#### University of Pécs Institute of Pharmaceutical Technology and Biopharmacy

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## Main points of the lecture

- Types of heat transfer
- Heat exchanger
- Heat transfer in pharmacy
- Heat transfer in industry
- Evaporation
- Distillation
- Cooling

#### The Heat

**heat** is <u>energy</u> that spontaneously passes between a system and its surroundings in some way other than through <u>work</u> or the transfer of matter

Pécsi Tudományegyetem

Gyógyszertechnológiai Intézet

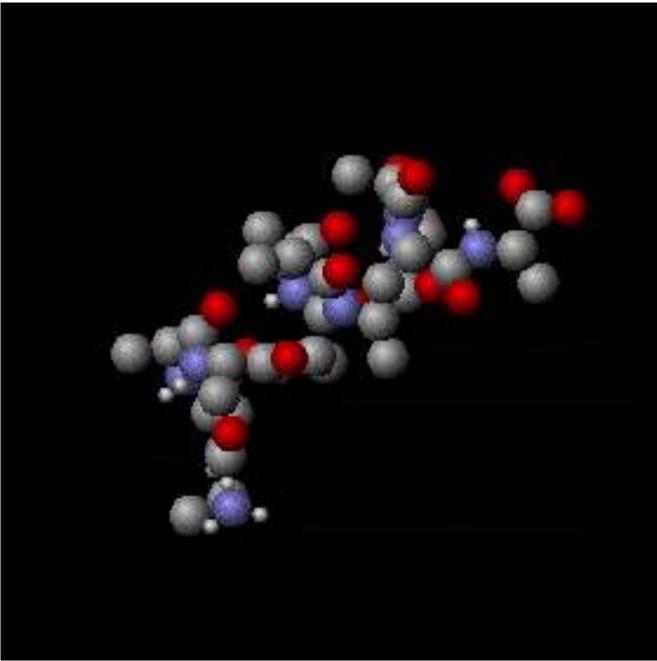


- The heat is closely intertwined with the main laws of thermodynamics.
  - The first law states that the change in the <u>internal energy</u>  $\Delta U$  of a <u>closed</u> <u>system</u> is equal to the amount of <u>heat</u> Q supplied *to* the system, minus the amount of <u>work</u> W done by the system on its surroundings.
  - The second law of thermodynamics states that there is no such process that results a flow of heat from a lower temperature place to a higher temperature place.

## The driving force for heat transfer is the difference in temperature



## WHAT IS TEMPERATURE?



 By en:User:Greg L - http://en.wikipedia.org/wiki/Image:Thermally\_Agitated\_Molecule.gif, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=1615355 • Temperature is a measure of the average kinetic energy of the particles in an object.

### The three main types of heat transfers







#### Conduction

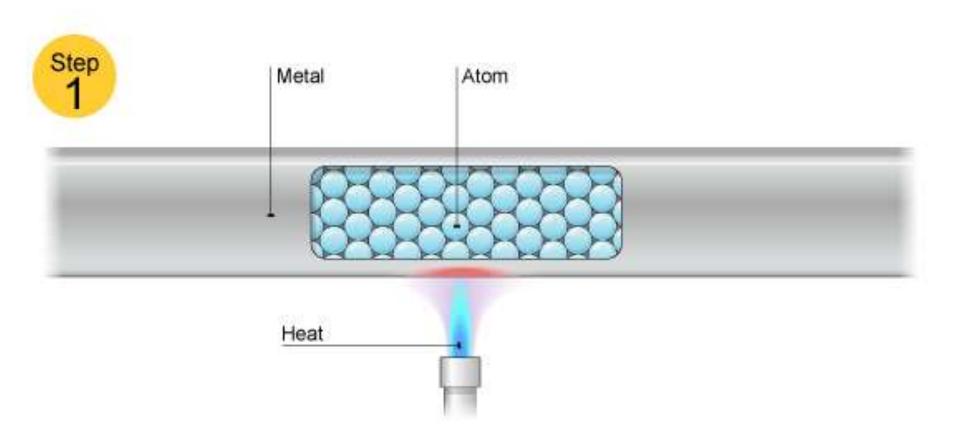
a particle (molecule or atom) with higher temperature (higher kinetical energy) if in a contact with a particle with lower temperature will pass some of the energy to it, this way the temperature of the second particle will increase, and the process of heat transfer is accomplished

## Conduction

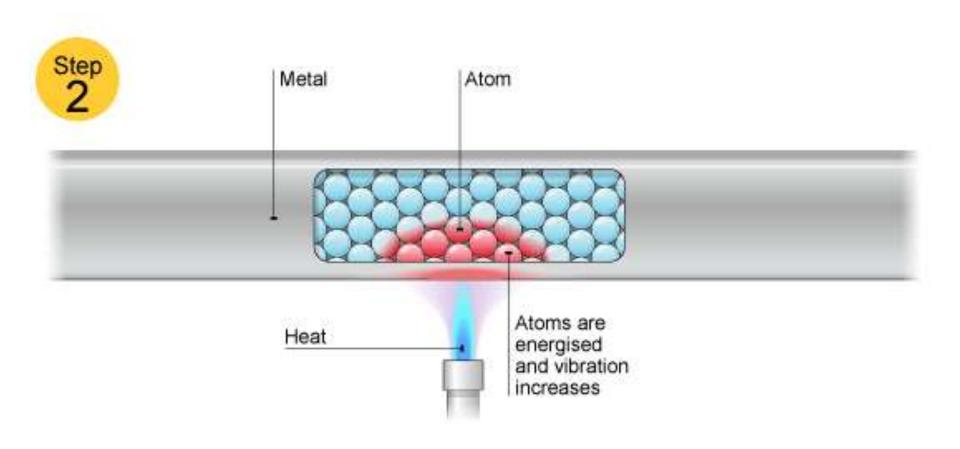
- It is purely molecular scale transfers of kinetic energy (heat diffusion)
- This is usually the way of heat transfer by solid systems.
- The location of particles of the material or system is not changing
- The parts of the system contacting with each other can transfer the heat and give it to each other (the flow of heat depends upon the transfer of vibrational energy from one molecule to another)

In the case of gases and liquids, the leading way of the heat transfer is convection, because of the particles movement.

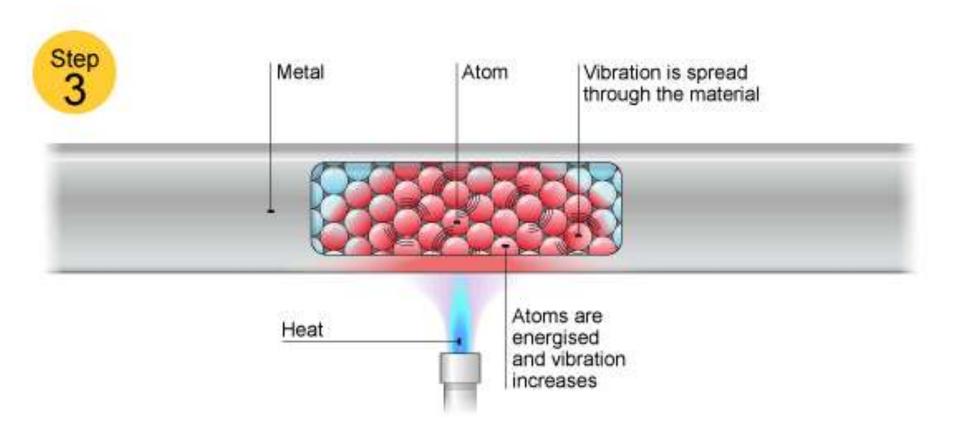
#### Conduction



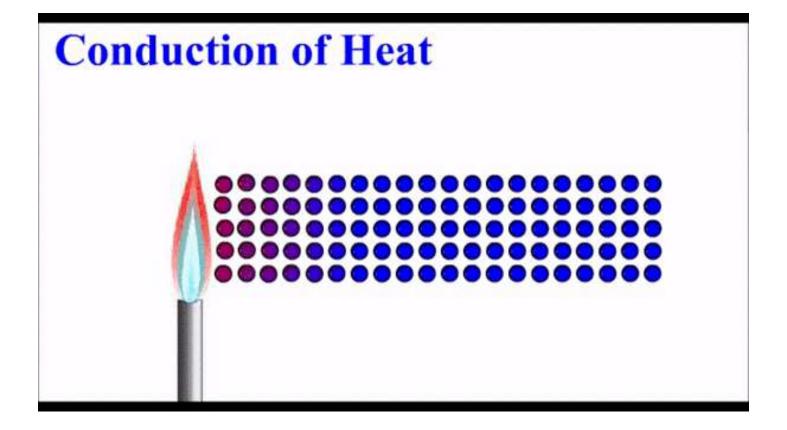
#### Conduction



#### Conduction







#### Conduction

The Fourier I. law is the principle of the conductivity.

$$\varphi = -\lambda \frac{A}{L} \Delta T$$

φ: conductivity (the rate of heat flow)A: surface

- $\lambda$ : thermal conductivity coefficient
- $\Delta T$ : temperature gradient
- L: thickness

The negative mark of the convection coefficient shows the direction of the heat transfer which points from the higher to the lower temperature area.

#### Conduction

#### Thermal conductivity coefficient ( $\lambda$ ):

•Depends on the material of which the body is made and on its temperature

#### **Conductivity:**

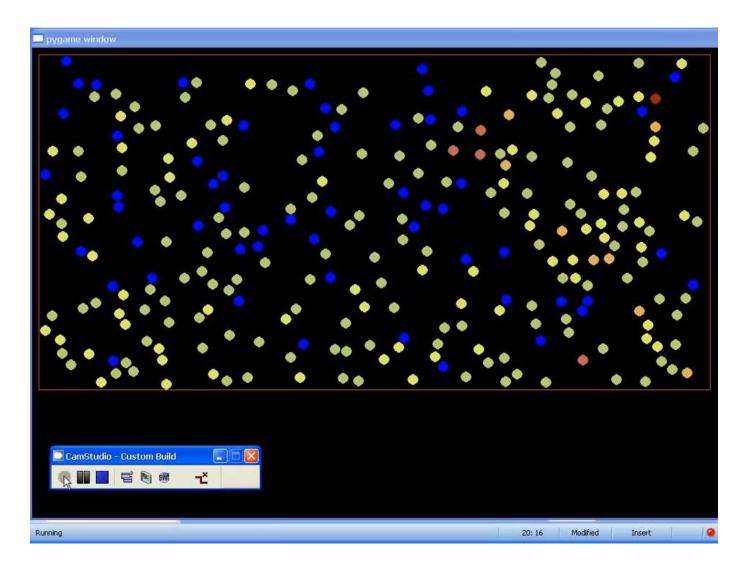
- High in metals, although values vary widely
- Nonmetallic solids normally have slower conductivities
- Carbon is an exception among non metals, because it has relatively high conductivity and chemical inertness wide use in heat exchanger

#### Convection

- Convective heat transfer involves the combined processes of <u>conduction</u> (heat diffusion) and <u>advection</u> or convection (heat transfer by bulk <u>fluid flow</u>)
- Usually in the case of gases and liquids
- Convection can occur in the case of thin layers.
- The heat can be propagated by the difference of density from the cooler- to the warmer-place.

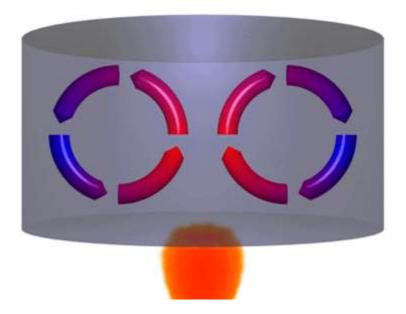
#### Convection

#### In the fluid or body location of the particles changes

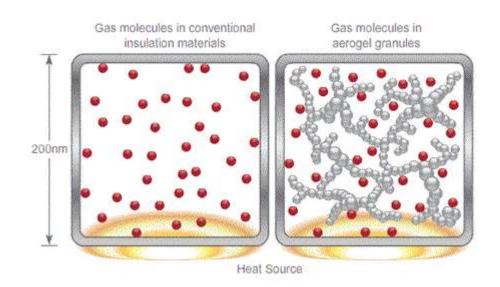




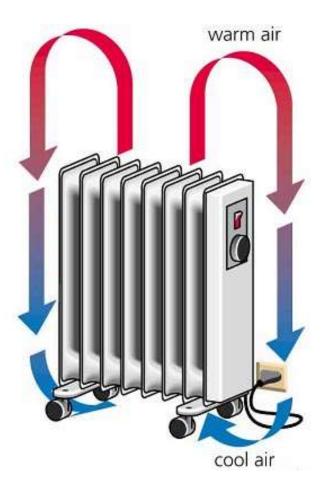
• the heat is transferred with the fluid flow, caused by the difference in density of colder and warmer zones of the fluid

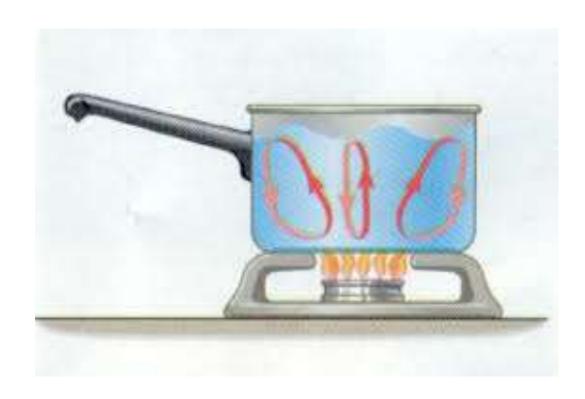


#### Convection



#### Convection





#### Convection

If the liquid or gas contacts with solid surface, then heat transfer occurs.

Heat transfer ( $\varphi$ ) Temperature difference ( $\Delta T$ ) Surface, what is perpendicular to the direction of the convection (A), Convection coefficient ( $\alpha$ )

$$\varphi = -\alpha A \Delta T$$



#### **Thermal Radiation**

Without media (in vacuum, too)
Heat transfer by *electromagnetic waves*The radiation of the warmer system is absorbed by the cooler system.



#### **Thermal Radiation**

Stefan-Boltzmann law

$$\varphi = \varepsilon \sigma A T^4$$

 $\varphi$  heat transfer

 $\varepsilon$  emissivity (emission coefficient)

 $\sigma$  radiation constant of the system (Stefan-Boltzmann constant)

A surface/area

T absolute temperature

The value of  $\varepsilon$  and  $\sigma$  depends on the quality, radiation frequency and temperature.

The  $\varepsilon$ -value of absolute black body is 1, in fact  $\varepsilon < 1$ .

#### Heat-induced changes



Polymorphism



These changes can be followed and detected by termoanalytical methods.

#### Heat transferring media



Pharmaceutical relevance of heat transfer

#### Liquid dosage forms

preparation of ,,infusa", or ,,decocta"
evaporation
distillation
sterilization

Pharmaceutical relevance of heat transfer

#### Semi-solid dosage forms

melting
ointments-,
suppositories

Pharmaceutical relevance of heat transfer

#### Solid dosage forms

promotion of dissolution processincrease of dissolution speed

## **HEAT EXCHANGER**

The heat transfer can be carried out:

- *Directly* by contact with materials
- *Indirectly* without any direct contact with materials

In pharmaceutical technology the indirect heating is principally used

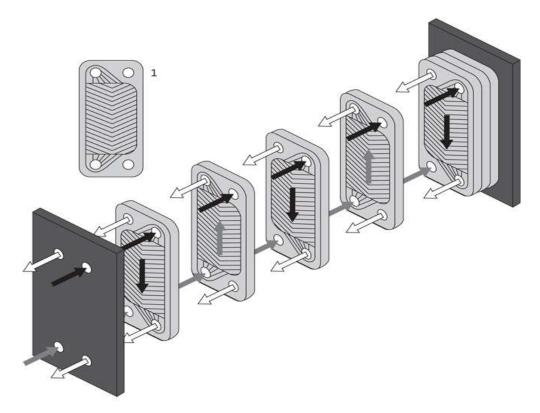
### **HEAT EXCHANGER**

#### Heat exchanger devices:

- 1. Plate heat exchanger
- 2. Cape heat exchanger /Duplicator
- 3. Tube bundle heat exchanger

## **HEAT EXCHANGER 1. Plate heat exchanger**

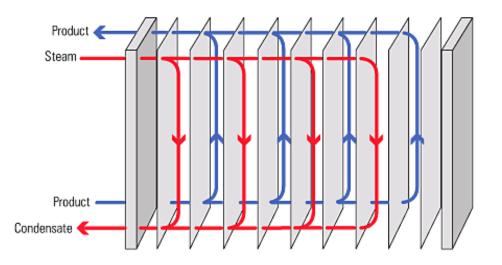
Consist of a number of specially press patterned plates bolted between two pressure plates.



**Turbulence** is created in the liquid flow channels, **giving very high heat transfer coefficients** and resulting in a compact, efficient heat exchanger.

## HEAT EXCHANGER1. Plate heat exchanger

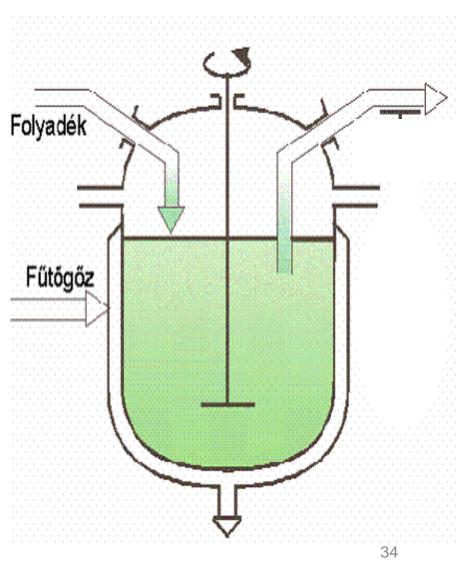




## HEAT EXCHANGER2. Cape heat exchanger/Duplicator

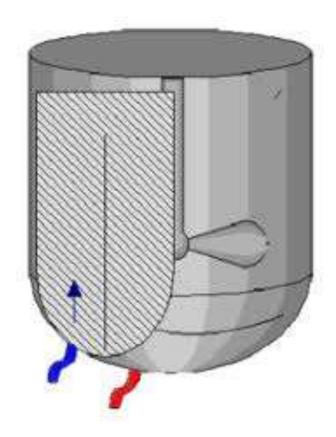
- Two-layered

   equipment, which is
   considered containers,
   surrounded by the
   external covering
   plate, called cape area
- Heat transfer is provided by transmisssion of warm water, steam or oil



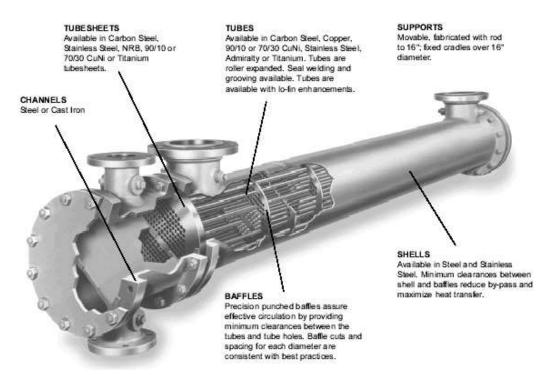
## HEAT EXCHANGER 2. Heating jacketed reactor/Duplicator

A jacketed tank is a tank with an outer jacket designed to containg heating or cooling media. Product is heated or cooled while being mixed, blended or agitated. Jacketed tanks are not thermally efficient and they cannot be used in a continuous operation.



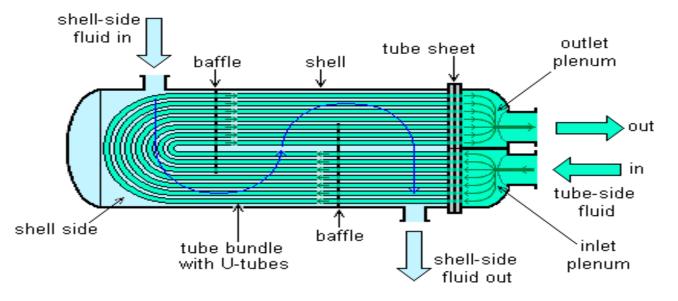
### HEAT EXCHANGER 3. Tube bundle heat exchanger

- the most common type of heat exchanger used in the chemical process industry.
- consists of a shell filled with a bundle of tubes



#### HEAT EXCHANGER 3. Tube bundle heat exchanger

#### U-tube heat exchanger



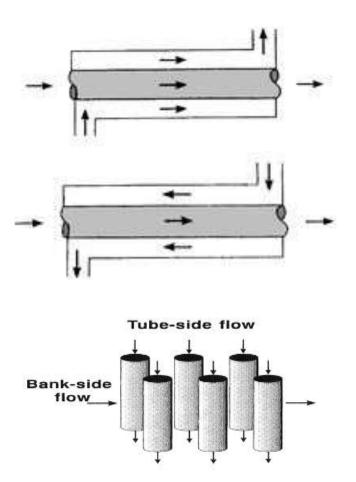
A fluid or gas flows through the tubes while another fluid or gas flows through the shell causing heat transfer through the tube walls.

## HEAT EXCHANGER2. Tube bundle heat exchanger

Heat transfer can be:

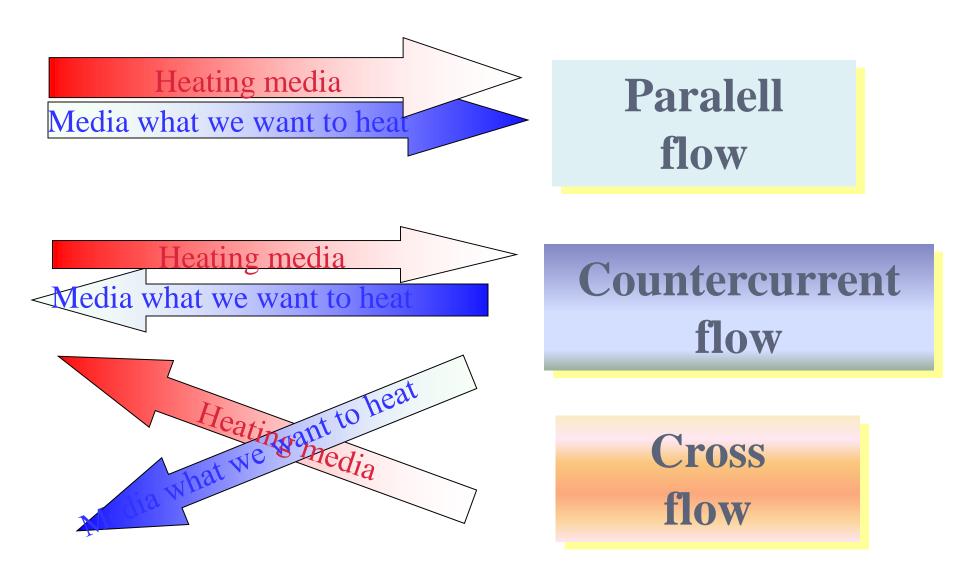
Direct/paralell flow

Countercurrent flow



Cross flow

#### Flows of heat exchangers



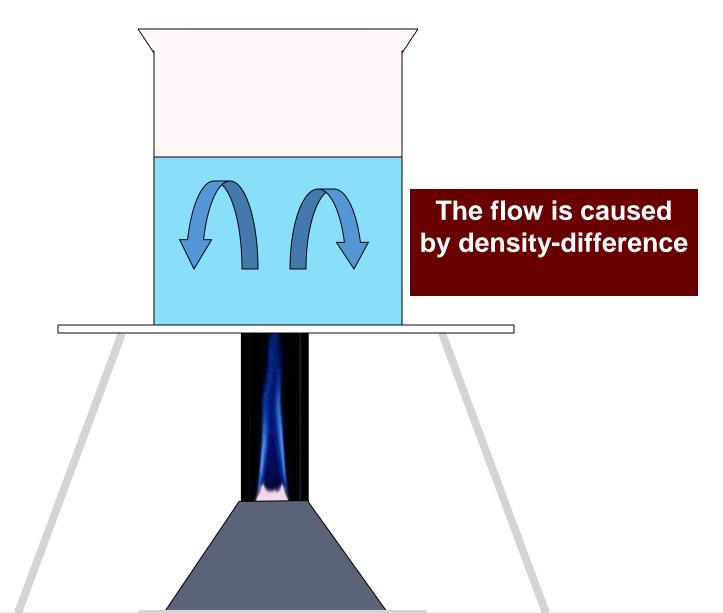
# Heat transfer

in pharmacy

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#### **Heating of liquids**

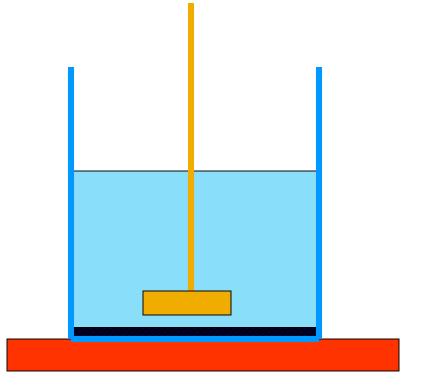


#### Pharmaceutical relevance of heat transfer

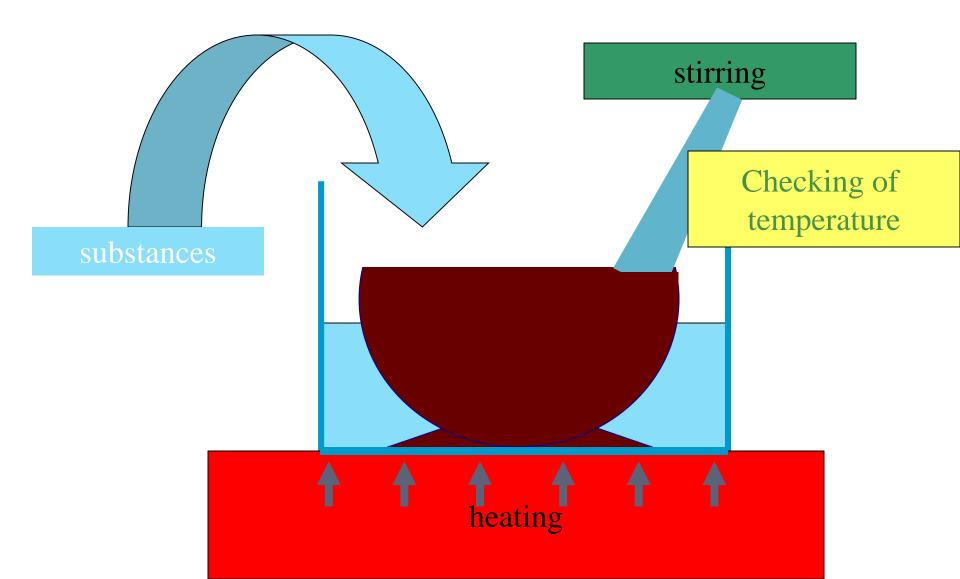
#### **Preparation of syrups**

Stirring and mild heating (avoid local over-heating and caramelisation)

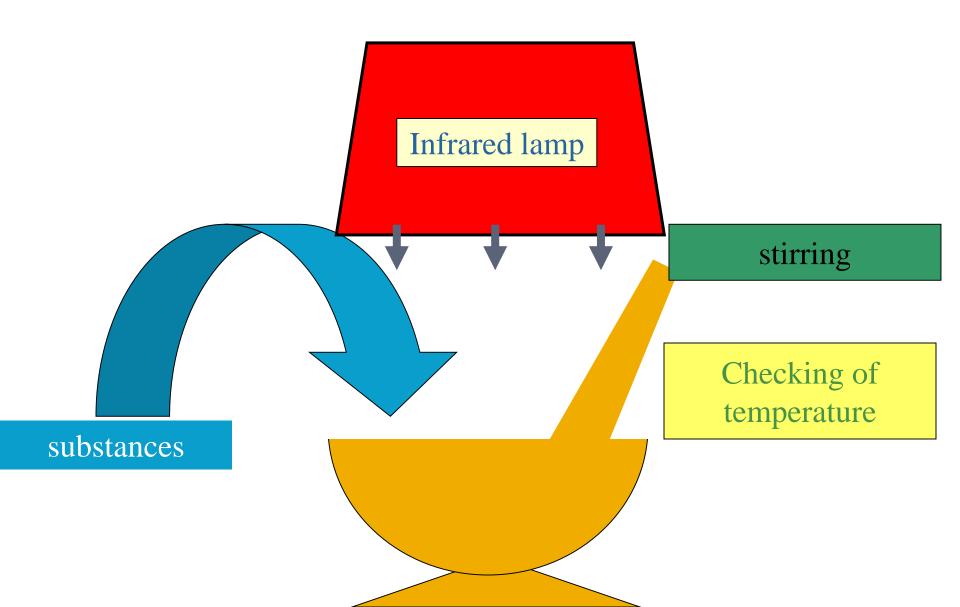
Boiling at the point of foaming (clarification) Supplementation after cooling.



## Melting of substances for preparation of ointments and suppositories

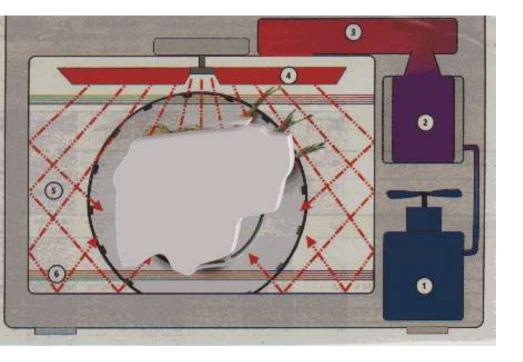


## Melting of substances for preparation of ointments and suppositories



#### Microwave Unit Design





The electron tube (magnetron) converts the AC electric energy (50 Hz) to high-radiation energy at frequency 2.45 GHz.

The rotating fans and the metal walls of the equipment can reflect the waves resulting a homogenous energy field. The object (what we want to heat) can be rotated for the perfect, uniform warming.

#### Heating with microwaves

During heating with microwaves **internal heating** can develop, thus the heat absorbtion is more even consistant, and the process of heat transfer lasts much shorter.

The temperture increase of heated material depends on:

- Time of heating
- Composition
- Dielectric properties of components
- Water and salt content of composition

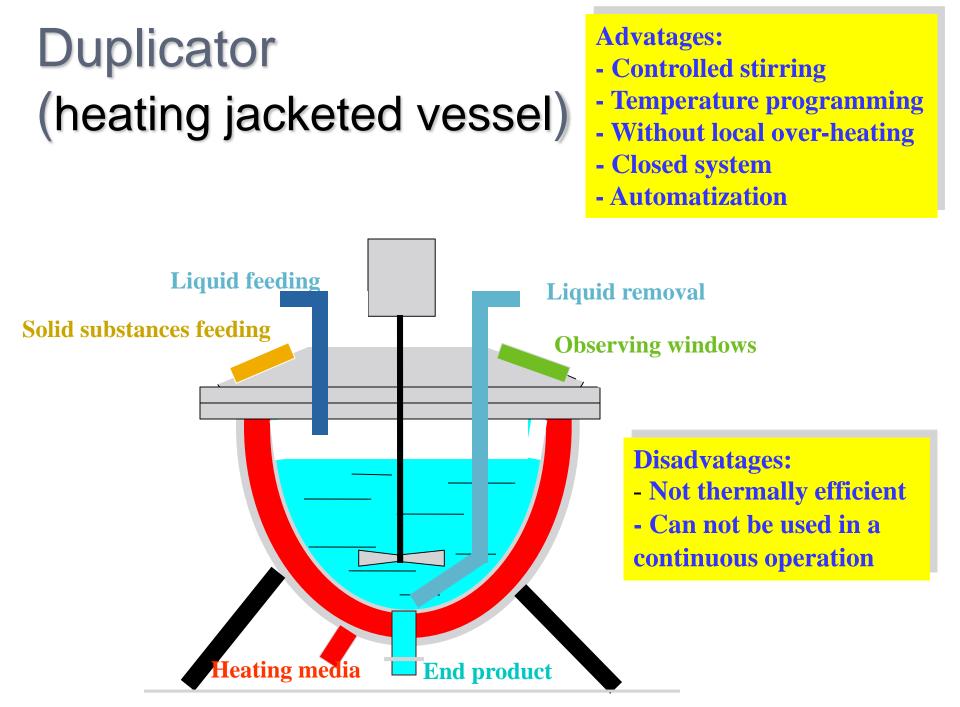
The disadvantage of heating with microwaves is the possibility of **selective heating**, which is caused by the different dielectric properties of the different ingridients.



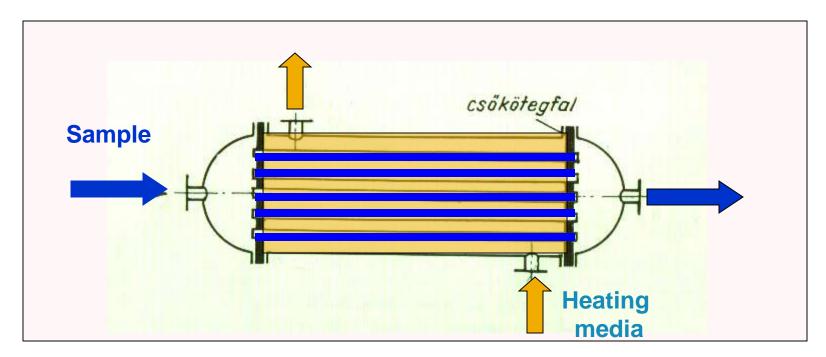
in industry

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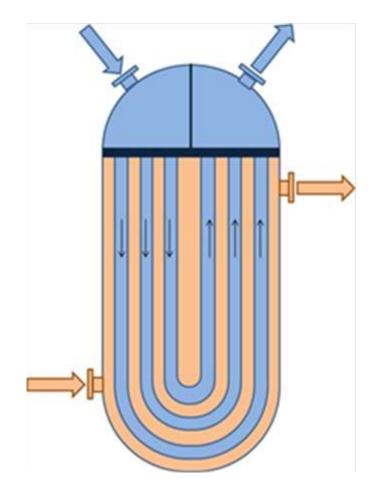
#### Straight-tube heat exchanger

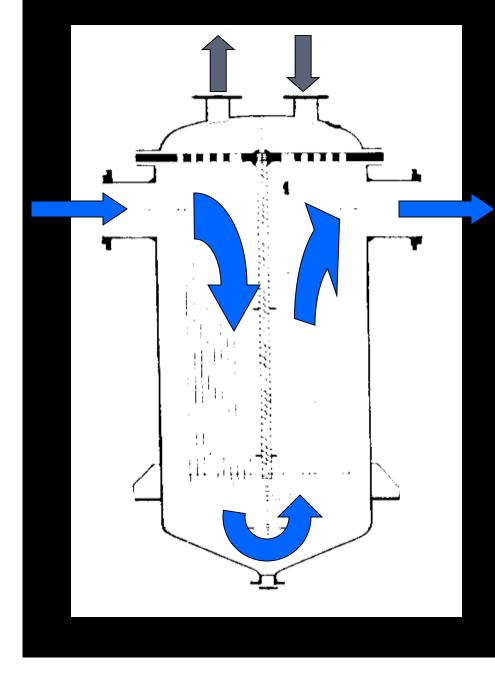


Tube heat exchanger consists of a series of tubes. One set of these tubes contains the fluid that can be either heated or cooled. The second fluid runs over the tubes that are being heated or cooled. Typically used for high-pressure applications (with pressures greater than 30 bar and temperatures greater than 260 °C).

#### Paralell or countercurrent flow.

#### Hairpin heat exchanger







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#### The solvent is eliminated from solution.

The aims:

- to concentrate the solution
- extraction of the dissolved substances
- extraction of the solvents



#### Heat is transferred to the solution, due to which a part of solvent transforms to steam phase and departs from solution:

#### **Steps of evaporation:**

- 1. solution should be heated untill the boiling point
- 2. steams create, depart from fluid phase.
- 3. the leftover solution concentrates more and more
- 4. if the solution becomes totally concentrated, then by further steam removal, crystal form of subsatuce will appear.

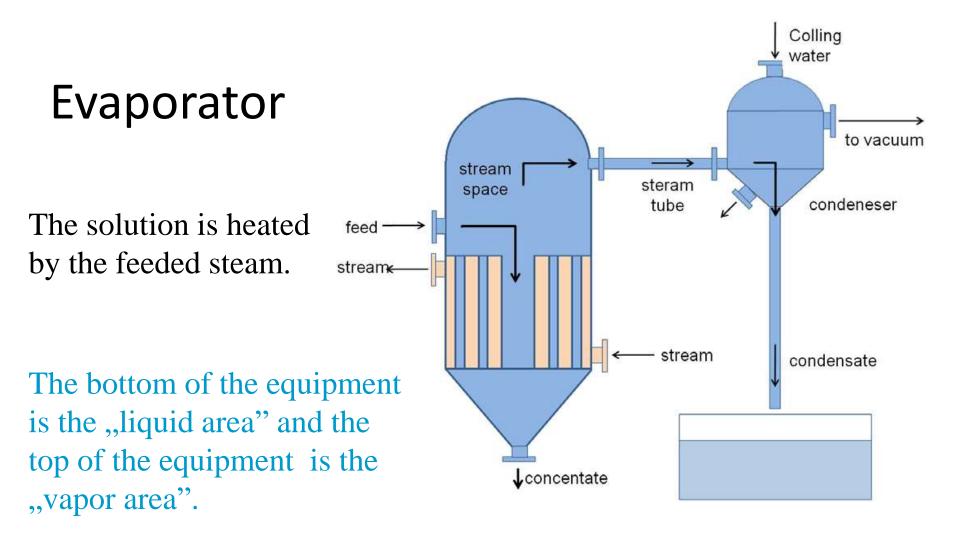


## **During evaporation the following parameters of solution are changing:**

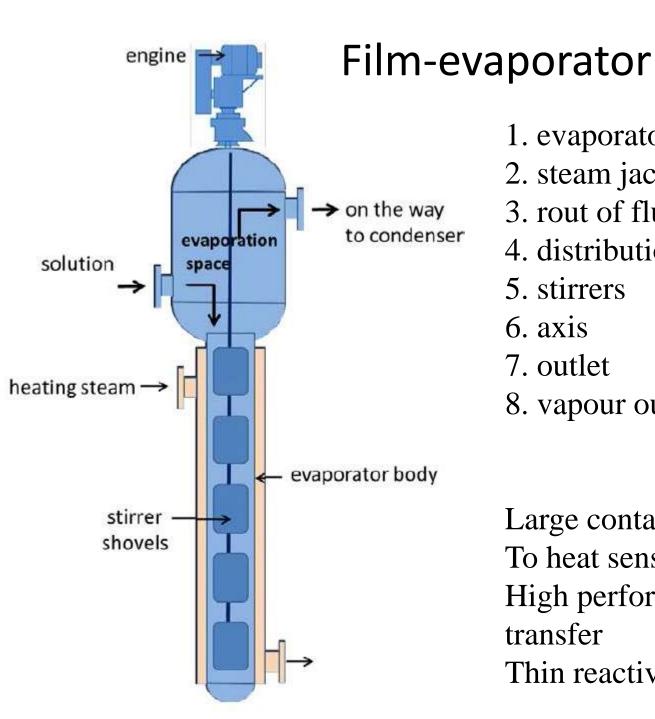
Concentration
Density
Viscosity
Boiling point

## Evaporation

At the end of evaporation, due to the increase of density and viscosity, bubble formation becomes gradually more difficult and more intense mixing is required. The internal circulation of liquid slows down, thus performance of evaporator decreases.



The drop collector is placed on the top of the evaporator

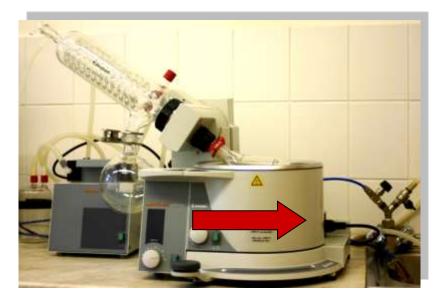


- 1. evaporator body
- 2. steam jacket
- 3. rout of fluids
- 4. distribution or drip tray
- 5. stirrers
- 6. axis
- 7. outlet
- 8. vapour outlet

Large contact surface. To heat sensitive materials High performance in heat transfer Thin reactive layer (0.1-0.5mm)

## Evaporation with water-cooling, stirring and vacuum

The efficacy of the evaporation may be increased if vacuum is applied. We can work on lower temperature if we reduce the pressure (,,enhance of vacuum"). The rotation of the flask is controlled.



Smooth heating of the material. The flow rate of the cooling water can be controlled.

LABOROTA (ROTADEST, ROTAVAPOR)

Faster, safer, efficient and milder evaporation.



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## Distillation

#### The distillation is a process in which a liquid mixture is separated into its component part by vaporization.

The different types of liquids can be separated from each other if their volatility are properly different.

## Distillation

#### The main aims are:

- cleaning,
- separation,
- extraction

Heat reduction or cooling is used:

- at storage of basic materials and preparations,
- distillation,
- crystallization,
- freeze-drying,
- preparation of different dosage forms
- condensate steams,
- reducing solubility.

#### Properties of applied cooling media are:

- non-toxic,
- not environmentally harmful,
- not flammable and explosive,
- large heat of vaporization,
- specific volume of steam has to be low,
- evaporation on atmospheric pressure,
- low viscosity,
- not expensive,
- does not have unpleasant odor,
- does not cause corrosion.

#### **Types of cooling:**

- Natural cooling: carried out by suitable natural media (air, water)
- Artifcial cooling: If there is no available, suitable, natural cooling medium in appropriate amount and appropriate temperature or the temperature of cooled medium has to decreased more than the natural cooling medium, or has to kept on that temperature, artificial cooling is needed.

#### Several artificial cooling mixture in practice

Cooling medium	Composition (m/m%)	Achievable temperature (°C)
Dry ice		-79
Dry ice—aceton		-86
Dry ice—ether		-100
Liquid air		-187
Liquid nitrogen		-195,8
Liquid helium		-268,6
NaCl—ice	23,5 : 6,5	-40-70
NH <sub>4</sub> CI—ice	19: 81	-21,2
CaCl <sub>2</sub> —ice	59:41	-15,8
36% HCl—ice	25:75	-54,9

The cooling process can be performed by

- cooling bath (cold water, crushed ice, mixture of eutectic salt and ice, dry ice, liquid nitrogen)
- perfusion of cooling medium





#### In pharmacy:

 consistent and slow cooling of melted ointment materials is performed with manual stirring in patendula with pestle, in order to create the appropriate gel structure.

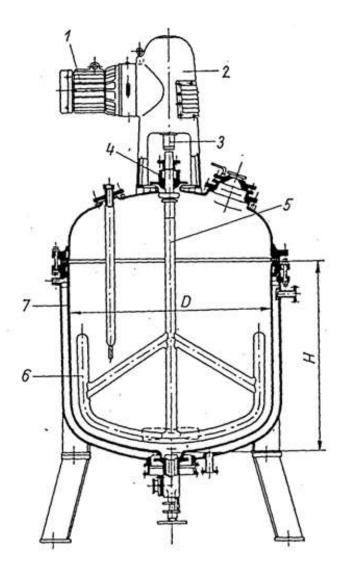




#### In idustry:

 cooling and mixing of ointments have to be regulated and carried out in devices (frequently in duplicators).





## **Storage temperatures**

- room temperature (15–25°C): the main part of pharmaceutical materials and preparation
- between 8-15 °C :*Mucuses*, syrups, ointments from Hungarian Pharmacopoeia (Ph. Hg. VII) and nutrition are stored in cool place.



### Storage temperatures

•between 2-8 °C : According to standards insulin preparations and eye drops from FoNo have to be kept in refrigerators.

•under -15 C°: Oculogutta rifampicini FoNoVII. preparation has to be stored in freezer. Its expiry date besides this storage is 1 month, but after unfolding until only 5 day can be used. In the meantime it has to be stored on 2-8 °C.



## Storage temperatures

Medicines in high amount are stored in **cooling rooms**, in the case of storage of higher stock in factories and wholesalers products are kept in **cooling halls**.





# • Thank you for your attention!