Operation of drying

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Operation of Drying

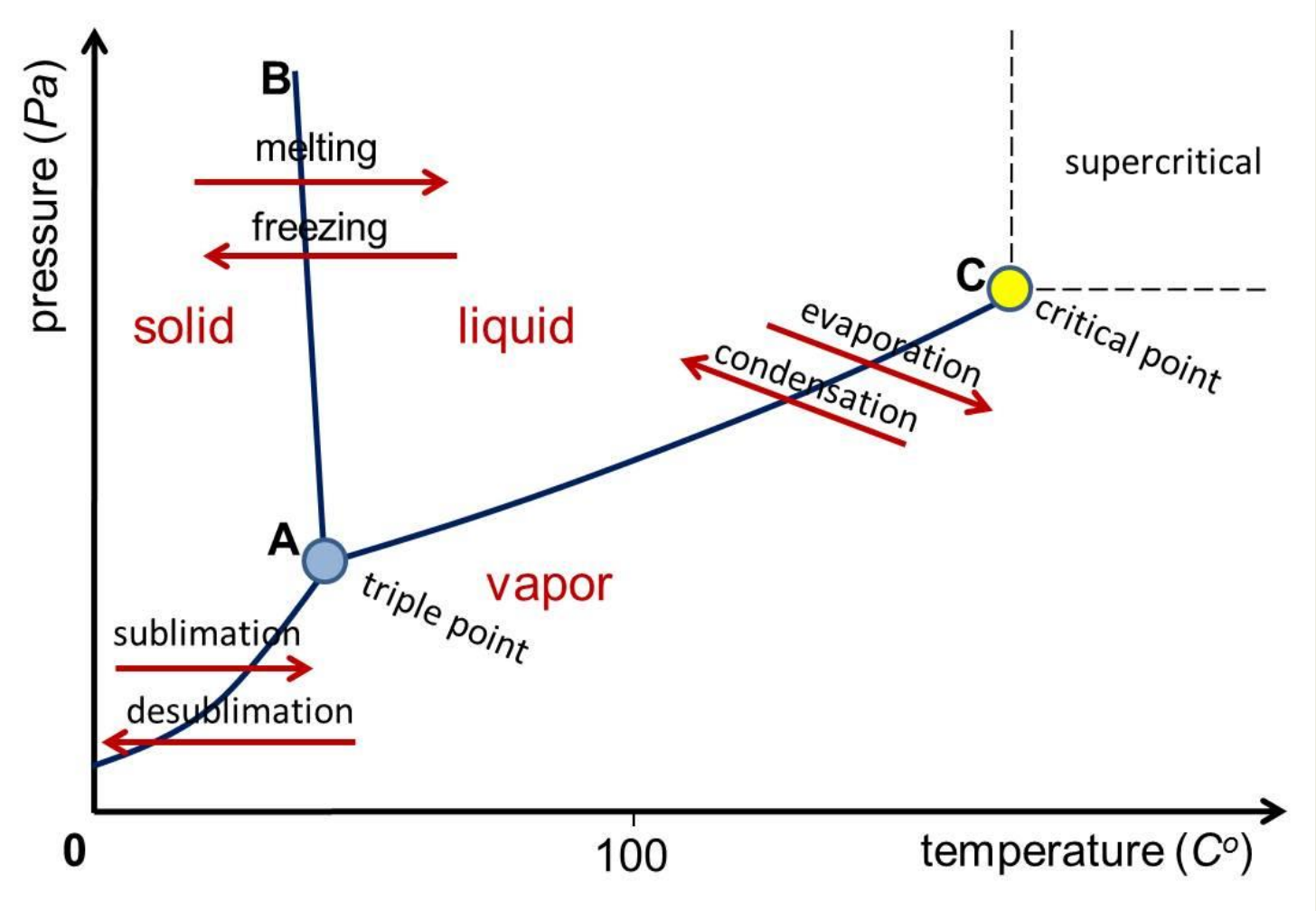
Definition of drying

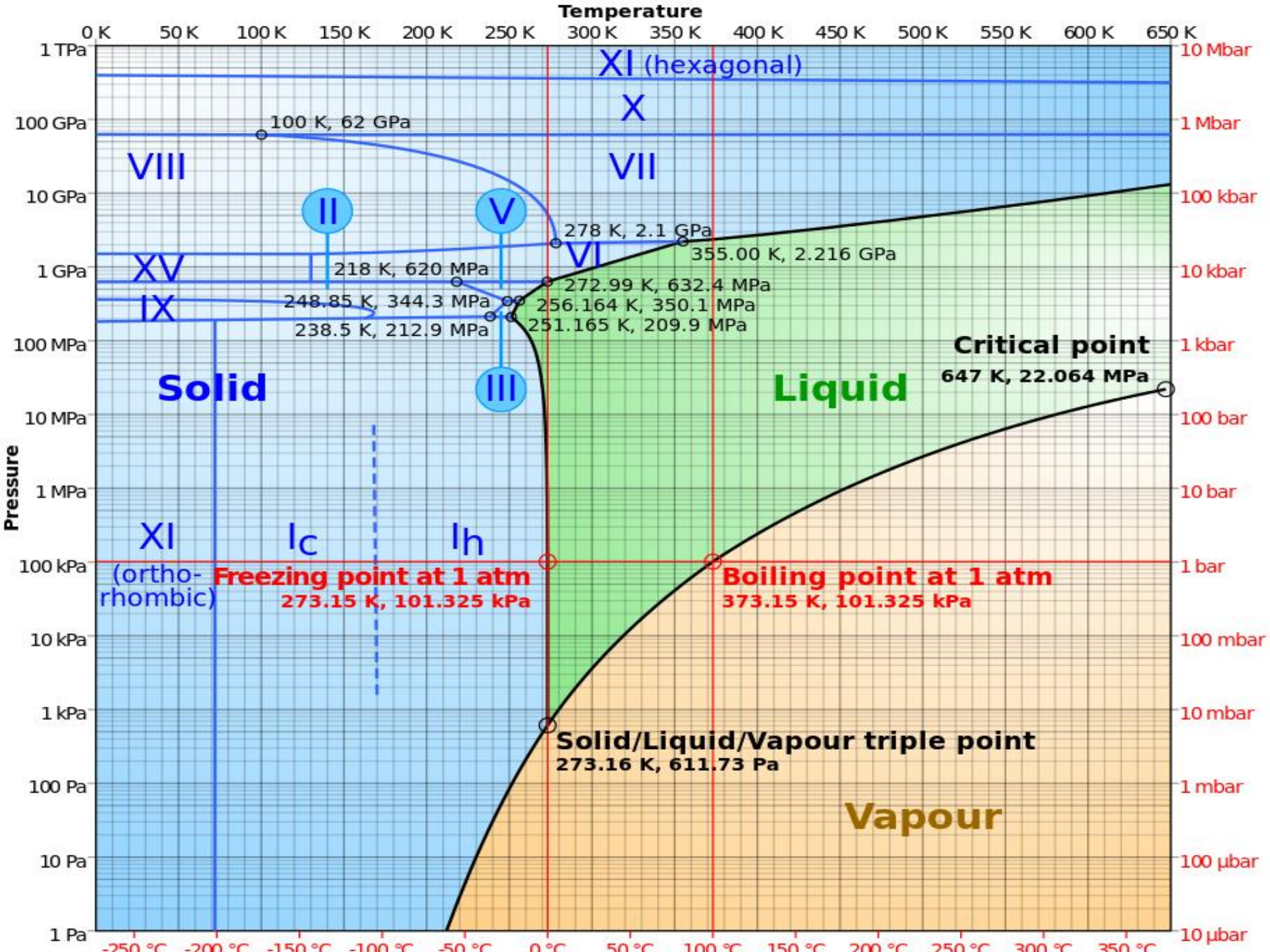
Drying is an operation of *mass transfer* and usually heat transmission in one, in which moisture is removed from the wet material.

The direction of component transfer (moisture evaporation) is from the stock to the air.

Theory of Drying

Phase diagram




Temperature
0 K
50 K
100 K
150 K
200 K
250 K
300 K
350 K
400 K
450 K
500 K
550 K
600 K
650 K
Pressure
1 TPa
100 GPa
10 GPa
1 GPa
100 MPa
10 MPa
1 MPa
100 kPa
10 kPa
1 kPa
100 Pa
10 Pa
1 Pa
10 Mbar
1 Mbar
100 kbar
10 kbar
1 kbar
100 bar
10 bar
1 bar
100 mbar
10 mbar
1 mbar
100 µbar
10 µbar
-250 °C
-200 °C
-150 °C
-100 °C
-50 °C
0 °C
50 °C
100 °C
150 °C
200 °C
250 °C
300 °C
350 °C
XI (hexagonal)
X
VIII
VII
II
V
VI
XV
IX
III
100 K, 62 GPa
278 K, 2.1 GPa
355.00 K, 2.216 GPa
218 K, 620 MPa
272.99 K, 632.4 MPa
248.85 K, 344.3 MPa
256.164 K, 350.1 MPa
238.5 K, 212.9 MPa
251.165 K, 209.9 MPa
Solid
Liquid
Vapour
Critical point
647 K, 22.064 MPa
XI
(ortho-
rhombic)
Ic
Ih
Freezing point at 1 atm
273.15 K, 101.325 kPa
Boiling point at 1 atm
373.15 K, 101.325 kPa
Solid/Liquid/Vapour triple point
273.16 K, 611.73 Pa

Drying practice

stationary-layer processes

Freeze drying

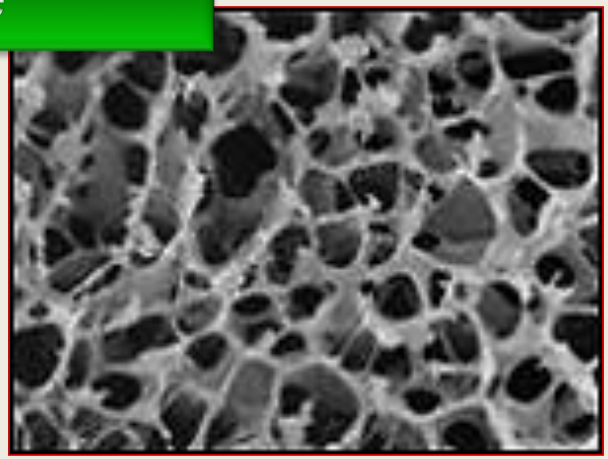
Definition:

Freeze-drying or lyophilisation is an effective way of drying materials without harming their structure. It makes use of the physical phenomenon of sublimation, which involves *the direct transition* between the solid state and the gaseous state without passing through the liquid phase. To achieve this, the frozen product is dried under vacuum, without being allowed to thaw out.

Examples of freeze dried products are antibiotics, bacteria, vaccines, diagnostic medications, protein-containing and biotechnological products, cells and tissues, and chemicals.

Drying practice

stationary-layer processes



Freeze drying

Advantages:

- heat sensitive ingredients can be dried without any significant change
- the biological samples and ingredients can remain their original biochemical, physiological, therapeutic properties after the drying process
- porous (with a large internal surface) structure is created
- rapid and complete dissolution (rehydration) of the dried material is possible.

Drying practice

stationary-layer processes

Freeze drying

Disadvantages:

- high investation cost
- expensive operation, significant energy need

Drying practice

INTRODUCTION

While the common application of pharmaceutical freeze drying is in the production of:

- injectable dosage forms.

The process is also used in the production:

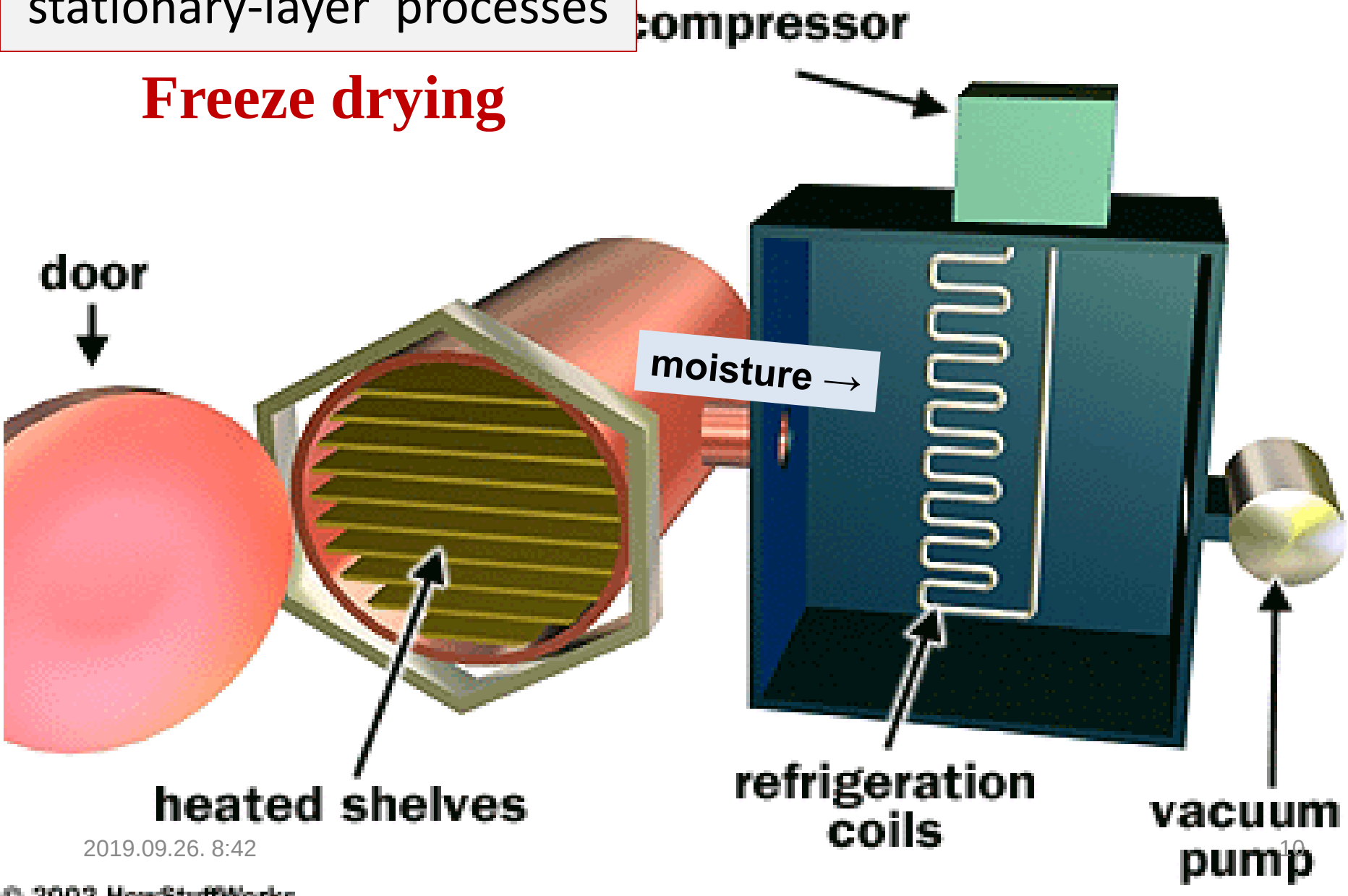
- of diagnostics and
- for oral solid dosage forms,
  where a very fast dissolution rate is desired.

Drying practice

Drying practice

stationary-layer processes

Freeze drying



Drying practice

stationary-layer processes

Steps of freeze drying

1. Freezing
2. Sublimation of water from the frozen mass (primary drying)
3. Heating of mass
4. After-drying (secondary drying)
5. Closing

Drying practice

stationary-layer processes

Steps of freeze drying

1. Freezing

Usually done by the freeze drying machine, it is important to reduce the temperature below the triple point where no liquid phase can appear

Material is cooled down to or below -40 °C, thus material is freezed

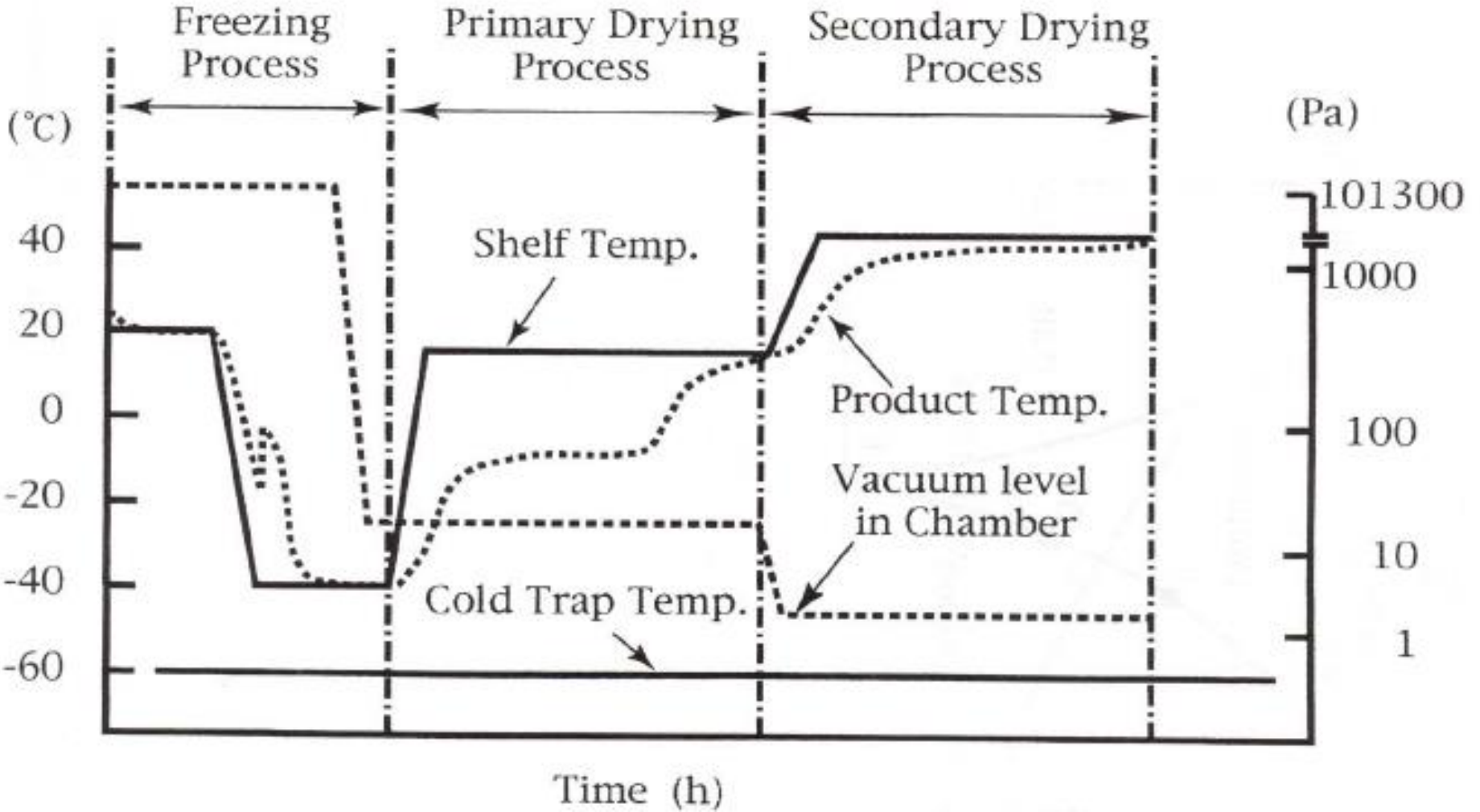
Air is the commonly used cooling medium, in some cases liquid CO_2 or liquid nitrogen can be used

Drying practice

stationary-layer processes

Steps of freeze drying

1. Freezing



Drying practice

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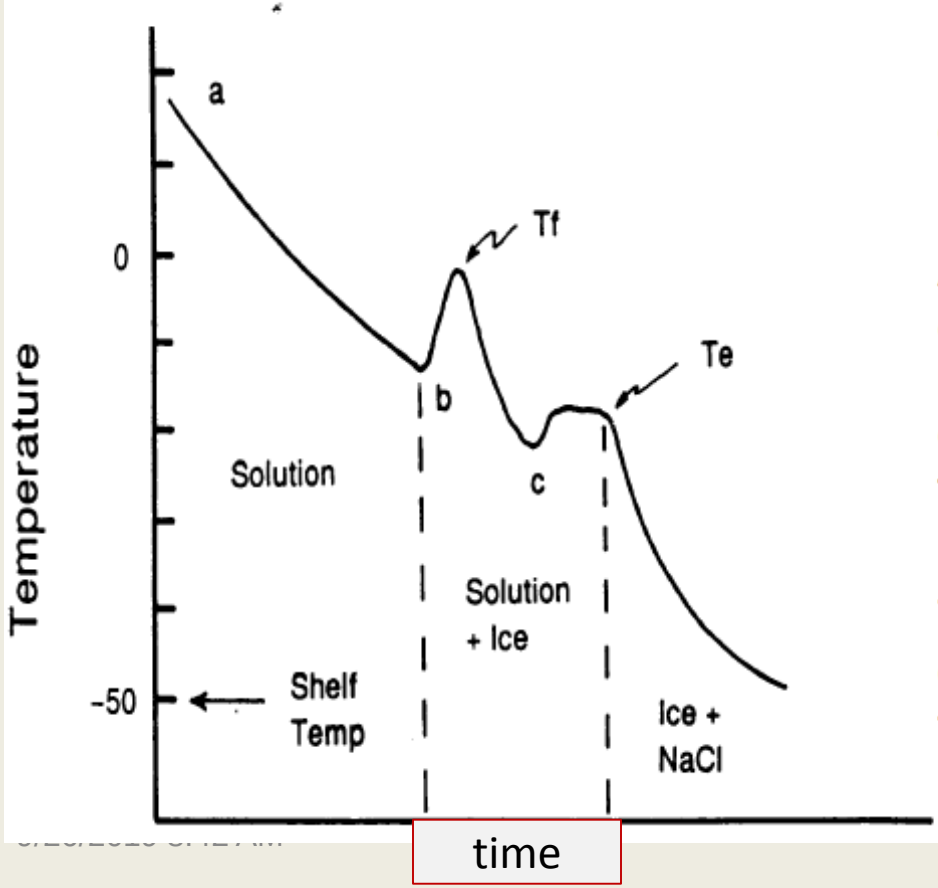
1. Freezing

TEMPERATURE VS. TIME FOR FREEZING OF NACL / WATER



When eutectic crystallization is initiated, the temperature of the product increases to the eutectic temperature (**Te**).

After eutectic crystallization is completed at the point **Te**, no more liquid is present and no changes in microstructure of frozen system take place.

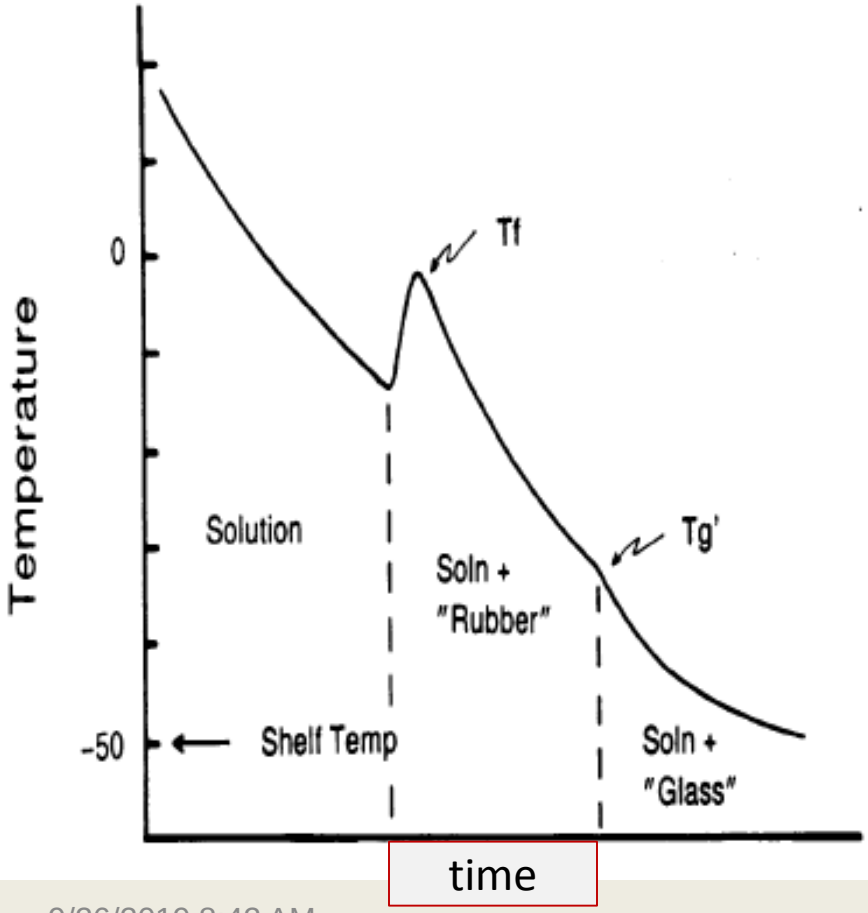
Then, the product temperature decrease more rapidly toward the shelf temperature.

Drying practice

stationary-layer processes

1. Freezing

TEMPERATURE VS. TIME FOR FREEZING OF AMORPHOUS SOLUTE



In the most cases, the solute does not readily crystallize during freezing.

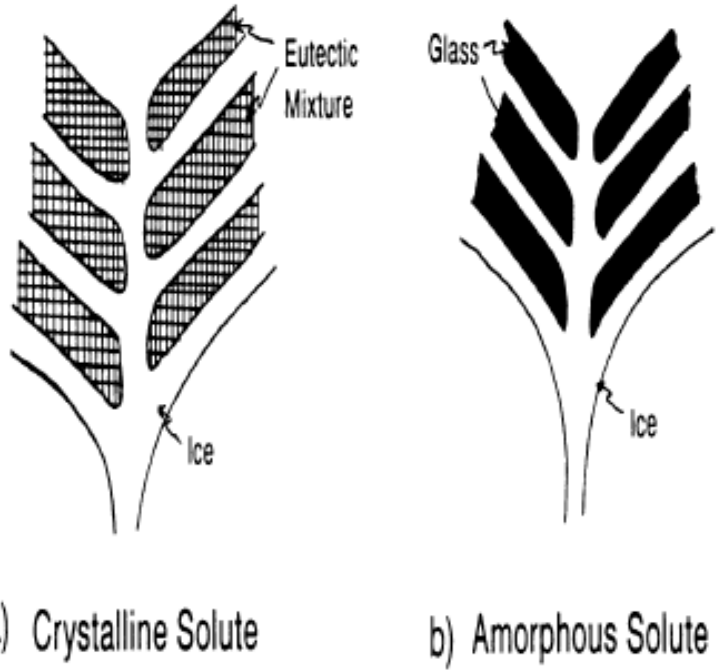
The first part of curve is the same, then a secondary (eutectic) crystallization does not occur, but a slight change in slope of the temperature vs. time curve is observed at **Tg** (glass transition temperature).

Drying practice

stationary-layer processes

1. Freezing

DRAWING OF MICROSTRUCTURE FOR CRYSTALLINE AND AMORPHOUS SOLUTES UPON FREEZING



a) Crystalline Solute

b) Amorphous Solute

For the *crystalline* (a), the interstitial material consists of a mixture of eutectic ice and crystalline solute.

When the ice is removed by sublimation, a crystalline solid with very little water is left.

For the *amorphous* system (b), the interstitial glassy material must be rigid enough to support its own weight after the ice is removed

in order to keep the microstructure established during freezing.

Drying practice

stationary-layer processes

Steps of freeze drying

2. Sublimation of water from the frozen mass

In this phase the pressure is reduced alowing solvent to sublimate

More then 95% of solvent is removed

This phase is very slow, it can take several days

Drying practice

stationary-layer processes

Steps of freeze drying

3.Heating of mass

Lose of heat has to be in balance with heat transfer in order not to cool down and warm up excessively

If materials cools down more than needed, process of drying slows down, but if it warms up, it can be able to melt.

Heat transfer should be adjusted to the sensitivity of material.

Drying practice

stationary-layer processes

Steps of freeze drying

4.After-drying

If the most of the vapor is eliminated from the material, than material can be heated with higher speed

On appropriate vacuum, temperature of material can be kept in 30-40 C^0

Moisture content of the end product have to be < 1%

Drying practice

stationary-layer processes

Steps of freeze drying

5.Closing

- Packaging of end product have to be perfect, hermetically closed, in most cases with protective inert gas
- Dryed product is sensitive to air moisture and oxidation

Drying practice

stationary-layer processes

DEVELOPMENT

The development of a suitable formulation and a freeze-dry cycle requires knowledge of some basic properties, such as:

- eutectic temperature
- temperature effect on solubility
- thermal properties of the frozen solution
- degree of super-cooling
- heat transfer properties of the freeze-dryer shelves, the metal trays, the containers and the frozen product
- equipment design and equipment capability.

Drying practice

stationary-layer processes

Homemade freeze dryer

stationary-layer processes

Industrial freeze dryer

stationary-layer processes

Freeze dryers

Industrial freeze dryer

stationary-layer processes

Industrial freeze dryer

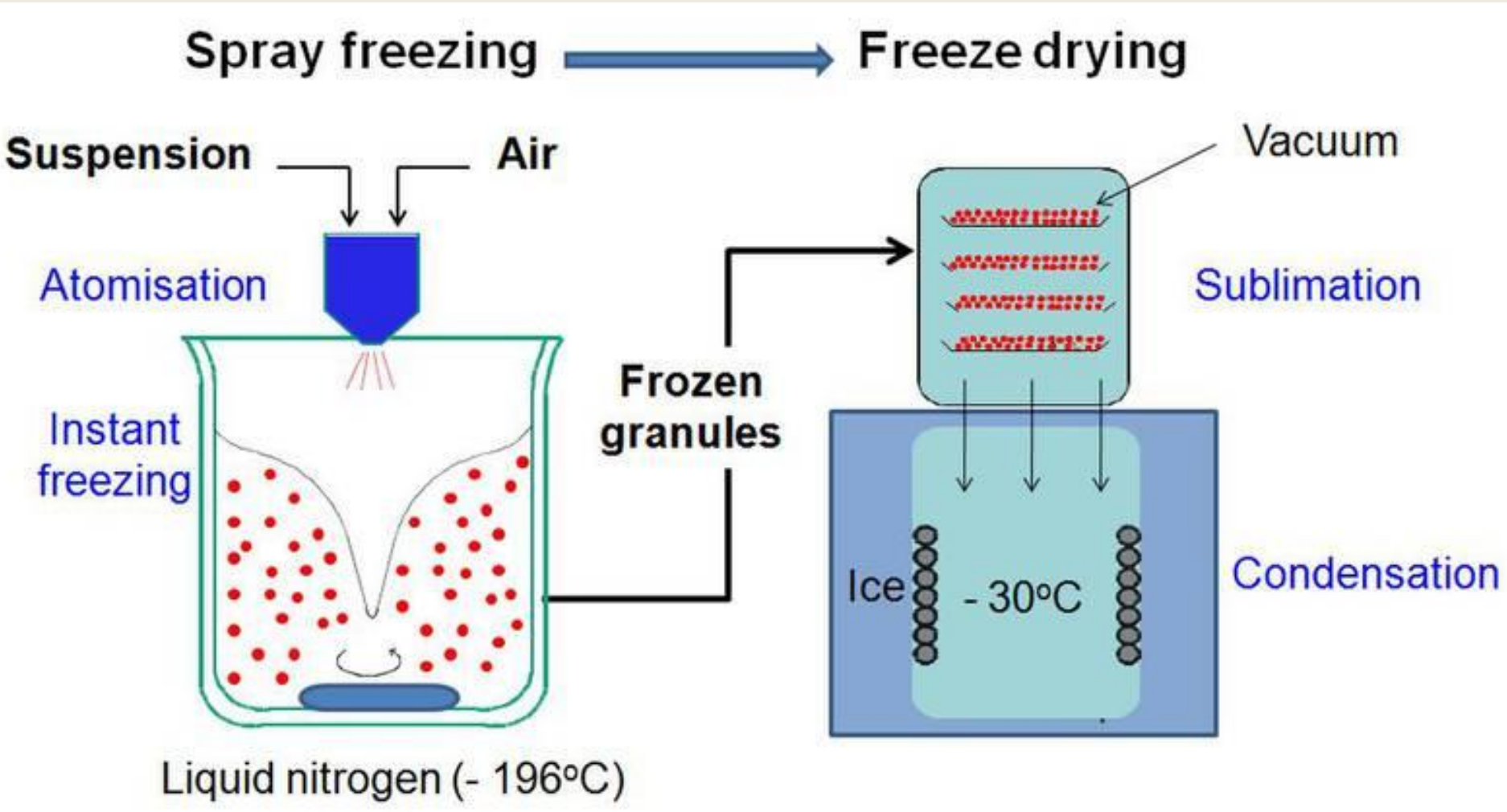
- https://www.youtube.com/watch?v=twEnPTkCu9k

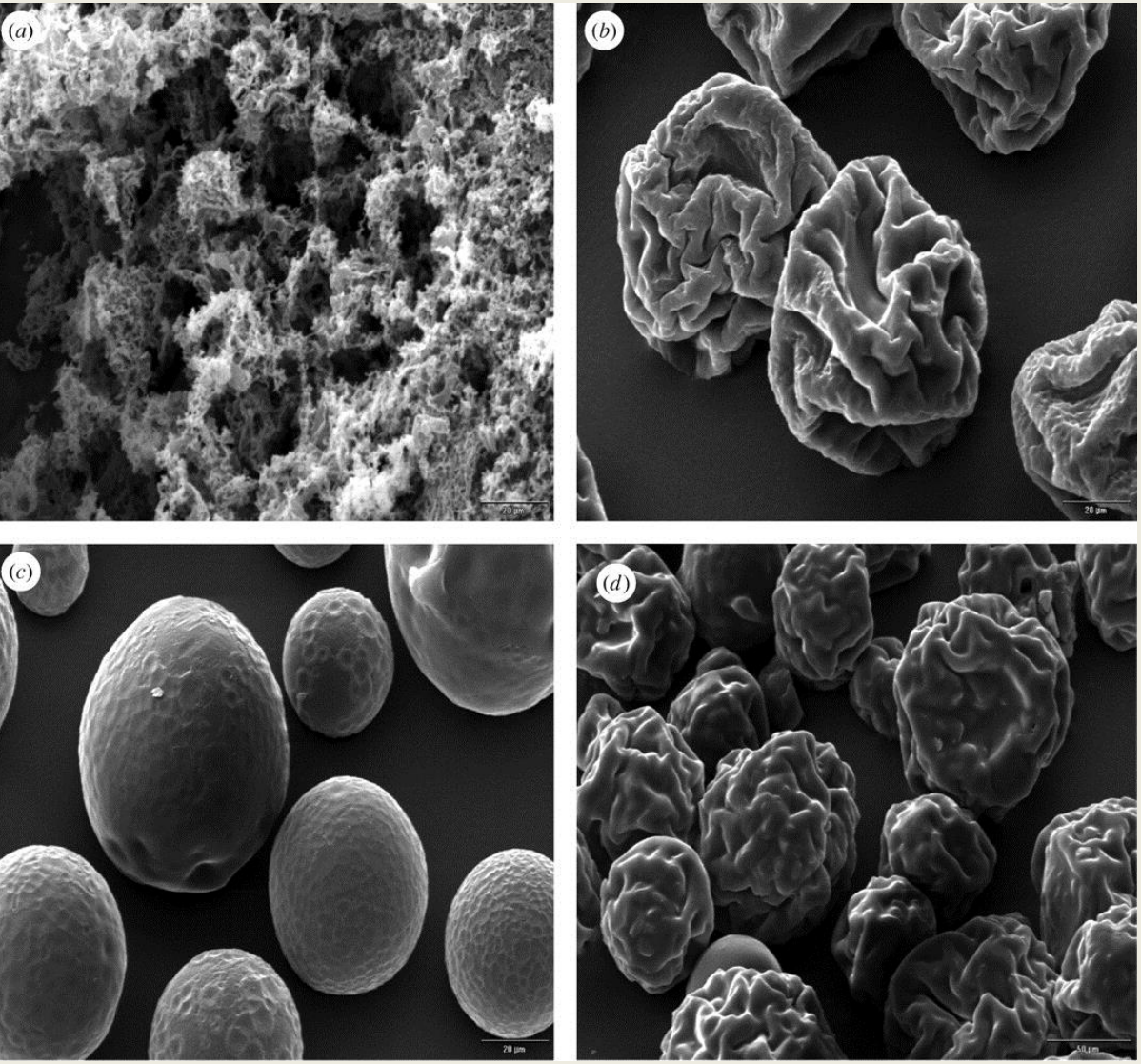
Freeze dryd products

- increase the shelf life of the products such as:
  - live virus vaccines
  - biologics and other injectables
- reconstitution in vials and more recently in prefilled syringes:
- stability of therapeutical proteins and monoclonal antybodies:
- manufacturing of raw materials for pharmaceutical products.
- dry powders of probiotics are often produced by bulk freeze-drying of live microorganisms such as Lactic acid bacteria and Bifidobacteria

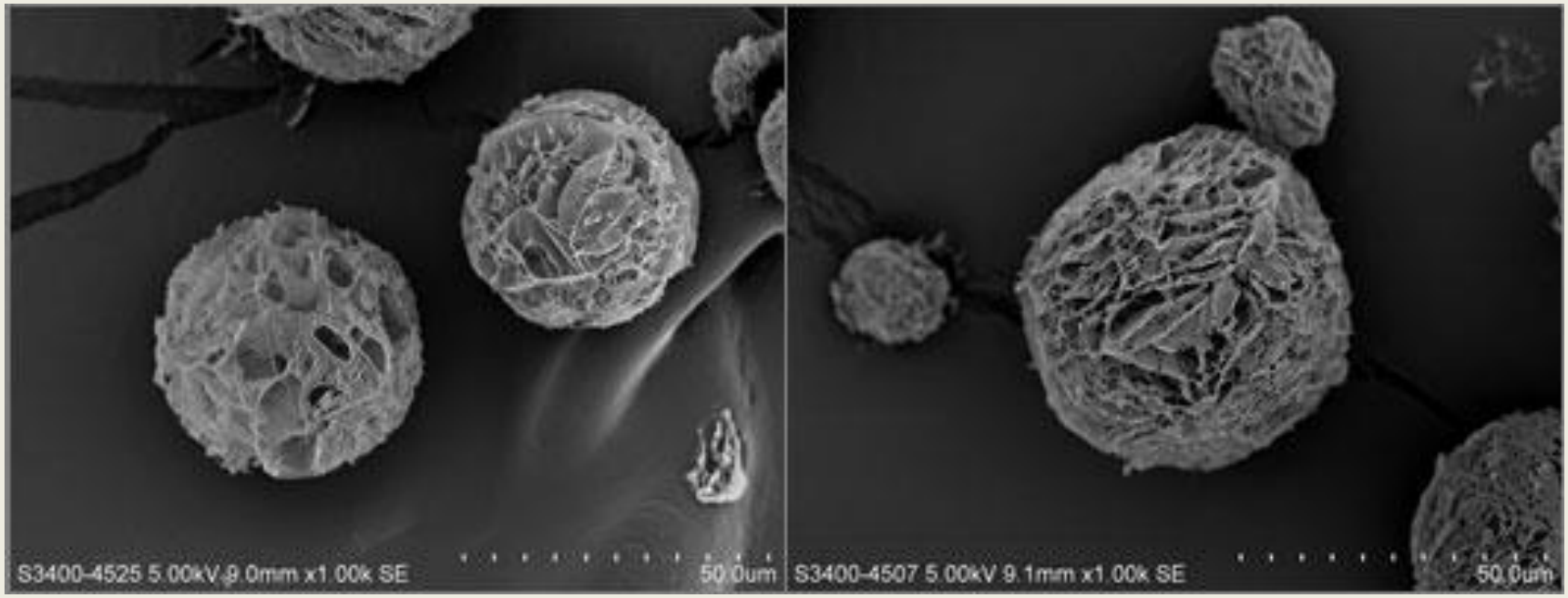
Zyprexa Velotab 5mg

- Pharmaceutical preparation prepared by lyophilization (Zydis)
- Due to its structure, the tablet disintegrates in the mouth
- It contains the active substance olanzapine


Spray freezing
Freeze drying
Suspension
Air
Atomisation
Instant freezing
Liquid nitrogen (- 196°C)
Frozen granules
Vacuum
Sublimation
Ice
- 30°C
Condensation



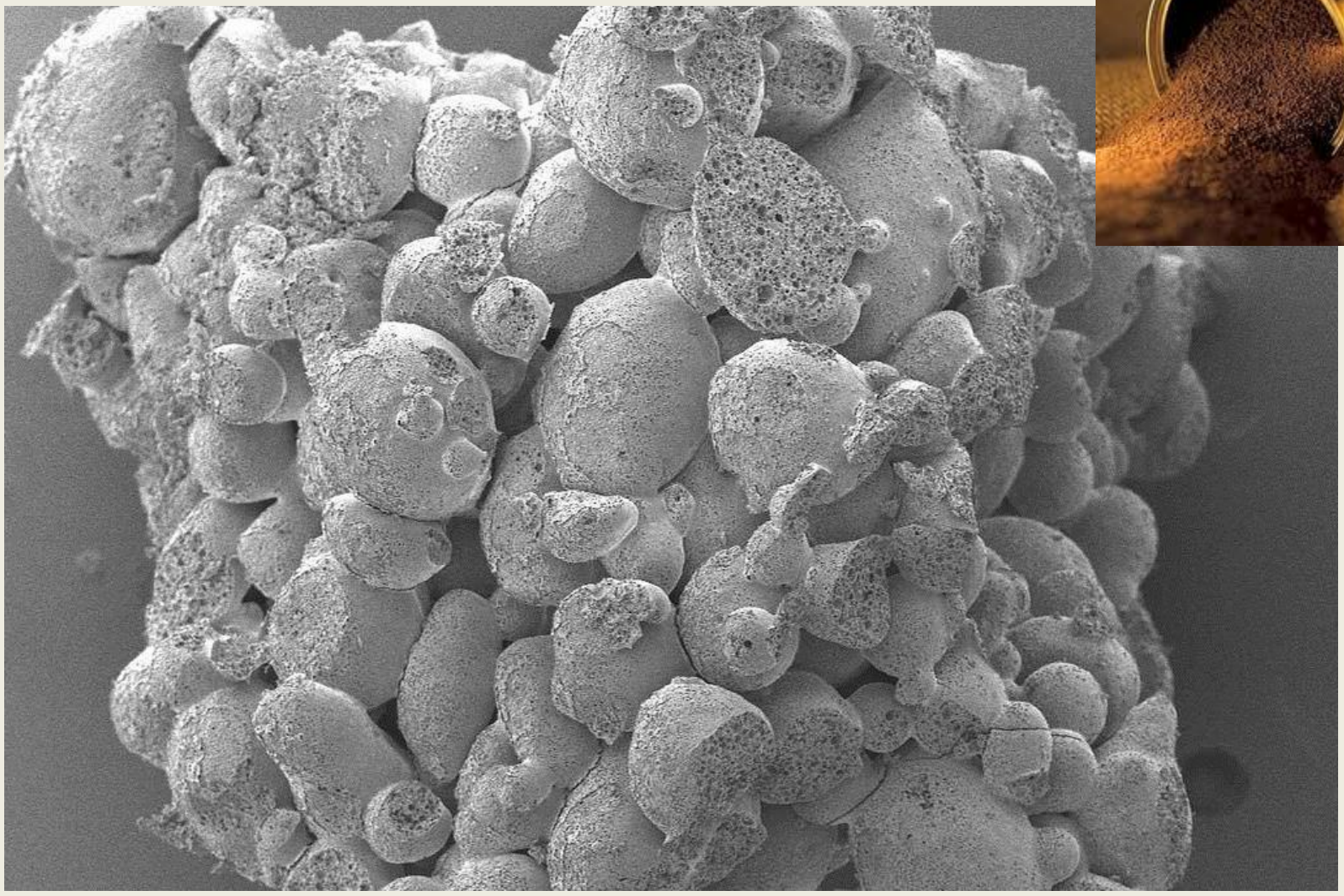
- (*a*) Pure insulin powder from a 5 mg ml−1insulin solution at pH 2.0 (magnification 2500×)
- (*b*) SFD microparticles from a pure TMDD (3 : 3 : 3 : 1) 35% (w/w) solution freeze-dried at −10°C and 100 mtorr (magnification 1000×)
- (*c*) at –30°C and 100 mtorr (magnification 2500×).
- (*d*) SFD microspheres from a TMDD (3 : 3 : 3 : 1) 35% (w/w) solution loaded with 25% insulin (magnification 500×).



- Scanning electron microscopic image of inhalable dry powder of nucleic acids prepared by spray freeze drying

Instant coffee freeze dried

Spray freezed-freezy dried coffee



Thank you
for your attention!!!