Classification of the operation

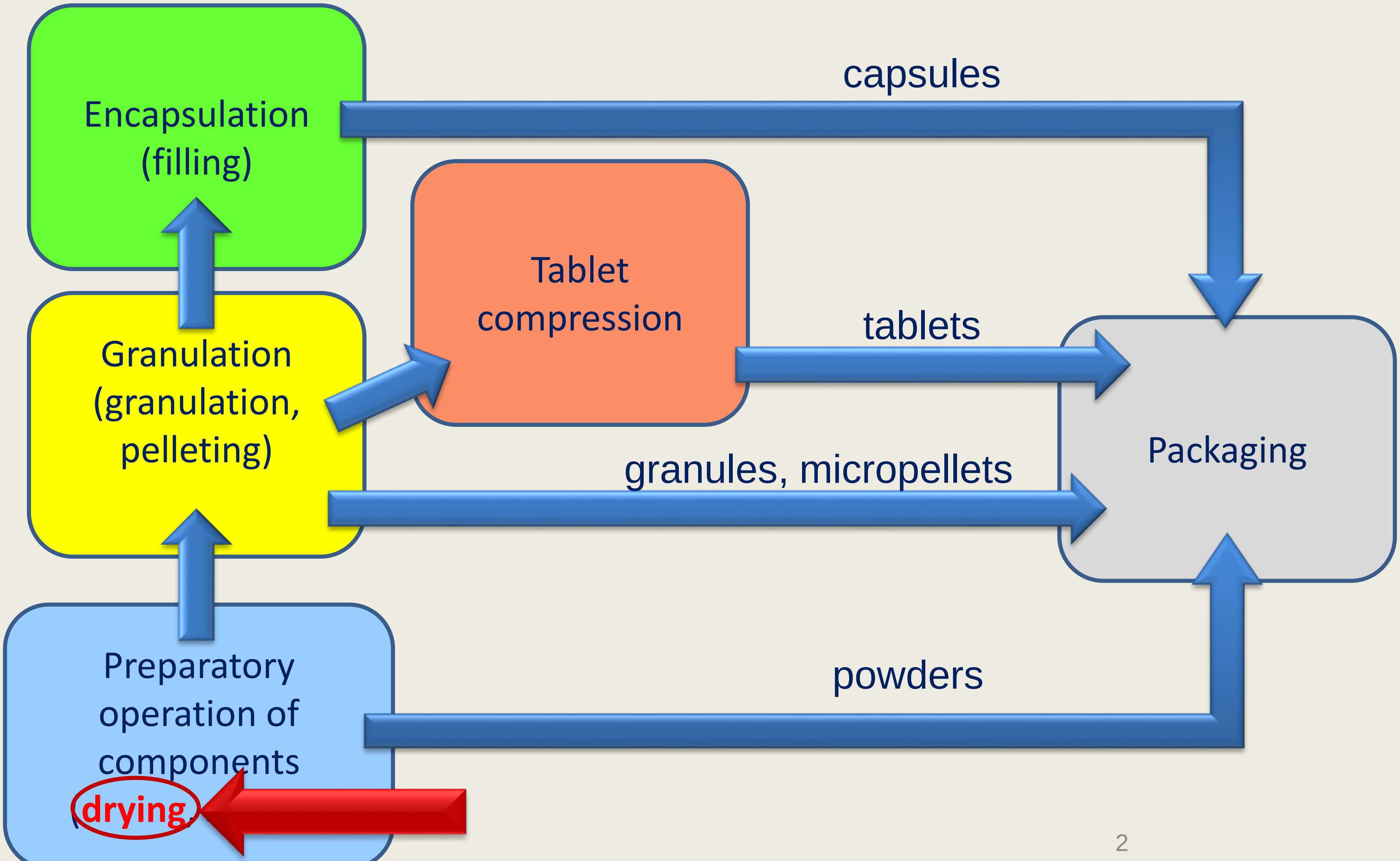
- ***Preparatory operation:***
  - includes the operations, which assist to be able to **perform other operations** (e.g. crystallization, drying)

- ***Compiling operation:***
  - when the substances are produced into **one coherent product** (e.g. mixing, pressing)

- ***Final operation:***
  - includes final operations performed in order to form the **final form of the product**.(e.g. **drying**, filling, coating, packing). Packing also in this group of operation.

The importance of drying

The order of the preparation steps of solid dosage forms



Operation of drying

University of Pécs

Institute of Pharmaceutical Technology and Biopharmacy

Operation of Drying

Definition of drying

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

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

Operation of Drying

Aim of drying

1. Removal of the moisture

- Preparatory step for the following operations (spray drying, granulation, tableting)

2. Setting of moisture content

- to ensure the stability
  - (physical, chemical, biological)
- Improve production

Operation of Drying

The moisture content determines the following technological properties of product, like:

- » density,
- » adhesiveness,
- » flowability,
- » mechanical strength,
- » mixing,
- » moisture absorbing capabiity.

Drying

On a laboratory (pharmacy) scale, desiccators (latin: exsiccator) are used.

Silica gel (a common laboratory and packaging desiccant) does not directly take water from a solid; instead it acts by **removing the water from the air**, thereby reducing its relative humidity to around 5-10%.

Others desiccants:

- *Sodium hydroxide,*
- *Calcium chloride,*
- *Calcium sulfate,*
- *Activated charcoal, and*
- *Molecular sieves.*

Desiccator

Theory of Drying

Theory of Drying

Main types of moisture

The moisture binding can be

- **unbound** (easily removable) and
- **bound** moisture.

Theory of Drying

Main types of moisture (1)

Unbound moisture (adhesive surface moisture or free moisture) forms a **continuous film on the surface** of substances.

In ***macrocapillaries*** (d > 10^{-7} m) the effect of capillary force has little effect, **vapor pressure** is **equal** with the pressure of saturated vapor:

$$p_v = p_{vt}$$

p_v: vapor pressure,
p_{vt}: pressure of saturated vapor

Theory of Drying

Main types of moisture (2)

Physically bound moisture is usually bound in pores or capillary vessels.

In ***microcapillaries*** (d < 10^{-7} m) it is significant,

vapor pressure is **lower** than the pressure of saturated vapor, due to the curved surface of moisture:

$$p_v < p_{vt}$$

p_v: vapor pressure,

p_{vt}: pressure of saturated vapor

Theory of Drying

Main types of moisture (3)

Crystal water, which is ***chemically bound*** (strongest type), classifies as difficult to remove.
It is built in between lattice points of the crystal lattice in a strictly determined stoechimetrical proportion characteristic of the substance.

anhydrate form	hydrated form
$MgSO_4$	$MgSO_4$*$7H_2O$
Na_2SO_4	Na_2SO_4*$10H_2O$
$CaSO_4$	$CaSO_4$*$2H_2O$

Theory of Drying

Main types of moisture (4)

Hygroscopic materials can **adsorb** a significant amount of moisture if they are contact with air.

Some ingredients ($CaCl_2$) can adsorb (steam water from the air) the water from the air in a proper ratio, therefore they **can dissolve in their own crystal water.**

(Stock solutions are prepared to solve this problem.)

Theory of Drying

Moisture content

$$m = m_d + m_m$$

m = mass of substance,
m_m = mass of moisture content,
m_d = mass of dry substance.

At a total drying:

$$m_m \to 0 \quad \Rightarrow \quad m_m = 0 \quad \Rightarrow \quad m = m_d$$

Theory of Drying

Absolute humidity is the mass of water vapor per air volume (φ_a)

Absolute humidity is the ***water content*** *of air expressed in gram per cubic meter.*

$$\varphi_a = \frac{m_v}{V}$$

m_v = mass of water vapor,
V = volume air

Theory of Drying

Relative humidity *of* air volume (RH or φ)

Relative humidity is the **ratio** of the **partial pressure** of water vapor to the **equilibrium vapor pressure** of water at a given temperature. Relative humidity depends on **temperature** and the **pressure** of the system of interest.

At **low temperatures** It requires **less** water vapor to attain **high** relative humidity.

In warm or hot air **more water vapor** is required to attain high relative humidity.

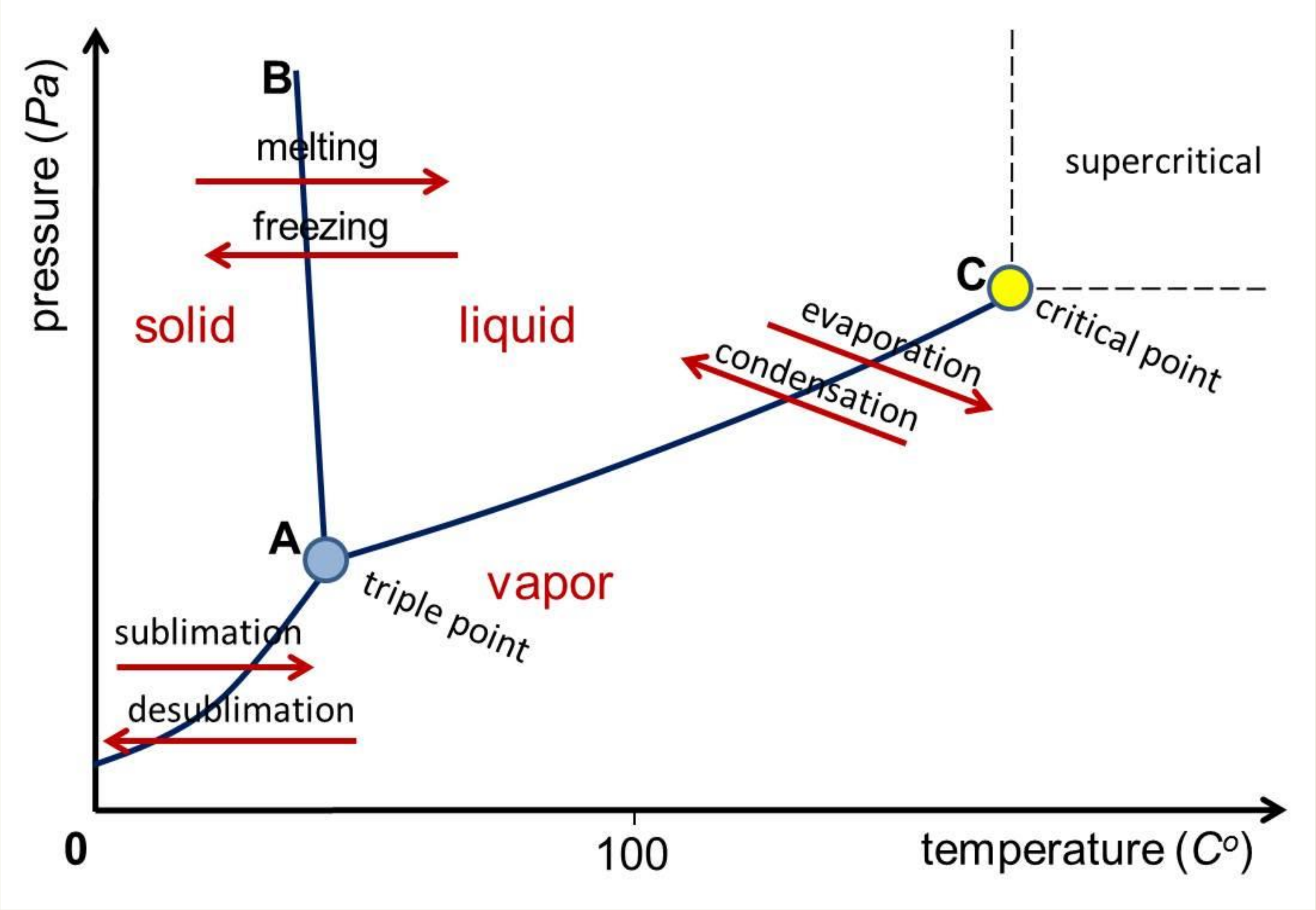
$$\varphi = \frac{p_v}{p_{vt}}$$

p_v = vapor pressure,

p_{vt} = pressure of saturated vapor.

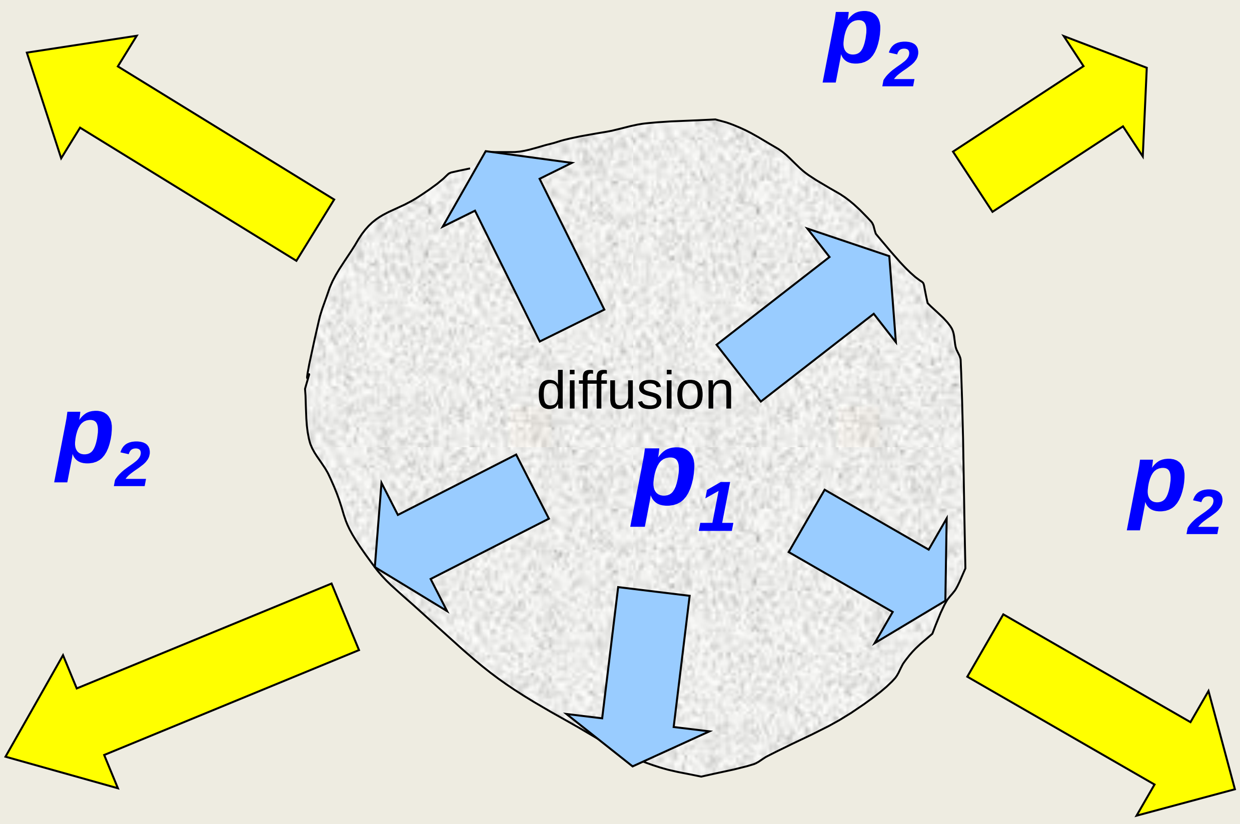
Theory of Drying

Phase diagram



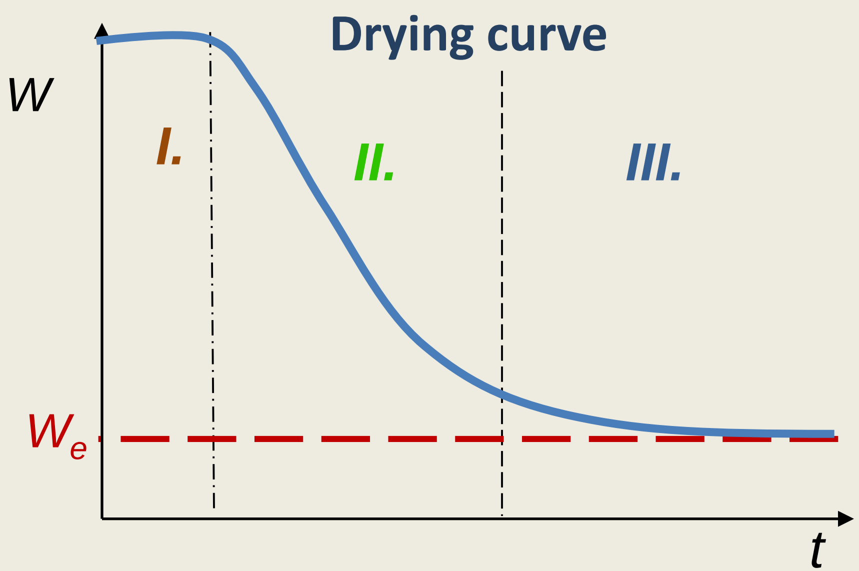
Kinetics of Drying

Theory of Drying



Theory of Drying

Kinetic of drying



W_e = equilibrium moisture content

I. **Warm-up** phase

II. **Constant rate** phase
(the evaporating moisture from the surface is ensured by the **inner moisture diffusion** to the surface)

III. **Decreasing rate** phase
(internal moisture **reduces**, thus speed of diffusion **decreases** with the evaporation from the surface)

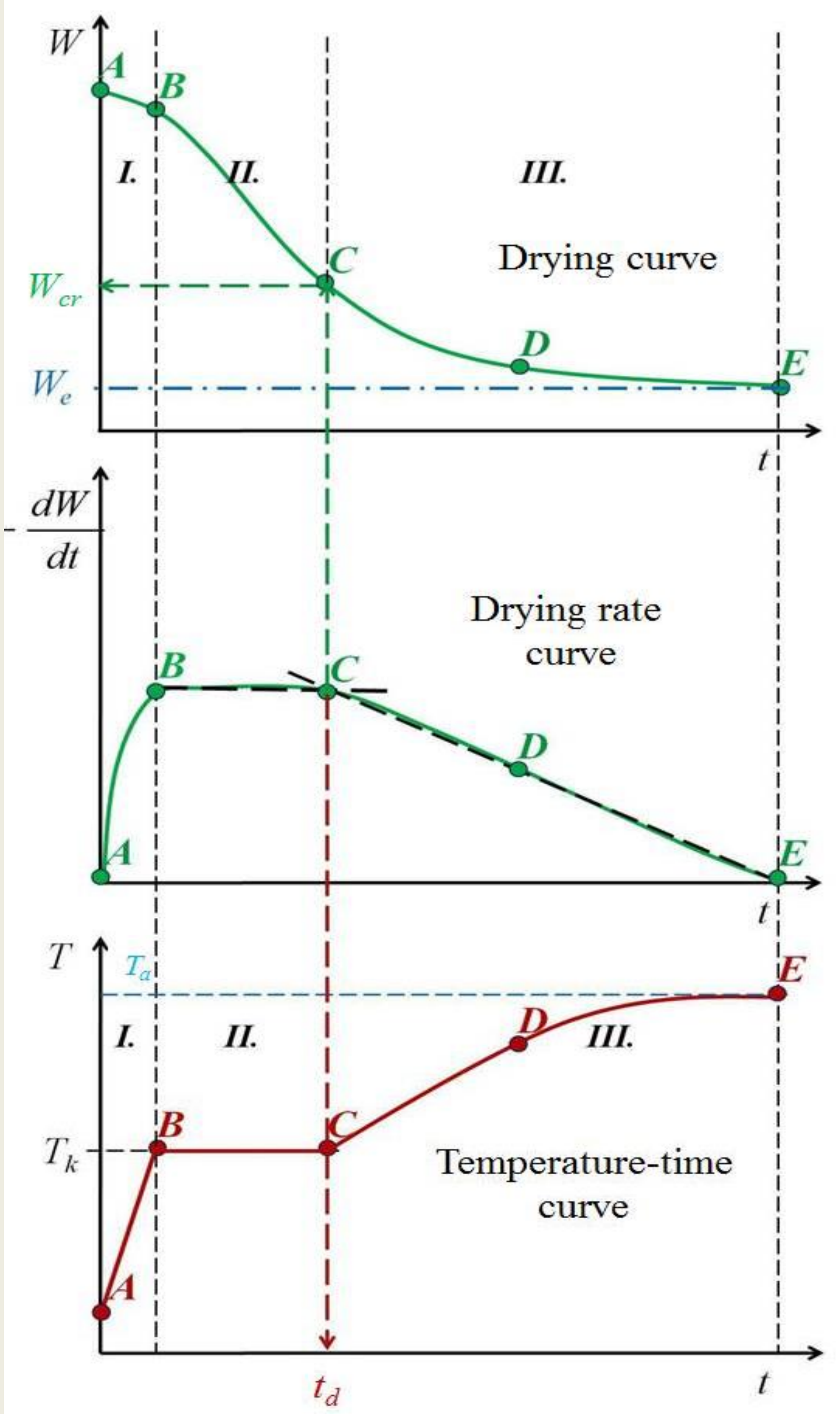
Kinetics of drying

Drying, drying rate and temperature-time curves

Drying curve,
W=f(t)

Drying rate curve,
dW/dt=f(t),
differencial curve of drying curve

Temperature-time curve of the dried material
T=f(t)



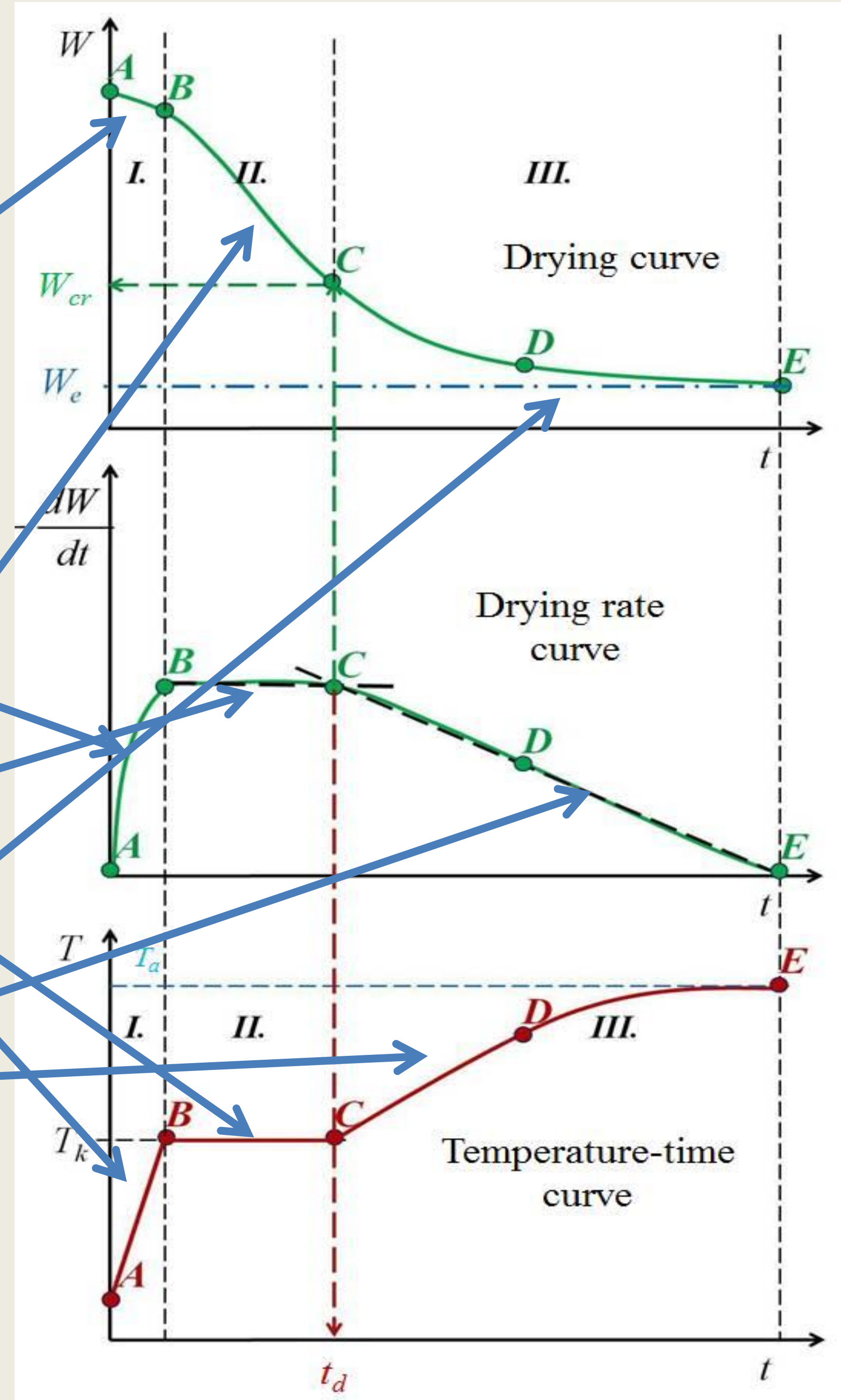
Kinetics of drying

Drying, drying rate and temperature-time curves

I. Warming stage

II. Linear (constant) rate stage (diffusion)

III. Decreasing rate stage (decreasing moisture content)



Kinetics of drying

Drying, drying rate and temperature-time curves

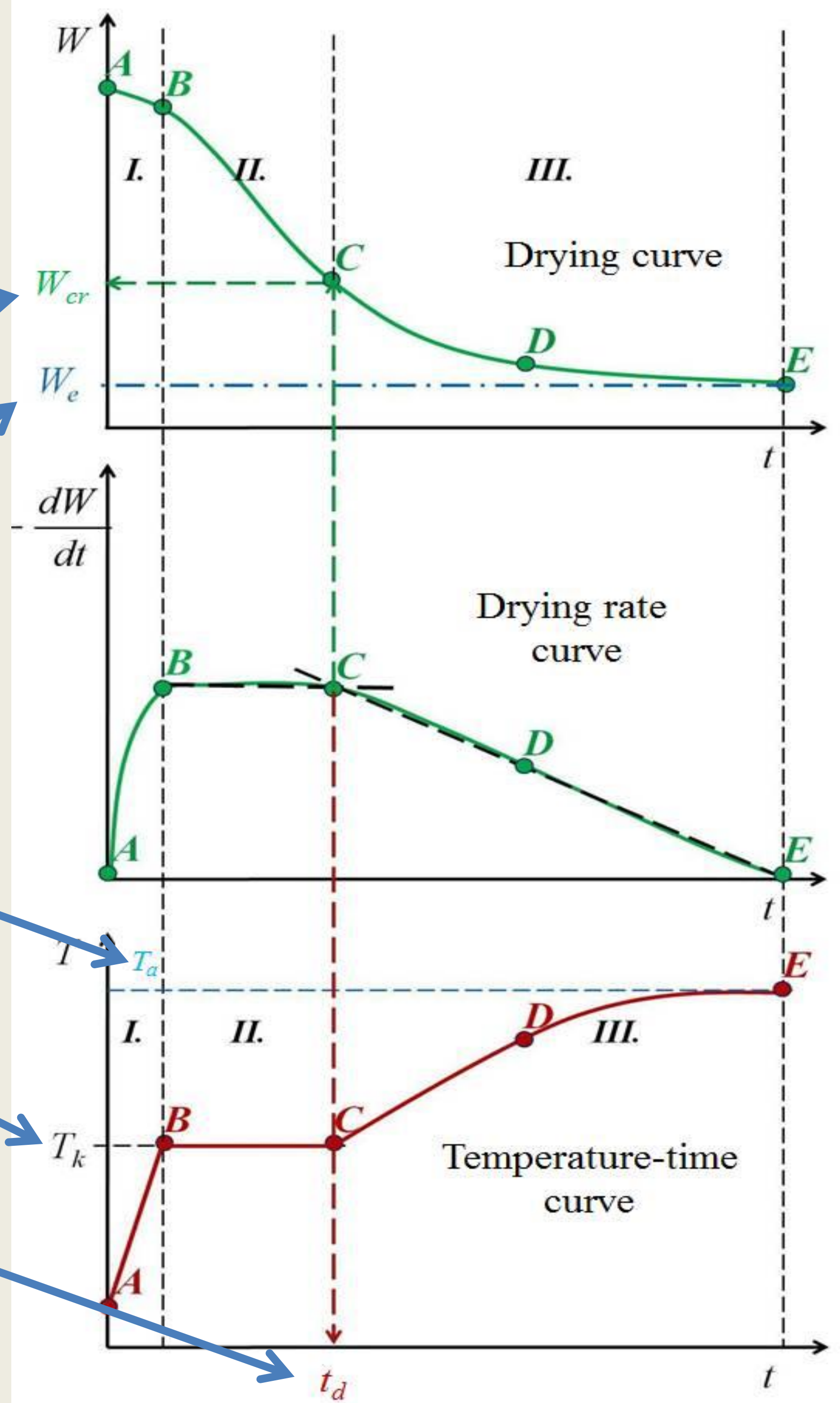
W_{cr} = moisture content corresponding to the critical point (II.→III.stage)

W_e = equilibrum moisture content

T_a = temperature of drying air

T_k = temperature of material in the steady rate stage

t_d = duration (time) of drying



Drying equipments

Drying equipment

Classification of drying equipment

Operation	Movement of material	Method of heat transfer	Movement of drying medium and material	Pressure in drying space
disconti-nuous	stationary-layer	convectional	direct flow	athmospheric
continuous	moving-layer	contact (conduction of heat)	counter flow	low / vaccum
		radiation of heat	cross flow	high (supercritical)
		- dielectric (microwave)		

Drying equipment

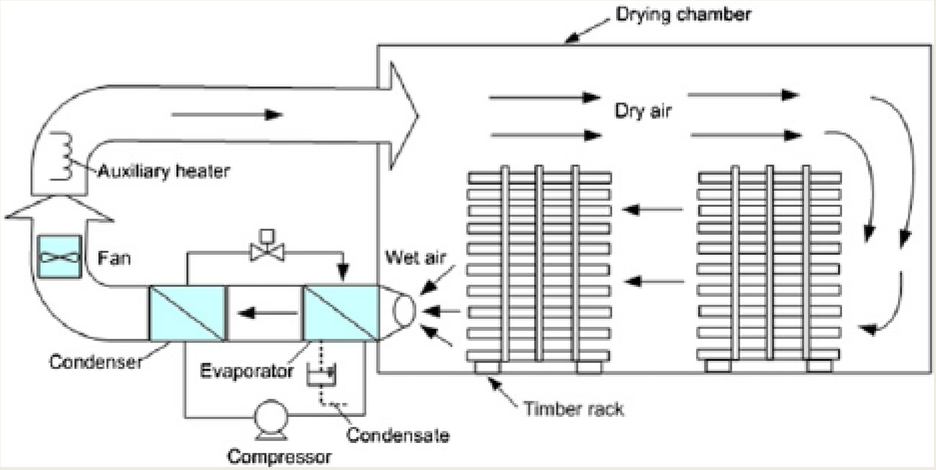
stationary-layer processes

Drying practice

stationary-layer processes

Tray-dryer

- discontinuous operation
- on normal atmospheric pressure or
- vacuum,
- with or,
- without air flow

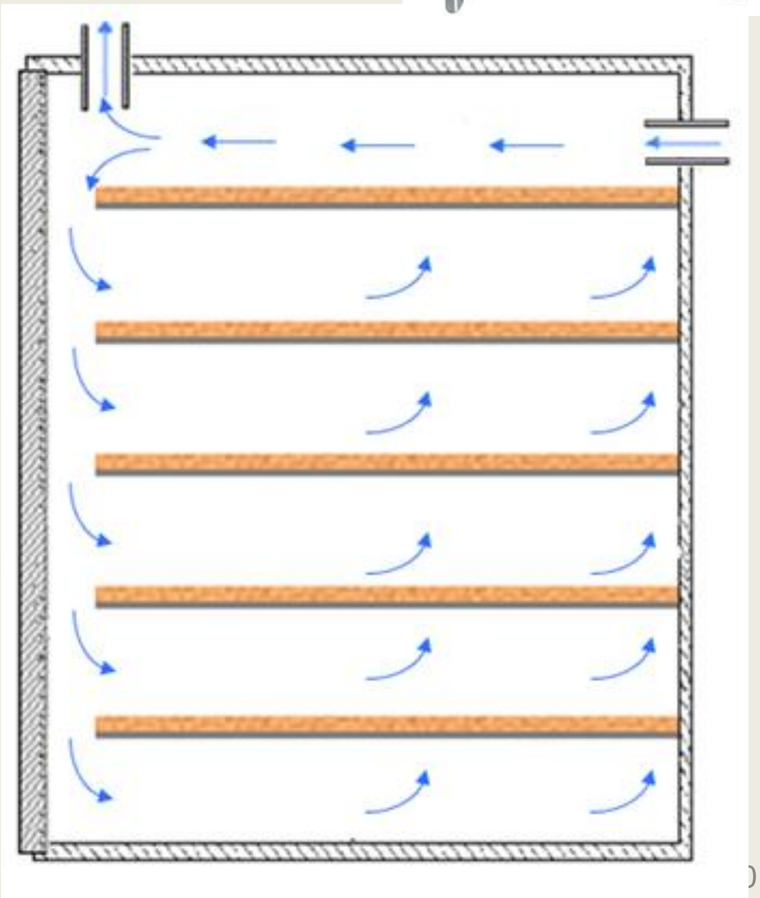


Drying practice

stationary-layer processes

Tray-dryer

Wet powder or granulation is placed onto perforated, sieve-like trays, then which are placed directly into racks in a drying chamber (oven).



Drying practice

stationary-layer processes

Vacuum dryer

The main characteristics of the vacuum dryers are:

1) the vacuum dryer can dry the material to a very low point of moisture,
2) under the circumstance of lower temperature, the vacuum dryer work with a higher drying rate (drying speed is slow),
3) the thermal efficiency is higher than that of others,
4) the solvent can be recycled,
5) the structure of the vacuum dryer is very simple, and it is very easy to clean this kind of dryers while it is very hard to accumulate materials on the turn-on wall,
6) it cannot work continuously,
7) the effective heating area is smaller and it is difficult to become large-scale.

Drying practice

stationary-layer processes

Vacuum dryer

drying for heat sensitive materials

Microwave Drying (Dielectric)

The microwaves are electromagnetic waves.
Their wavelength is between 1 mm - 1 m, frequency is 300 MHz - 300 GHz.

The microwaves are generated by magnetron (what is a specific electron tube).

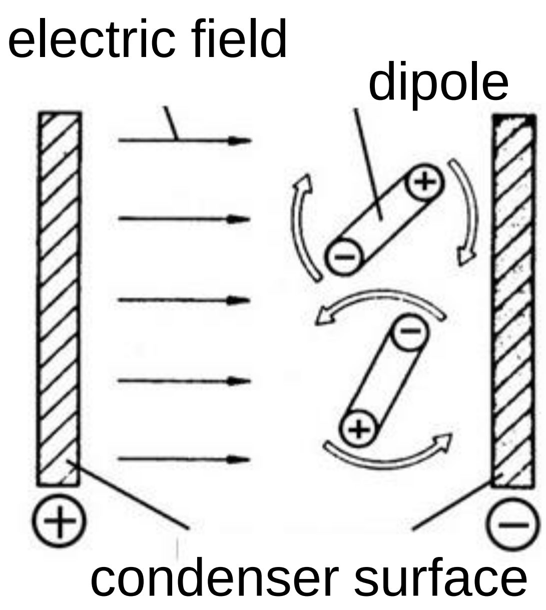
Pharmaceutical technological application:

- heating,
- melting,
- drying,
- granulation,
- sterilization of materials.

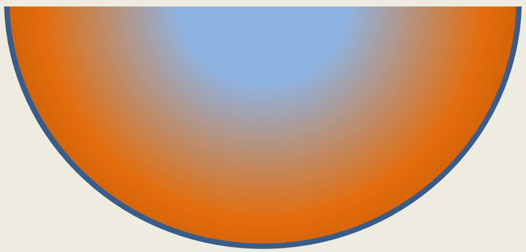
Drying practice

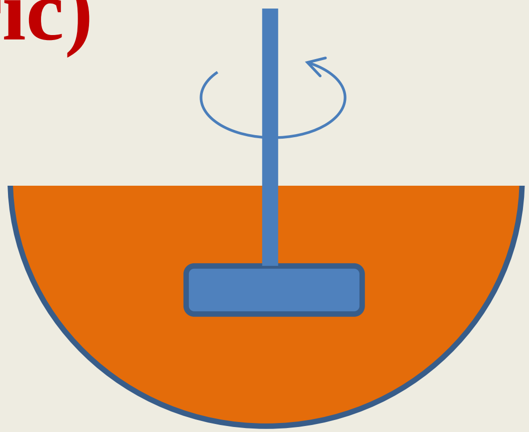
Microwave Drying (Dielectric)

The water molecule has a dipole charge.
One part of the electric energy transforms into heat.
On increased temperature, the water can leave the mass easier.

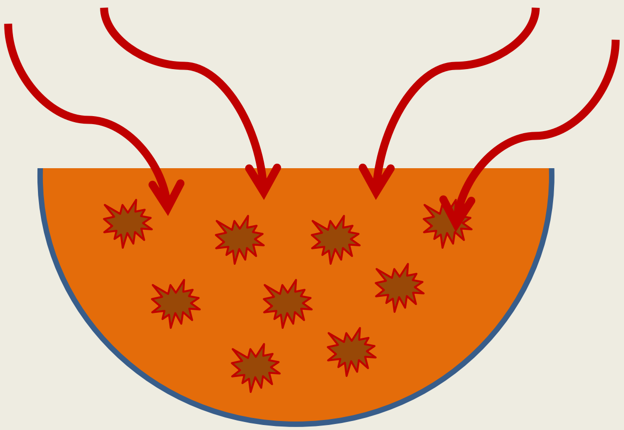


Microwave Drying (Dielectric)





We can avolid the local over-heating.
In most cases the convection is not enough for perfect mixing of the mass and even distribution of drying, thus stirrers have to be applied.



The microwaves can heat all parts of the mass equally.

Drying practice

stationary-layer processes

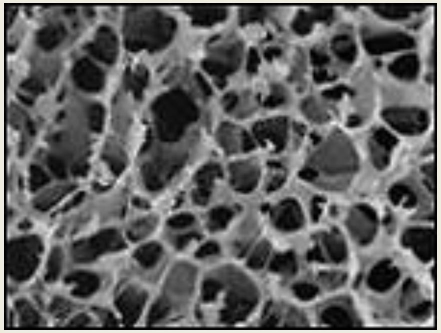
Freeze drying

Synonyms:

- vacuum-sublimation
- cryodehydration
- lyophilization
- cryosiccation

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 structure is created (with a large internal surface).
- Rapid and complete dissolution of the dried material is possible (rehydration).

Drying practice

stationary-layer processes

Freeze drying

Disadvantages:

- high cost,
- expensive operation,
- significant energy is needed.

Drying practice

stationary-layer processes

Steps of freeze drying

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

Drying practice

stationary-layer processes

Freeze dryers

Drying practice

stationary-layer processes

Industrial freeze dryer

Drying practice

stationary-layer processes

DDS

Zyprexa Velotab 5mg

- Technology: Zydis
- Orodispersable tablet-quick effect
- API: olanzapine

Drying practice

stationary-layer processes

Belt dryer

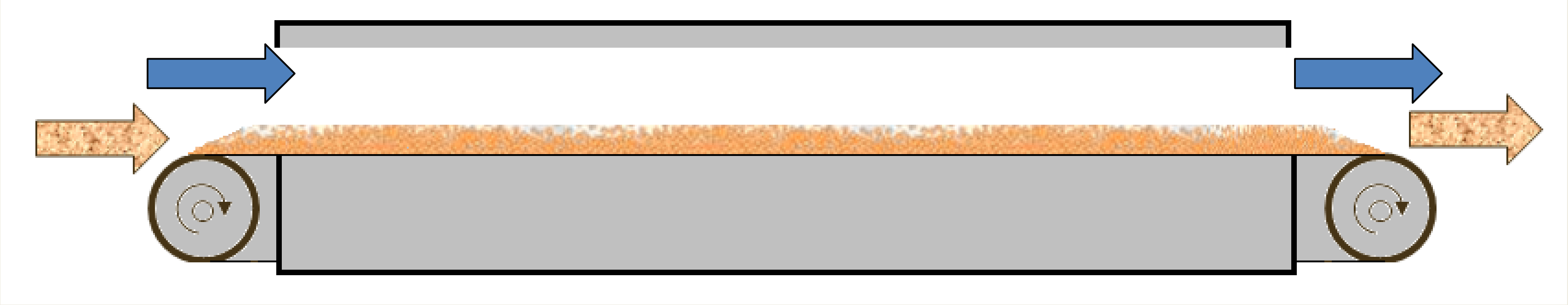
- **continuous operation**
- **drying temperature can be decreased,**
- **evaporated solvent can be recovered**

Drying practice

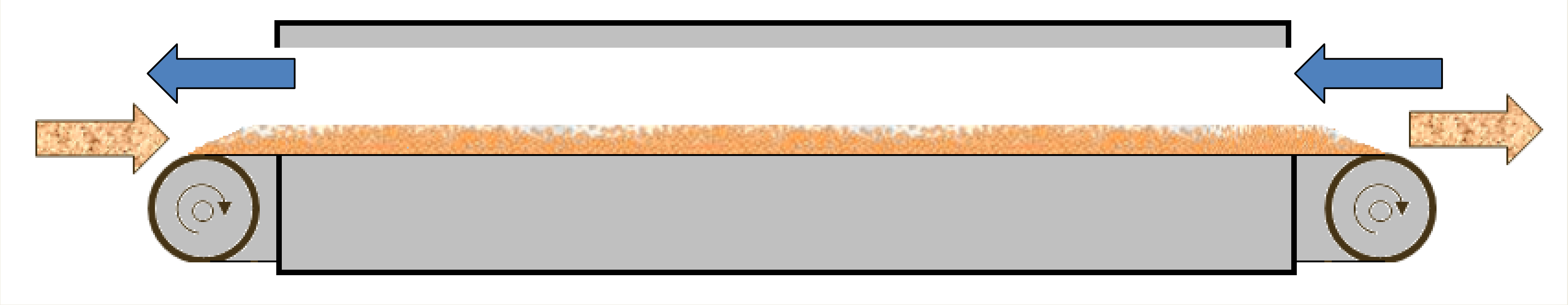
stationary-layer processes

Belt dryer

direct flow



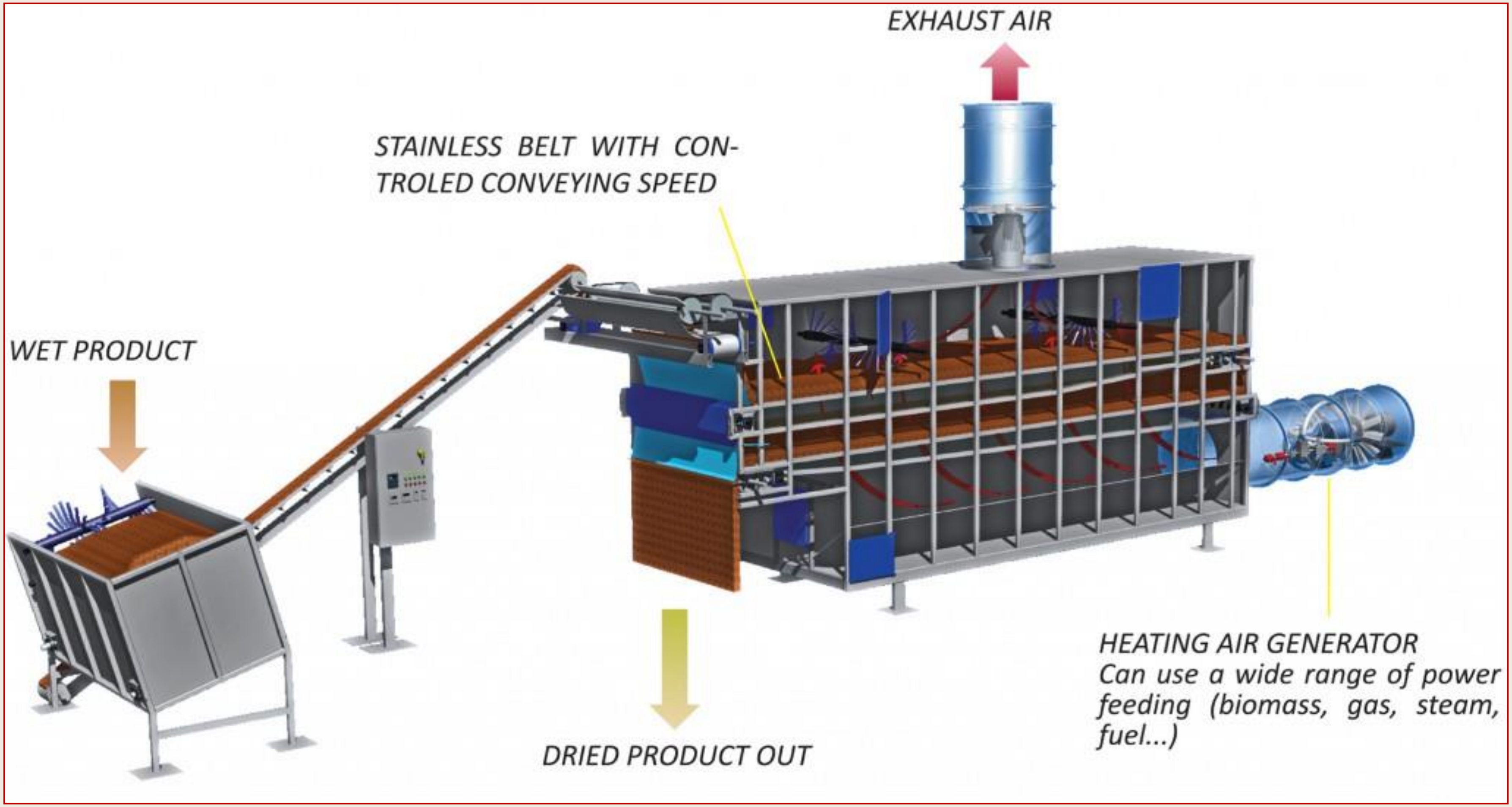
counterflow



Drying practice

stationary-layer processes

Belt dryer



Drying equipment

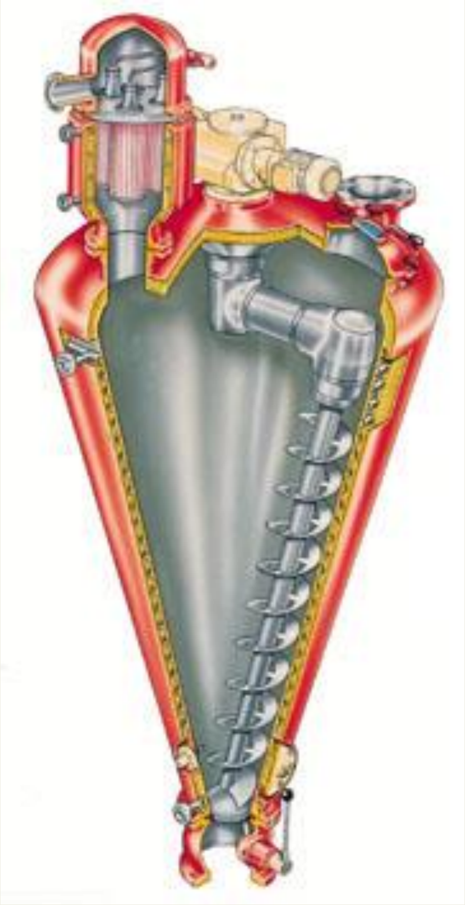
Moving-layer processes

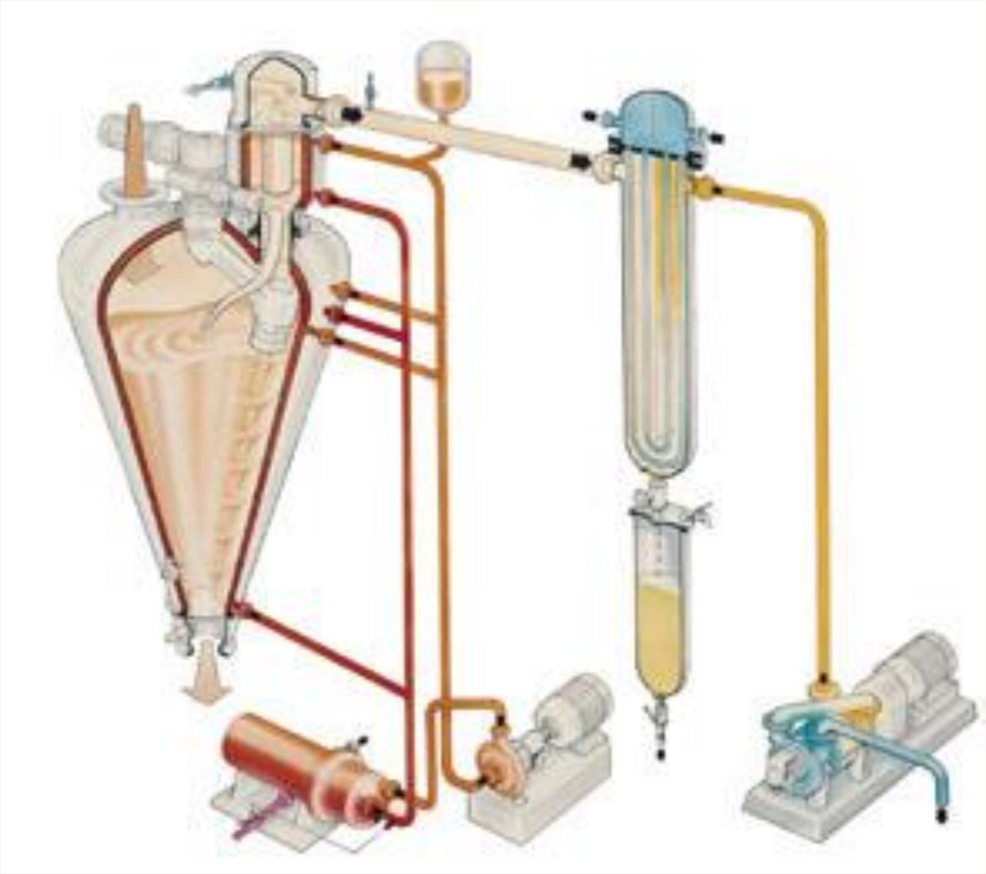
Drying practice

Moving-layer processes

Vacuum dryer

Discontinuous operation,
Moving layer (by mixing)



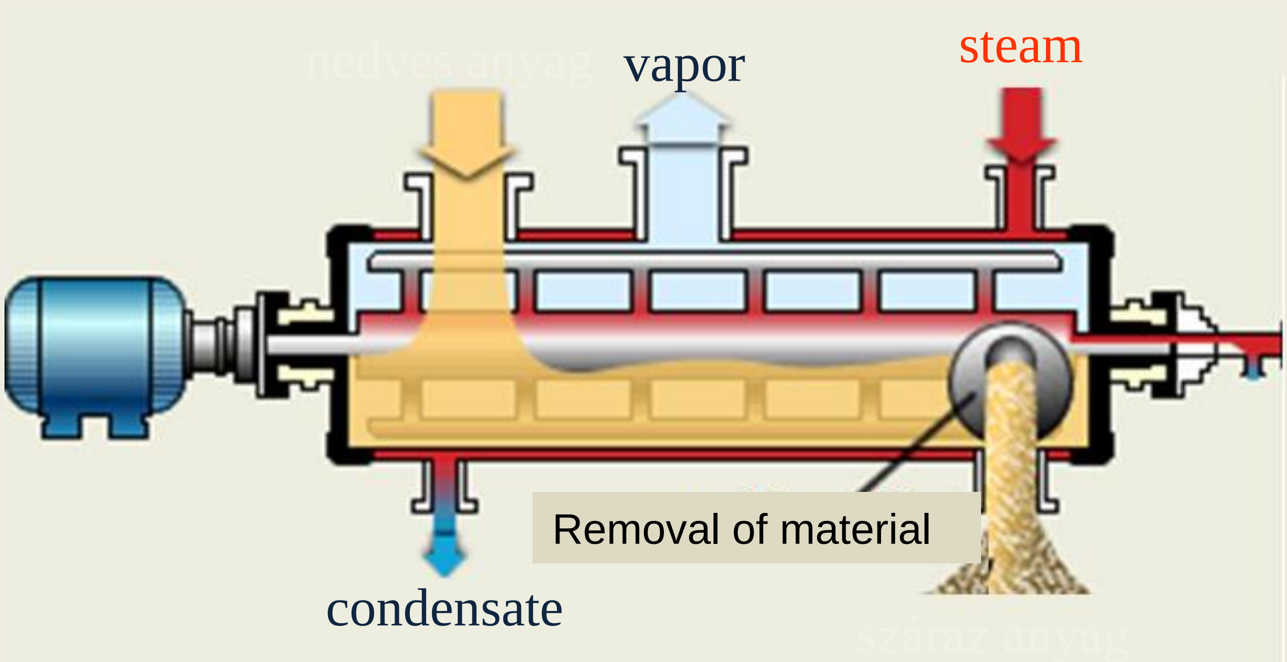


Drying practice

Moving-layer processes

Rototherm - industrial equipmemnt

Continuous operation, high energy is needed



Drying practice

Moving-layer processes

Fluid-dryer

- allows intensive and fast drying,
- particles collide with each other,
- creation of fine powder can occur,
- high of energy is needed,
- discontinuous operation.

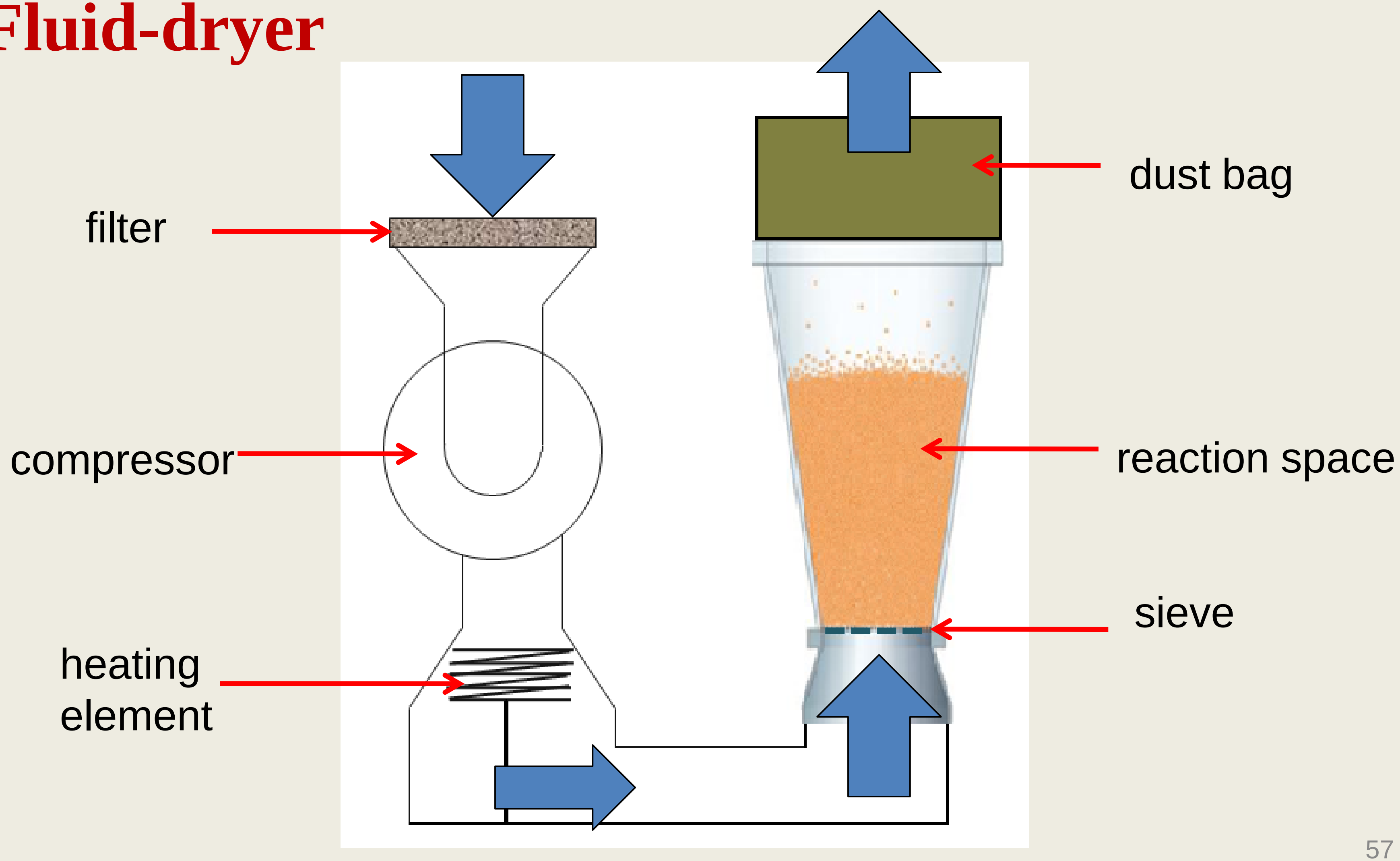
Three functions of the drying medium are the following:

- heat transfer
- it moves the particles,
- transfer the vapor.

Drying practice

Moving-layer processes

Fluid-dryer



Drying practice

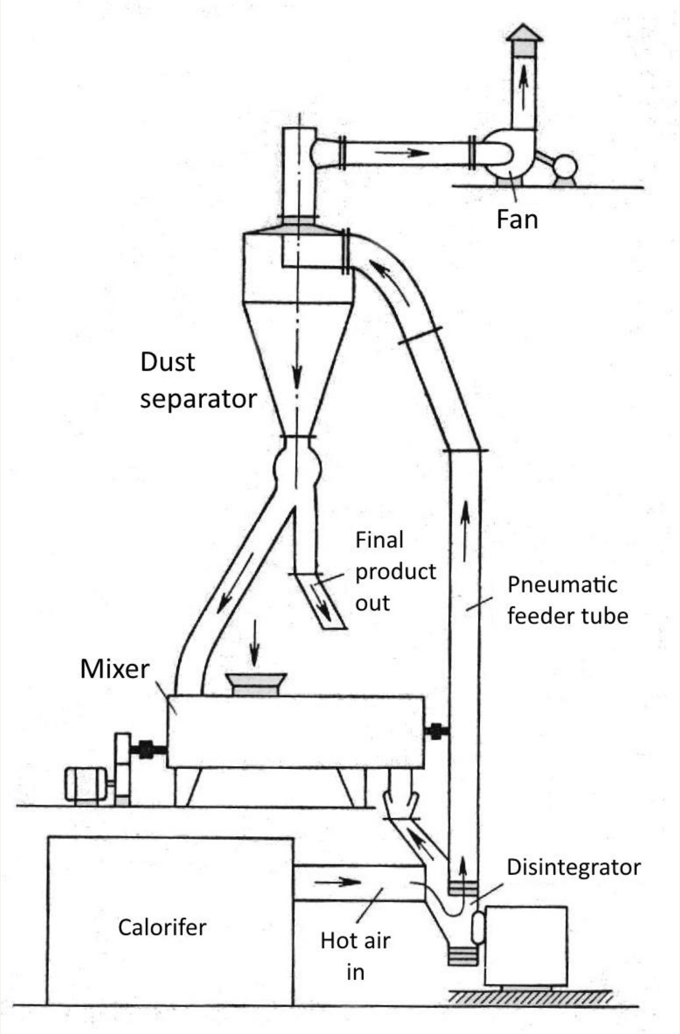
Moving-layer processes

Pneumatic dryer

The air moves the sample and dries it.

Continuous operation.

Lot of energy is needed.



Drying practice

Moving-layer processes

Spray drying

The most important part of a spray dryer is the nozzle, which influences the structure and quality of end product.

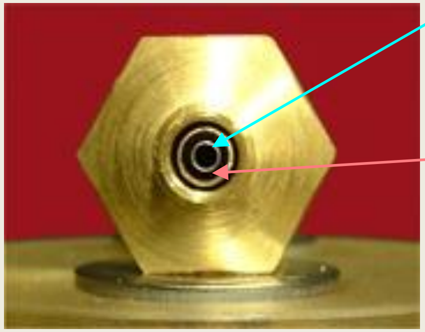
More homodisperse distribution and high particle density of the end product can be achieved by appropriately applied pressure.

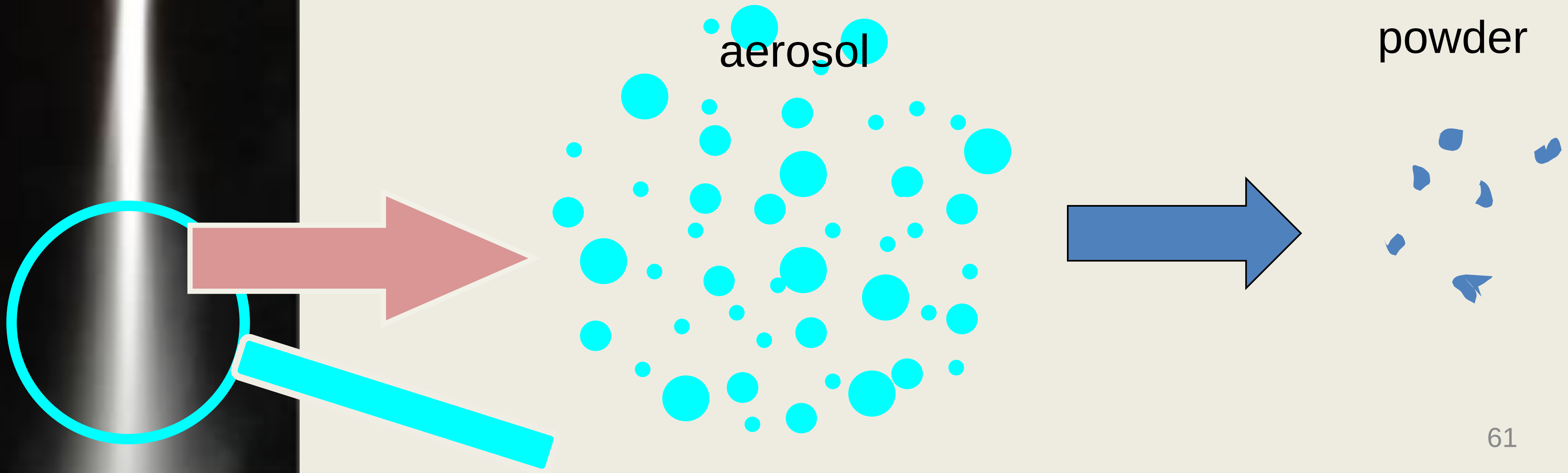
Drying practice

Moving-layer processes

Spray dryer

Nozzle spray drying



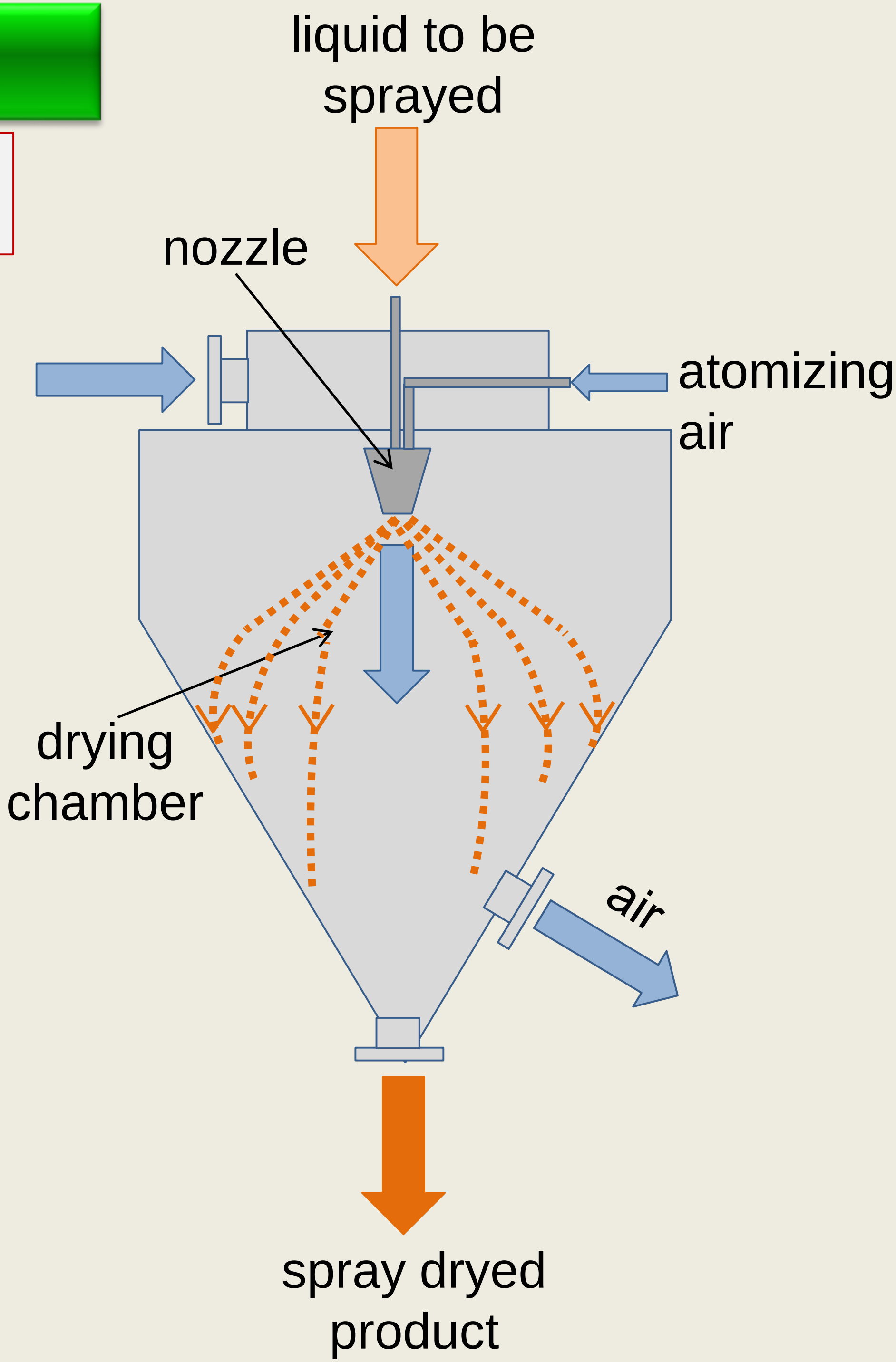


Drying practice

Moving-layer processes

Spray dryer

Nozzle spray dryer



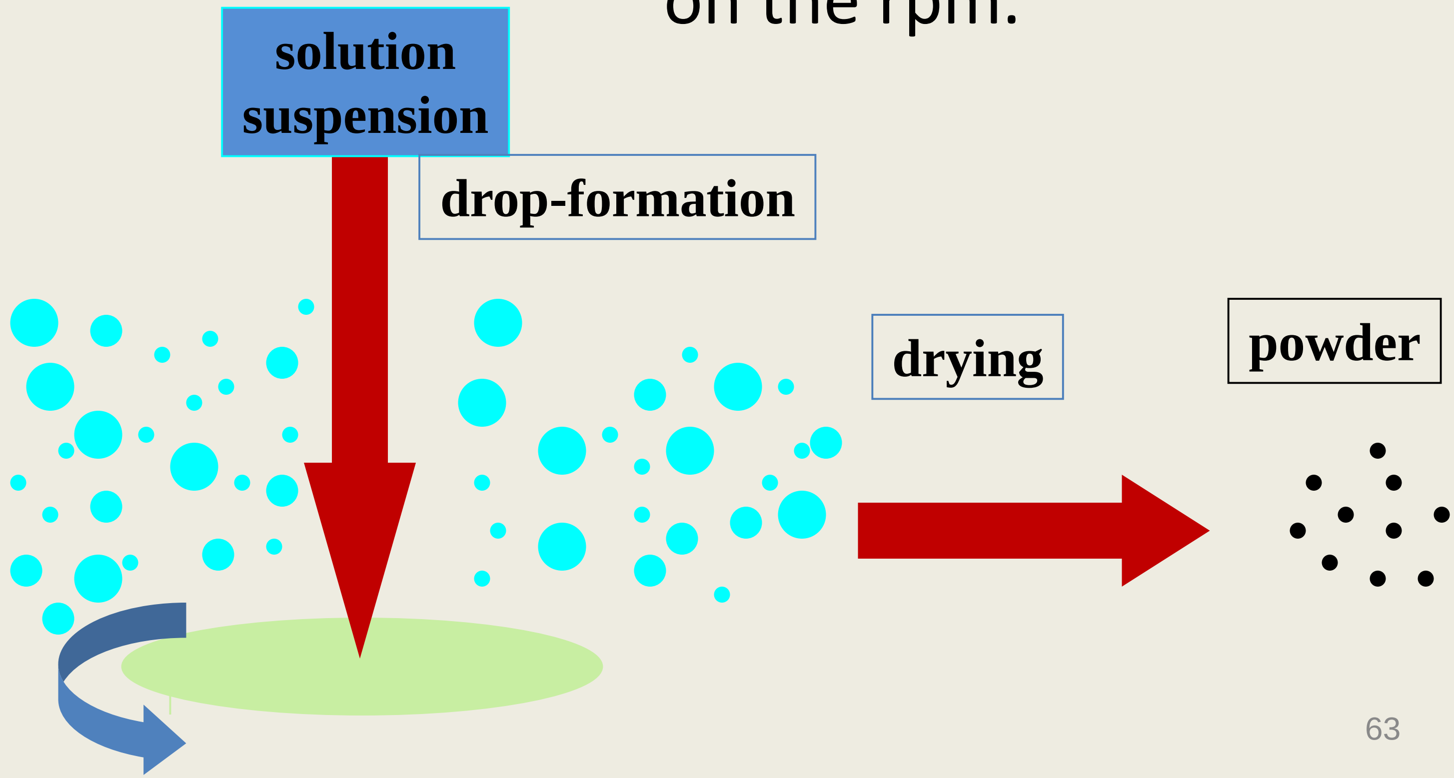
Drying practice

Moving-layer processes

Spray dryer

Rotary disk dryer

- High speed rotary disk,
- Mechanical effect,
- The particle size depends on the rpm.

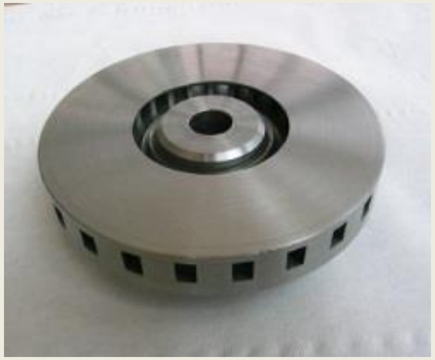


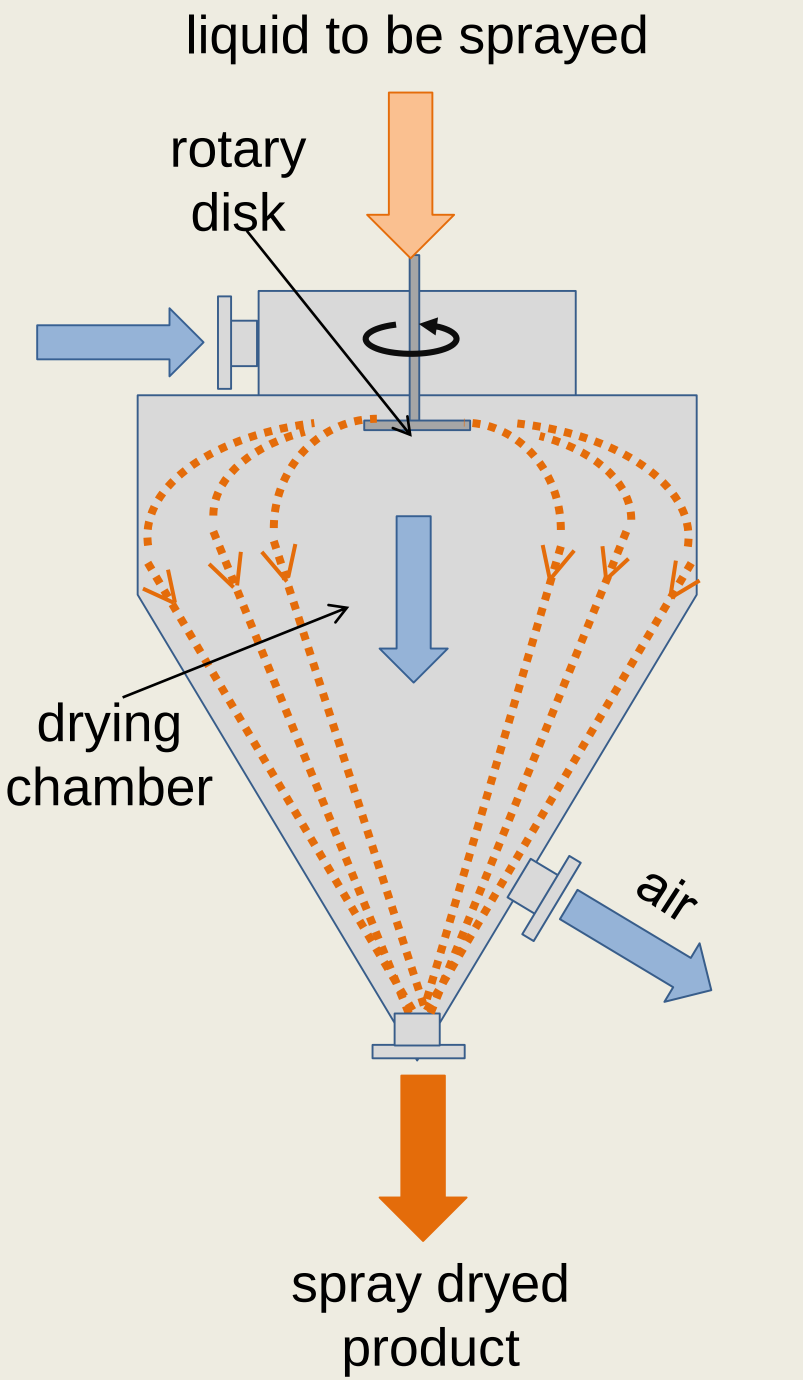
Drying practice

Moving-layer processes

Spray dryer

Rotary disk dryer

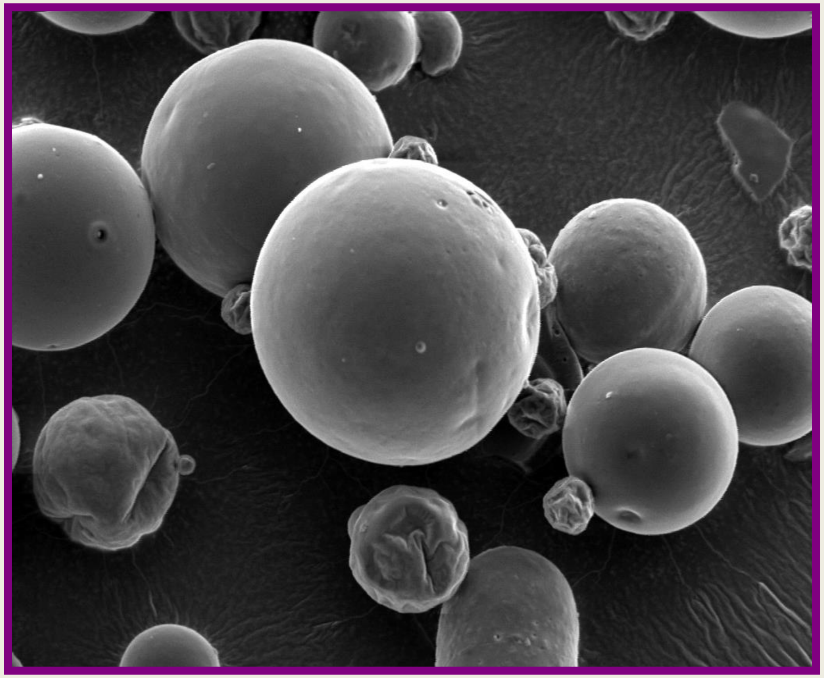




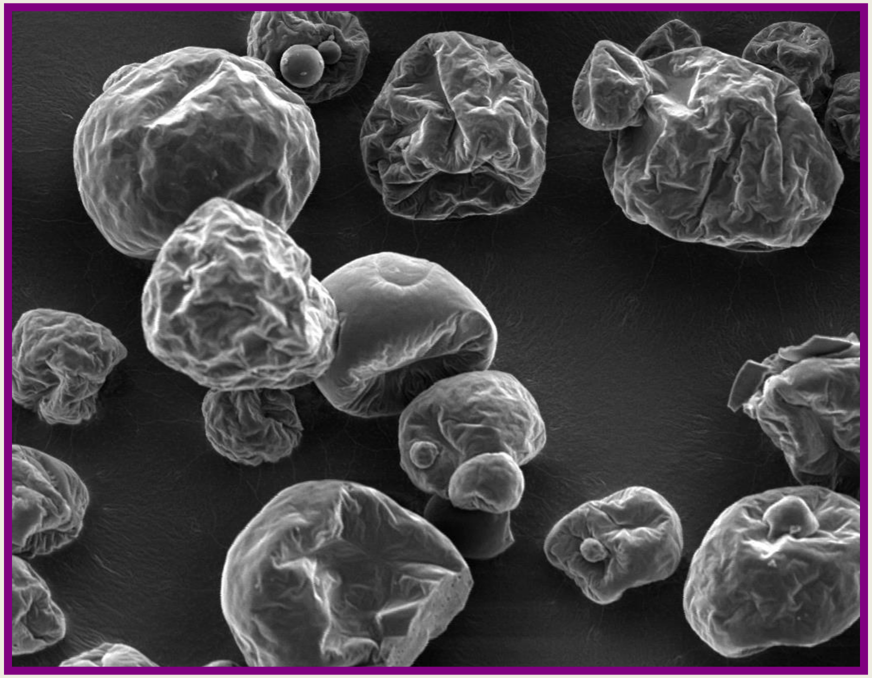
Drying practice

Moving-layer processes

Spray dryed products



with rotary disk



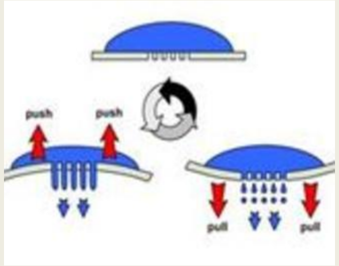
with nozle

Drying practice

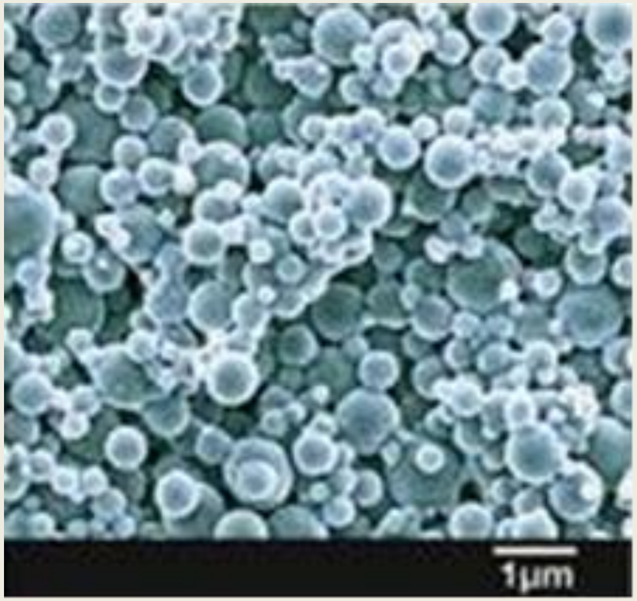
Moving-layer processes

Spray dryer

Nano Spray Dryer B-90



Piezoelectric nozzle head



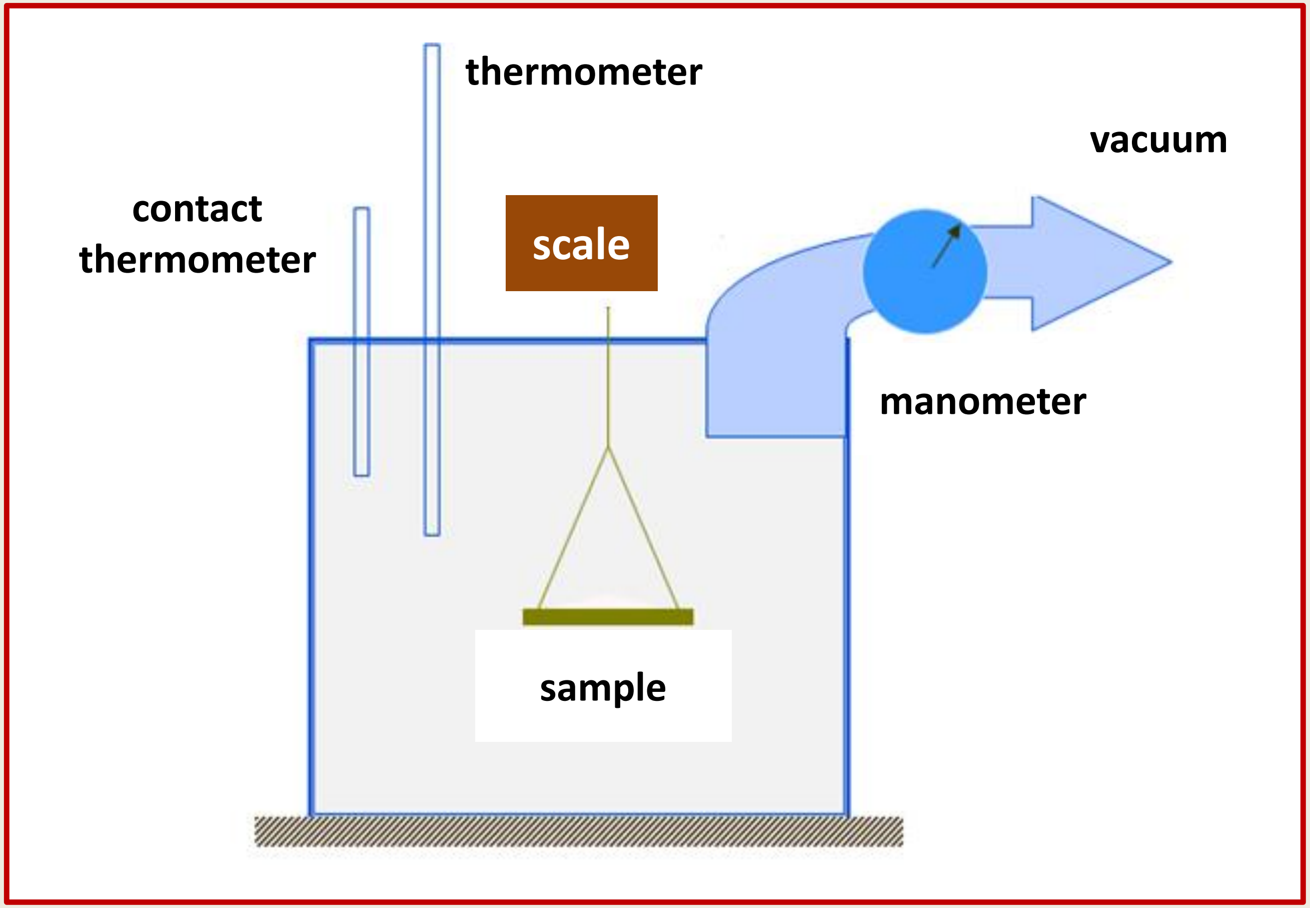
Determination of moisture content

(quality control)

Determination of moisture content

Gravimetry

Continuous heating and weighing



Determination of moisture content

Gravimetry

Moisture determination

by microwaves or infrared radiation.

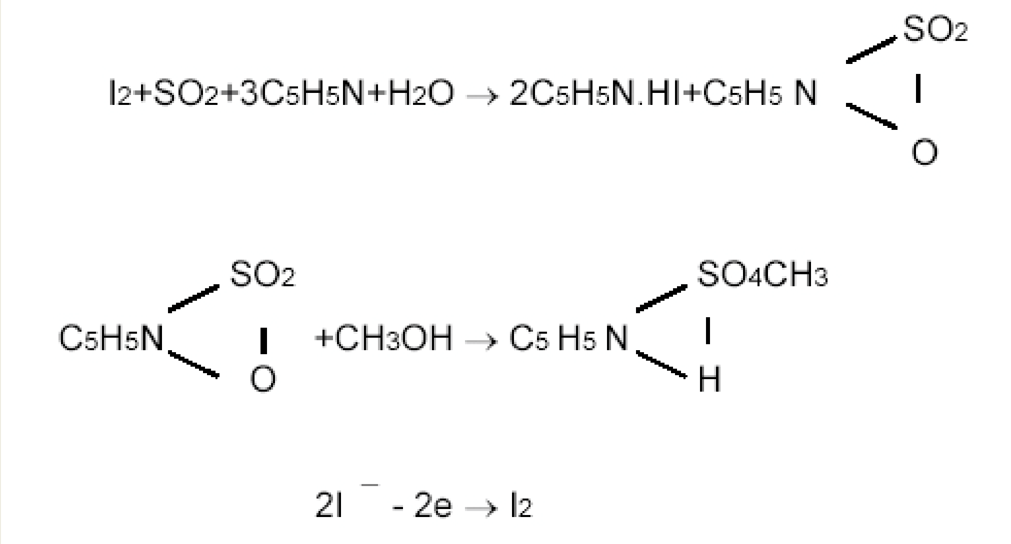
Determination of moisture content

Karl Fischer titration

The iodine can react with the sulfur-dioxid in the presence of water. Water can be accuratelly determined.

$$I_2 + SO_2 + 2H_2O \rightarrow 2HI + H_2SO_4$$

In practice, the reaction can assist with methanol and pyridine.



Determination of moisture content

Spectroscopy

NMR

- H_2O is determined according to hydrogen atoms (quantitative determination of protons)
- free and bound water are distinguished

IR spectroscopy

- difficult to calibrate

NIR

- absorbed water can measured in different wavelength
- does not harm the material
- fast method

Thank you
for your attention!!!