Solvents, solutions, syrups, flavour corrigents, elixirs, mixtures

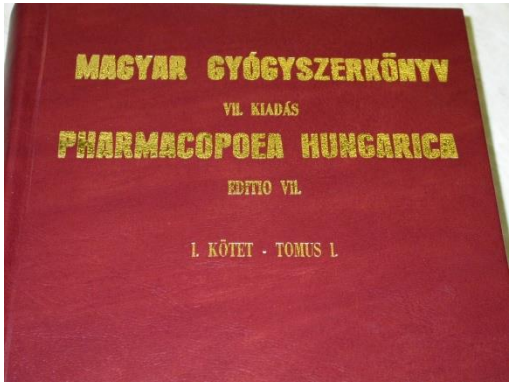
Institute of Pharmaceutical Technology and Biopharmacy

Dissolution/solvation

- is a procedure in which solid, liquid or gaseous compounds are dispersed in molecular- or colloidal-size with solvent(s).

- If the dissolved compound's size is less than 1 nm, it is a molecular solution.
- If the dissolved compound's size is between 1-500 nm, it is a colloidal solution.

Solution(s)

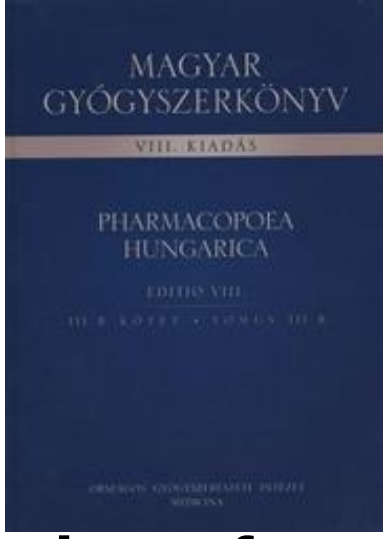


Ph. Hg. VII. :

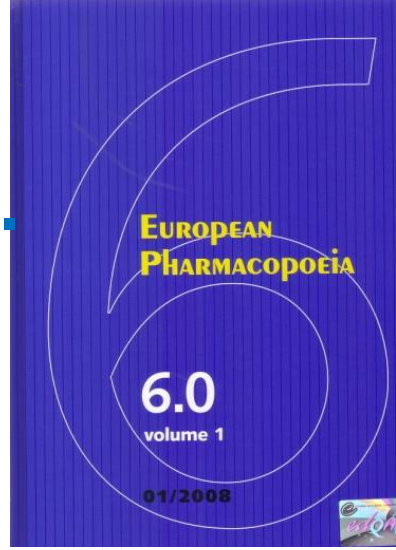
- „Solutions are clear liquids, free of sediment, prepared by dissolving of APIs in appropriate solvents applicable both for internal or external use.”

- homogeneous disperse system

Ph.Hg.VIII.



Ph.Eur.6-8.



- Solutions:

Liquid preparations for oral use
/Praeparationes liquidae peroraliae

Liquid preparations for cutaneous application
/Praeparationes liquidae ad usum dermicum

i.e.:Solutions for irrigation
Gargles
Mouth washes
Oromucosal solutions
Rectal solutions

Solutions

Composition: API(s) + solvent(s)

Type of solutions according to the substances:

- simple (one substance is dissolved)
- complex (more substances are dissolved)

Type of solutions according to the application:

- external or internal use

Concentration:

- Amount of a measured substance is expressed in percent by weight (%m/m)
- Concentration of the alcohol is expressed in percent by volume (%V/V) at 20°C
- Special cases (API/solvent):
  - injection: mg/ml
  - infusion: mmol/ml

Solubility. In statements of solubility in the section headed Characters, the terms used have the following significance referred to a temperature between 15 °C and 25 °C.

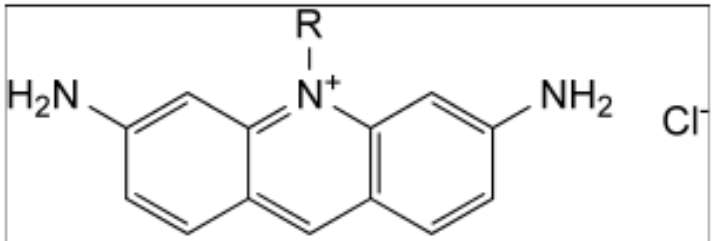
Descriptive term	Approximate volume of solvent in millilitres per gram of solute			
Very soluble	less than	1		
Freely soluble	from	1	to	10
Soluble	from	10	to	30
Sparingly soluble	from	30	to	100
Slightly soluble	from	100	to	1000
Very slightly soluble	from	1000	to	10 000
Practically insoluble	more than			10 000

The term "partly soluble" is used to describe a mixture where only some of the components dissolve. The term "miscible" is used to describe a liquid that is miscible in all proportions with the stated solvent.

Ph. Eur.

ACRIFLAVINIUM MONOCHLORIDE

Acriflavinii monochloridum



R	Mol. Formula	M_r
H	$C_{13}H_{12}ClN_3$	245.7
CH_3	$C_{14}H_{14}ClN_3$	259.7

DEFINITION

Mixture of 3,6-diamino-10-methylacridinium chloride and 3,6-diaminoacridine hydrochloride.

Content: 95.0 per cent to 105.0 per cent (anhydrous substance).

CHARACTERS

Appearance: reddish-brown powder, hygroscopic.

Solubility: freely soluble in water, sparingly soluble in alcohol, very slightly soluble in methylene chloride.

Solvents (Ph.Eur.)

- Aqua …… - different types
- Ethanolum (96 per centum)

  (Alcoholum 96%, Alcoholum 70%)
- Glycerolum (85 per centum)

  (Glycerinum)
- Propylenglycolum
- Macrogola (type 400)

  (Macrogolum 400)
- Paraffinum liquidum
- Triglycerida saturata media

  (Oleum neutrale)
- Helianthi annui oleum raffinatum

  (Oleum helianthi)

Aqua - water

- ***Aqua ad injectabilia – water for injections***
  - Made from tapwater/purified water by destillation
  - *It is sterilized*
  - It is used for parenteral preparations

- ***Aqua valde purificata – highly purified water***
  - Used fo preparations with high microbiological criteria, when ‘water for injection’ is not necessary

Aqua - water

- ***Aqua purificata – purified water***
  - Most common preparations
  - Making by: distillation
    ion exchanging,
    reverse osmosis

- ***Aqua ad dilutionem solutionium concentratarum ad haemodialysim***
  - Water used to dilute the concentrated hemodialysing solutions.

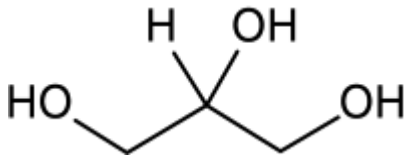
Ethanolum (*96 per centum) - ethanol*

CH_3-CH_2-OH

- **Ph. Hg. VIII.**
  - **Ethanolum *(96 per centum)***
  - **Other name: Alcoholum 96%**
    - **93,1-94,6 %m/m, or 20°C: 95,5-96,5 %V/V**
  - Alcoholum dilutum 70% Ph.Hg.VII.
    - 61,3-63,5 %m/m, or 20°C: 69,0-71,0 %V/V

Glycerolum (***85 per centum***)-glycerol

$C_3H_8O_3$



- trivalent alcohol
- 85,0-88,0 %m/m
- ***description***:
  - clear, transparent, syrupy liquid
  - odourless, sweet taste
  - hygroscopic
- ***storage***:
  - protected from light, well-closed container
- ***solubility***:
  - miscible with water and alcohol
  - insoluble in ether, chloroform, fatty oils

Propylenglycolum CH_3-CHOH-CH_2OH

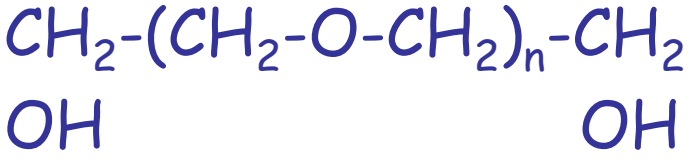
(propylene glycol)

- divalent alcohol
- ***description:***
  - clear, colourless, syrupy liquid
  - odourless, sweetish, causes warm feeling on the tongue
  - hygroscopic
- ***solubility:***
  - miscible with water, ethanol, glycerol, chloroform, acetone
  - miscible with ether
  - insoluble in petrol-ether, fatty oils

Macrogola (macrogols)

- Mixture of ***ethylen-oxyd-polimers***
- The physical characteristics depends on its molecular weight
  - between 200-600 – clear, colourless, viscousy liquid
  - above 1000 – tender/soft wax
  - between 4000-6000 – hard wax

- Ph.Hg.VII:
  - Macrogolum 400 n=7-9
  - Macrogolum 1540 n=28-36
  - Macrogolum 4000 n=68-84



Paraffinum liquidum

(Paraffin, liquid)

- Viscous mixture of saturated hydrocarbons (obtained from crude oil/mineral oil)
- Clear, colourless, tasteless, nearly odourless (mild odour)
- Non-miscible with water, alcohol, glycerol
- Miscible with ether, chloroform, oils
- *The liquid paraffin is an apolar solvent*

Triglycerida saturata media

Oleum neutrale Ph.Hg.VII.

- Mixture of the triglicerids of saturated fatty acids which carbon numbers are between 8-12.
- Description
  - colourless or pale yellow fluid, odoureless, tasteless
- density: 0,938-0,958 $g.cm^{-3}$
- apolar
- storage:
  - Well-closed container, protected from light, unlimited time
- solubility:
  - soluble in alcohol, ether, benzole
- Good solvent of volatile oils, steroids, vitamins

Helianthi annui oleum raffinatum –

Sunflower oil, refined

- The refined oil of the ripe seeds of sunflower, „Helianthus annuus” obtained by mechanical extrusion or by extraction
- Triglycerides of linol- and oleic acid
- Storage:
  - filled full to the brim
  - keep in dark and cool place.
- Becomes rancid:
  - at double bonds, peroxide radicals develop → typical odour and taste change
  - this reaction can be catalyzed by metals and light.

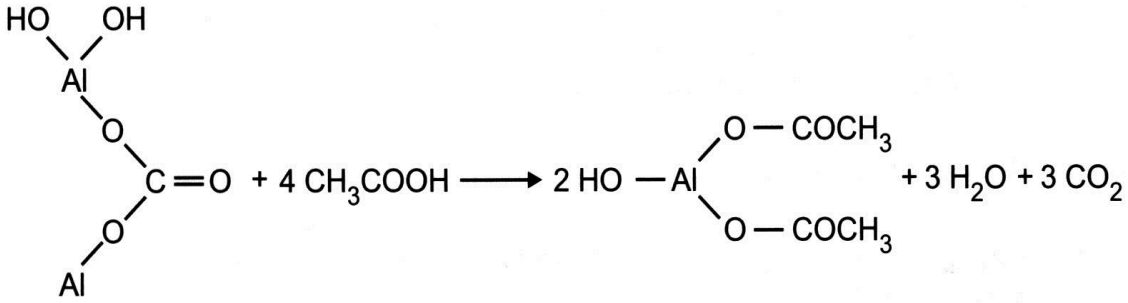
Three important galenicals used in Hungary

1. Aluminium aceticum tartaricum solutum Ph.Hg. VII.
2. Aqua calcis FoNo VII.
3. Solutio acidi borici 2% FoNo VII.

Aluminium aceticum tartaricum solutum (Ph.Hg.VII.)
Solution of aluminium-acetate-tartarate
(Burow solution) :

1. $Al_2(SO_4)_3*18\,H_2O + 3CaCO_3 \rightarrow Al_2(OH)_4CO_3 + 3\underline{CaSO_4}*2H_2O + 10H_2O + 2CO_2$

2.



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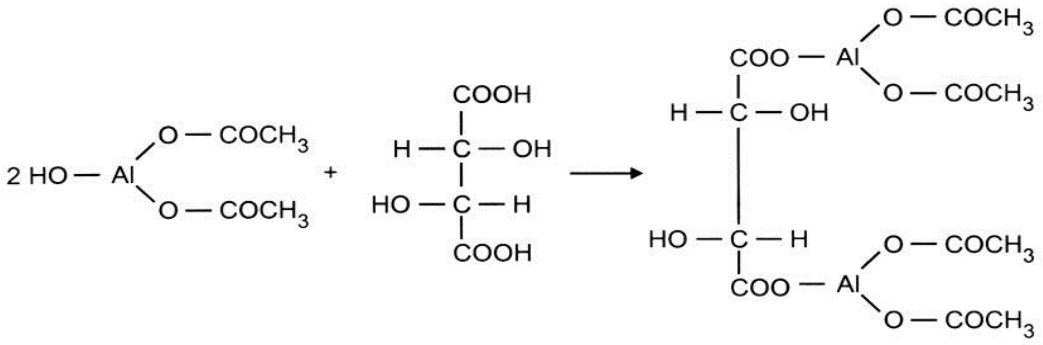


Aqua calcis (FoNo VII.)
Calcareous (chalky) water:

Characteristic: 0.13-0.17% $Ca(OH)_2$

colorless, odorless, alkaline taste, transparent liquid

Preparation: the quicklime (CaO) should be slaked slowly (step by step (Danger!!)

This results a white mass (hot!!!) containing: $Ca(OH)_2$ and $CaCO_3$.

This mass should be rinsed with suitable amount of water.

Shake well, then let the solid particles to be settled on the bottom of the bottle. It should be used by careful pouring out of the stock pot.

After depletion, it can be re-used by supplementing the sediment with the proper amount of water until the Ca level is above 0.13%

Solutio acidi borici 2% (2% boric acid solution) FoNo VII.

***Characters**:* colourless, odourless, tasteless, mild alkaline pH. It is miscible with water and alcohol.

***Preparation**:* the boric acid is dissolved in a 10% benzalkonium-chloride solution mixed with water applying gentle heating.

***Incompatibility**:* alkaline media

***Application**:* external use, mild antiseptic effect (because it absorbs vitamin-B_6).

Stock solutions

❖ **Application of stock solutions:**

a., active ingredients have better physical stability

(hygroscopicity: Zn-chloride, Ca-bromide, Na-bromide;

crumbling: Al-sulphate),

b., low solubility of substance

(phenylmercury borate)

c., substance is difficult to measure in small amount

(benzalkonium chloride, thiomersal, phenylmercuric borate),

Stock solutions

facts to remember

- They are not given directly to the patient
- They are basic preparations, which are used to make other pharmaceutical preparations.
- The most common stock solutions are listed between the galenicals (i.e.: FoNo VII.)

Concentration of stock solutions:

(50%, 33.3%, 10%, 0.1%) easy application

Nomenclature after the name of the active ingredient: ‘solutum’

FoNo VII.:

Benzalkonium chloratum solutum 10%,
Thiomersalum solutum 0.1%

- FoNo VI. :

Benzalkonium chloratum solutum 10%,
Calcium bromatum solutum 33.3%,
Natrium bromatum solutum 33.3%,
Phenylhydrargyrum boricum solutum 0.1%
Thiomersalum solutum 0.1%
Zincum chloratum solutum 50%.

Storage: maximally 1 year!!!

SYRUPS

Ph. Hg. VII.

Syrups are orally used concentrated solutions, (emulsions or suspensions) which are sweet containing sugars (sucrose, invert sugar, glucose, fructose) or hexits (mannitol, sorbitol).

Ph.Eur. 6

„Syrups are aqueos preparations chracterised by sweet taste and viscous consistency. They may contain sucrose at a concentration of at least 45 per cent m/m. The sweet taste can also be obtained by using other polyols or sweetening agents. Syrups usually contain aromatic or other flavouring agents. Each dose from a multidose container is administered by means of a device suitable for measuring the prescribed volume. The device is usually a spoon or a cup for volumes of 5 ml or multiples thereof.”

Labelling: „The label states the name and concentration of the polyol or sweetening agent.”

1., „dry” syrups

(ie.: syrups containing antibiotics)

2., water based solutions of sugars

(ie.: Sirupus simplex)

3., made from fruit juice

(ie.: Sirupus rubi idaei)

4., made by extracts from herbal drugs with sugar

(ie.: Sirupus aurantii)

5., medicinal syrups

(ie.: Sirupus laxans)

Steps of preparation of syrups

1. Sugars or hexits + solvents

↓

2. *Heating (carefully to avoid caramelization), dissolving*

↓

3. *Refining*

↓

4. *Filtration, preserving (conservation)*

Refining

- There are colloidal ballast materials in the sugar, which are precipitated during this procedure – this is the aim of the process

  Two methods:

  -short period of boiling
  (the resulting foam can be easily removed)

  -with adsorbents
  (kaolinum ponderosum, talc, MgO).

- after refining the syrups they sometimes should be left to sediment

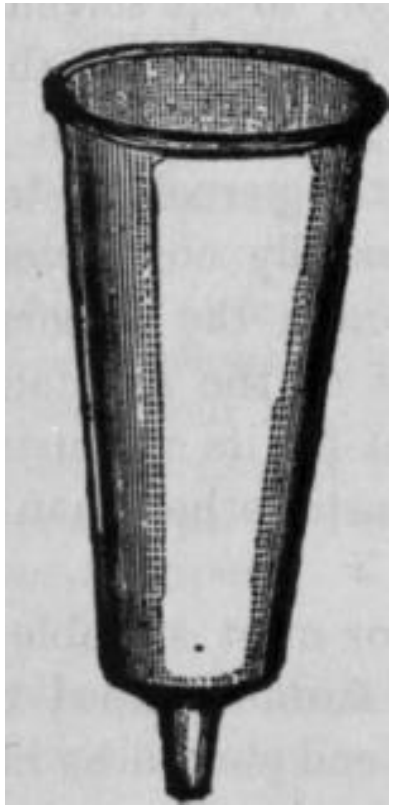
- **the evaporated liquid during the process has to be suppplemented before filtration.**

Filtration

sintered-glass filter G2 and G3

Preparation of syrups without heating

- sugar sieved using nominal dimension of aperture: 2,00 mm is filled into a percolator



- the solvent is added to this system, and the sugar is percolated repeatedly with it until the product will be transparent.

- advantage: development of inverted sugar is avoided

Microbiological stability

❑ the concentrated sugar solutions have dehydrating effect to micro-organisms, thus they have antimicrobial effect

❑ However the syrup will be used in diluted form, so the addition of antimicrobial preservative is necessary.

• benzoic acid and sodium salt, sorbic acid and potassium salt, (0.1% concentration)

•methyl p-hydroxybenzoate (in Solutio conservans Ph. HG. VII.)

•mixture of methyl p-hydroxybenzoate and propyl p-hydroxybenzoate (0,10 -0,15%)

❑ **condensing water** at room temperature may be disadvantageous regarding to the stability! (keep the syrups up to the brim and shake before use)

Application of flavours:

- correction of bitter tastes is the most difficult task in the therapy (bitterness of 1 molecule of quinine-chloride can only be corrected with 3300 molecules of sugar)

- (The cacao-syrup was one of the best choice to the correct bitter tastes, but it was deleted by official institutes because of the reproducibility of the flavour)

- nowadays, we use: syrup of liquorice root (Liquiritiae rhizoma et rhadix)

- to correct bitter-metalic taste: anise, raspberry, lemon or blackcurrant are the most useful.

Important requirements:

1. appropriate taste correcting ability,

2. microbial stability,

3. chemical stability.

Taste correcting ability of fruit syrups

- The worst: Sirupus simplex,

  The best: Sirupus fragariae (strawberry syrup)

- the flavour quality must be authorized by

National Public Healt Center – National Institute for Food and Nutrition Science /OKK-OÉTI /

Other flavours:

- honey (mel),
- honey with cocoa (mel-cocoa),
- caramel syrup,
- aspartame
- saccharimidum natricum / Saccharin sodium:

  they are synthesized sweetener,

  1 tablet equals 5 g sugar
- diluendum, aromatic waters (will be mentioned later)

„Taste masking” agents:

They are not sweet, but they can cover the receptors of taste buds to decrease the intensity of the unpleasant tastes.

Their taste masking effect is increasing with the viscosity until it achieves a limit.

Syrup preparations in Hungary

Sirupus simplex (Simple syrup) Ph.Hg.VII.

Saccharosum, Acid.sorbic., Aqua destill.

Sirupus aurantii (Orange syrup) Ph.Hg. VII.

Tinct.aurantii pro sirupo, Saccharosum, Aqua destillata

Sirupus liquiritiae (Liquorice syrup) Ph.Hg.VII.

Extr.liquiritiae fluidum, Sir.simplex., Sol.conserv.

Sirupus rubi idaei (Raspberry syrup) FoNoVII.

Vinum rubi idaei, Saccharosum, Aqua destill.

Sirupus sorbitoli (Sorbitol syrup) FoNo VII.

Sorbitum, Sol-conserv., Aqua destill.

Sirupus fragariae (Strawberry syrup)

Sirupus ribis rubri (Currant syrup)

Pharmaceutical syrups

Sirupus laxans (Laxative syrup) (Ph. Hg. VII. – FoNoVII., FoNoVet III.)

Sennae folium, Foeniculi fructus

Natrium sulfuricum

Saccharosum, Sol. conserv. Aqua destill.

Sirupus kalii chlorati (FoNo VII.)

Sirupus zinci (FoNo VII.)

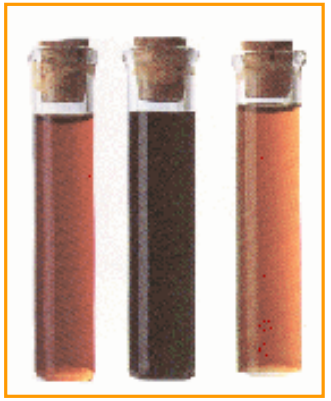
ELIXIRS, MIXTURES

Elixirs are solutions, (emulsions or suspensions) containing high concentration of sugar and ethanol and salts for oral use.

Elixirium thymi compositum (Ph.Hg.VII.)

Thyme-elixir

Tinctura aromatica
Tinctura thymi
Tinctura aurantii pro sirupo
Natrium bromatum solutum 33,33 %
Sirupus simplex



The word of elixir (arabic origin) means: „philosopher stone”

Mixtures are heterogenous disperse systems (usually made by tinctures dilution) containing particles near the colloidal range.

The suspended ingredients sediment slowly, because of the colloidal range.

Labelling:„Shake well before use!”

FoNo VII. **Mixtura antirheumatica**
+ Mixtura pectoralis
Mixtura solvens

ALCOHOLIC SOLUTIONS

- **Their solvents may be alcohol(s) or the mixture of alcohol(s) and water.**

  (If you see just „alcohol”, then we mean about this „ethanol 96%”.)

- **Nomenclature:**

  a., *Spiritus*..... *(*Spiritus salicylatus)

  b., with adjective *(Solutio iodi alcoholica)*

  c., no indication in the name (*Solutio conservans)*

Ph. Hg. VII

- Solutio conservans
- Solutio iodi alcoholica
- Spiritus camphoratus
- Spiritus anisatus

OILY SOLUTIONS

Oily solutions are used external or internal. Oils are used in the most cases to dissolve in them *menthol, camphor, volataile oils, vitamins, hormones.*

- Oleum borozinci
- Oleum jecoris
- Oleum pro inhalatione
- Oleum ricini
- Paraffinum aromaticum

Aromatic waters–
Aqua aromatica

Diluends-
Diluenda

Diluendum (plural: Diluenda) is a concentrated aromatic water

Preparation process:

- solubilization (Diluendum menthae)
- dilution of tincture

- Keep in weel-closed glass and protected it from light
- Storage time: max. 1 year

The aromatic waters can be prepared from diluends with dilution in range 1:10 or 1+9.

FoNo VII.

Diluendum benzaldehydi

Benzaldehydum
Alcoholum 96 %
Aqua destillata

Diluendum menthae

Aetheroleum menthae piperitae
Polysorbatum 20
Alcoholum 96 %
Aqua destillata

Aromatic waters are water or alcohol based solutions of essential oils and other aromatic substances, which are transparent or mild opalescent.

„Aromatic waters are clear, transparent or slightly opalescent aqueous or alcoholic liquids containing dissolved volatile (essential) oils or other aromatic substances. The taste and odour of aromatic waters is characteristic to the dissolved volatile oils or aromatic substances.”

- They may be solutions or emulsions (disperse system).

Decoction- DECOCTUM

Infusion- INFUSUM

FoNo VII.:

The decoctions (decocta) and

infusions (infusa) are obtained by water based extracts or water diluted tinctures of herbal drugs applying high temperature.

Ph. Hg. VII.:

Preparation process:

-dilution of tincture

-dissolution of dry-extracts that prepared with cryosiccation

Preparation process:

- the properly chopped herbal drugs are placed in a flask.
- the drugs should be wetted with the extraction fluid in a mortar.
  (the temperature of extraction fluid should not be too high, because it can cause coagulation of the proteins and colloidal substances. This process can delay the extraction.)
- the drug should be placed in a flask, then it should be placed in a „Schulek-steampot”.
- leave decoctions in the steam for 40 min, infusions for 20min
- the decoctions must be filtered at the end this procedure immediately but the infusions at room temperature.

Preparation process:

- other substances, that are prescribed to the preparation may be added to filtered and cooled extract.

- in case of herbal drugs with no strength- if nothing else is prescribed:
  100 g extract can be prepared from 3 g herbal drug

- Preparations made from dilution of tinctures can occur in two cases:

1 g ipecacuanha radix equal 10 g Ipecacuanha tincture

1 g „saponariae albae radix" equal 2 g „Tinctura saponariae"

Drops-guttae

Liquid preparations for oral use (praeparationes liquidae peroraliae):

Liquid preparations for cutaneous application (praeparationes liquidae ad usum dermicum)

- Oculogutta / otogutta / nasogutta

Ph. Eur. 6.0

Liquid preparations for oral use (praeparationes liquidae peroraliae):

„Oral drops are solutions, emulsions or suspensions that are administered in small volumes such as drops by the means of a suitable device.”

Labelling:

„The label states the number of drops per millilitre of preparation or per gram of preparation if the dose is measured in drops.”

Ph.Hg.VIII.

- **Standard drop:**

  a drop, that is measured with standard pipette.

- **Standard pipette:**

  A pipette compies with the following test:
  20 drops of water at 20±1 °C flowing freely from the pipette held in the vertical position at a constant rate of 1 drop per second weighs 1000±50 mg.

- **Drop number:**

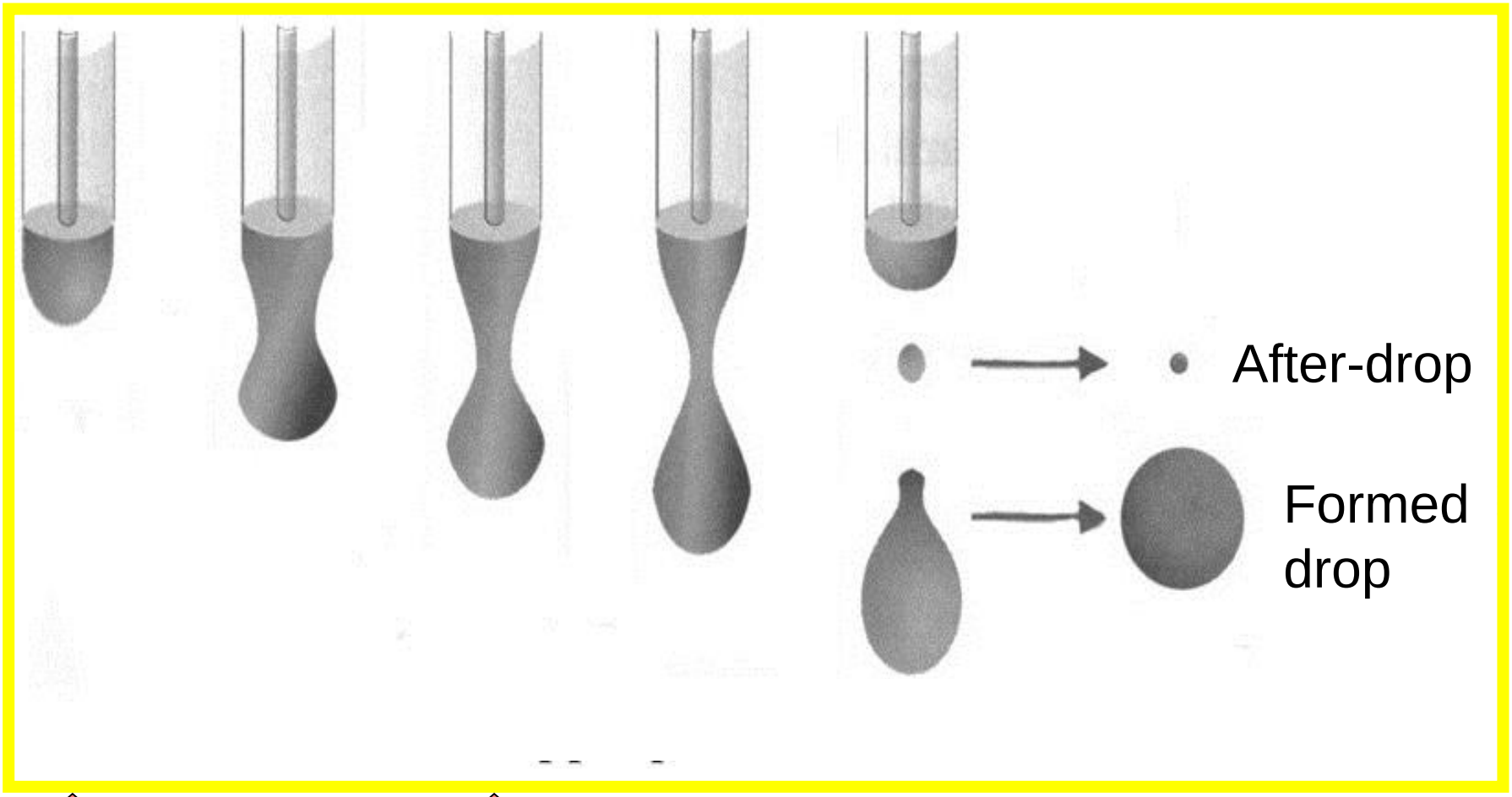
  The number of standard drops of 1 g liquid (tables: Ph.Hg.VII. IV.volume, Table I, or FoNo VI.)

  The medical FoNo gives the drop number of the preparations by their prescription (monograph).

The weight of drops depends on:

- viscosity of the liquid
- surface tension
- adhesion
- properties of the droper's surface
  (matter, size, shape, position, statement of fat-free)
- temperature
- dropping speed
- surrounding medium

Forming of a drop



Dispensing of drops

if made in the pharmacy:

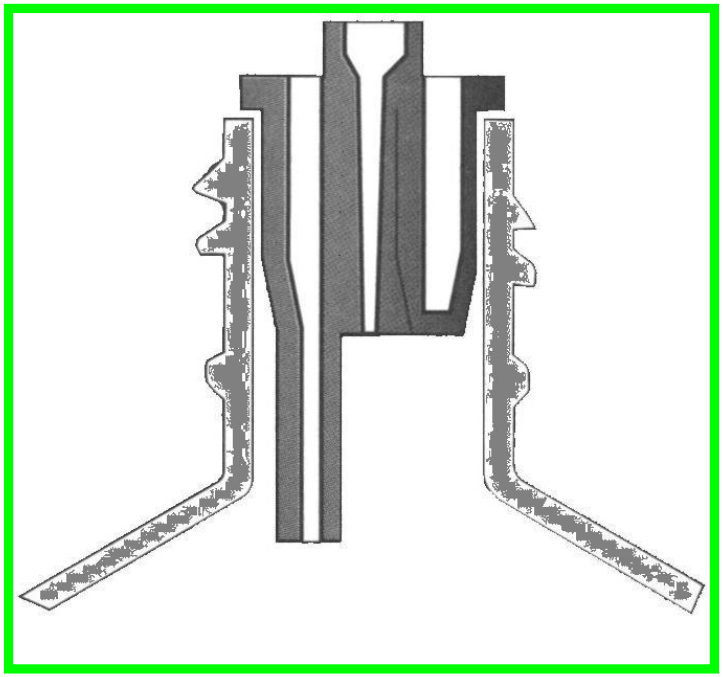
- with glass pipette, 3 mm inner hole, or

- with pipette cap

Labelling:

„The label states the number of drops per millilitre of preparation or per gram of preparation if the dose is measured in drops.”

Dispensing of drops



By manufacturer's preparations integral dropper is applied (central dropper adapter).

In the central position:
pipette
On the left side:
pressure compensator tube (aeration tube)

High efficacy: 60 drops/min

COLLOID DISPERSE SYSTEMS

MUCILAGE

THE COLLOID SOLUTION

is a disperse system, where the linear extent of the dispersed phase is between 1-500nm.

MUCILAGES (colloid disperse system):

SOLUBILITY OF MACROMOLECULES:

❖The difference in dissolution process against the small molecules is called: ***swelling***. During the process the molecule structure changes, it looses a part of their intermolecular bounds without separation. If more solvent is added to the system, they separate from each other and they will be dissolved in the solvent like colloid sized particles.

❖The properties of dissolved macromolecules can influence the solution's rheological (e.g.: fluidity, viscosity…) character.

❖The ***shearing stress*** is an applied force, which can result in the demolition of the reticular structure of macromolecules. This force can produce linear macromolecular structure. The viscosity of the system is decreasing: this is ***pseudoplastic*** property.

MUCILAGES:

STABILITY OF MACROMOLECULES:

- dehydration can cause the ***flocculation*** of the mucilages (electrolites, non-electrolites –poliols: sorbitol, mannitol, sucrose, glycerol or alcohols)

- The pH-value can also produce depolimerisation of macromolecules that leads to the decrease of viscosity.

MUCILAGES:

Application of mucilages:

a. *Increase viscosity:* clysma, emulsion, suspension, eye drops, nasal drops

b. *Ointment base materials* (in high concentration): hydrogels

c. *Binders:* granules, tablets

d. *Electrode gels: by* ECG, by EEG

e. Application during *ultrasound examinations*

CLASSIFICATION OF MACROMOLECULES:

1. According to their charge the macromolecule may be

- cationic

(polielectrolytes with amino groups)

- anionic

(polielectrolytes with carboxy groups)

- amphoter

(amino and carboxylic groups)

- non-ionic

2. According to their origin:

- natural: starch, tragacanth , pectin,
gelatine, acacia, agar

- semisynthetic : cellulose derivatives

- synthetic : polyvinyl-pyrrolidone, polyvinyl- alcohol

Ph.Hg. VII:

Mucilago methylcellulosi

Appearance: colourless or yellowish, transparent or opalescent, viscuous liquid

Mucilago hydroxyaethylcellulosi

Appearance: colourless or mild yellowish, transparent, viscuous liquid, it contains 3% of hydroxyethylcellulose

FoNo VII:

Solvens viscosa

Solvens viscosa pro oculoguttis

Mucilago ad catheterem

Enema
(CLYSMA, MICROCLYSMA)

The clysma (enema) is a liquid preparation administered rectally.

- The clysma can also be applied with pressure. Applying „high” pressure it can achive the colon.

- According to the volume of the liquid:

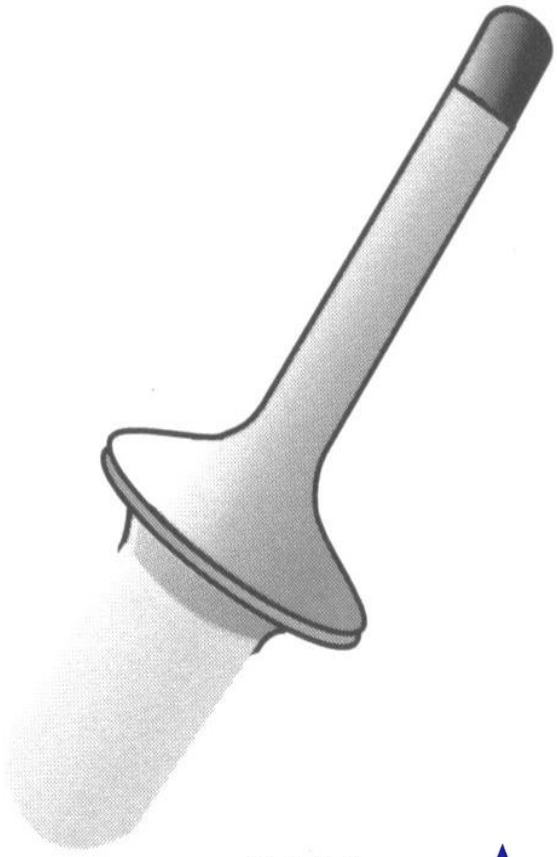
macroclysma (50-1000 ml)

microclysma (2-10 ml).

Purpose of application of clysma:

- purifying ~
- nutrition ~
- medical ~

The rectal and per oral doses of active ingredient are equal.



Rektiola

The main excipient of clysmas are mucilages:

- increase the viscosity of preparation,
- coat the rectal lumen in a thin layer decreasing the irritation of the mucosa.
- assist the connection between the active ingredient and the rectal mucosa

The most commonly used substances:

Gelatine, dextrane, polyvidone, cellulose-derivatives

Ph. Eur. 6

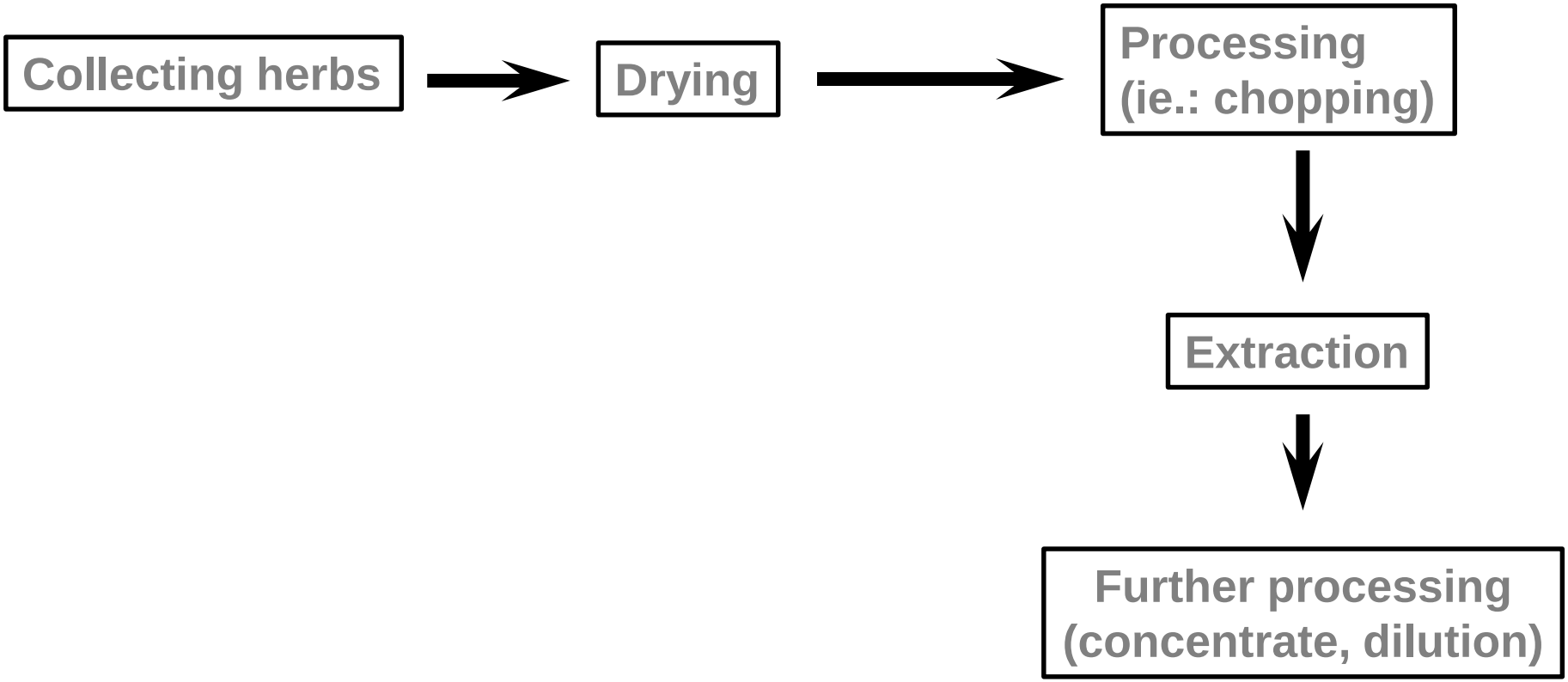
Extracts - EXTRACTA

„Extracts are preparations of liquid (liquid extracts and tinctures), semi-solid (soft extracts) or solid (dry extracts) consistency, obtained from herbal drugs or animal matter, which are usually in a dry state.”

Types: liquid (liquid extracts and tinctures)
semi-solid (soft extracts)
solid (dry extracts)

- „Standardised extracts”: are adjusted within an acceptable tolerance to a content of constituents with known therapeutic activity, standardisation is achieved by blending batches of extras.”
- „Quantified extracts”: are adjusted to a defined range of constituents, adjustment are made by blending batches of extracts.”
- „Other extracts”: are essentially defined by their production process (state of herbal drug or animal matter to be extracted, solvent, extraction conditions) and their specifications.

What happens to herbal and animal drugs?



Ph. Eur. 6

Extracts - EXTRACTA

Preparation process can be carried out with:

- ethanol or other suitable solvent,
- maceration,
- percolation
- or other validated method.

Unwanted matter may be removed after extraction.

Protected from light

Types of extracts

- **Extracta fluida (liquid extracts)**
  - „Liquid extracts are liquid preparations 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.”
- These preparations are adjusted according their solvent content (or API content)

Liquid extracts may be filtered, if necessary.

- A slight sediment may form during storage, which is acceptable as long as the composition of the liquid extract is not changed significantly.
- Labelling: the ethanol content in percent %V/V in the final extract.

Types of extracts

- **Extracta spissa (soft extracts)**
- „Soft extracts are semi-solid preparations obtained by evaporation or partial evaporation of the solvent used for extraction.”

- The dry matter content at least 70%.

Types of extracts

- **Extracta sicca (dry extracts)**
- „Dry extracts are solid preparations obtained by evaporation of solvent used for their production.”
- Dry extracts have water content of maximally 5 %m/m.
- The dry matter content (with excipints, other substances and vehicles) at least 95%.
- Storage: airtight container (and protected from light)

The extraction is a diffusion type procedure, where the required substances are extracted with a suitable solvent from the properly dried and grinded herbal drug or animal matter.

Most important active ingredients:

alcaloids, essential oils, saponins, steroids, and bitter substances, tannin, flavonoids, vitamins, glycosides, etc.

Other substances:

carbohydrates (starches, sugars, pectin), proteins, mucilage, waxes, resins, fats, enzymes, pigments.

The purpose of such basic extraction procedures for crude drugs are to obtain the therapeutical portion and eliminate the inert material with an appropriate solvent known as *Menstruum*.

Fick's law of diffusion:

$$\frac{dn}{dt} = -qD\frac{dc}{dx}$$

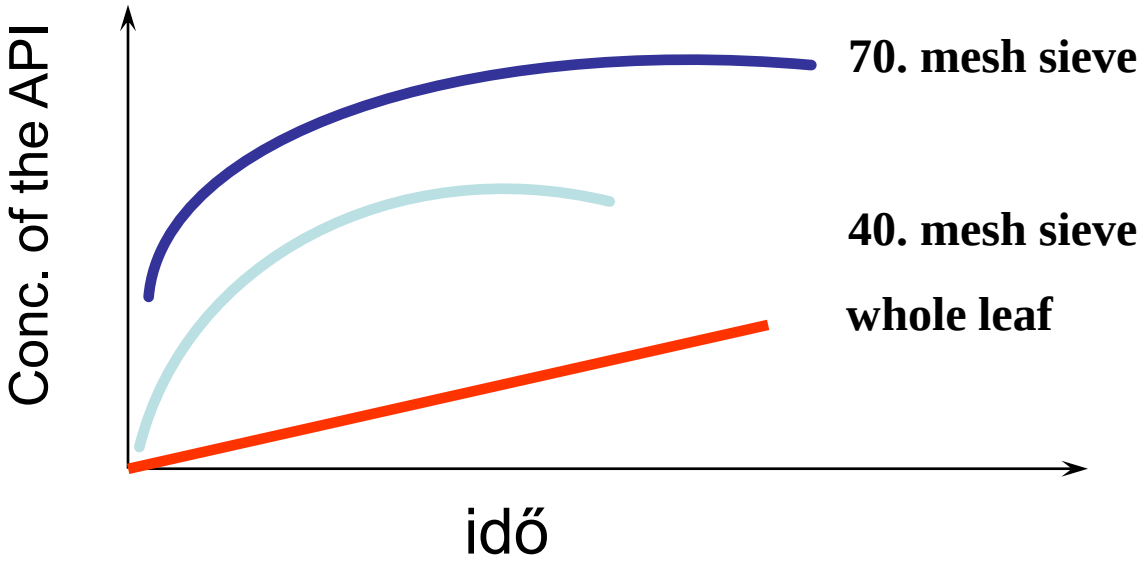
$$M = D \cdot F \cdot t \cdot \frac{C_2 - C_1}{l}$$

M	mass
D	diffusion contant
F	area
t	time
C_2-C_1	concentration difference
l	thickness of the diffusion layer

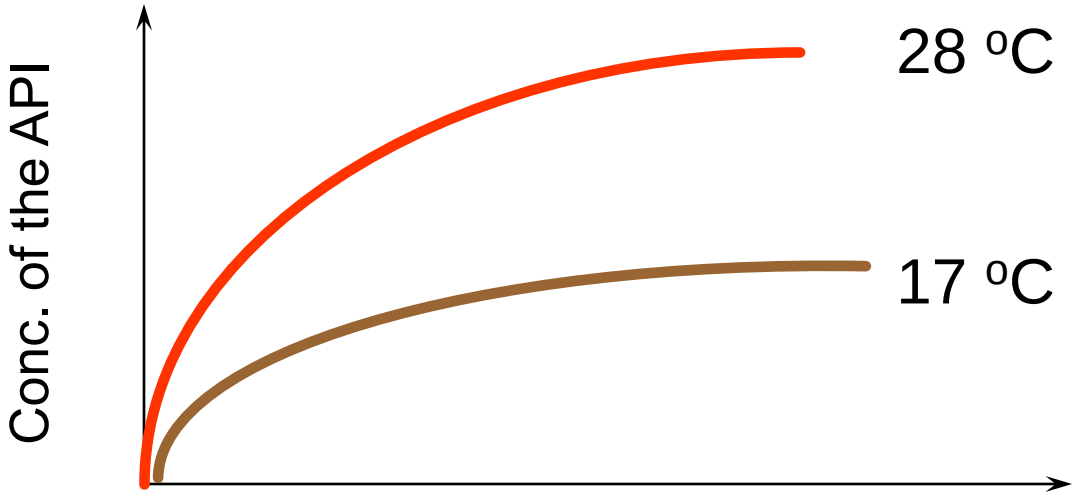
Factors:

- surface
- concentration gradient
- temperature
- moisture of the herbal drug or animal matter
- solvent
- pH
- viscosity
- surfactants

Factors affecting extraction



chopping



temperature

Processes of manufacturing herbal drugs

1. ***Extraction***
2. ***Compression***
3. ***Sedimentation***
4. ***Evaporation***

Processes of extraction:

I. maceration
II. turbo-exraction
III. flow-trough extraction
IV. counter-flow extraction

I. Double maceration

•**Repeated maceration may be more efficient than a single maceration, since an appreciable amount of active ingredient may be** left behind in the herbal or animal matter.

•**multi-step operation**
•**the extraction process can be accelerated with stirring**

- Efficacy of the **single maceration:65-70%**
- Efficacy of the double **maceration:80-90%**

Advantage:

- easy
- reproductibility

Disadvantage:

- time
- substance loss (retained by drug)

Maceration may be applied:

- water soluble, but heat-sensitive material (active ingredient or sovent is volatile),
- we need just the cold extractable components (Althaeae folium),
- preliminary operation (step)

The efficiency of the maceration

$$W = \frac{a(M - x)}{a(M - x) + 1}$$

W: maceration %

M : amount of solvent
(in ratio of the amount of drug)

a : constant

x: the absorbed solvent by drug
(in ratio of the amount of drug)

II. Turbo-extraction

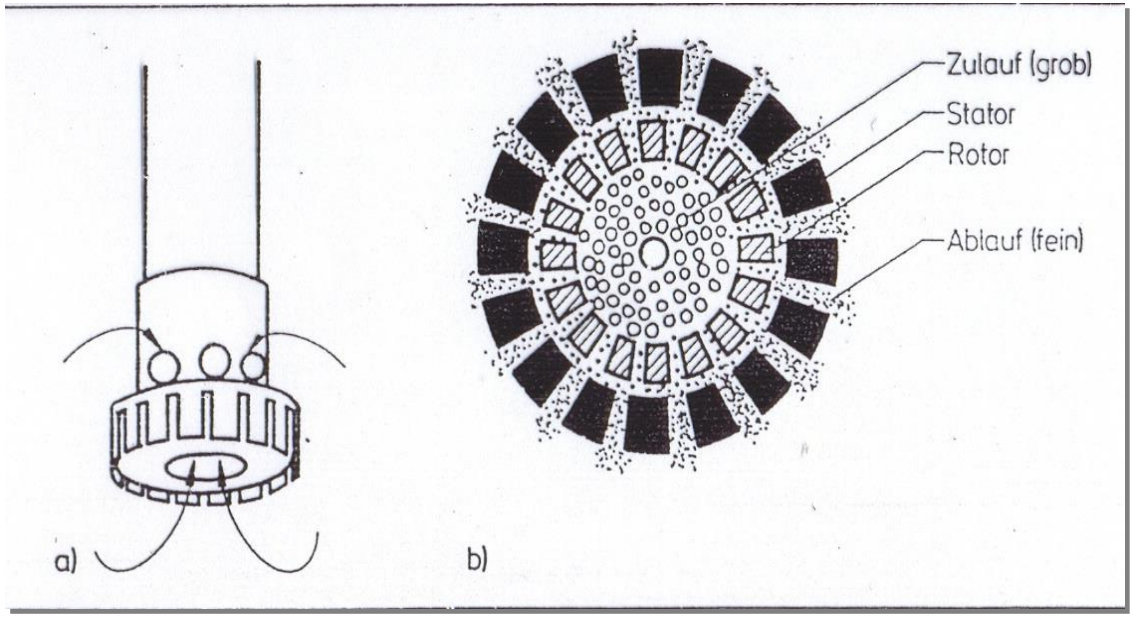
Steps of the procedure:

- start the solvent filled high-speed (rpm) mixer (stirrer)
- add the herbal or animal matter to the solvent (menstruum)
- stir it for 5-10 min.
- **The amount of the extracted active ingredient equals to a 6-day maceration.**
- **Two type of equipments:**

  a., equipment with *chopper blades*

  b., equipment with *stator and rotor*

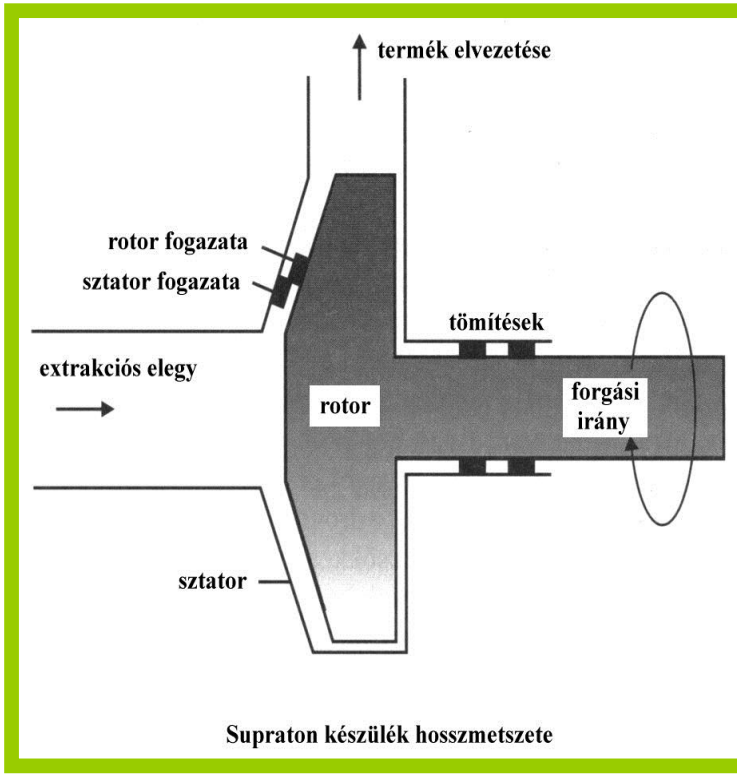
a., Equipment with chopper blades



b., Equipment with stator and rotor

- **Particles pass into the narrow gap between the stator and the rotor. The procedure is occurring by the collision of the particles between the stator and rotor.**

- **This process can cause an increase of the kinetic energy which leads to small particles and the heating of the solvent.**



Vibro-extraction:

- **with ultrasound**
- **the ultrasound causes vibration in the system that accelerates the diffusion and increases the permeability of the cell memranes.**
- **It is a very effective method.**
- **A 30 minutes vibro-extraction process equals with 8-day maceration.**

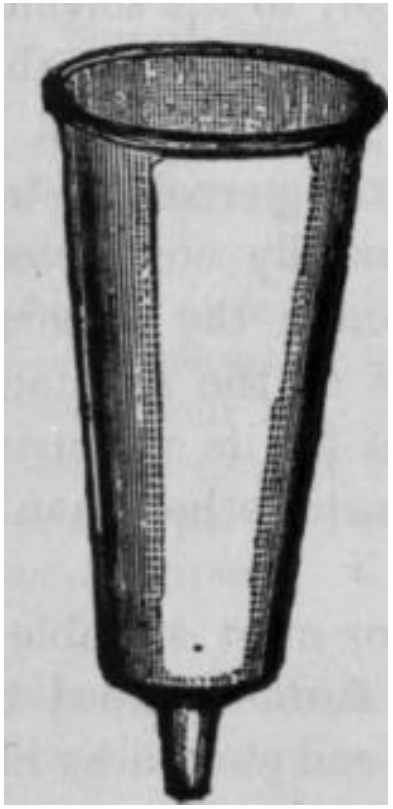
- **Warning!**

Avoid heavy metal contamination

Degradation of hydrolysis and oxidation sensitive drugs

III. A Flow-through extraction

1. Percolation:

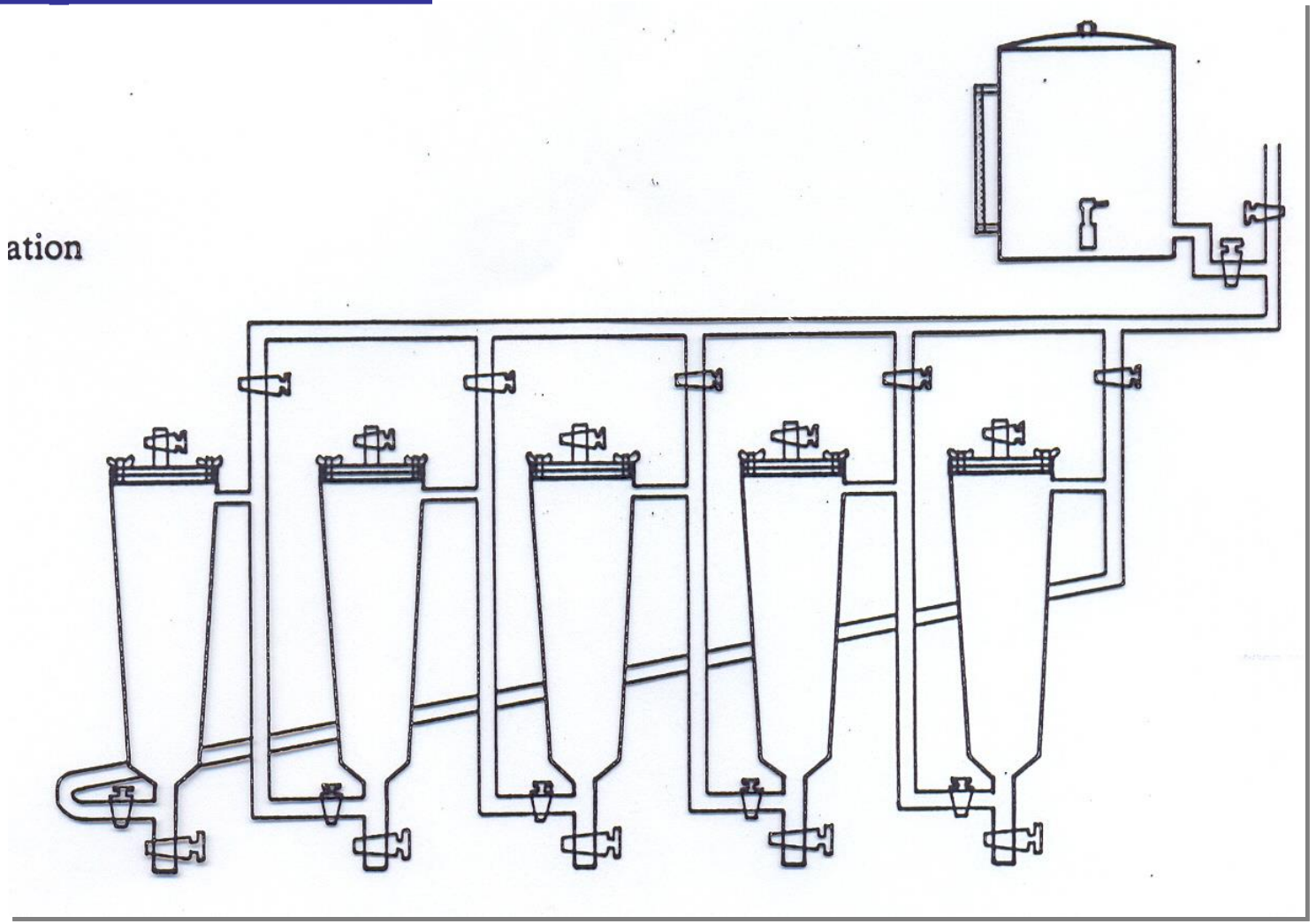


This is an extraction process, which occurs in an appropriate extraction equipment – percolator.

The solvent (menstruum) is added to a cylinder containing the powdered matter.

The menstruum percolates (infiltrates) through the matter and dissolves its components that are removed from the bottom of the container.

Re-percolation:



Perforator:

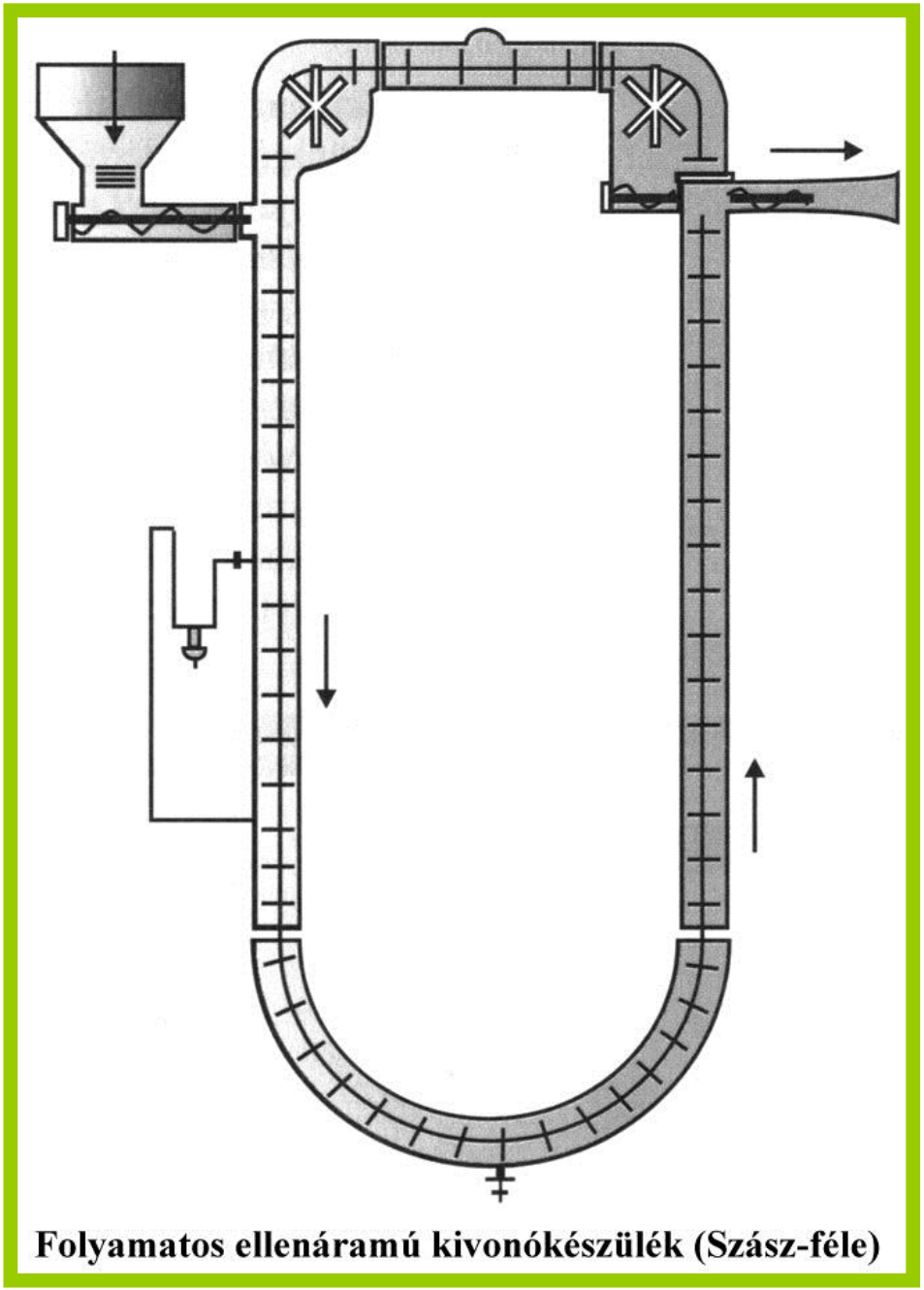
- flow-trough extraction **with 100% efficacy**
- **low amount of menstruum**
- **the solvent of the extract can be evaporated and using the purified menstruum can be performed in another extraction after first extaction(this circulation can be made until it is needed)**
- continuous extraction procedure

IV. counter-flow extraction

- opposite direction of the movement of the the drug and the menstruum occurs
- the concentration gradient between the cells and the mentruum is constant.

- equipments:

-U- shaped extractor.

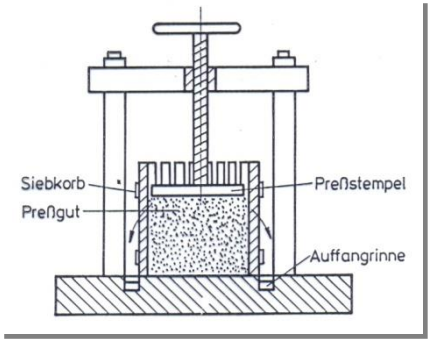


Folyamatos ellenáramú kivonókészülék (Szász-féle)

1. ***Extraction***

2. ***Compression:***

Extracted herbal or animal matter should be compressed. In order to do this step, extracted matter should be placed in a pressing machine in an appropriate filter from textile material.



3. ***Sedimentation***

4. ***Evaporation***

Aim: to reach an appropriate consistency

In vacuum evaporation apparatus evaporation temperature should not exceed 55°C
The temperature is in correlation with the evaporation time
Important if the extract contains easily volatile or thermosensitive constituents.

the required amount of previously dried lactose:

$$x = \frac{97 \cdot A}{a} - T \ ,$$

Where: **x = amount of diluent (g),**

A = amount of evaporatable active ingredient (g)

a = the required amount of active ingredient of the product (%),

T = the dry matter in the whole extract fluid (g).

Storage:

- well closed container, protected from light,
- at room temperature (fluid and dry extract) or
- cool place (semi-liquid extract),
- preserve dry extracts over a moisture adsorbing material.

TINCTURES

Ph.Eur.6.0 **Tincturae**

„Tinctures are liquid preparations that are usually obtained using either 1 part of herbal drug or animal matter and 10 parts of extraction solvent, or 1 part of herbal drug or animal matter and 5 parts of extraction solvent.”

Ph. Hg. VII.: Tinctures are liquid extractions that are usually obtained using either alcohol or aether as extraction solvent to prepare a product with characteristic odour, colour and taste.

Preparation and tests of tinctures

- Store the herbal drug or animal matter over a moisture absorbing material (for a few days)
- maceration (1:5)
- percolation (1:10)
  - amount of the extraction solvent is prescribed
  - press the drug
  - join the different extracts (first, second portions)
  - sedimentation (~ for a few days), decantation, filtering
  - completing to the required mass (weight) with extraction solvent.

Storage

- protected from light
- dark place

- room temperature 15-25 ºC
- cold or cool 8 -15 ºC
- in refrigerator 2 - 8 ºC
- in a deep-freeze <- 15°C

- seperately odoured medications
  strong effect drugs and sedatives
- poison cabinet poisons, (narcotics, abused medications)

Storage

- Storage is approved by the national offices of pharmaceutical attendance (in Hungary: National Institute for Quality- and Organizational Development in Healthcare and Medicines)

- ***Galenical preparaitions:***
  - Ph.Hg.VII. max. 5 years
  - FoNo VII. 1 year

- ***FoNo VII. preparations max. 6 months***

Storage

- *Solutions are made in pharmacy:*
  - Preparations made according the FoNo VII.
    - extemporaneous
    - 3 mounths
    - 1 mounth
    - max. 6 mounths
  - See the guides of national offices

Solution or elixir?

Thank you for your attention!