Extracts, extraction, extrusion

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EXTRACTS - EXTRACTA

Classes according to:

- **Physical states**:
  - **liquid** (liquid extracts, tinctures)
  - **semi-solid** (soft extracts)
  - **solid** (dry extracts)
- **Types**:
  - **Standardized** extracts:
    known **therapeatic activity**
  - **Quantified** extracts:
    defined range of constituents
  - **Other** extracts:
    defined by their **production process**

EXTRACTS - EXTRACTA

Extracts are peaparations of

- **liquid**,
- **semi-solid** or
- **solid** consistency,

obtained from

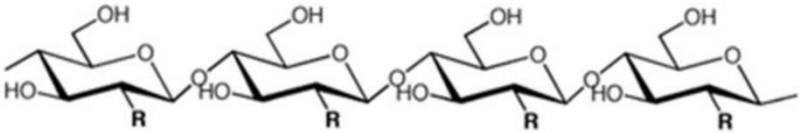
- **herbal** drugs or
- **animal** matters,

which are usually in a **dry** state.

EXTRACTS - EXTRACTA

Herbal drugs

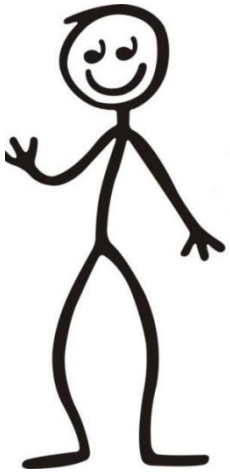
EXTRACTS - EXTRACTA



Cellulose: **R** = OH
Chitin: **R** = $NHCOCH_3$
Chitosan: **R** = NH_2

Chitin (β-(1-4)-poly-N-acetyl-d-glucosamine) is widely distributed in nature and is the second most abundant polysaccharide after cellulose.
It is often converted to its more deacetylated derivative, chitosan.
Chitin and chitosan are **biocompatible**, **biodegradable**, and **non-toxic**.

EXTRACTS - EXTRACTA



Leaves, roots, etc.

Extraction

Extract

Body fluids, tissues

Urine – Blood serum – etc.

Extract

EXTRACTS - EXTRACTA

Production:

- Ethanol or other suitable **solvents**
- Different *batches* may be *blended* **before the extraction**

Extracts are produced by

- using ethanol or other suitable solvets,
  - **maceration**,
  - **percolation** or
  - other, suitable validated methods.

Unwanted matter may be removed after extraction!

Labelling

- **Name** of the herbal drug or animal matter used,
- Whether the extract is **liquid, soft or dry**, or whether it is a **tincture**,
- For **standardized** extracts: **the content of constituents** with known therapeutic activity,
- For **quantified** extracts: the content of constituents (**markers**) used for quantification,
- The name and amount of any **excipient** used including stabilizers and antimicrobial preservatives,
- **Solvents** used for extraction

Groups of extracts (1)

Tincturae (Tinctures)

Liquid preparations which are usually obtained using

1 part of herbal drug or animal matter and
5 or 10 parts of extraction solvent.

Production:

- maceration
- percolation

Solvent: ethanol (suitable concentration)

Labelling: the ratio of

- starting material to extraction liquid
- starting material to final tincture.

Groups of extracts (2)
Extracta fluida (Liquid extracts)

Liquid preparation of which, in general,

1 part by mass or volume is equivalent to 1 part by mass of the dried herbal drug or animal matter.

Liquid extracts may be filtered, if necessary.

A slight sediment may form on standing, which is acceptable as long as the composition of the liquid extract is not changed significantly.

Labelling:
the ethanol content in per cent (V/V %) in the final extract.

Groups of extracts (3)
Extracta spissa (Soft extracts)

Semi-solid preparations obtained by evaporation or partial evaporation of the solvent used for extraction. Their consistency is between the consistency of liquid and dry extracts.

Groups of extracts (4)
Extracta sicca (Dry extracts)

Solid preparations obtained by **evaporation of the solvent** used for their production.

Their **loss of drying** and water content should **not be greater than 5%**.

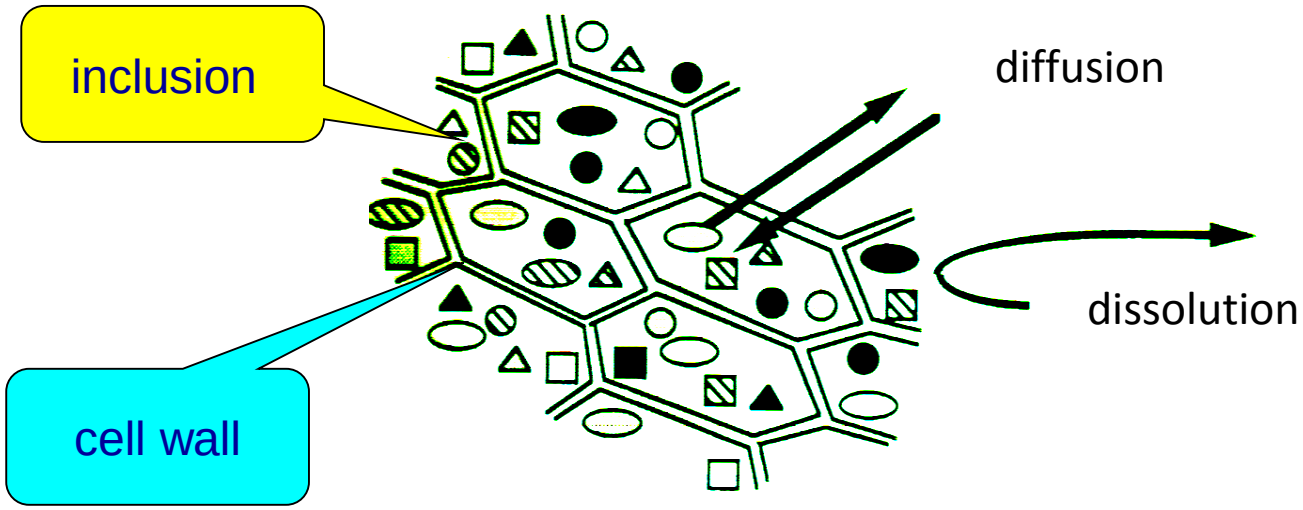
Ginseng and dry extract

BASIC OPERATIONS

EXTRACTION

Extraction

Extraction is the **removal process** of one or more components from a liquid, semisolid or solid material.



Extract (contains dissolved materials)
Raffinate (leftover solution)

Extraction

Main steps of the process:

1. Extraction solvent **penetrates** into cells.
2. Substances are **dissolved** in solvent (active and escort/accompanying substances).
3. From the solution created in the cells (cell solution) the components **diffuse** into the extraction solvent due to concentration gradient.

Extraction

Difussion process in which active and accompanying substances are extracted from the herbal drug with a suitable solvent.

Main active substances:

- alkaloids,
- volatile oils,
- saponins,
- steroids,
- amara (bitter substances),
- tannins,
- flavonoids,
- vitamines etc...

Accompanying substances:

- carbohydrates (starch, sugars, pectin),
- proteins,
- mucilages,
- waxes,
- resins,
- fats,
- enzymes,
- colouring agents

Steps of producing extracts

Preparation of herbal drug

1. collection,
2. drying,
3. grinding

Extraction (maceration, percloration)

Extrusion

Sedimentaion, filtration

Evaporation

Adjusting of API content

Diffusion

The process is driven by the **concentration difference**

Fick equation

$$M = DAt\frac{C_2 - C_1}{l}$$

M	= mass (diffusing quantity)
D	= diffusion constant
A	= area
t	= time
C_2-C_1	= concentration gradiens
l	= thickness of the diffusion layer

Factors influencig the extraction:

- surface,
- concentration of cell solution and extractant solution,
- temperature,
- humidity of herbal drug,
- pH-value,
- viscosity,
- surface-active agents.

*Role of the **surface**:*

If the particle size decreases:

- » increasing surface **velocity of diffusion is increasing**
- » BUT: ***too small particle size***
  - can make the filtration more difficult
  - has disadvantegeuos/negative effect because of adsorption

Degree of adsorption should be always smaller than diffusion force.

Concentration of cell solution and extractant solution:

Extraction is a process which has **equilibrium** (balance) between cell solution and extraction solution at the end, thus it is **needed to have concentration difference during the process** $(c_1-c_2) > 0$.

It can be ensured by:

- increasing the volume of extraction solvent (not economical),
- re-newing the extraction solvent:
  - a, *discontinuous* (eg. maceration two times),
  - b, *continuous* (percolation).

Role of temperature

- Increasing temperature results increasing in the velocity of diffusion
- ***In the case of thermosensitive APIs particular attention is needed***

During warm extraction

- ***Proteins may coagulate,*** become unextractable,
- Starch can form a colloidal dispersion, thus it can pass into the extract.

Extraction

Nernst's distribution coefficient (k)

$$k = \frac{x_e}{x_r}$$

x_e equilibrium concentration of distributing material **in extract**

x_r equilibrium concentration of distributing material **in raffinate**.

phase proportion (f)

$$f = \frac{m_e}{m_r}$$

m_e mass of extract,

m_r mass of raffinate.

Extraction factor

$$E = kf = \frac{x_e m_e}{x_r m_r}$$

Extraction

Herbal drug preparations can be produced from herbal drug with variant **procedures**:

- *extraction,*
- *distillation,*
- *extrusion,*
- *separation,*
- *purification,*
- *evaporation,*
- *fermentation*.

Extraction

General requirements about extraction solvents:

- dissolves selectively the desired material,
- extraction solvent and carrier solvent should not dissolve in each other,
- not to be harmless for the extract (no chemical reaction with the API),
- should have low evaporation heat and boiling point,
- not to be corrosive,
- not to be flammable or explosive,
- not to be toxic,
- to be cheap and recyclable.

(Carbohydates, mucilages and proteins cannot be extracted by non-polar solvents.)

Extraction

Main tasks during extraction are:

1.) **intensive contact and mixing** of delivering phase and absorbing phase,
2.) insurance of **appropriate time interval** in order to perform the transport of valuable component,
3.) **separation** of raffinate and extract, namely the two phases created during extraction.

Classification of extraction operations:

1.) at ***liquid-liquid*** *extraction, LLE* the initial material and solvent is in liquid state of matter (solvent extraction),
2.) *at* ***solid-liquid*** *extraction, SLE* the initial material is a complex solid material and its soluble components are extracted by extractant
3.) at ***supercritical extraction***, *SCE* the initial material is solid (or liquid mixture), and the extractant is high pressure gas in fluid state.

1. Liquid-liquid extractors

- Continuous or discontinuous/phased procedure similarly to solid-liquid extraction.
- Operate with separation based on **density difference**.

According to their structure and operation, they can be classified to the following groups:

A. ***column extractor,***

B. ***centrifugal extractor,***

C. ***mixer-settler extractor***

A. Column extractor

counter flow

Gravitational settling

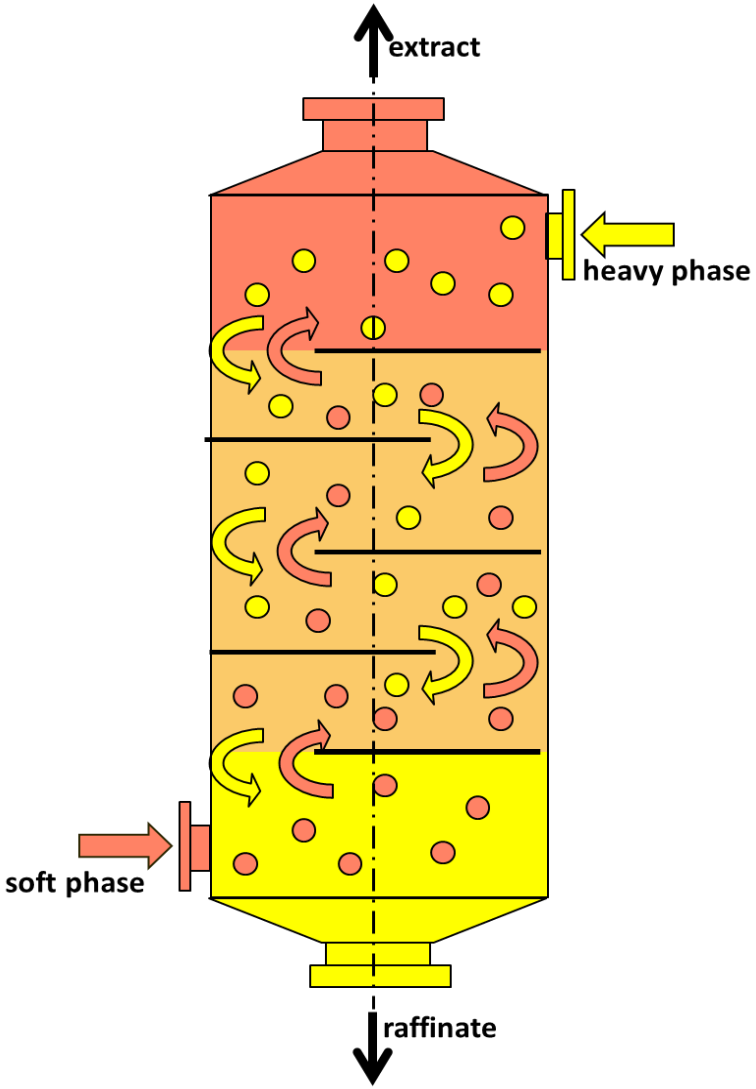
Baffle plates

mixing

Extract and raffinate

is separated only

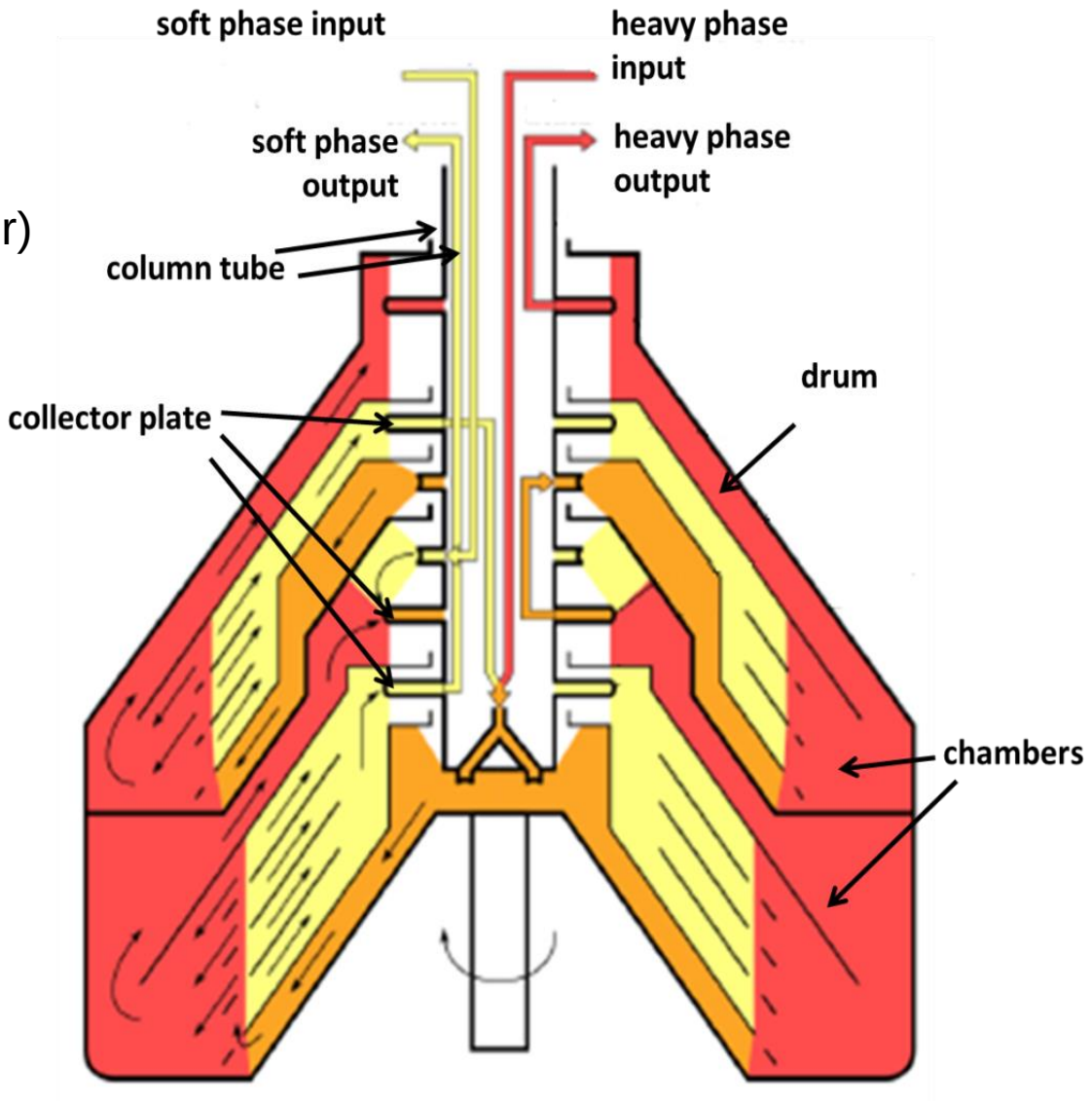
with gravitational settling.



B. Centrifugal extractor

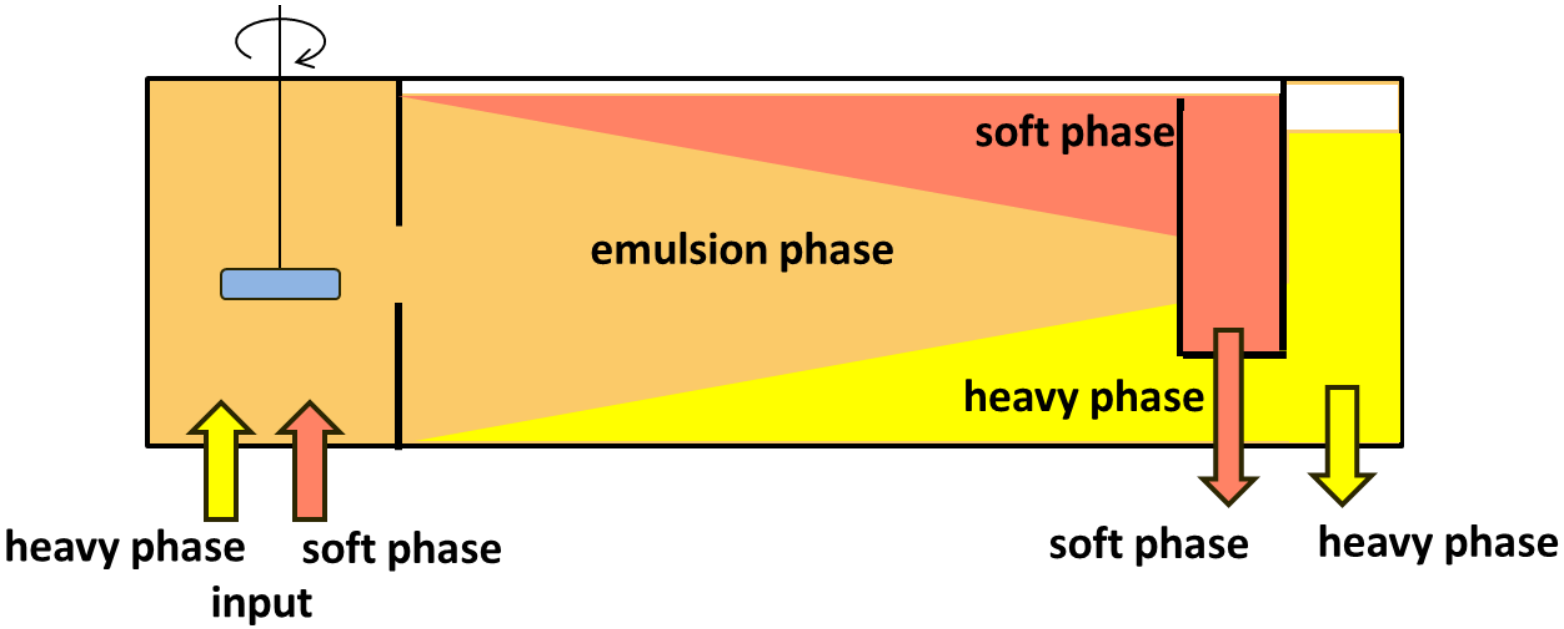
Highest efficacy

(Luwesta type extractor)



C. Mixer-settler extractor

Counter flow
Gravitational separation
Mixed than separated in settler container



2. Solid-liquid extraction

- Components of solid phase are **dissolved in liquid extractant**.
- **Osmosis** and **diffusion** have highlighted roles.
- Extraction is **assisted** frequently **with heating**, but heat sensitivity has to be carefully considered.

Main steps of extraction:

- contact with extractant,
- swelling,
- extraction,
- separation,
- re-extraction of solid phase,
- extraction of components from pooled liquid phase with variant separation methods (e.g. evaporation).

2. Solid-liquid extraction

Methods of **solid-liquid** extraction:

A. *soaking (maceration),*
B. *flow-trough methods (percolation),*
C. *turboextraction,*
D. *vibroextraction,*
E. *counterflow extraction.*

A. Maceration

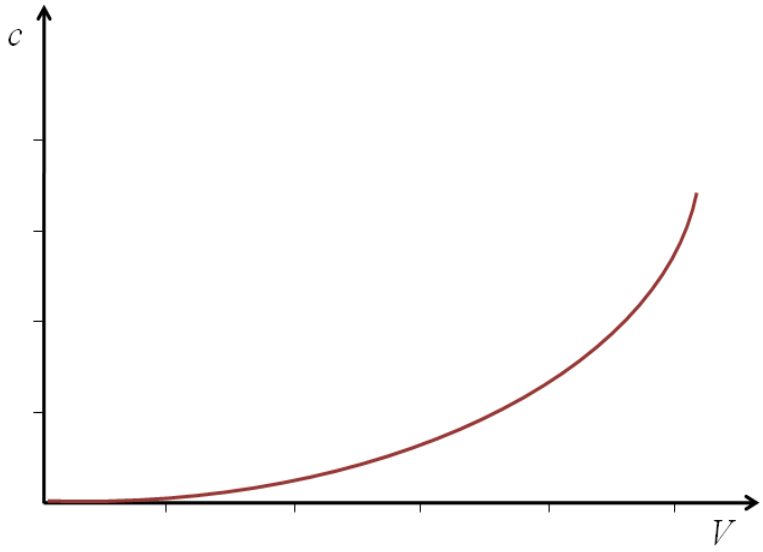
Maceration is used, if:

- The API is water-soluble and heat sensitive,
- The extraction solution is heat sensitive and volatile,
- We need only the components, which are soluble in room temperature (e.g. Althaeae folium),
- Before certain extraction methods.

A. Maceration

$$c = c_o V^k$$

C = equlibrium concentration of maceratum
C_o = initial concentration of drug
V = volume of solvent
K = material constant



- discontinuous,
- room temperature,
- sliced/reduce drug is moistened (swell the cells for 10 minutes),
- the amount of solvent is 5-10 times higher than the amount of drug,
- total extraction time is **hours or days**.

A. Maceration

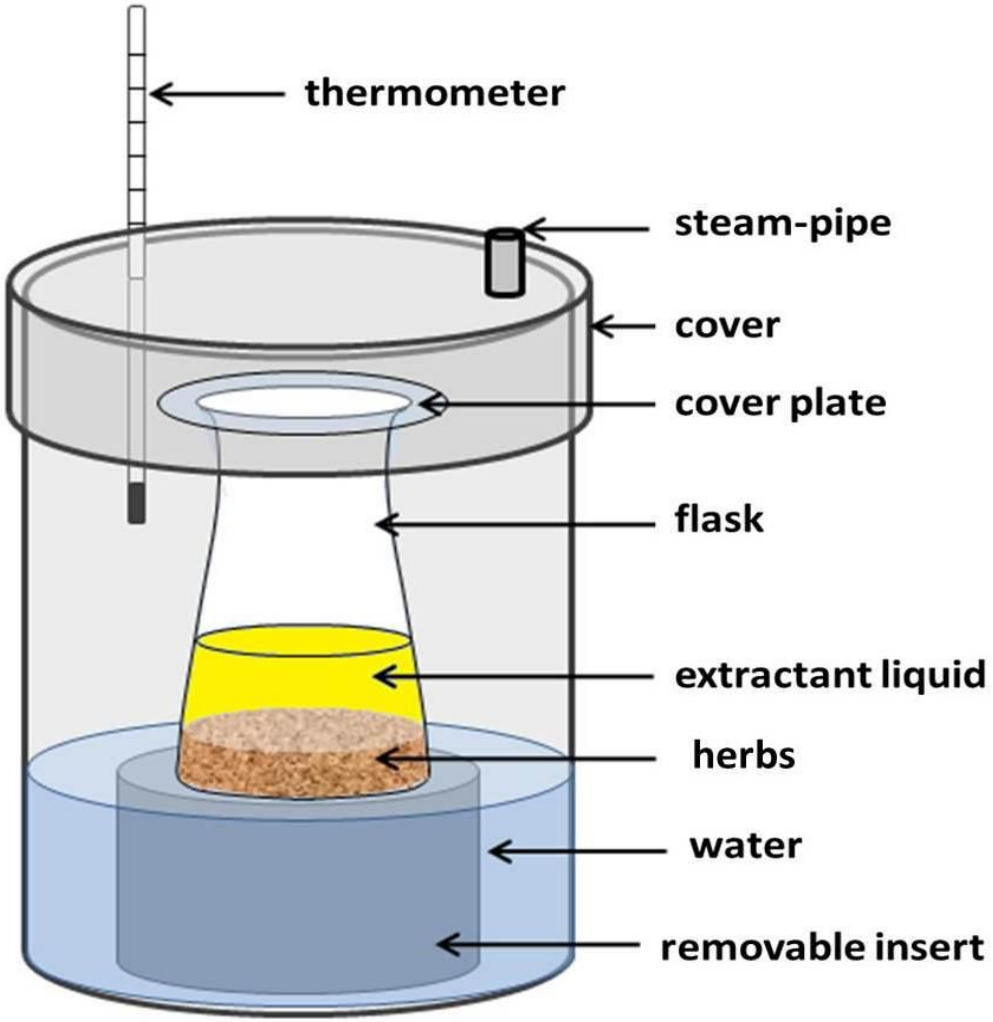
Advantages of maceration:

- **whithout any serious equipment**
- Requires **minimal work**
- **From equal quality of herbal drugs** we can produce **extracts with equal API-content**

Disadvantages of maceration:

- Requires **too much time,**
- **Too much loss** due to remaining much amount of API in the resiude/raffinate

A. Maceration



Schulek's steampot

Produce **decoctions** and **infusions** (dosage forms)

A. Maceration

Decoctions (*decocta*) and ***infusions*** *(infusa)* are the **aqueous extracts of herbal drugs** performed in higher temperature.

Main steps of their preparation:

- herbal drug sliced/reduced,
- previously performed soaking (room temperature),
- flask has to be taken into Schulek's steampot, and required period of time is allowed in steam chamber
  - till **20 min in the case of infusions**,
  - till **40 minutes at decoctions**,
- after prescribed time,
  - decoctions have to removed immediately and filtered while hot, and
  - infusions are filtered after cooling down.

A. Maceration

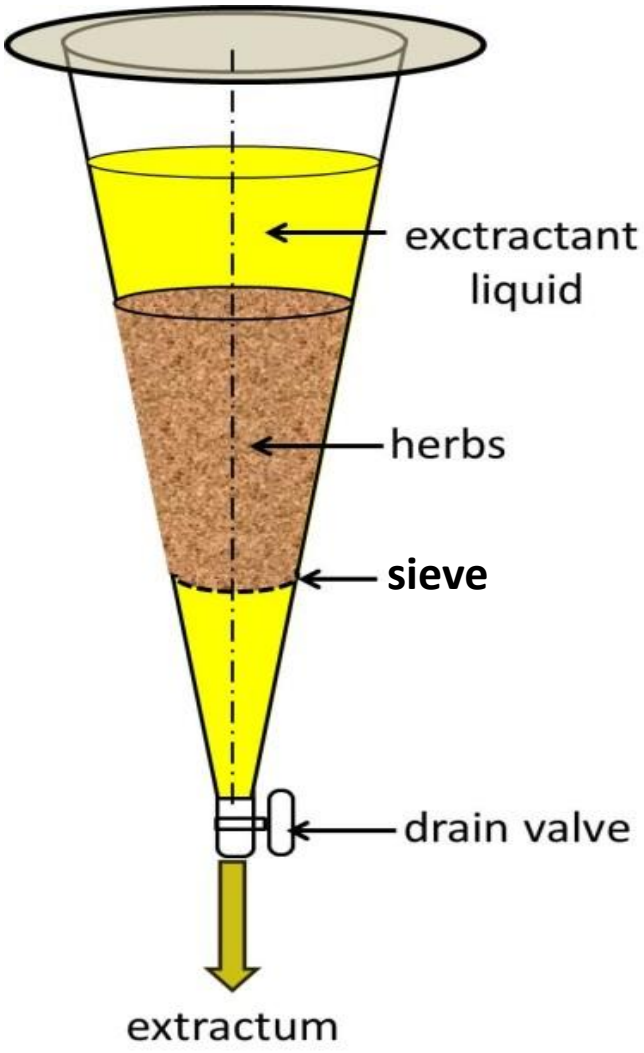
	Infusion/ Infusum	Decoction/ Decoctum
Swelling	+	+
Steam	20 min.	40 min
Filtration	After cooling	Immediately

B. **Flow-through** method: **Percolation**

*This is an extraction process, which is carried out in a **suitable extraction equipment.***

The solvent is filled into the cylindrical placed powdered drug.

The solvent percolates (infiltrates) the drug and dissolves its components that are removed at the bottom of the container.



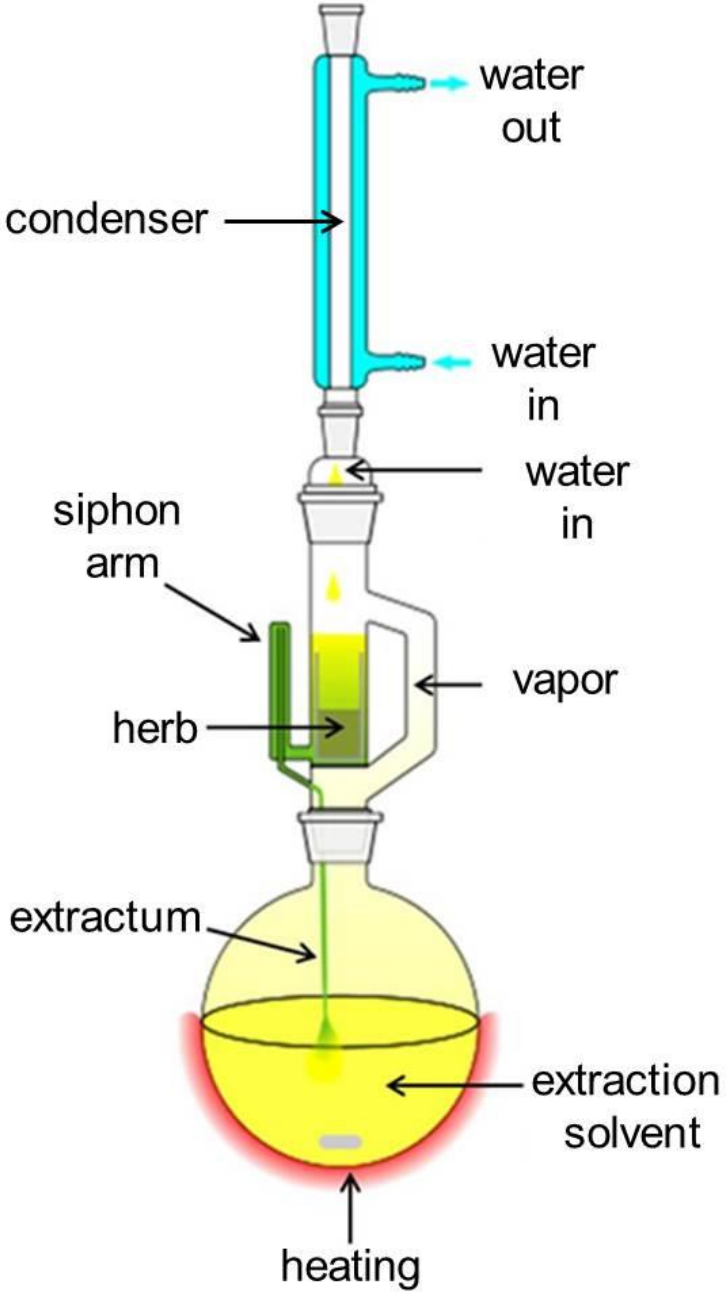
(dis)continuous

room temperature

B. Flow-trough method

Soxhlet-extractor

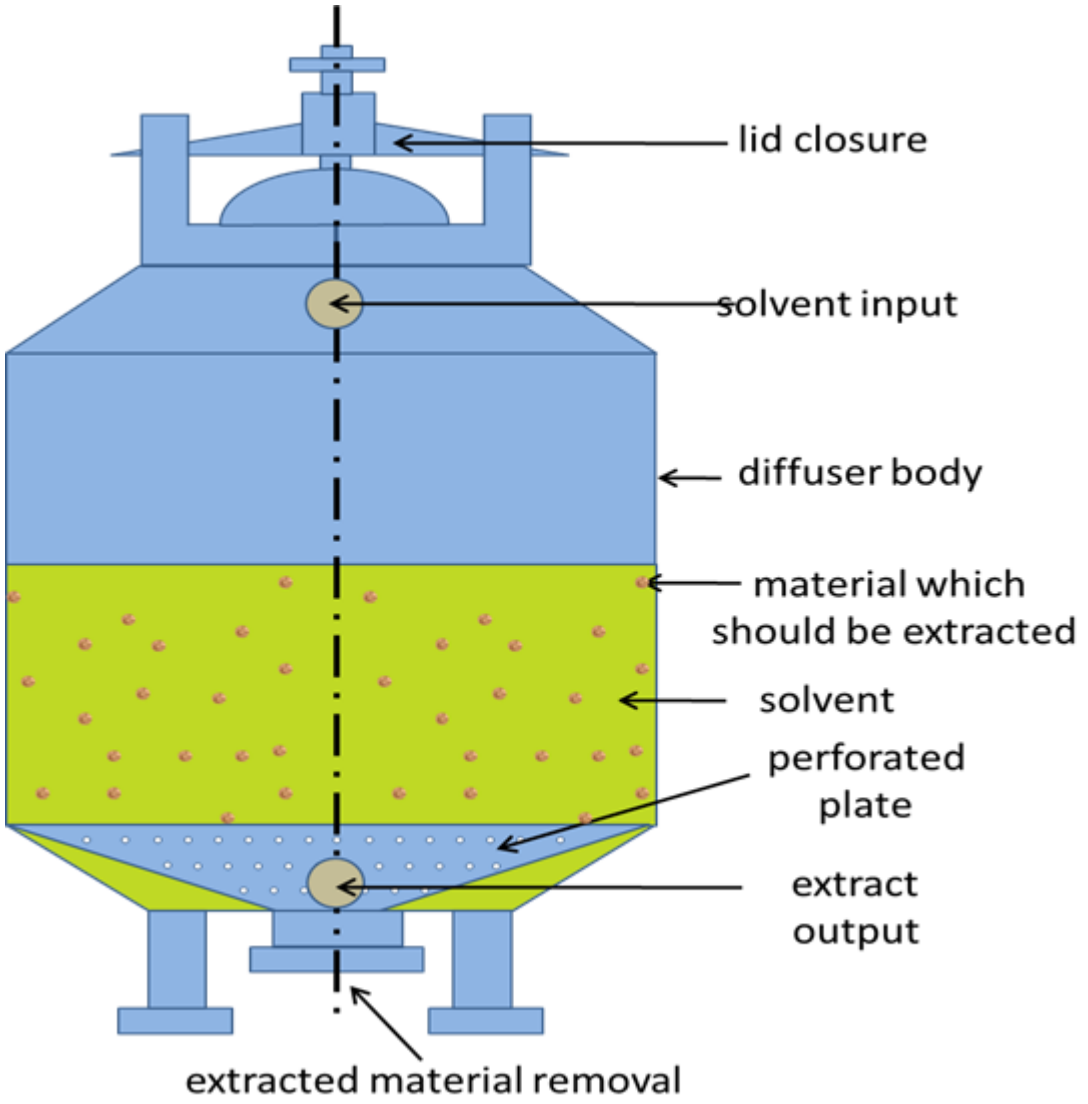
- recirculating solvent several times
- high concentration difference
- discontinuous
- 15-20 hours



B. **Flow through** method: **Diffuser**

Discontinuous

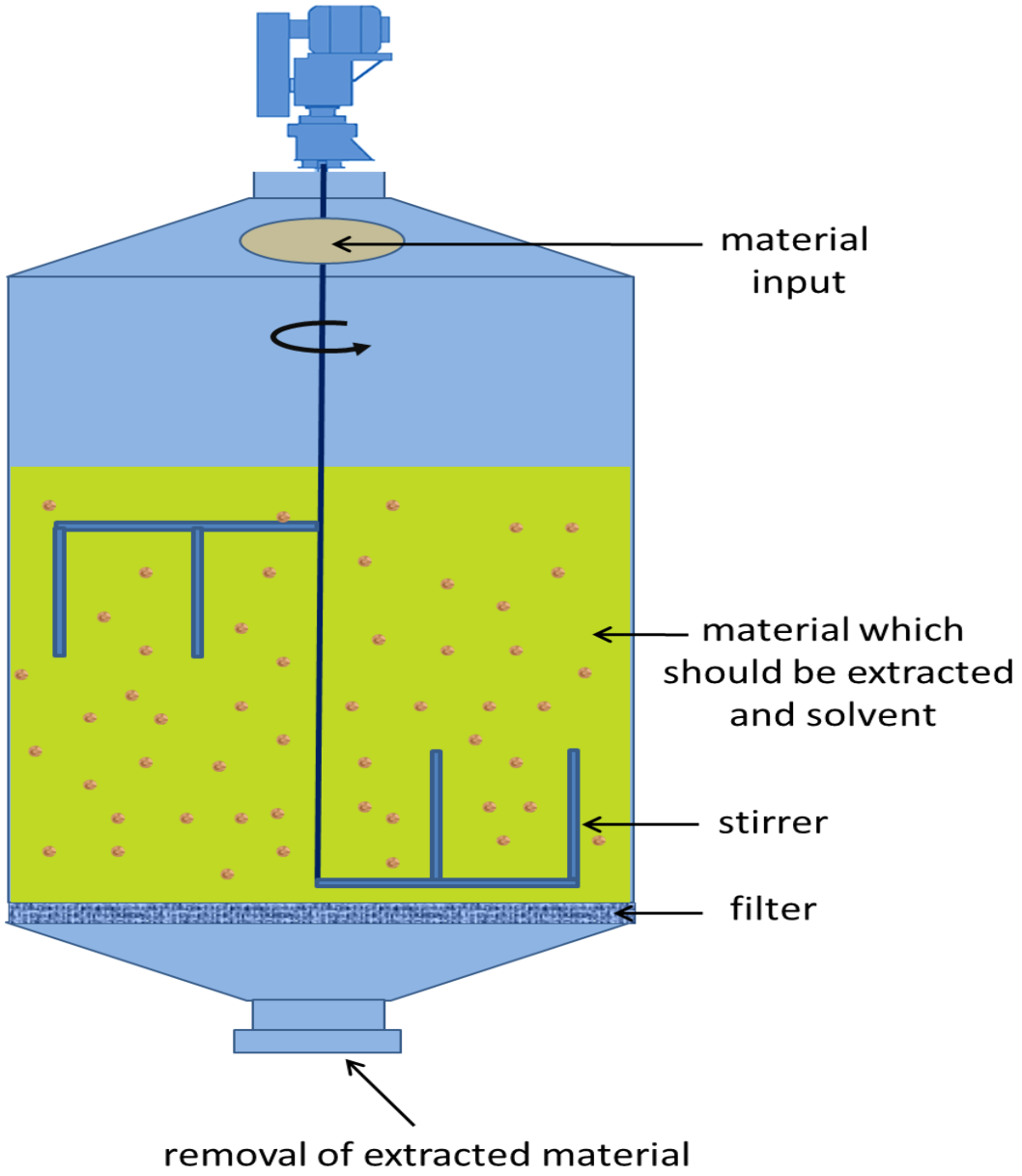
Industrial device



B. **Flow trough** method: **Mixer-settler extractor**

discontinuous

mixed



C. Turboextraction

- Stirring with ***high rpm*** (8000-13000 rpm),
- ***Temperature*** of extractant is ***increasing*** (heat-sensitive APIs),
- ***5-10 min = 6 days maceration*** (API-content of the extract),
- Because particle size of the herbal drug is very small due to grinding, extract can be separated from the grinded herbal drug only with ***vaccum filtration.***

D. Vibroextraction

- **Vibration** used by **ultrasound** can increase the permeability of the cell's wall and so the diffusion speed as well.
- Extraction is supported by **ultrasound**
- **Higher efficacy** (**30 min = 8 days maceration)**

NOTE!

APIs that are sensitive for hydrolysis and oxidation, can be broken down during the process!

E. Counter-flow extractor

- Herbal drug and extractant move in **opposite** direction.
- Concentration gradient can be found between cell solution and the extractant during the whole process, thus extraction has **higher efficacy.**

Extractors:

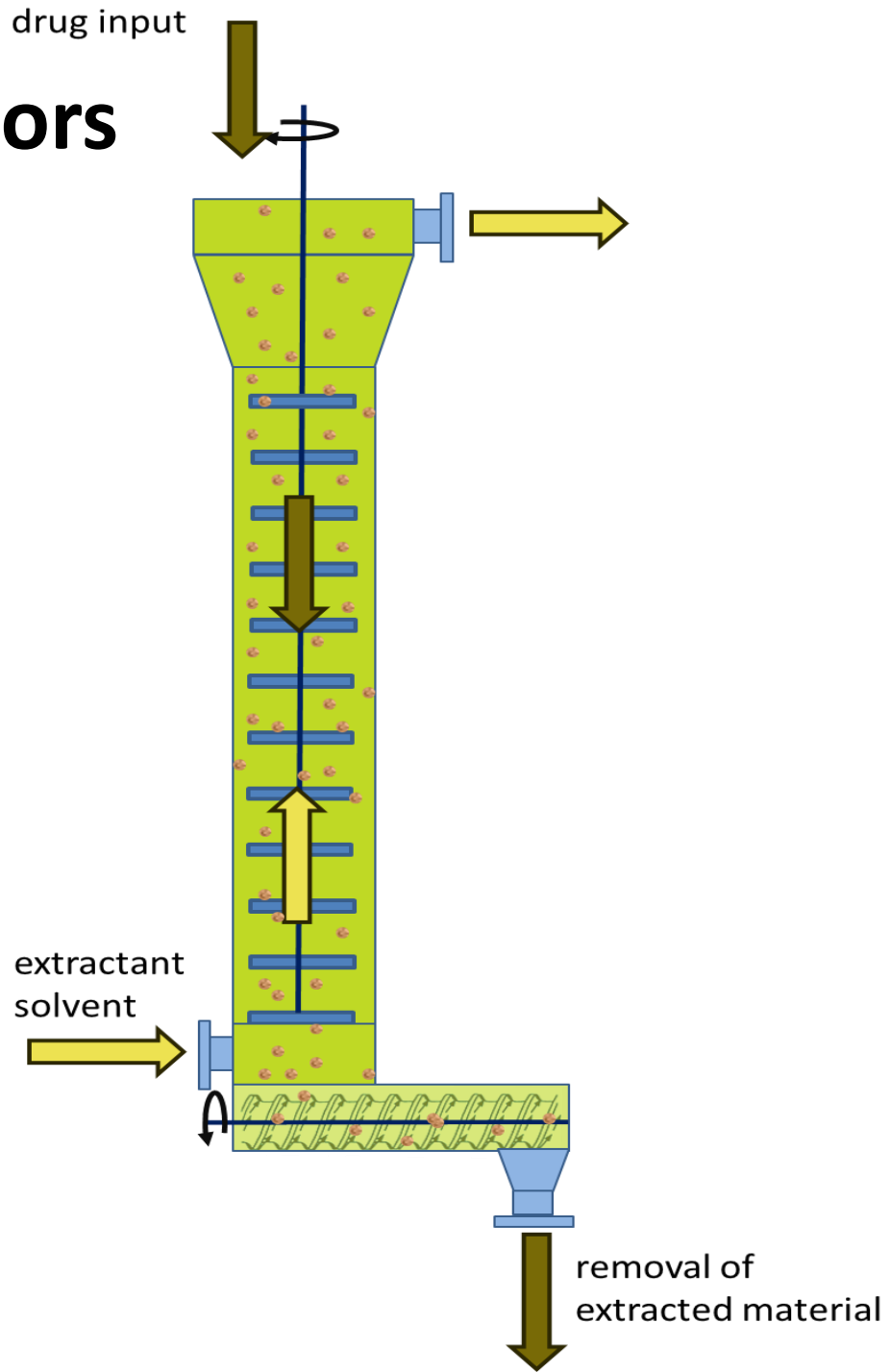
- Bonotto extractor
- Bollmann extractor
- Hildebrandt extractor
- U-extractor

E. Counter-flow extractors

Bonotto extractor

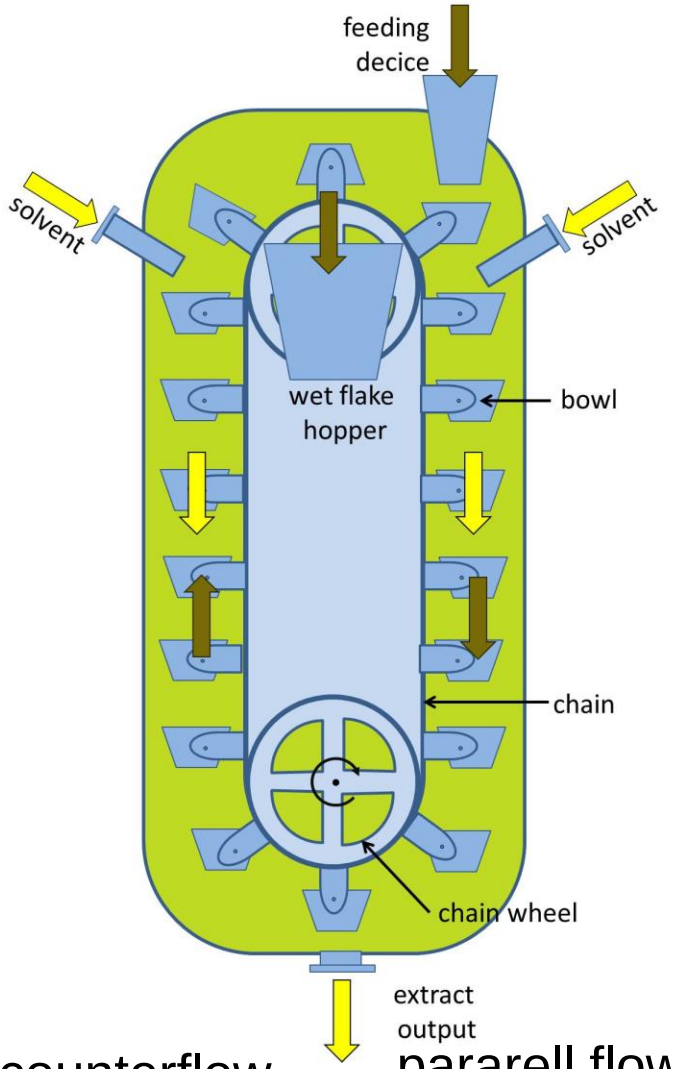
Continuous

Screw system

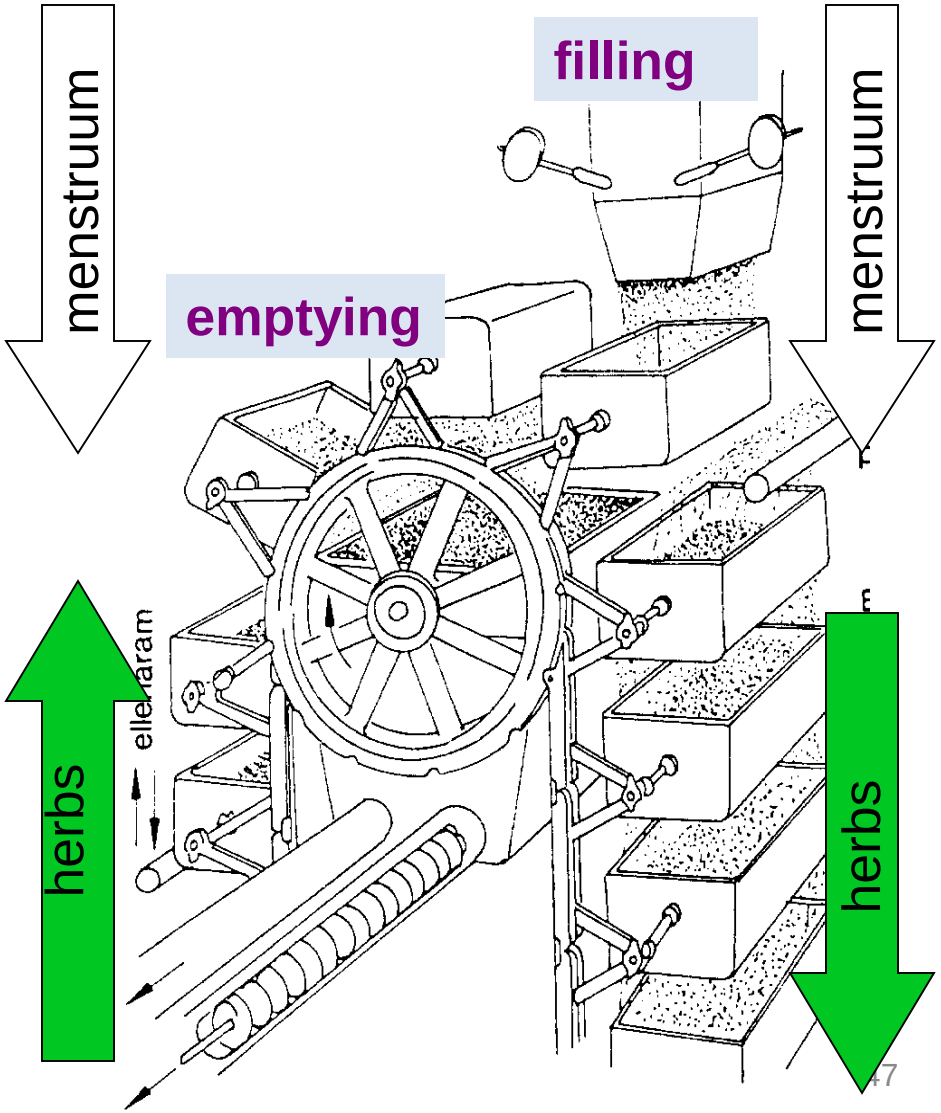


E. Counter-flow extractors

Bollmann extractor



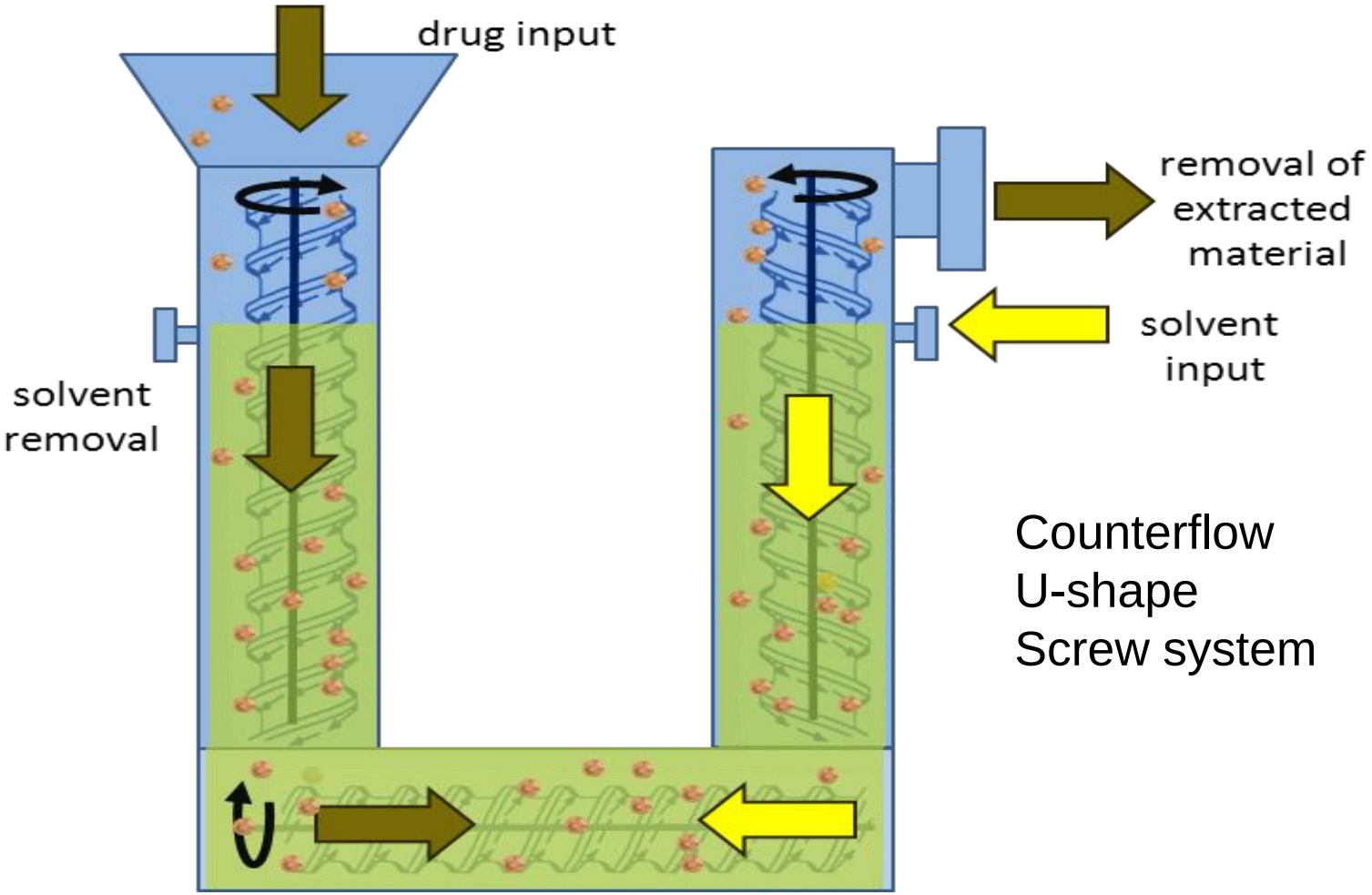
counterflow



pararell flow

E. Counter-flow extractors

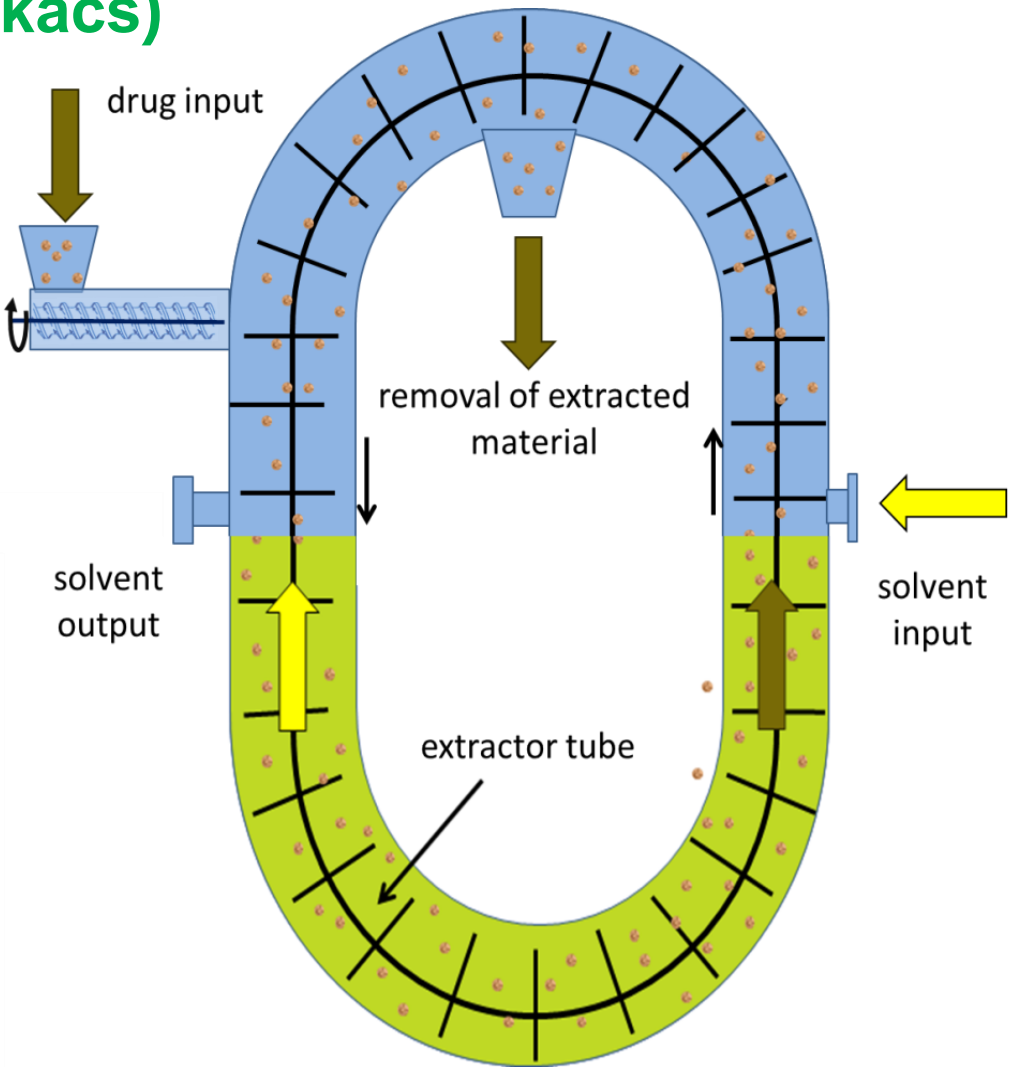
Hildebrandt extractor



Counterflow
U-shape
Screw system

E. Counter-flow extractors

U - extractor (Szász-Takács)



counterflow

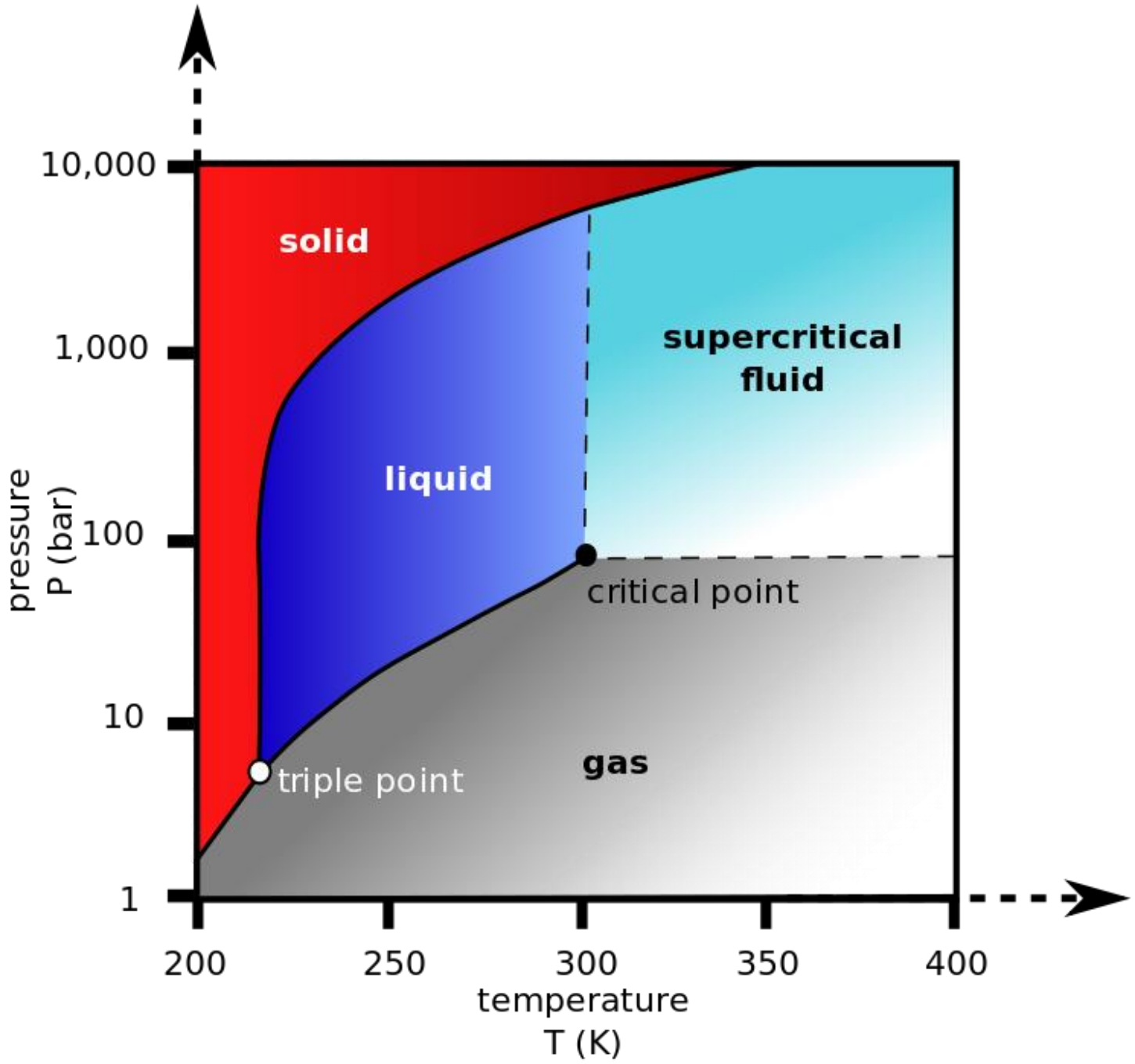
Highest efficacy

3. Supercritical Fluid Extraction

In the viewpoint of selectivity it is important that most of applied **gases** (carbon dioxide, methane, ethane, nitrous oxide, etc.) **have apolar property**, but composition of extractant can be modified by **adding cosolvents** (e.g. water, methanol, ethanol, acetone, hexane or other organic solvents).

Carbon dioxide can be used for extraction from herbs, since its critical temperature is **low**, thereby is especially able to extract biologically active, heat sensitive compounds.

- not harmless,
- not polluting,
- no reaction with treated material,
- not flammable and corrosive,
- leaves without any rest/remainder from preparation.


10,000
1,000
100
10
1
pressure
P (bar)
solid
liquid
supercritical
fluid
critical point
triple point
gas
200
250
300
350
400
temperature
T (K)

BASIC OPERATIONS

Extrusion

Extrusion

Extrusion is mostly used for the separation of **solid** and **liquid** phases in preparing galenics (e.g. tinctures) from herbal drugs.
In this sense extrusion means the **separation of cell-fluids and cells lysated through crushing by the application of pressure**.

The ***efficacy of extrusion (φ)*** can be calculated from

- the weight ratio of the extruded liquid (m_{juice}) and
- the substance to be extruded (m_{charge}):

$$\varphi = \frac{m_{\text{juice}}}{m_{\text{charge}}} 100\ \%$$

Extrusion

Factors affecting the ***efficacy of extrusion*** are:

- **liquid content** of substance to be extruded,
- **structure** of substance to be extruded,
- **amount** of applied pressure,
- **rate of pressure rise,**
- **duration** of applied pressure.

Extrusion

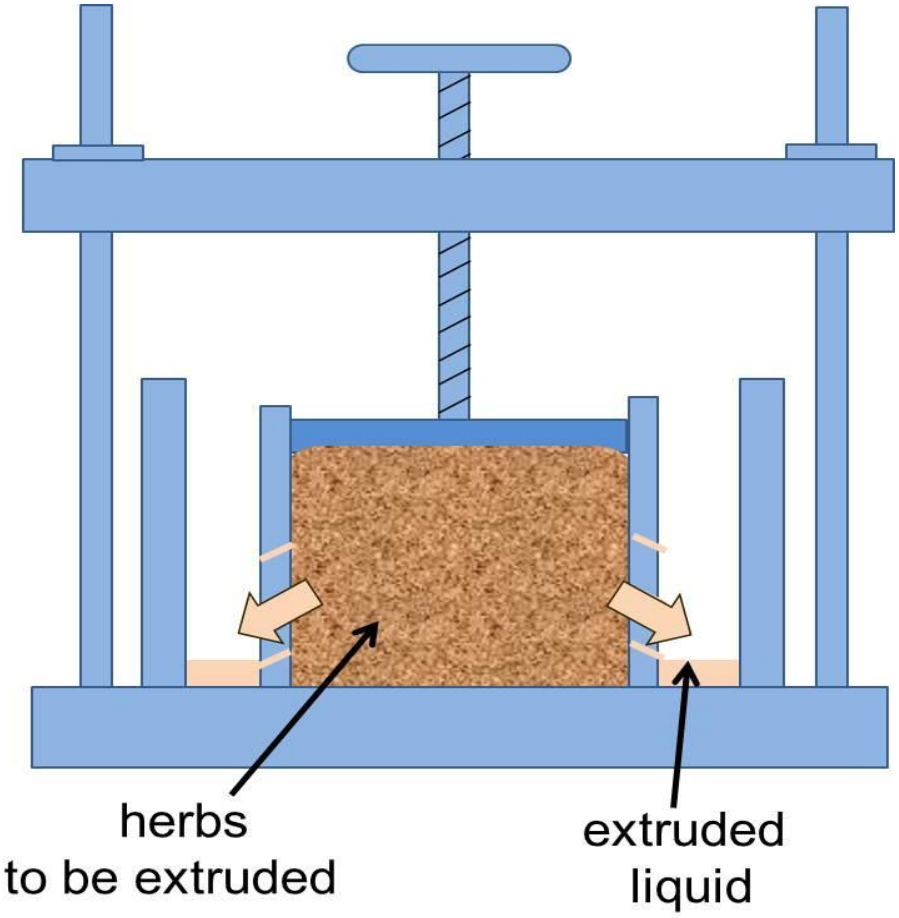
Distinguishing by the source of pressure, there are **manual** (for smaller amount) **and machine powered** (industrial-scale) extruders:

1) mechanical,
2) hydraulic (oil) ,
3) pneumatic (compressed air).

Extrusion

Basket type extruder

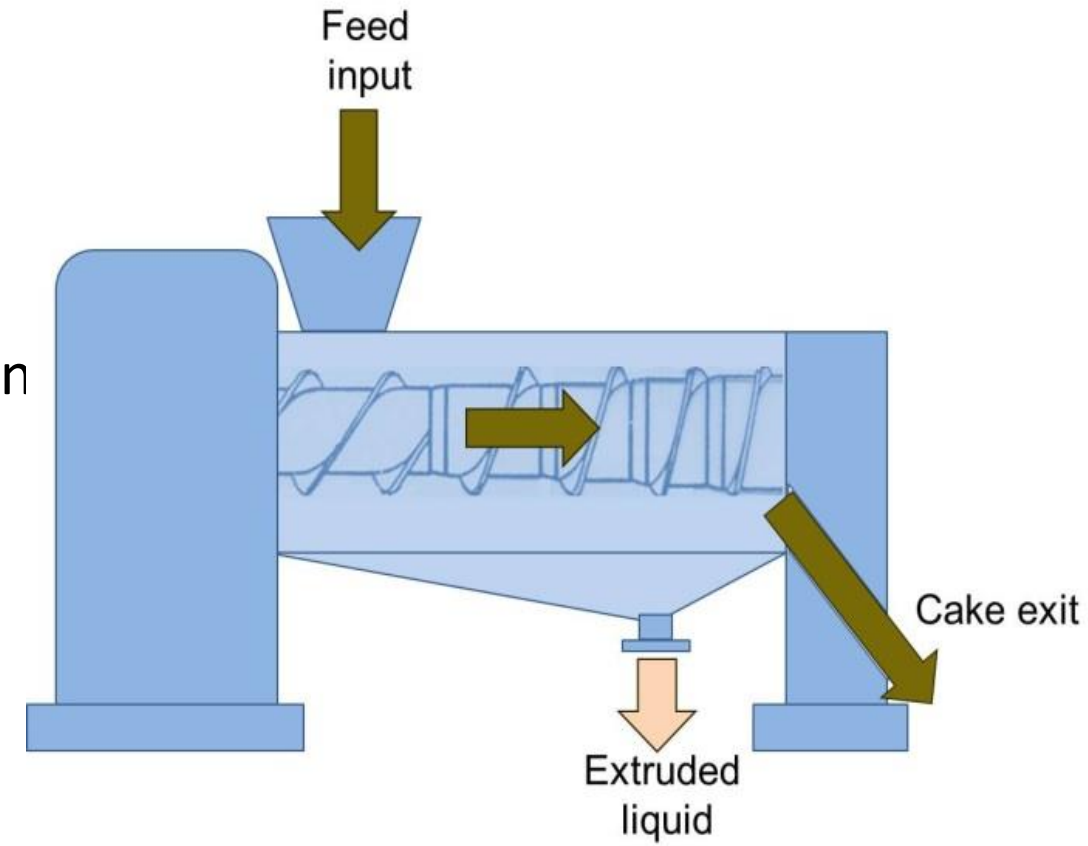
Manually powered
Screw extruder



Extrusion

Screw extruder

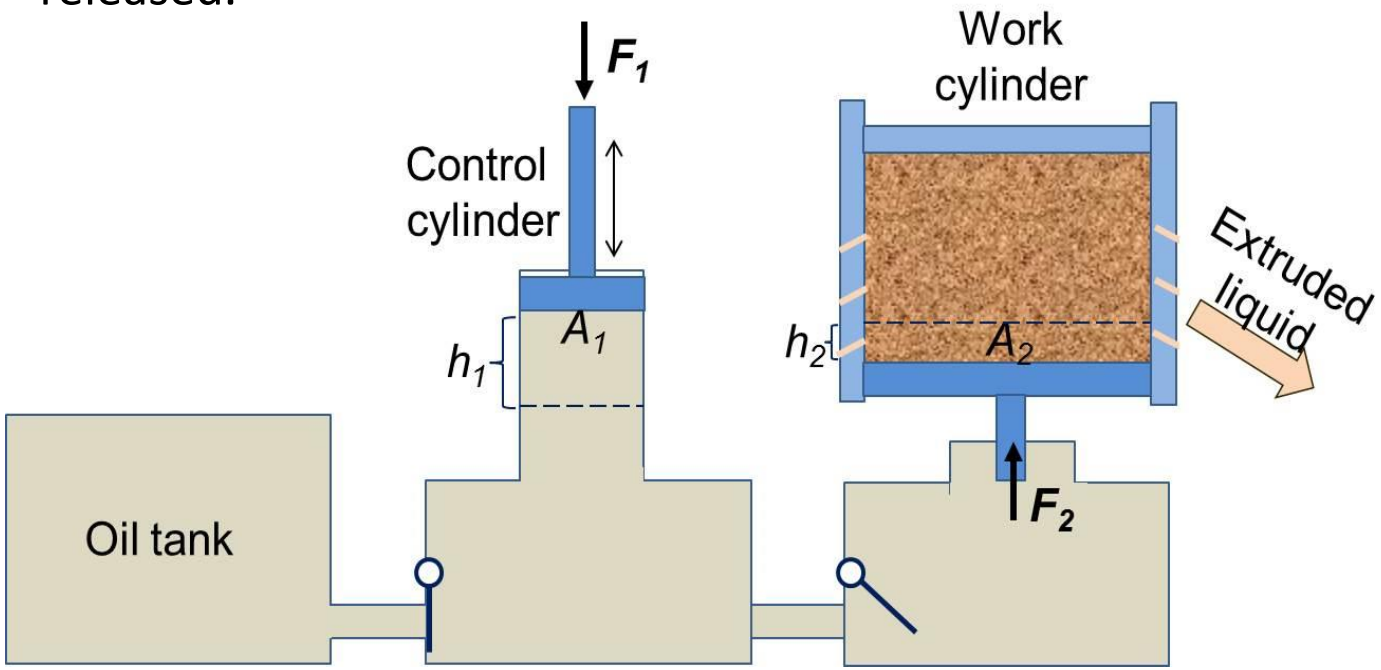
Continuous operation
Machine powered
Adjustable speed of rotation



Extrusion

Bramah press

Hydraulic pressure is exerted to the material from which the moisture is released.



The application of hydraulic extrusion will not save work, but it yealds higher force with less motion (Pascal's law)

$$F_2 = F_1 \frac{h_1}{h_2}$$

Thank you
for your attention!