Pharmaceutical Unit Operations - DRYING

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PHA 3005-Pharmaceutical Technology- I

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Definition of Drying

Many pharmaceutical operations, including those used to produce active pharmaceutical ingredients and excipients, use water or organic solvents as essential processing aids.

However, the continued presence of these processing aids may harm manufacturing operations or the safety and stability of the final pharmaceutical product.

Drying is a common unit operation used to reduce the levels of water or organic solvent in pharmaceutical materials to acceptable levels.

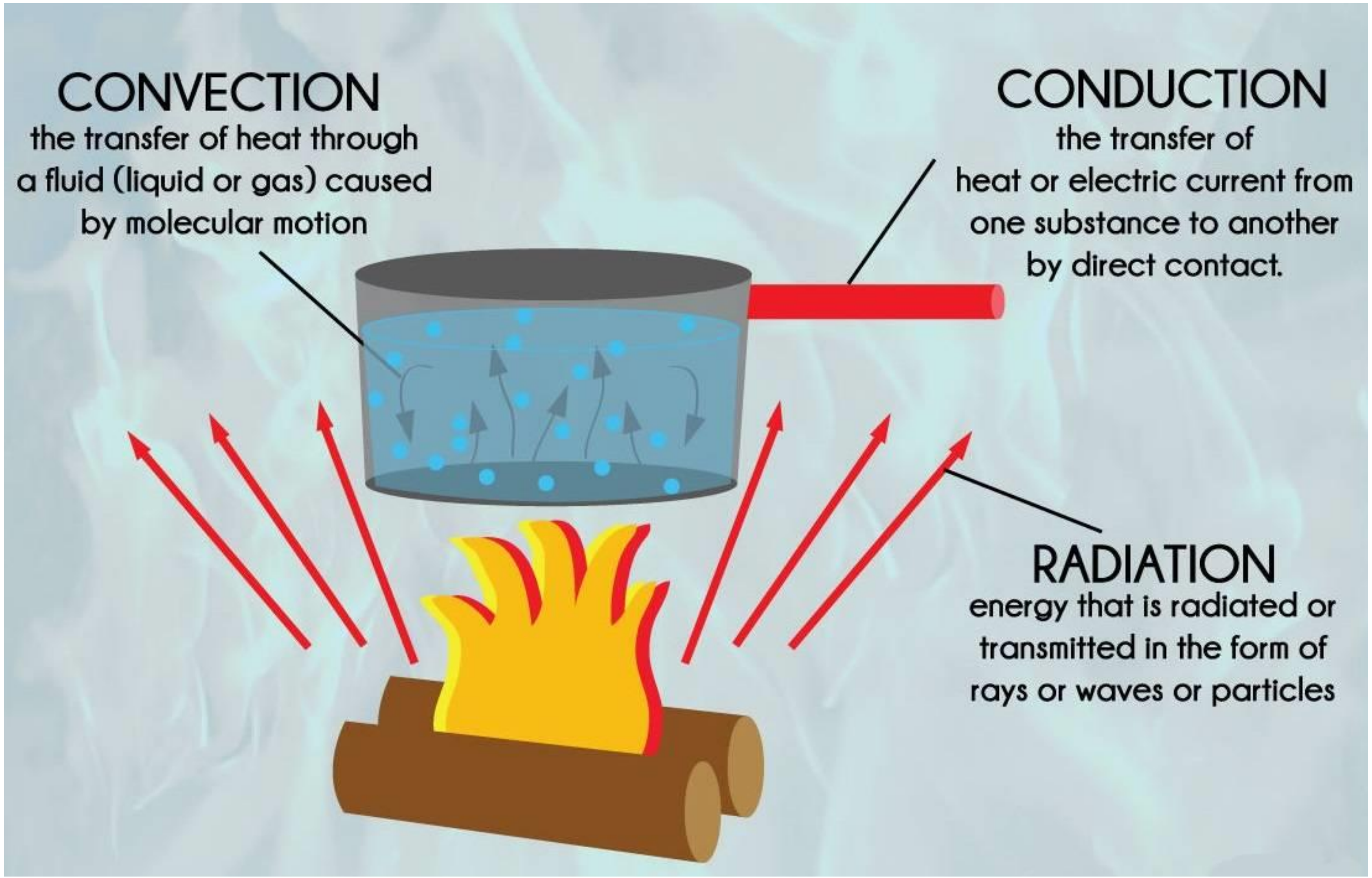
Drying process in pharmaceutical technology

- The granules to be pressed into tablets or filled into capsules are dried
- Tablets, granules, particles are dried during coating processes
- Nanoparticles, microspheres and microcapsules are dried after preparation
- Materials are dried to assist grinding process
- Freeze-drying (lyophilization) process
- Drying processes applied in the preparation of sterile injection powders

Besides,

- Obtaining plant-derived medicines, the plants must be dried prior to extraction, the resulting extracts should be dried
- Purification and drying of inorganic salts (sodium chloride, calcium carbonate etc.)
- To obtain dry powder form of drugs and excipients

Mechanisms of Heat Transfer



Humidity is measured by:

- **Gravimetric method:**

Air is passed over a certain substance of known weight, which can absorb moisture, such as phosphorus pentoxide. The absolute humidity of the air is calculated from the change in the weight of the substance

- **Mechanical Hygrometers:**

Contains a spring or composite bar that expands or contracts depending on the ambient humidity.

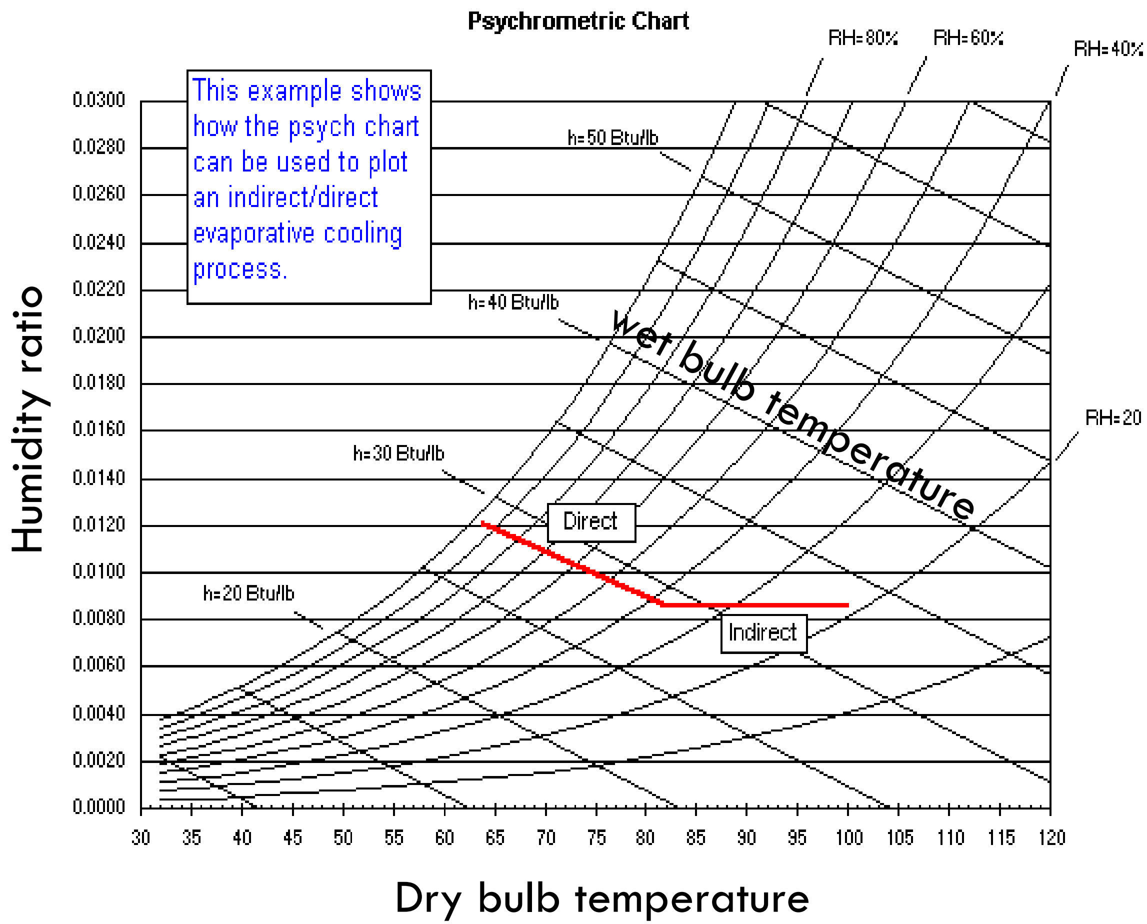
- **Electronical Hygrometers**

- **Psychrometers**

Psychrometer

A psychrometer is a pair of identically shaped thermometers, one of which is covered with a wet sleeve. It measures humidity by taking both a wet-bulb and a dry-bulb temperature reading.

With those two values known, the other properties of the air, including its moisture content, can be determined by computation or by reading a psychrometric chart.



Relative Humidity Table (in percent)

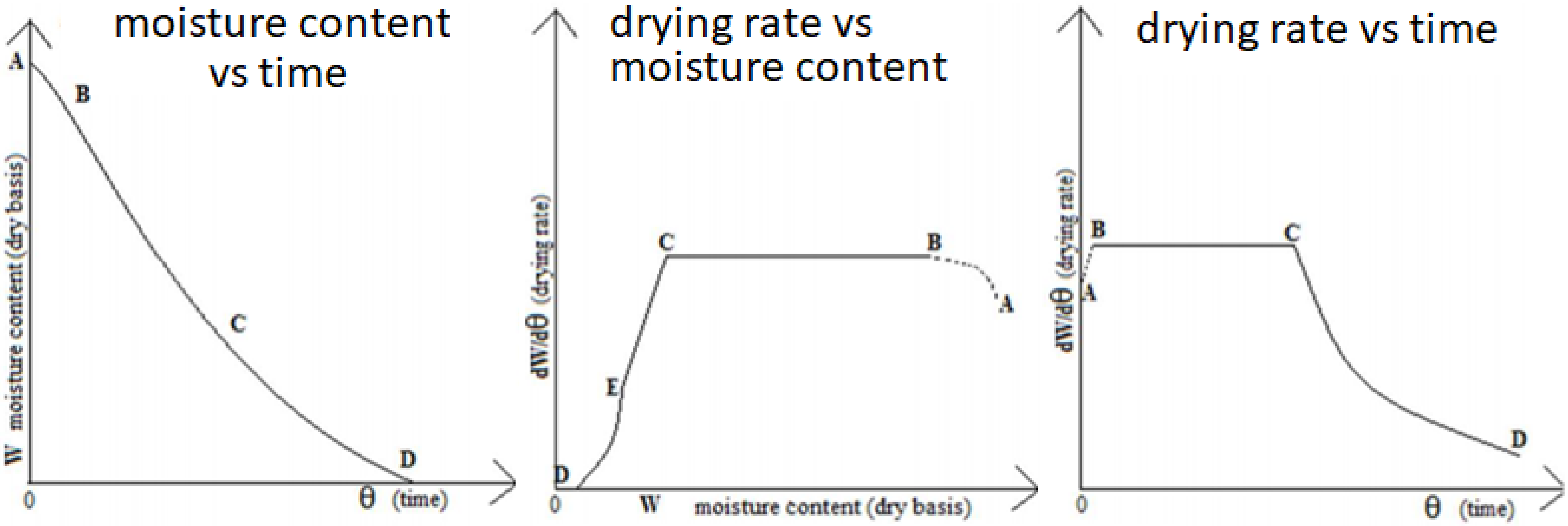
Dry Bulb	Dry Bulb Minus Wet Bulb (degrees celsius)									
°C	1	2	3	4	5	6	7	8	9	10
10	88	77	66	55	44	34	24	15	6	
11	89	78	67	56	46	36	27	18	9	
12	89	78	68	58	48	39	29	21	12	
13	89	79	69	59	50	41	32	22	15	7
14	90	79	70	60	51	42	34	25	18	10
15	90	81	71	61	53	44	36	27	20	13
16	90	81	71	63	54	46	38	30	23	15
17	90	81	72	64	55	47	40	32	25	18
18	91	82	73	65	57	49	41	34	27	20
19	91	82	74	65	58	50	43	36	29	22
20	91	83	74	67	59	53	46	39	32	26
21	91	83	75	67	60	53	46	39	32	26
22	91	83	76	68	61	54	47	40	34	28
23	92	84	76	69	62	55	48	42	36	30
24	92	84	77	69	62	56	49	43	37	31
25	92	84	77	70	63	57	50	44	39	33

Introduction to Drying Process

Drying can be described by three processes operating simultaneously:

- The first process is energy transfer from an external source to the water or organic solvent in the material.
- The second process is the phase transformation of the water or organic solvent from a liquid or liquid-like state to a vapor state.
- The third process is the transfer of the vapor generated away from the pharmaceutical material and out of the drying equipment.

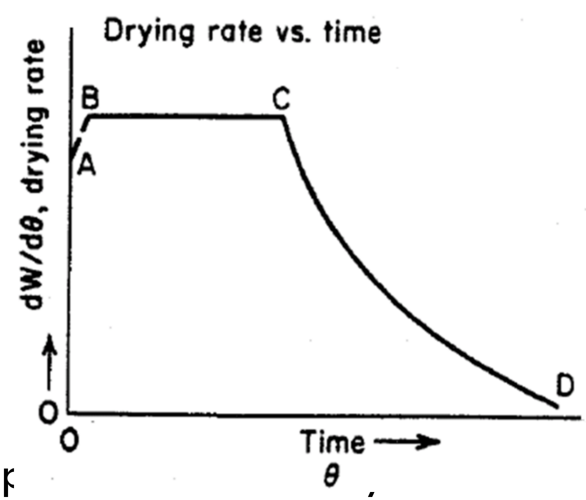
Periods of Drying



- Warm up period (A-B)
- Constant Rate Period (B-C)
- Falling rate period (C-D)

First phase → heating up

- Heat is transferred to the product.
- Product is heating up from the inlet condition to the process condition. The rate of evaporation increases dramatically during this period with mostly free moisture being removed.



Second phase → constant rate period

- Free moisture persists on the surfaces and the rate of evap the moisture content reduces. During this period drying rates are high, and higher inlet air temperatures than in subsequent drying stages.

Third phase → falling rate period

- This is the phase during which migration of moisture from the inner side of each particle to the outer surface becomes the limiting factor that reduces the drying rate.

The point C, where the drying rate begins to decrease, is called "critical moisture content".

Drying Methods

The following points should be considered when selecting the drying method to be applied to the material to be dried:

1) Drying properties of the material
2) Properties of dry matter obtained
3) Properties related to drying process
4) Operating conditions

Classification of dryers

I. Drying of solids with moisture

*Stationary (Static) bed dryers

a) batch types of static bed dryers

b) Continuous types of static bed dryers

*Moving bed dryers: vacuum dryers

*Fluid bed dryers

II. Drying of liquids in solution, suspension and slurry

*Pneumatic systems

*Freeze drying

According to heat transfer mechanism:

1- Direct dryers:

Heat reaches the material to be dried by hot air via convection.

2- Indirect Dryers:

Heat is transmitted by conduction. Heat reaches the material to be dried by the container wall on which they are placed. Therefore the material is in contact with the hot surface.

3- Dryers with IR radiation:

Drying occurs by absorption of IR light. Microwave dryers are in this class.

I. Drying of solids with moisture

1- Stationary (Static) bed dryers:

- Tray Dryers
- Tunnel Dryers
- Microwave Dryers

- There is no movement between the particles of the material to be dried.
- The drying air or heated trays are in contact with the surface.

2-Moving bed dryers:

- Rotary Dryers
- Rotating Tray Turbo Dryers
- Vacuum dryers

- The particles are in motion by gravity or mechanical stirring.
- Heat and mass transfer is faster than system 1.

3-Fluid bed dryers

- ✓ Particles are suspended in an air stream or gas stream.
- ✓ That is to say a solid mixture in gas, similar to a boiling liquid.
- ✓ There is a faster drying than system 1 and 2.

Tray Dryers

- It operates by passing hot air over the surface of a wet solid that is spread over trays arranged in racks.
- Tray dryers are the simplest and least-expensive dryer type.

Tunnel Dryers

- They make the trays mobile. The material to be dried are fed from one end in the air heated tunnel for drying and collected from the other end.
- The source of heating can be of

1) Hot air circulation
2) Infrared
3) Microwave or
4) Radio frequency.

Microwave Dryers

- By applying microwave energy to pharmaceutical systems to be dried, dielectric materials such as water and solvents with dissolved salts absorb the energy thereby increasing molecular vibration.
- They can be;

- stand-alone cabinets,
- fluid bed,
- vibrational capabilities,
- combination dryers with vacuum

Rotary Dryers

- The cascading rotary dryer is a continuously operated direct contact dryer.
- It consists a slowly revolving cylindrical shell that is typically inclined to the horizontal a few degrees to aid the transportation of the wet feedstock which is introduced into the drum at the upper end and the dried product withdrawn at the lower end.

Rotating Tray Turbo Dryers

- Consists of a stack of slowly **rotating** circular **trays.**
- Material is fed onto the top **tray.**
- After one revolution the material is wiped onto the next lower **tray.**
- Here it is mixed, leveled, and then after one revolution, is wiped to the next **tray** where the operation is repeated.

Vacuum Dryers

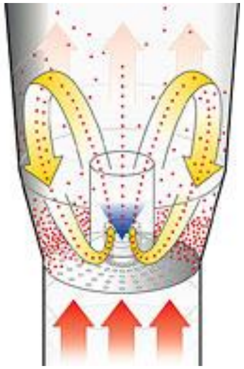
- The total pressure surrounding the pharmaceutical material is reduced to levels below the saturation pressure of the solvent at the interface between the wet and dry layers causing generation of vapor.
- Vacuum can be supplied by conventional pumps, blowers, or steam jets.
- Heating fluid circulates through a jacket and enters and exits through dynamic seals along the axis of rotation.
- With suitable vacuum levels, drying can be cost-effective at relatively low product temperatures.
- Vacuum drying is particularly advantageous for heat- or oxygen-sensitive products, for reducing the risk of dust explosions, and for applications requiring solvent recovery or extremely low residual solvent levels

Fluid Bed Systems

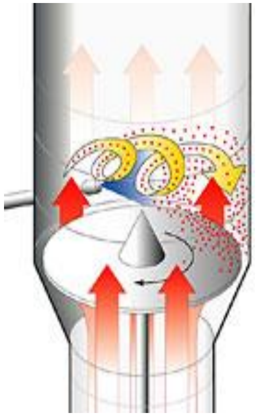
- Fluid bed-drying is a widely used example of the direct heating classification.
- Drying is accomplished by suspending the particles to be dried directly in a stream of heated air or other gaseous media.
- The intimate contact and high surface areas available for transfer result in fast, efficient drying, often making fluid bed the approach of choice for high-volume products

Fluid bed dryers

Top Spray

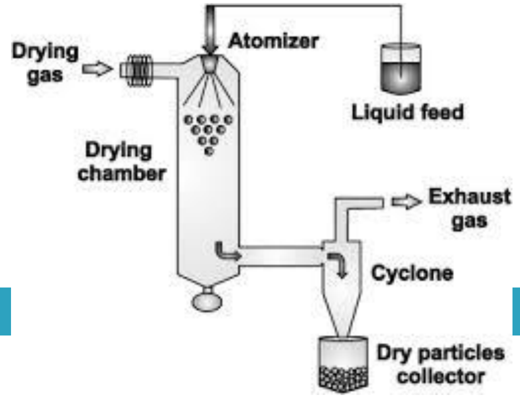


Bottom Spray
(Wurster coating)



Tangential Spray
(Rotor pellet coating)

Spray dryers



- Spray drying is a technique to generate powders by transforming the feed from a liquid state into a dry form, by spraying the feed into a hot drying medium.
- The feed can be a solution, suspension, dispersion, or emulsion.
- The spray drying process mainly consists of five steps:

Concentration: Before introduced to the spray dryer, feedstock is usually concentrated.
Atomization: Favors evaporation to a dry powder, by having optimum properties.
Droplet-Air Contact: In the chamber, atomized liquid contacts with hot gas, leading to evaporation of a majority of the water or solvent contained in the droplets within a few seconds.
Droplet Drying: Water or solvent evaporation takes places.
Separation: Cyclones, bag filters, and electrostatic precipitators may be used for the final separation stage

ADVANTAGES

- rapid,
- continuous,
- reproducible
- single-step
- suitable for scaling without major modifications
- the possibility to dry a broad spectrum of compounds including heat-sensitive substances without major detrimental effects
- Can be used to encapsulate drugs, extracts, aromatic oils, pigments, and flavors within different types of carriers such as polymeric nanoparticles (NPs) and microparticles.

Freeze drying (lyophilization)

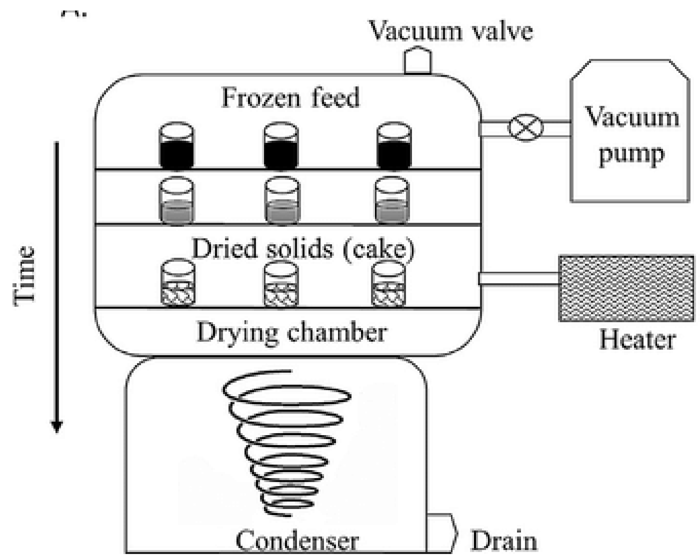
A drying process employed to convert solutions of labile materials into solids of sufficient stability for distribution and storage

-the removal of ice or other frozen solvents from a material through the process of sublimation and the removal of bound water molecules through the process of desorption.

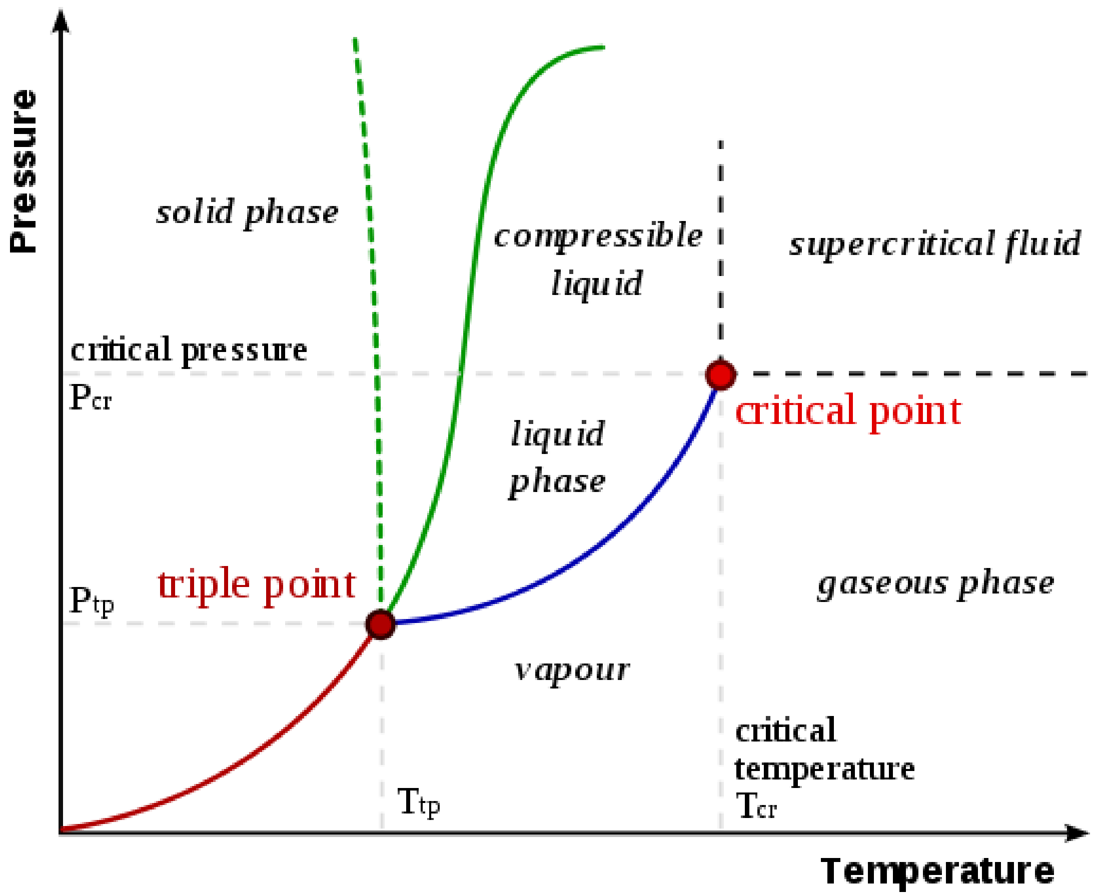
Sublimation is the transition of a substance from the solid phase directly to the gas phase without passing through an intermediate liquid phase.

A typical production scale freeze dryer consists of:

- Refrigeration System
- Vacuum System
- Control System
- Product Chamber or Manifold
- Condenser



triple point



defined as the point at which

- -solid,
- -gas,
- -liquid

coexist as three separate phases.

Lyophilization is carried out below the triple point to enable conversion of ice into vapor, without entering the liquid phase

Sublimation in the freeze drying process can be described as:

1. FREEZE - The product is completely frozen, usually in a vial, flask or tray.

1.VACUUM - The product is then placed under a deep vacuum, well below the triple point of water.

3. DRY – Heat energy is then added to the product causing the ice to sublime.

    1. PRIMER DRYING
    2. SECONDER DRYING

Application areas

- preparation of sterile powders for injection,
- To obtain the peptide-protein active substances as dry raw materials,
- Blood products, biological materials, bacterial strains, vaccines and sera are dosed in special containers and stored in lyophilized form under aseptic conditions,

- Some special drug forms and

drug delivery systems are prepared

- Widely applied in the production of fruit and coffee extracts.

Advantages of lyophilization

- Ease of processing a liquid, which simplifies aseptic handling
- Enhanced stability of a dry powder
- Removal of water without excessive heating of the product
- Enhanced product stability in a dry state
- Rapid and easy dissolution of reconstituted product

Disadvantages of lyophilization

- Increased handling and processing time
- Need for sterile diluent upon reconstitution
- Cost and complexity of equipment