conductive or radiative methods to dry solid masses
  - Efficient drying relies upon large surface areas, efficient heat transfer, efficient mass transfer and efficient vapour removal

- Types of dryers
  1. Fluidised-bed dryer **(Convection)**
  2. Vacuum oven **(Conduction)**
  3. Microwave **(Radiation)**
  4. Spray dryer
  5. Freeze-dryer

$$Q = UA\Delta B$$

Q = Rate of transfer

U=Overall transfer coefficient

A=Surface Area over which transfer takes place

ΔB=Driving force for transfer

For mass transfer = pressure or concentration gradient

For heat transfer = temperature gradient

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Fluidised-bed Dryers

- Powder particles fluidised in a stream of air and granulated
  - Drying by convection
  - Turbulent conditions allow lead to high heat and mass transfer rates

- Advantages (For drying specifically)
  - High drying rates
  - Uniform drying: All particles exposed to drying in homogenous fashion
  - Solute migration is minimal
  - Large amounts of up to 1500kg available

- Limitations
  - Equipment is expensive
  - Excessive size reduction by attrition
  - Generation of static electricity

BEWARE!!!
- Do not mix up fluidised-bed **drying** and fluidised-bed **granulation**

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Vacuum Oven

- Method not used as commonly anymore in large-scale production
  - Drying by conduction
  - Used more on smaller scale

- Process
  1) Reduce pressure in sealed chamber with vacuum
  2) Heat shelves
  3) Water boils at lower temperature
  4) Vacuum removes vapour

- Advantages
  - Low temperatures used for drying
  - Low risk of oxidation

- Limitations
  - Scale issues and uniformity of drying
  - Solute migration on powder tray

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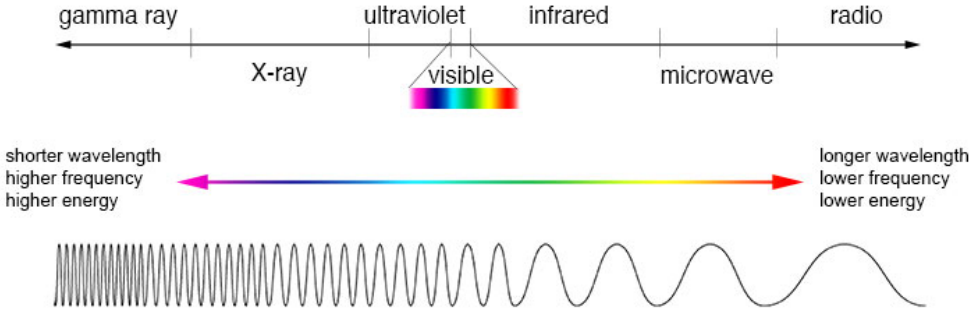
Microwave Dryers



- Efficient heating and drying method
  - Drying by radiation
- Process
  1) Magnetron produces microwaves
  2) Electromagnetic radiation beamed through window
  3) Resonance of electrons in solid mass transfers energy
  4) Heat is generated
- Advantages
  - Low temperatures used
  - Rapid heat transfer
  - Efficient because surroundings remain cool
  - Powder can be stationary
  - Uniform drying (good penetration)
  - Equipment is highly refined

- Limitations
  - Batch size smaller than for other methods
  - Radiation hazard

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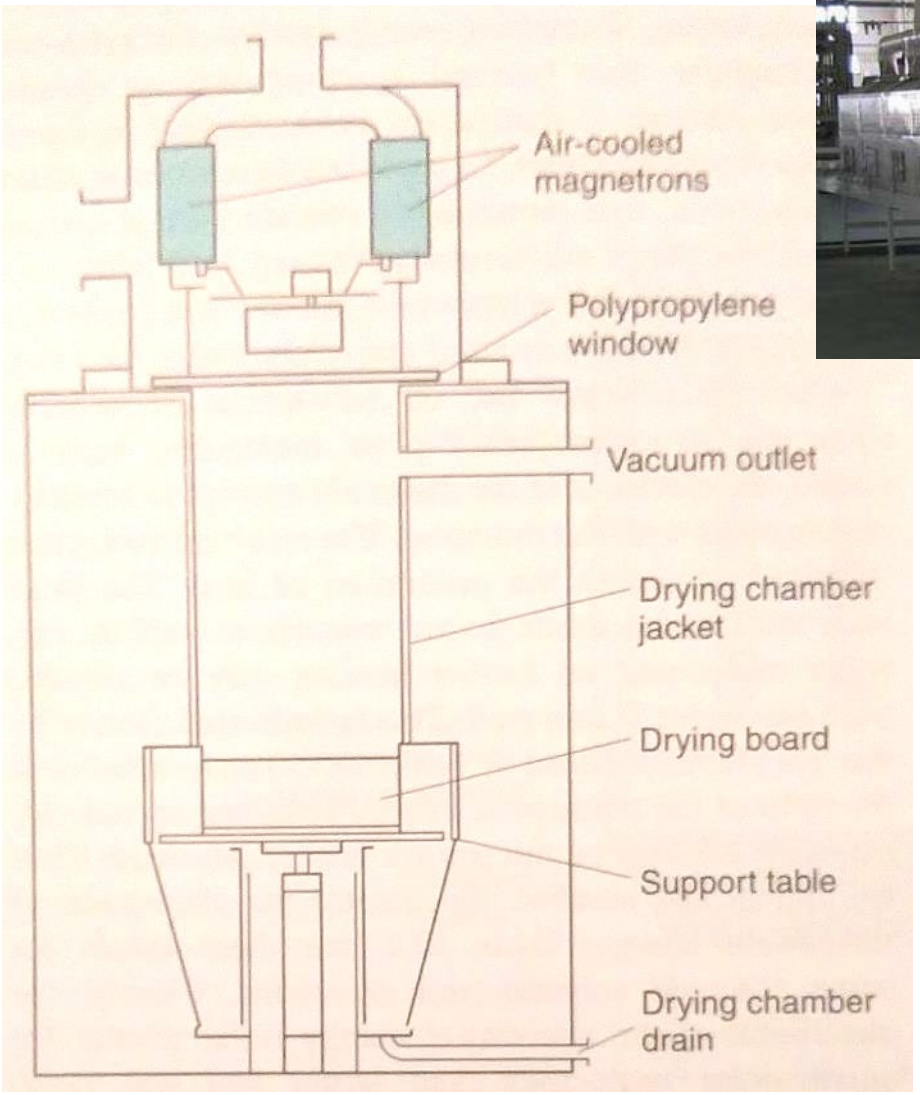
Microwave Dryers



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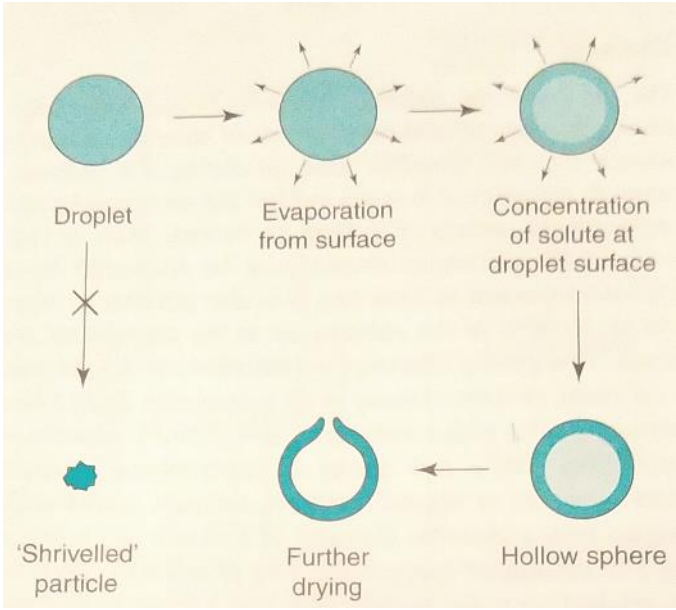
Spray Drying

- Spray drying is a method of drying a solution or suspension of particles
  - Generates large surface area by producing droplets that are dried
  - Droplets dry into solid particles

- Process
  1) Liquid preparation fed into spray dryer
  2) Pressurised air and atomiser disperses liquid into drying chamber as droplets
  3) Droplets dried in warm air currents and by attrition
  4) Dry product collected

- Advantages
  - Low temperature (latent heat)
  - Rapid heat transfer
  - Uniform drying
  - Uniform particle size shape (spherical) and distribution

- Limitations
  - Expensive
  - Overall heat transfer is inefficient
  - Polymorphism and amorphism risk



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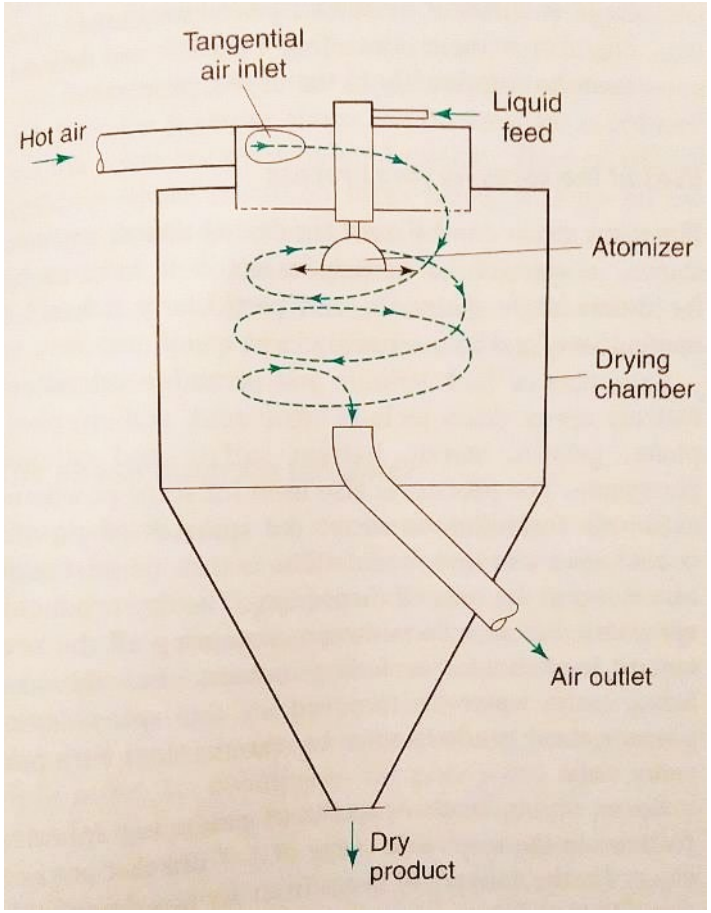
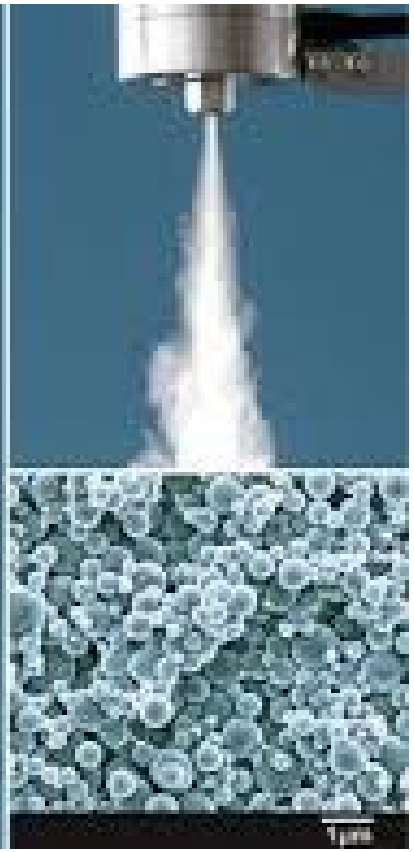
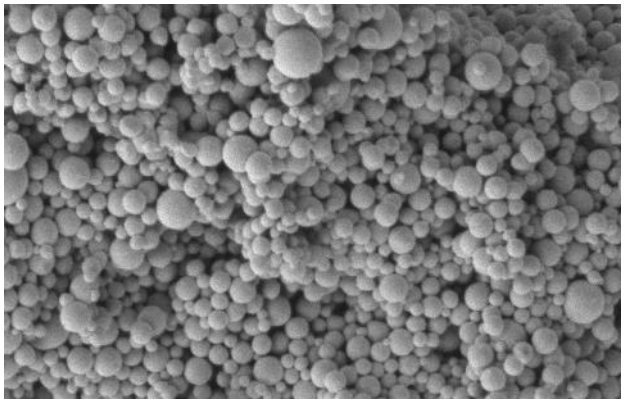
Spray Drying







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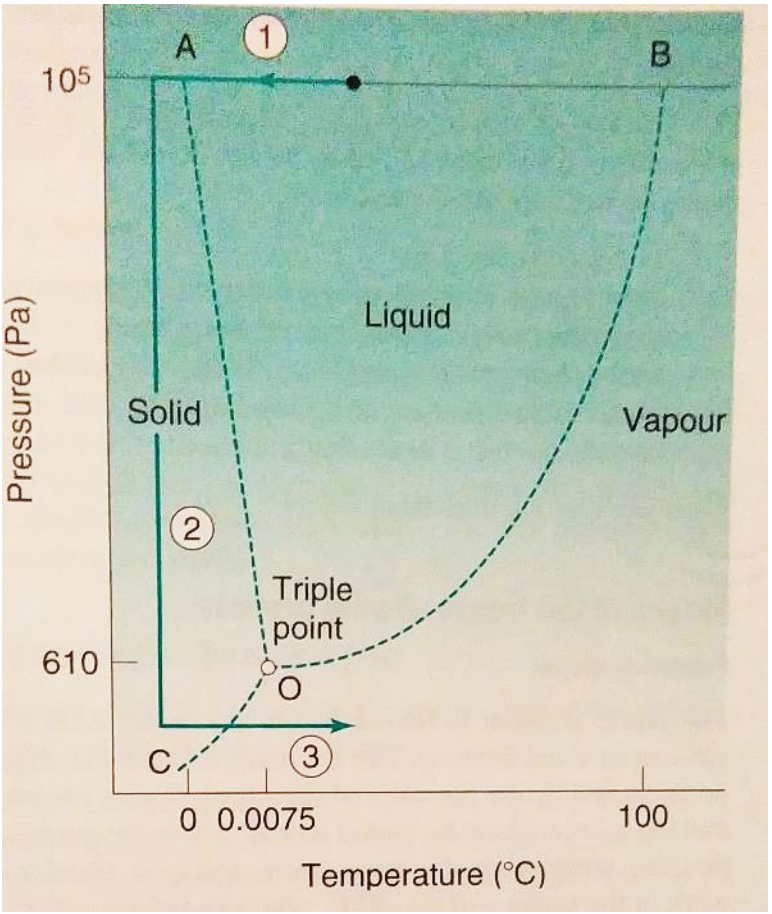
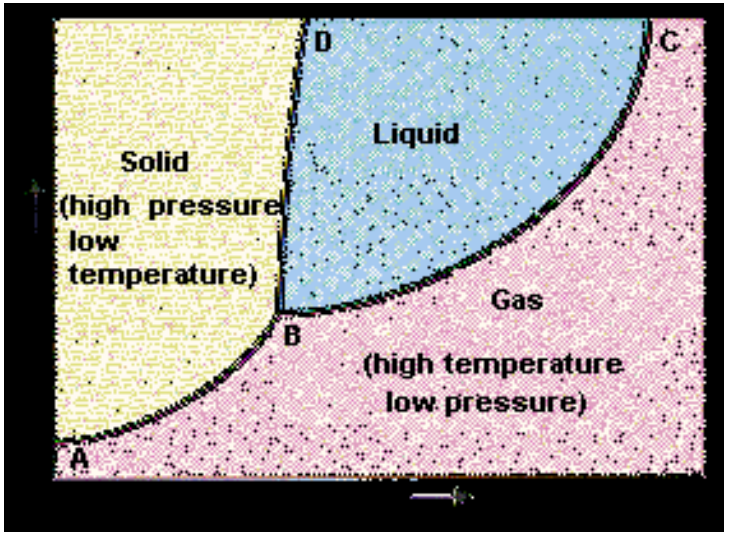
Freeze-Drying: Lyophilisation of Heat-Sensitive Materials

- Drying process of choice for extremely thermolabile substances
  - Removal of liquid by freezing and sublimation
  - Low temperatures and low pressures used
  - Phase diagram of water





- Process for liquid with melting point B
  1. Reduce temperature to point below freezing point of liquid at atmospheric pressure (A)
  2. At this temperature, reduce the pressure using a vacuum to a point below the triple point of liquid (C)
  3. At this pressure, increase the temperature for sublimation to occur

  (i.e. drying by going directly from solid to gas)

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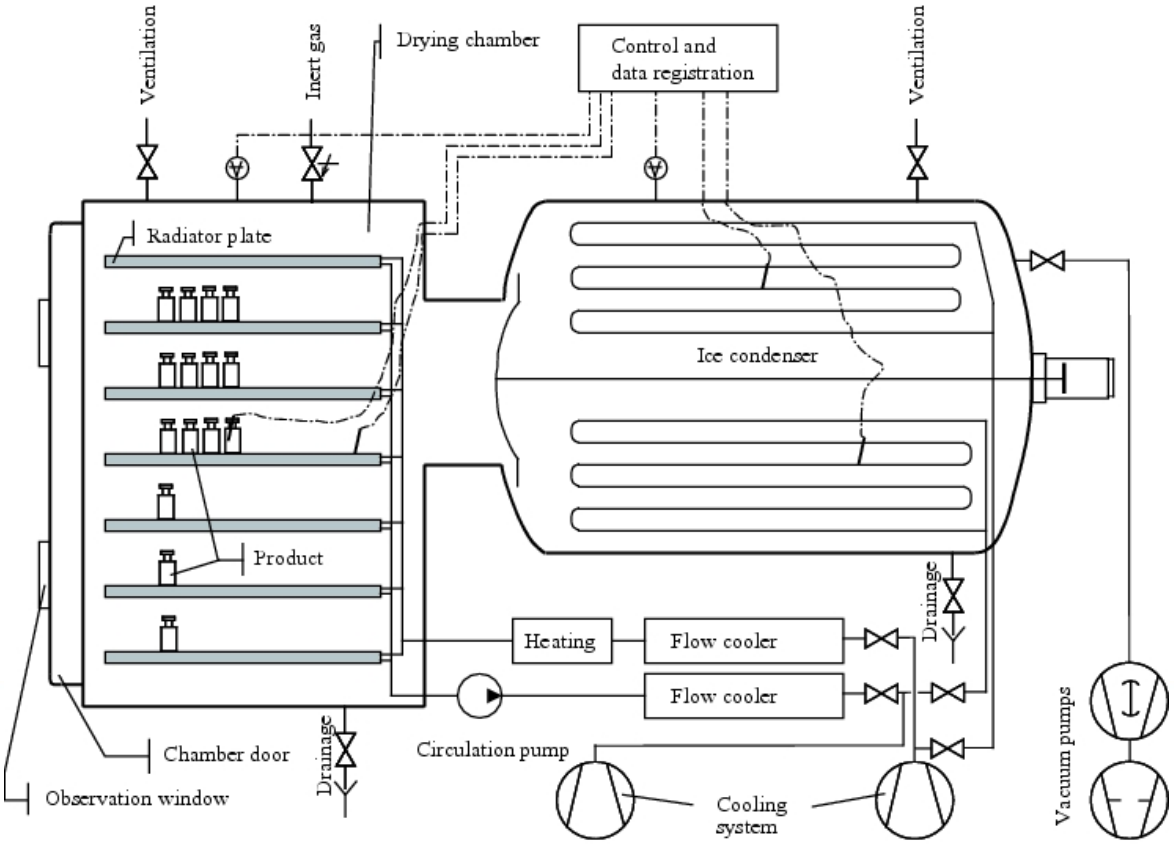
Freeze-Drying: Lyophilisation of Heat-Sensitive Materials

- Advantages
  - Very low temperatures used for drying (stability)
  - Little oxidation
  - Product formed is light and porous
  - Can be used for protein formulation
- Limitations
  - Expensive
  - Time-consuming
  - Product formed is hygroscopic



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Solute Migration

- Essentials
  - Phenomenon in drying where solutes concentrate on particle surfaces during removal of solvent
  - Important factor to for uniformity of content within granules

- How does solute migration happen?
  - Evaporation occurs at particle interface with environment
  - Solvents moving to interface ferry dissolved solutes with high affinity for the solvent
  - Removal of solvent causes precipitation of solute at surface

- Solute migration and granule drying fall into two categories
  1. Intergranular migration: Solutes move from granule to granule
  2. Intragranular migration: Solutes move to periphery within granule

- The consequences of inappropriate solute migration
  - Non-uniform drug distribution
  - Loss of drug
  - Migration of soluble binders
  - Mottling of coloured tablets

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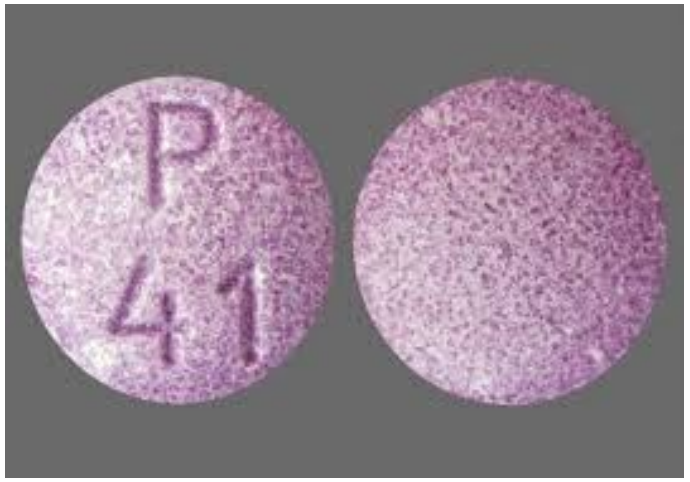
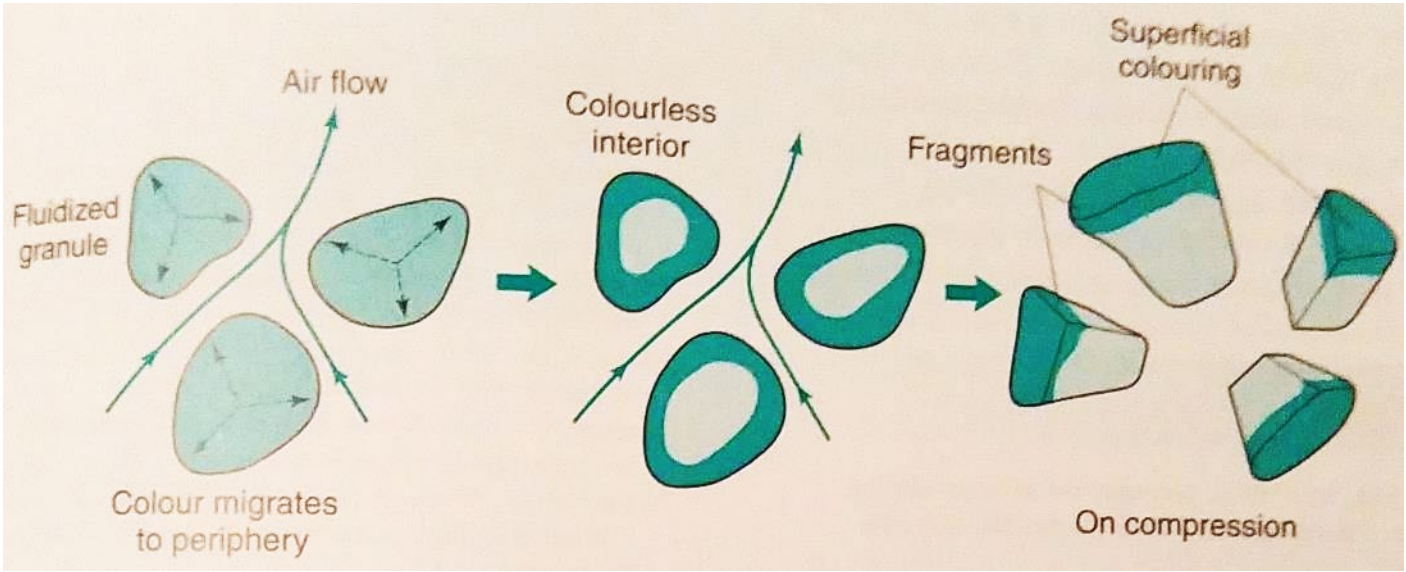
Solute Migration

- Factors affecting solute migration
  - Nature of ingredients in powder
  - Viscosity of granulating fluid
  - Method of drying
  - Initial moisture content



- Methods of reducing solute migration
  - Use minimum quantity of granulating fluid
  - Disperse fluid homogenously
  - Use smallest granules possible
  - Use alternative drying method



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Further Reading

- Aulton's Pharmaceutics Chapter
  - Drying

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