evropský sociální fond v ČR
EVROPSKÁ UNIE
MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY
OP Vzdělávání pro konkurenceschopnost
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

PHYTOPHARMACEUTICALS

academic year 2018/19

LECTURE 2 – Application forms, mode of administration. Herbal tea preparations.

Dr. Ivana Daňková
Dept. of Natural Drugs, Faculty of Pharmacy, VFU Brno

Plant drugs – terminology

Pharmacopoeial names of plant organs:

- ***radix*** = root (e.g. Liquiritiae radix, liquorice)
- ***rhizoma*** = rhizome (e.g. Zingiberis rhizoma, ginger)
- ***cortex*** = bark (e.g. Salicis cortex, willow bark)
- ***lignum*** = wood (e.g. Juniperi lignum, Quassiae lignum)
- ***herba*** = whole aerial (above-ground) part of plant
  = stem + leaves + flowers (e.g. Thymi herba, thyme)
- ***folium*** = leaves (e.g. Sennae folium)
- ***flos*** = flowers, or inflorescences (e.g. Calendulae flos, marigold flower)
- ***fructus*** = fruit (e.g. Anisi fructus, aniseed)
- ***semen*** = seed (e.g. Lini semen)
- ***pericarpium*** (fructus sine semen) = pericarp (e.g. Aurantii pericarpium
  = orange fruit pericarp; Phaseoli fructus sine semen)

Plant drugs terminology

- binomial terminology – first part of a drug name is according the plant (usually name of plant genus or species), second part is according the plant organ
  - *Sambucus nigra* → Sambuci flos
  - *Salvia officinalis* → Salviae folium
  - *Mentha piperita* → Menthae piperitae folium
  - *Atropa belladonna* → Belladonnae radix
- exceptions:
  - one name → Aloe, Lycopodium
  - more names → Crataegi folium cum flore
  - name of drug is different from plant name →
    e.g. Liquiritiae radix (*Glycyrrhiza glabra*),
    Cynosbati fructus *(Rosa canina)*

Plant drugs terminology

- !! older terminology of plant drugs – the opposite order of names of plant drugs or galenical preparations (in older literature and pharmacopoeias, e.g.:
  - **Valerianae radix** (now) ↔ Radix valerianae (formerly)
  - **Salviae officinalis folium** (now) ↔ Folium salviae officinalis (formerly)
  - **Gentianae tinctura** (now) ↔ Tinctura gentianae (formerly)
  - **Althaeae sirupus** (now) ↔ Sirupus althaeae (formerly)

    BUT **Sirupus simplex**

Plant drugs terminology

- other terms:
  - ***Etheroleum, etherolea*** = essential oils (e.g. *Anisi etheroleum*)
  - ***Olea plantarum pinguia*** *(Olea herbaria)* = vegetable fatty oils (e.g. *Helianthi oleum*)
  - ***Mucilago*** = mucilage (e.g. *Acaciae mucilago*)
  - ***Oleoresinum, oleoresina*** = oleoresin (e.g. *Capsici oleoresina*)
  - **Balsamum** = balm (e.g. *Balsamum peruvianum*)
  - **Pix** = tar (e.g. *Pix lithantracis* = coal tar)
  - etc.
- names of galenical preparations
  - ***Extractum*** = extract
  - ***Tinctura*** = tincture (e.g. *Gentianae tinctura* x *Tinctura amara*)
  - ***Solutio*** = solution (e.g. *Lactulosi solutio*)
  - ***Sirupus*** = syrup (e.g. *Althaeae sirupus* x *Sirupus simplex*)
  - ***Spiritus*** = spirit (e.g. *Spiritus anisi compositus*)
  - ***Guttae*** = drops
  - ***Tabulettae*** = tablets
  - ***Capsulae*** = capsules
  - ***Unguentum*** = ointment

Plant drugs constituents

- Chemical constituents of plants:
  - **active principles** = effective constituents, the substances mainly responsible for the use of the drug
  - constituents that can influence the main constituents = *co-effective principles*
  - dietetically significant components
  - auxiliary components
  - concomitant components
  - ballast components

Biologically active secondary metabolites

The most important groups of active constituents:

- alkaloids
- flavonoids and relative compounds
- phenolics, polyphenolics
- saponins
- essential oils (terpenes or phenylpropanoids)
- anthraquinones
- tannins
- bitter principles
- polysaccharides, mucilage…

Alkaloids

- are highly biological active and highly toxic (depending on dose)
- !!! the most of alkaloid drugs **are not suitable** as phytopharmaceuticals due to their toxicity – alkaloid drugs are rather used for isolation of active compounds
- Examples of highly biologically active alkaloids:
  - morphine (*Papaver somniferum*) – analgesic
  - codeine (*Papaver somniferum*) – antitussive
  - papaverine (*Papaver somniferum*) – spasmolytic
  - quinine (*Cinchona* sp.) – antimalarial, analgesic
  - emetine (*Cephaelis ipecacuanha*) – emetic (vomiting)
  - atropine (*Atropa bella-donna*) – parasympatholytic, anticholinergic
  - etc.

ALKALOID DRUGS

Papaver somniferum, poppy plant
Papaveris fructus

codeine – antitussive

morphine – analgesic

papaverine – spasmolytic

Atropa belladonna, deadly nightshade
Belladonnae folium, B. radix

atropine, scopolamine
– anticholinergic agents

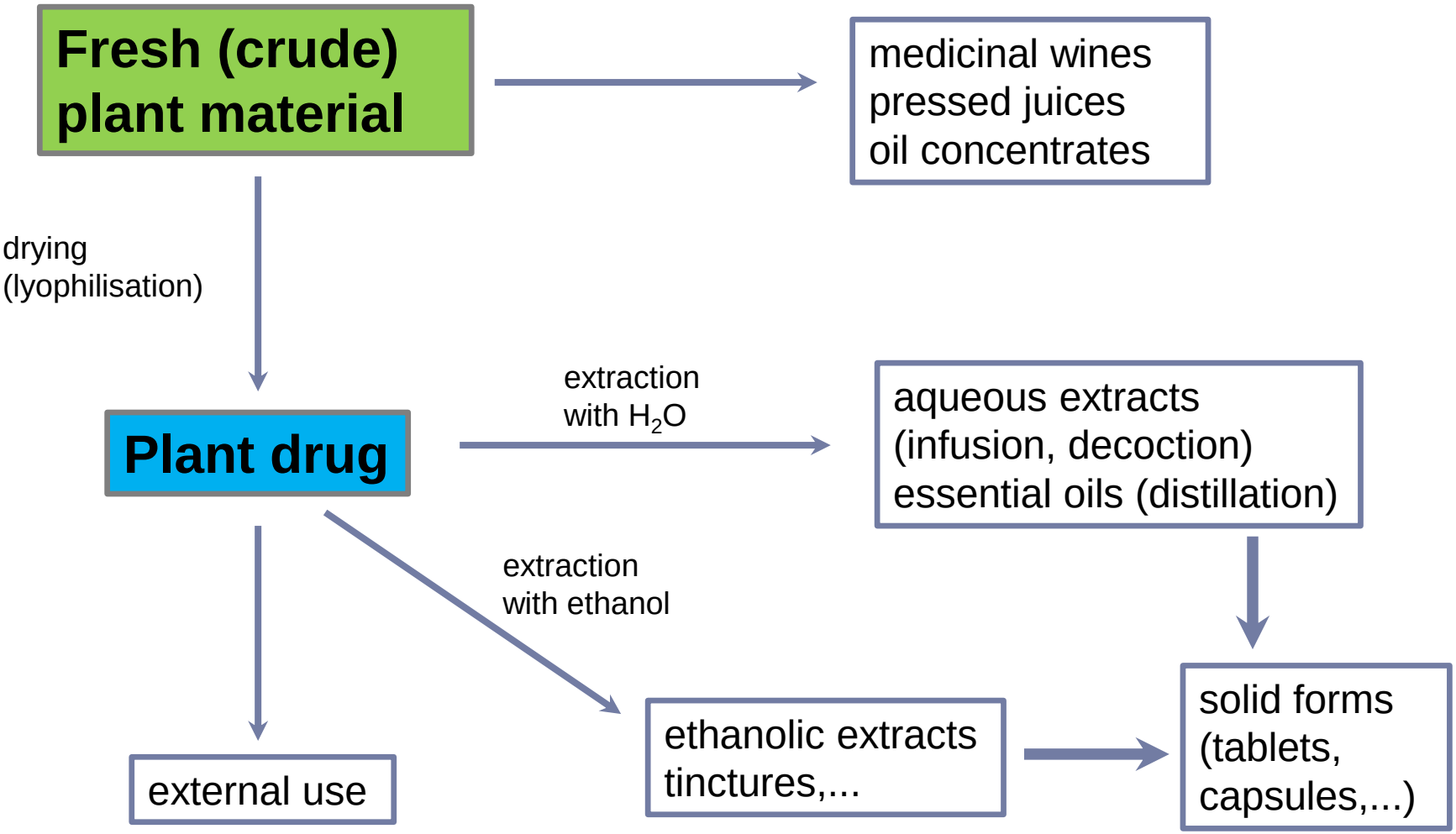
Cinchona pubescens
Cinchonae cortex

quinine
– antimalarial, analgesic

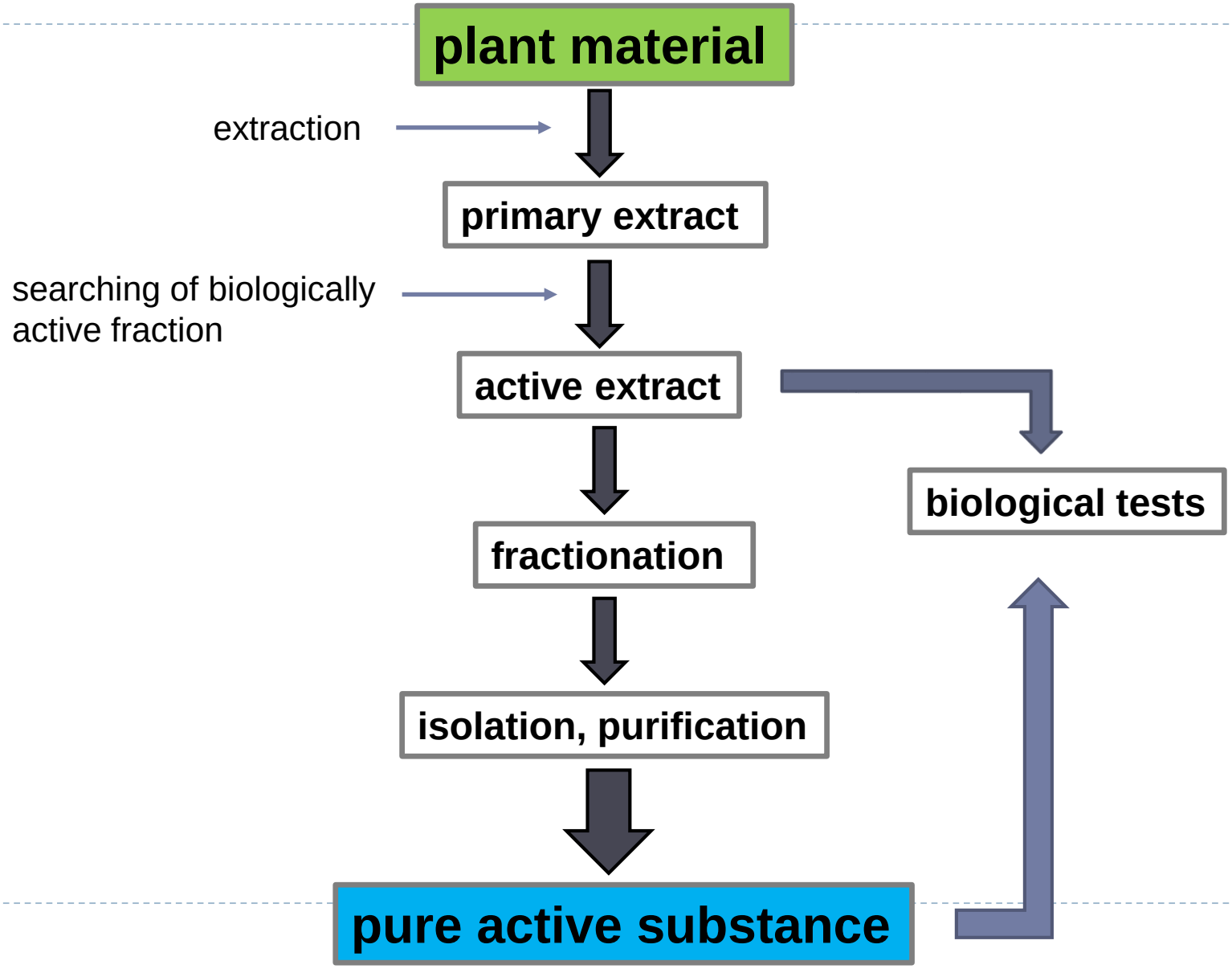
Mode of administration

- internal use – orally
  - herbal teas
  - drops, syrups, aromatic waters, aromatic spirits...
  - lozenges (pastilles)
  - tablets, capsules
- external use
  - inhalation
  - on skin – water/alcoholic preparations, ointments, creams
  - compress, bath,...

Medicinal preparations



General procedure for isolation of active principles



Herbal tea preparations

- Plantae medicinales ad potionem aquosam (ČL 2009) = medicinal plant drugs for tea preparations
- monocomponent = a herbal medicinal product consisting solely of one plant drug
- polycomponent = „species“, remedies – consisting of more plant drugs, optimum 4-6 drugs (maximally 8)
  - **remedium basis** – main component responsible for biological effect
  - **remedium adjuvans** – a drug that support the effect of the main component
  - **remedium corrigens** – a drug that influences the taste and smell
- drugs are treated (cut) according to the requirements
- herbal teas are loose or in tea bags

Herbal teas – dosage

- **tea bags** – approx. 1.5-2 g of treated plant drug or mixture of drugs (package – usually 20 tea bags in a box)
  - usually for internal use – one tea bag per cup (150-250 mL of water)
- dosage of **loose teas** (package – usually 50/100 g)
  - for internal use – teaspoon or tablespoon per cup
  - for external use – to a bath, as a compress, for inhalation

Herbal teas - monocomponent

- **monocomponent -** a herbal tea consisting only of one plant drug
- the name of product according to the plant drug, in case of medicinal herbal teas is necessary also **Latin name** of plant drug
  - Plantain leaf, Plantain tea, *Plantaginis folium*

Herbal teas - polycomponent

- **polycomponent** - a herbal tea consisting of more plant drugs, „species“
- herbal tea formulas must comply with legal requirements and demonstrate evidence of **quality, efficacy** and **safety**
- the name of product usually according to the indication/ pharmacological effect of tea mixture

Herbal teas – polycomponent

- Tea for cough
  (Megaphyt Pharma)
  - Thymi herba
    Matricariae flos
    Sambuci flos
    Tiliae flos
  - 20 tea bags/1,5 g

- Species Pectorales
  (Leros)
  - Plantaginis folium
    Althaeae radix
    Farfarae folium
    Menthae piperitae herba
    Liquiritiae radix
    Verbasci flos
    Foeniculi fructus
  - loose tea, 100 g

Herbal teas – polycomponent

- the name of product sometimes according to „designed to“ („for who“), e.g.:
  - Herbal tea for women
  - Herbal tea for nursing mothers (lactating women)
  - Herbal tea for children
  - etc.

Medicinal preparations

- Mode of extraction (techniques) – water extracts, tea:
  - **maceration**
  - **infusion**
    decoction
  - pressing
  - distillation (isolation of essential oils)

Medicinal preparations

- **MACERATION**
  - solvent: **cold/lukewarm water** (at room temperature)!
  - in a ratio of drug to water = usually 5:100
  - time of extraction – **several hours** (3-12 hours)
  - examples of suitable plant drugs – **mucilage drugs**, e.g. *Malvae flos, Althaeae folium*

Medicinal preparations

- **INFUSION**
  - solvent: **hot water**
  - suitable for **soft structures** (flowers, leaves, herbs…), plant drugs with **essential oils**…
  - in a ratio of drug to water = 2-10 :100
  - pour **hot (boiling) water** over the plant drug, cover
  - time of extraction – usually (5-) **10-15** (-30) minutes
  - pass through a tea strainer

Medicinal preparations

- **DECOCTION**
  - solvent: **boiling water**
  - suitable for **hard structures** (roots, bark, hard fruits…), plant drugs containing tannins…
  - in a ratio of drug to water = 5-10 :100
  - **boil** (!) the drug with water
  - time of extraction – usually **10-15 minutes**
  - pass through a tea strainer

Comparison between **infusion** and **decoction**

	INFUSION	DECOCTION
Plant material	Soft structure (leaves, flowers,...)	Hard, woody structure (bark, root,...)
Menstruum (Solvent)	Hot/Boiling water	Boiling water
Procedure	Infusing the drug with hot water	Boiling the drug with water
Time of extraction	Calculated as soon as the water is added to drug	Calculated as soon as the water begins to boil
Adjustment of final volume	No adjustment	Adjustment is necessary
Apparatus	Infusion earthenware pot	Any covered apparatus
Storage	Used fresh within 12 hours	Used fresh and when stored in refrigerator used within few days

Extractum, extracta

- aqueous/alcoholic extracts:
  - **liquid** (Extractum fluidum) – drug : solvent = 1:5, 1:10; e.g. *Matricariae extractum fluidum*
  - **semi-solid**, paste (Extractum spissum) – residual solvent 15-25 %
    e.g. *Capsici acris extractum spissum normatum*
  - **dry** (Extractum siccum) – residual solvent max. 5 %; e.g. *Ginseng extractum siccum normatum,*
    Ginkgo bilobae extractum siccum normatum
- suitable for preparation of drops, syrups and other application forms (tablets, capsules,…)

Extract classification in Ph. Eur. (2009)

- Standardised extracts
  - adjustment to a defined content of a constituent with known therapeutic activity
- Quantified extracts
  - adjustment to a defined range of constituents (active markers)
  - active markers are generally accepted to contribute to the therapeutic activity
- Other extracts
  - neither constituents with known therapeutic activity nor active markers are known
  - monographs define a lower limit of a constituent (analytical marker)

Standardised Extracts in Ph. Eur.

- Aloes extractum siccum **normatum**
- Belladonnae folii extractum siccum normatum
- Belladonnae folii tinctura normata
- Cinchonae extractum fluidum normatum
- Frangulae corticis extractum siccum normatum
- Hippocastani seminis extractum siccum normatum
- Ipecacuanhae extractum fluidum normatum
- Liquiritiae extractum fluidum ethanolicum normatum
- Myrtilli fructus recentis extractum siccum raffinatum et normatum
- Opii extractum siccum normatum
- Rhamni purshianae extractum siccum normatum
- Rhei extractum siccum normatum
- Sennae folii extractum siccum normatum
- Silybi mariani extractum siccum raffinatum et normatum

not necessary to know, do not memorize that

Quantified Extracts in Ph. Eur.

- Capsici oleoresina raffinata et **quantificata** (6.5-8.0 % capsaicinoids)
- Crataegi folii cum flore extractum fluidum quantificatum - Hawthorn leaf and flower liquid extract (0.8-3.0 % flavonoids)
- Ginkgonis extractum siccum raffinatum et quantificatum - Ginkgo dry extract (22.0-27.0 % flavonoids, 2.6-3.2 % bilobalide, 2.8-3.4 % ginkgolides)
- Hyperici herbae extractum siccum quantificatum - St. John‘s wort dry extract (0.1-0.3 % hypericins)
- Melissae folii extractum siccum quantificatum - Melissa leaf dry extract (in preparation, 3.0-6.0 % rosmarinic acid)

not necessary to know, do not memorize that

Other Extracts in Ph. Eur.

- Agni casti fructus extractum siccum
- Boldi folii extractum siccum
- Cynarae folii extractum siccum
- Harpagophyti extractum siccum
- Liquiritiae extractum siccum ad saporandum
- Matricariae extractum fluidum
- Melissae folii extractum siccum
- Menthae piperitae folii extractum siccum
- Oleae folii extractum siccum
- Passiflorae herbae extractum siccum
- Salicis corticis extractum siccum
- Saw palmetto extract
- Valerianae extractum aquosum siccum
- Valerianae extractum hydroalcoholicum siccum

not necessary to know, do not memorize that

Liquritiae extractum in Ph. Eur.

- Liquiritiae extractum fluidum ethanolicum **normatum**
  - Liquorice ethanolic liquid extract, **standardised**
  - 3.0-5.0 % of glycyrrhizic acid
  - the extract is produced from the herbal drug by a suitable procedure using ethanol 70% (V/V)
- Liquiritiae extractum siccum ad saporandum
  - Liquorice dry extract for flavouring purposes
  - „other“ extract
  - 5.0-7.0 % of glycyrrhizic acid
  - the extract is produced from the cut herbal drug by a suitable procedure using water

not necessary to know, do not memorize that

EUROPEAN PHARMACOPOEIA 7.0

Calculate the percentage content of 18β-glycyrrhizic acid, using the following expression:

$$\frac{A_1 \times m_2 \times p \times 0.979}{A_2 \times m_1 \times 5}$$

A_1 = area of the peak due to 18β-glycyrrhizic acid in the chromatogram obtained with the test solution;

A_2 = area of the peak due to 18β-glycyrrhizic acid in the chromatogram obtained with the reference solution;

m_1 = mass of the extract to be examined used to prepare the test solution, in grams;

m_2 = mass of *monoammonium glycyrrhizate CRS* used to prepare the reference solution, in grams;

p = percentage content of 18β-glycyrrhizic acid in *monoammonium glycyrrhizate CRS*;

0.979 = peak correlation factor between glycyrrhizic acid and monoammonium glycyrrhizate.

01/2011:1536

LIQUORICE ETHANOLIC LIQUID EXTRACT, STANDARDISED

Liquiritiae extractum fluidum ethanolicum normatum

DEFINITION

Standardised ethanolic liquid extract produced from *Liquorice root (0277)*.

Content: 3.0 per cent to 5.0 per cent of glycyrrhizic acid ($C_{42}H_{62}O_{16}$; M_r 823).

PRODUCTION

The extract is produced from the herbal drug by a suitable procedure for liquid extracts using ethanol (70 per cent *V/V*).

CHARACTERS

Appearance: dark brown, clear liquid.

It has a faint characteristic odour and a sweet taste.

IDENTIFICATION

Thin-layer chromatography (*2.2.27*).

Test solution. Place 1.0 g of the extract to be examined in a 50 mL round-bottomed flask, add 16.0 mL of *water R* and 4.0 mL of *hydrochloric acid R1* and heat on a water-bath under a reflux condenser for 30 min. Allow to cool and filter. Dry the filter and the round-bottomed flask at 105 °C for 60 min. Transfer the filter to the round-bottomed flask, add 20 mL of *ether R* and heat in a water-bath at 40 °C under a reflux condenser for 5 min. Allow to cool and filter. Evaporate the filtrate to dryness and dissolve the residue in 5.0 mL of *ether R*.

Reference solution. Dissolve 5.0 mg of *glycyrrhetic acid R* and 5.0 mg of *thymol R* in 5 mL of *ether R*.

Plate: *TLC silica gel F_{254} plate R*.

Mobile phase: *concentrated ammonia R, water R, ethanol (96 per cent) R, ethyl acetate R* (1:9:25:65 *V/V/V/V*).

Application: 10 µL as bands.

Development: over a path of 15 cm.

Drying: in air for 5 min.

Detection A: examine in ultraviolet light at 254 nm.

Results A: the chromatograms obtained with the test solution and the reference solution show in the lower half a quenching zone due to glycyrrhetic acid.

Detection B: spray with *anisaldehyde solution R*; heat at 100-105 °C for 5-10 min and examine in daylight.

Results B: the chromatogram obtained with the reference solution shows in the lower half a violet zone (glycyrrhetic acid), and in the upper third a red zone (thymol); the chromatogram obtained with the test solution shows in the lower half a violet zone corresponding to glycyrrhetic acid in the chromatogram obtained with the reference solution, and in the upper third, below the zone of thymol in the chromatogram obtained with the reference solution, a yellow zone due to isoliquiritigenin; further zones are present.

TESTS

Ethanol (*2.9.10*): 52 per cent *V/V* to 65 per cent *V/V*.

Methanol and 2-propanol (*2.9.11*): maximum 0.05 per cent *V/V* of methanol and maximum 0.05 per cent *V/V* of 2-propanol.

Ochratoxin A (*2.8.22*): maximum 80 µg per kilogram of extract.

ASSAY

Liquid chromatography (*2.2.29*).

Solvent mixture: *dilute ammonia R1, water R* (8:92 *V/V*).

Test solution. Dilute 1.000 g of the extract to be examined to 100 mL with the solvent mixture and centrifuge. Dilute 2.0 mL of the supernatant to 10.0 mL with the solvent mixture.

Stock solution. Dissolve 0.130 g of *monoammonium glycyrrhizate CRS* in the solvent mixture and dilute to 100.0 mL with the solvent mixture.

Reference solution (a). Dilute 5.0 mL of the stock solution to 100.0 mL with the solvent mixture.

Reference solution (b). Dilute 10.0 mL of the stock solution to 100.0 mL with the solvent mixture.

Reference solution (c). Dilute 15.0 mL of the stock solution to 100.0 mL with the solvent mixture.

Column:

– *size*: *l* = 0.10 m, Ø = 4 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *glacial acetic acid R, acetonitrile R, water R* (6:30:64 *V/V/V*).

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 10 µL.

Establish a calibration curve with the concentrations of the reference solutions (g/100 mL) as the abscissa and the corresponding peak areas as the ordinate.

Using the retention times and the peak areas determined from the chromatograms obtained with the reference solutions, locate and integrate the peak due to glycyrrhizic acid in the chromatogram obtained with the test solution.

Calculate the percentage content of glycyrrhizic acid using the following expression:

$$A \times \frac{5}{m} \times B \times \frac{823}{840}$$

A = concentration of monoammonium glycyrrhizate in the test solution, determined from the calibration curve, in g/100 mL;

B = declared percentage content of *monoammonium glycyrrhizate CRS*;

m = mass of the extract to be examined, in grams;

823 = molecular mass of glycyrrhizic acid;

840 = molecular mass of monoammonium glycyrrhizate (without any water of crystallisation).

pitted. Inside the testa a narrow, whitish endosperm and an embryo composed of 2 large, flattened, yellowish and oily cotyledons are present; the radicle points towards the hilum.

B. Reduce to a powder (355) (*2.9.12*). The powder is greasy to the touch. Examine under a microscope using *chloral hydrate solution R*. The powder consists of fragments of the outer epidermal cells of the testa filled with mucillage; collenchymatously thickened sub-epidermal layer seen in surface view as rounded cells with distinct triangular intercellular spaces often attached to the sclerenchymatous layer composed of elongated cells, some with strongly thickened and pitted walls; thin-walled pitted cells of the hyaline layer often remaining attached to the elongated sclereids and crossing them at approximately right angles; pigmented cells of the inner epidermis of the testa composed of moderately thickened polygonal cells filled with orange-brown pigment; parenchyma of the endosperm and cotyledons containing aleurone grains and fatty oil.

TESTS

Foreign matter (*2.8.2*): maximum 10 per cent of seeds with a dull coat and maximum 1.5 per cent of other foreign matter.

Swelling index (*2.8.4*): minimum 4.

Cadmium (*2.4.27*): maximum 0.5 ppm.

Loss on drying (*2.2.32*): maximum 8.0 per cent, determined on 1.000 g of the powdered drug (355) (*2.9.12*) by drying in an oven at 105 °C for 2 h.

Total ash (*2.4.16*): maximum 5.0 per cent.

04/2008:2378

LIQUORICE DRY EXTRACT FOR FLAVOURING PURPOSES

Liquiritiae extractum siccum ad saporandum

DEFINITION

Dry extract produced from *Liquorice root (0277)*.

Content: 5.0 per cent to 7.0 per cent of 18β-glycyrrhizic acid ($C_{42}H_{62}O_{16}$; M_r 823) (dried extract).

PRODUCTION

The extract is produced from the cut herbal drug by a suitable procedure using water.

CHARACTERS

Appearance: yellowish-brown or brown powder.

Very sweet taste.

IDENTIFICATION

Thin-layer chromatography (*2.2.27*).

Solvent mixture: *ethyl acetate R, methanol R* (50:50 *V/V*).

Test solution. To 0.30 g of the extract to be examined add 30 mL of *hydrochloric acid R1* and boil on a water-bath under a reflux condenser for 60 min. After cooling, extract the mixture with 2 quantities, each of 20 mL, of *ethyl acetate R*. Combine the organic layers and filter through a filter covered with *anhydrous sodium sulfate R*. Evaporate the filtrate to dryness *in vacuo* and dissolve the residue in 2.0 mL of the solvent mixture.

Reference solution. Dissolve 5.0 mg of *glycyrrhetic acid R* and 5.0 mg of *thymol R* in 5.0 mL of the solvent mixture.

Plate: *TLC silica gel F_{254} plate R* (5-40 µm) [or *TLC silica gel F_{254} plate R* (2-10 µm)].

Mobile phase: *concentrated ammonia R, water R, ethanol (96 per cent) R, ethyl acetate R* (1:9:25:65 *V/V/V/V*).

Application: 20 µL [or 10 µL], as bands.

Development: over a path of 15 cm [or 7 cm].

Drying: in air for 5 min.

Detection: spray with *anisaldehyde solution R* and heat at 100-105 °C for 5-10 min; examine in daylight.

Results: see below the sequence of zones present in the chromatograms obtained with the reference solution and the test solution. Furthermore, other faint zones may be present in the chromatogram obtained with the test solution.

Top of the plate	
Thymol: a red zone	
	A yellow zone
Glycyrrhetic acid: a violet zone	A violet zone (glycyrrhetic acid)
Reference solution	Test solution

TESTS

Loss on drying (*2.8.17*): maximum 7.0 per cent.

ASSAY

Liquid chromatography (*2.2.29*).

Solvent mixture: *water R, methanol R* (20:80 *V/V*).

Test solution. Place 0.200 g of the extract to be examined in a 150 mL ground-glass conical flask. Add 100.0 mL of the solvent mixture and sonicate for 2 min. Filter through a membrane filter (nominal pore size 0.45 µm).

Reference solution. Dissolve 50.0 mg of *monoammonium glycyrrhizate CRS* in the solvent mixture and dilute to 50.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

– *size*: *l* = 0.10 m, Ø = 4.0 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *glacial acetic acid R, acetonitrile R, water R* (6:30:64 *V/V/V*).

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 10 µL.

Run time: 3 times the retention time of 18β-glycyrrhizic acid.

Retention time: 18β-glycyrrhizic acid = about 9 min.

Identification of peaks: use the chromatogram supplied with *monoammonium glycyrrhizate CRS* and the chromatogram obtained with the reference solution to identify the peaks due to 18β-glycyrrhizic acid and 18α-glycyrrhizic acid.

System suitability: reference solution:

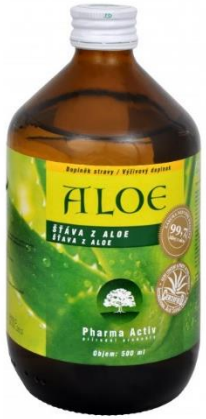
– the chromatogram obtained with the reference solution is similar to the chromatogram supplied with *monoammonium glycyrrhizate CRS*;

– *resolution*: minimum 2.0 between the peaks due to 18β-glycyrrhizic acid and 18α-glycyrrhizic acid.

Plant juices

- complex composition – important in phytotherapy
- content of hydrophilic components, not highly effective (no toxic) compounds
- processing of fresh (crude) material, immediately after harvesting (or after freezing) to prevent enzymatic degradation
- pressing using high pressure
- heat treatment – pasteurisation

- ALOE VERA GEL
  - *Aloe barbadensis*
  - juice of inner part of leaves, cold pressing
  - high content of polysaccharides, saponins, lignins, vitamins, minerals,…
  - low content of aloin
  - for internal/external use

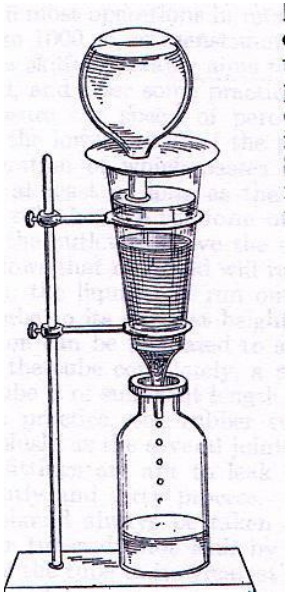


Etheroleum, etherolea

- = essential oils, volatile oils
- concentrated hydrophobic liquids containing volatile aroma (fragrant) compounds from plants
- generally extracted by distillation (often by using steam), using solvent extraction or by mechanical process without heating (pressing)
- wide biological effects – using in phytotherapy, aromatherapy
- for culinary purposes;
  in cosmetics, perfumes

Tinctura, tincturae

- alcoholic extracts of drugs or alcoholic solutions of dry extracts
- the solvent is only ethanol of suitable concentration (usually 60-70 %)
- Preparation:
  - usually maceration at normal temperature, in ratio of drug to ethanol = 1:5
  - percolation; in a ratio of drug to ethanol = 1:10 (suitable for extraction of alkaloids, glycosides, essential oils)
  - dissolution of semi-solid or dry extract in ethanol



percolator

Tinctura, tincturae

- **Tinctura simplex**
  – prepared of one drug
  - e.g. Arnicae tinctura
    Gentianae tinctura
    Valerianae tinctura…
- **Tinctura composita**
  – prepared of more drugs
  - e.g. Tinctura amara
    Tinctura aromatica…

Guttae, solutiones

- = drops and medicinal solutions
- homogenised dispersions of two or more components in water, ethanol, or glycerine (hydrophilic), or in oil (hydrophobic)
- Preparation:
  - dissolution of dry medicines in solvent
  - mixing of one-phase liquid systems
- Dosage:
  - drops – internal or external use
  - greater volume – e.g. gargles, mouthwash

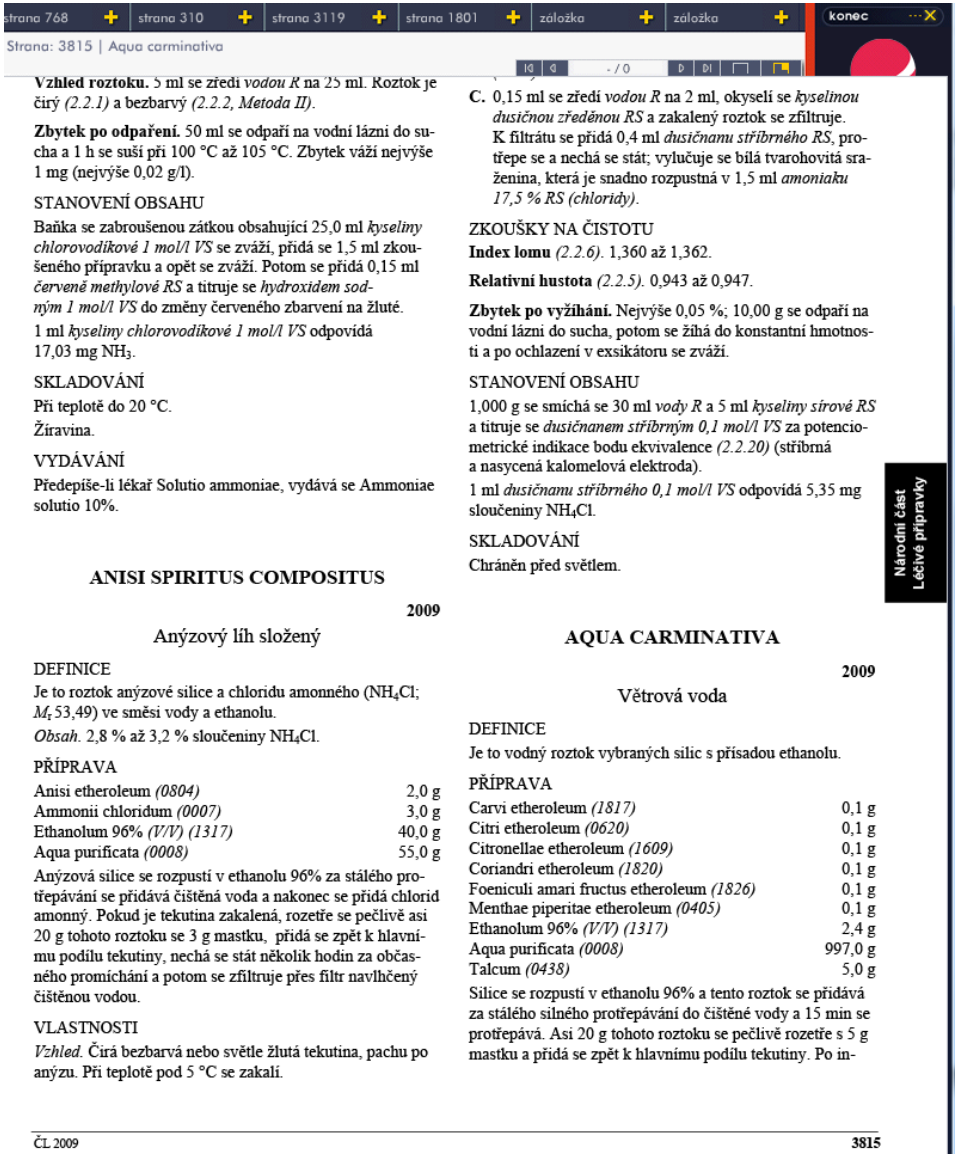
Oil concentrates

- extraction of water/alcoholic insoluble compounds
- high content of volatile compounds (essential oils, terpenic compounds)
- e.g. extraction of flowers with cold oil (fat) – „enfleurage“ → high-quality fragrant oils (suitable for perfumes)

Aromatic waters and spirits

- Aromatic waters
  - saturated aqueous solutions of essential oils with small addition of alcohol for better solubility
  - used for adjustment of taste and smell, or as medicines, e.g. *Aqua carminativa rubra*
- Aromatic spirits (alcohols)
  - solutions of essential oils or volatile compounds in alcohol, e. g. *Anisi spiritus compositus*
  - used for adjustment of taste and smell, or as medicines, especially as digestive, carminative and spasmolytic agents.
  - tinctures of fresh (non-dried) plants – Alcoholaturae

ČL 2009 = PHARMACOPOEIA BOHEMICA MMIX



strana 768 | strana 310 | strana 3119 | strana 1801 | záložka | záložka | konec

Strana: 3815 | Aqua carminativa

Vzhled roztoku. 5 ml se zředí *vodou R* na 25 ml. Roztok je čirý *(2.2.1)* a bezbarvý *(2.2.2, Metoda II)*.

Zbytek po odpaření. 50 ml se odpaří na vodní lázni do sucha a 1 h se suší při 100 °C až 105 °C. Zbytek váží nejvýše 1 mg (nejvýše 0,02 g/l).

STANOVENÍ OBSAHU

Baňka se zabroušenou zátkou obsahující 25,0 ml *kyseliny chlorovodíkové 1 mol/l VS* se zváží, přidá se 1,5 ml zkoušeného přípravku a opět se zváží. Potom se přidá 0,15 ml *červeně methylové RS* a titruje se *hydroxidem sodným 1 mol/l VS* do změny červeného zbarvení na žluté.

1 ml *kyseliny chlorovodíkové 1 mol/l VS* odpovídá 17,03 mg NH_3.

SKLADOVÁNÍ

Při teplotě do 20 °C.

Žíravina.

VYDÁVÁNÍ

Předepíše-li lékař Solutio ammoniae, vydává se Ammoniae solutio 10%.

ANISI SPIRITUS COMPOSITUS

2009

Anýzový líh složený

DEFINICE

Je to roztok anýzové silice a chloridu amonného (NH_4Cl; M_r 53,49) ve směsi vody a ethanolu.

Obsah. 2,8 % až 3,2 % sloučeniny NH_4Cl.

PŘÍPRAVA

Anisi etheroleum *(0804)*	2,0 g
Ammonii chloridum *(0007)*	3,0 g
Ethanolum 96% *(V/V) (1317)*	40,0 g
Aqua purificata *(0008)*	55,0 g

Anýzová silice se rozpustí v ethanolu 96% za stálého protřepávání se přidává čištěná voda a nakonec se přidá chlorid amonný. Pokud je tekutina zakalená, rozetře se pečlivě asi 20 g tohoto roztoku se 3 g mastku, přidá se zpět k hlavnímu podílu tekutiny, nechá se stát několik hodin za občasného promíchání a potom se zfiltruje přes filtr navlhčený čištěnou vodou.

VLASTNOSTI

Vzhled. Čirá bezbarvá nebo světle žlutá tekutina, pachu po anýzu. Při teplotě pod 5 °C se zakalí.

C. 0,15 ml se zředí *vodou R* na 2 ml, okyselí se *kyselinou dusičnou zředěnou RS* a zakalený roztok se zfiltruje. K filtrátu se přidá 0,4 ml *dusičnanu stříbrného RS*, protřepe se a nechá se stát; vylučuje se bílá tvarohovitá sraženina, která je snadno rozpustná v 1,5 ml *amoniaku 17,5 % RS (chloridy)*.

ZKOUŠKY NA ČISTOTU

Index lomu *(2.2.6)*. 1,360 až 1,362.

Relativní hustota *(2.2.5)*. 0,943 až 0,947.

Zbytek po vyžíhání. Nejvýše 0,05 %; 10,00 g se odpaří na vodní lázni do sucha, potom se žíhá do konstantní hmotnosti a po ochlazení v exsikátoru se zváží.

STANOVENÍ OBSAHU

1,000 g se smíchá se 30 ml *vody R* a 5 ml *kyseliny sírové RS* a titruje se *dusičnanem stříbrným 0,1 mol/l VS* za potenciometrické indikace bodu ekvivalence *(2.2.20)* (stříbrná a nasycená kalomelová elektroda).

1 ml *dusičnanu stříbrného 0,1 mol/l VS* odpovídá 5,35 mg sloučeniny NH_4Cl.

SKLADOVÁNÍ

Chráněn před světlem.

Národní část Léčivé přípravky

AQUA CARMINATIVA

2009

Větrová voda

DEFINICE

Je to vodný roztok vybraných silic s přísadou ethanolu.

PŘÍPRAVA

Carvi etheroleum *(1817)*	0,1 g
Citri etheroleum *(0620)*	0,1 g
Citronellae etheroleum *(1609)*	0,1 g
Coriandri etheroleum *(1820)*	0,1 g
Foeniculi amari fructus etheroleum *(1826)*	0,1 g
Menthae piperitae etheroleum *(0405)*	0,1 g
Ethanolum 96% *(V/V) (1317)*	2,4 g
Aqua purificata *(0008)*	997,0 g
Talcum *(0438)*	5,0 g

Silice se rozpustí v ethanolu 96% a tento roztok se přidává za stálého silného protřepávání do čištěné vody a 15 min se protřepává. Asi 20 g tohoto roztoku se pečlivě rozetře s 5 g mastku a přidá se zpět k hlavnímu podílu tekutiny. Po in-

ČL 2009 3815

ANISI SPIRITUS COMPOSITUS ČL2009

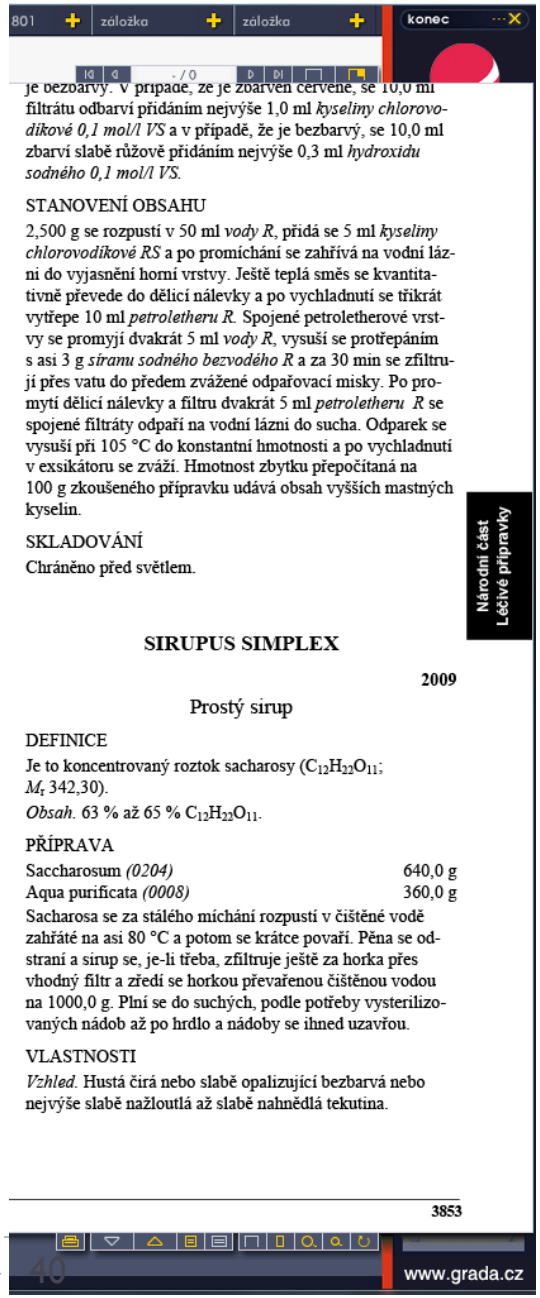
Anisi etheroleum	2,0 g
Ammonii chloridum	3,0 g
Ethanolum 96% (V/V)	40,0 g
Aqua purificata	55,0 g

AQUA CARMINATIVA ČL2009

Carvi etheroleum	0,1 g
Citri etheroleum	0,1 g
Citronellae etheroleum	0,1 g
Coriandri etheroleum	0,1 g
Foeniculi amari fructus etheroleum	0,1 g
Mentae piperitae etheroleum	0,1 g
Ethanolum 96% (V/V)	2,4 g
Aqua purificata	997,0 g
Talcum	5,0 g

Sirupus, sirupi

- = syrups
- a thick, viscous liquid consisting primarily of a solution of sugar in water, in water plant extract or in fruit juice.
- containing a large amount of dissolved sugars (mainly sucrose, or glucose, fructose), or polyols (alcoholic sugars, e.g. mannitol, sorbitol)
- **Sirupus simplex** (*Simple syrup*) = **64% (m/V)** aqueous solution of sucrose (saccharose) – this concentration has a preservative effect
- medicinal syrups contain dissolved medicinal compounds, plant extracts



je bezbarvý. V případě, že je zbarven červeně, se 10,0 ml filtrátu odbarví přidáním nejvýše 1,0 ml *kyseliny chlorovodíkové 0,1 mol/l VS* a v případě, že je bezbarvý, se 10,0 ml zbarví slabě růžově přidáním nejvýše 0,3 ml *hydroxidu sodného 0,1 mol/l VS*.

STANOVENÍ OBSAHU

2,500 g se rozpustí v 50 ml *vody R*, přidá se 5 ml *kyseliny chlorovodíkové RS* a po promíchání se zahřívá na vodní lázni do vyjasnění horní vrstvy. Ještě teplá směs se kvantitativně převede do dělicí nálevky a po vychladnutí se třikrát vytřepe 10 ml *petroletheru R*. Spojené petroletherové vrstvy se promyjí dvakrát 5 ml *vody R*, vysuší se protřepáním s asi 3 g *síranu sodného bezvodého R* a za 30 min se zfiltrují přes vatu do předem zvážené odpařovací misky. Po promytí dělicí nálevky a filtru dvakrát 5 ml *petroletheru R* se spojené filtráty odpaří na vodní lázni do sucha. Odparek se vysuší při 105 °C do konstantní hmotnosti a po vychladnutí v exsikátoru se zváží. Hmotnost zbytku přepočítaná na 100 g zkoušeného přípravku udává obsah vyšších mastných kyselin.

SKLADOVÁNÍ

Chráněno před světlem.

Národní část
Léčivé přípravky

SIRUPUS SIMPLEX

2009

Prostý sirup

DEFINICE

Je to koncentrovaný roztok sacharosy ($C_{12}H_{22}O_{11}$; M_r 342,30).

Obsah. 63 % až 65 % $C_{12}H_{22}O_{11}$.

PŘÍPRAVA

Saccharosum *(0204)*	640,0 g
Aqua purificata *(0008)*	360,0 g

Sacharosa se za stálého míchání rozpustí v čištěné vodě zahřáté na asi 80 °C a potom se krátce povaří. Pěna se odstraní a sirup se, je-li třeba, zfiltruje ještě za horka přes vhodný filtr a zředí se horkou převařenou čištěnou vodou na 1000,0 g. Plní se do suchých, podle potřeby vysterilizovaných nádob až po hrdlo a nádoby se ihned uzavřou.

VLASTNOSTI

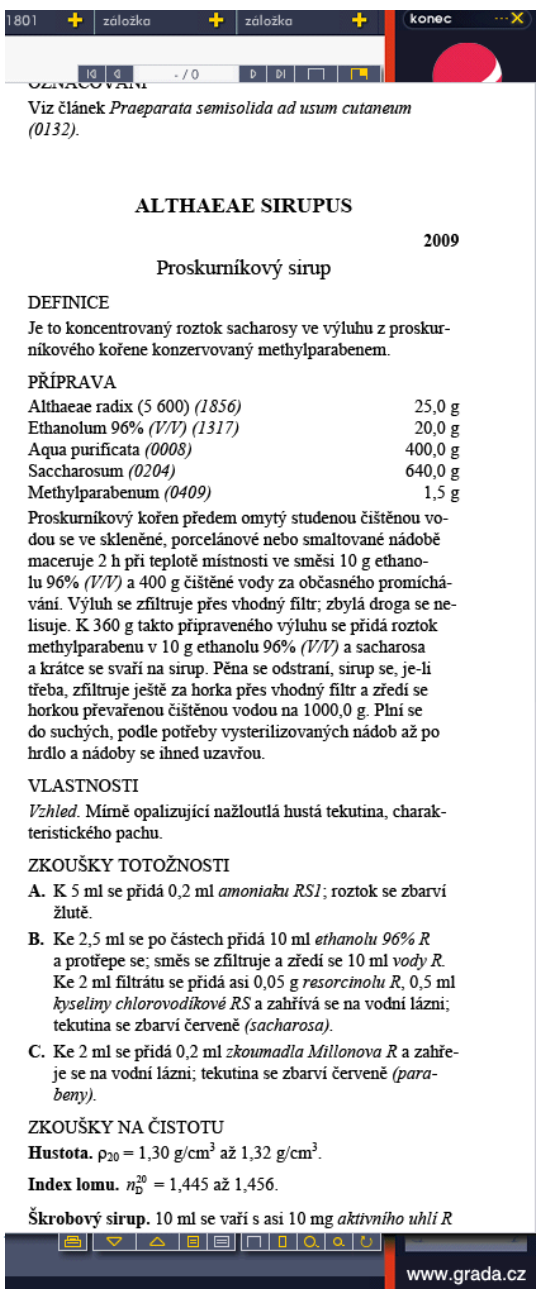
Vzhled. Hustá čirá nebo slabě opalizující bezbarvá nebo nejvýše slabě nažloutlá až slabě nahnědlá tekutina.

SIRUPUS SIMPLEX ČL2009

Saccharosum	640,0 g
Aqua purificata	360,0 g

ALTHAEAE SIRUPUS ČL2009

Althaeae radix	25,0 g
Ethanolum 96% (V/V)	20,0 g
Aqua purificata	400,0 g
Saccharosum	640,0 g
Methylparabenum	1,5 g



Viz článek *Praeparata semisolida ad usum cutaneum (0132).*

ALTHAEAE SIRUPUS

2009

Proskurníkový sirup

DEFINICE

Je to koncentrovaný roztok sacharosy ve výluhu z proskurníkového kořene konzervovaný methylparabenem.

PŘÍPRAVA

Althaeae radix (5 600) *(1856)*	25,0 g
Ethanolum 96% *(V/V) (1317)*	20,0 g
Aqua purificata *(0008)*	400,0 g
Saccharosum *(0204)*	640,0 g
Methylparabenum *(0409)*	1,5 g

Proskurníkový kořen předem omytý studenou čištěnou vodou se ve skleněné, porcelánové nebo smaltované nádobě maceruje 2 h při teplotě místnosti ve směsi 10 g ethanolu 96% *(V/V)* a 400 g čištěné vody za občasného promíchávání. Výluh se zfiltruje přes vhodný filtr; zbylá droga se nelisuje. K 360 g takto připraveného výluhu se přidá roztok methylparabenu v 10 g ethanolu 96% *(V/V)* a sacharosa a krátce se svaří na sirup. Pěna se odstraní, sirup se, je-li třeba, zfiltruje ještě za horka přes vhodný filtr a zředí se horkou převařenou čištěnou vodou na 1000,0 g. Plní se do suchých, podle potřeby vysterilizovaných nádob až po hrdlo a nádoby se ihned uzavřou.

VLASTNOSTI

Vzhled. Mírně opalizující nažloutlá hustá tekutina, charakteristického pachu.

ZKOUŠKY TOTOŽNOSTI

A. K 5 ml se přidá 0,2 ml *amoniaku RS1*; roztok se zbarví žlutě.

B. Ke 2,5 ml se po částech přidá 10 ml *ethanolu 96% R* a protřepe se; směs se zfiltruje a zředí se 10 ml *vody R*. Ke 2 ml filtrátu se přidá asi 0,05 g *resorcinolu R*, 0,5 ml *kyseliny chlorovodíkové RS* a zahřívá se na vodní lázni; tekutina se zbarví červeně *(sacharosa)*.

C. Ke 2 ml se přidá 0,2 ml *zkoumadla Millonova R* a zahřeje se na vodní lázni; tekutina se zbarví červeně *(parabeny)*.

ZKOUŠKY NA ČISTOTU

Hustota. ρ_{20} = 1,30 g/cm^3 až 1,32 g/cm^3.

Index lomu. n_D^{20} = 1,445 až 1,456.

Škrobový sirup. 10 ml se vaří s asi 10 mg *aktivního uhlí R*

Medicinal wines

- the base is usually **„malt wine“** – obtained due to the fermentation of malt extract (from germinated barley grains – *Hordeum vulgare*)
- the malt wine is enriched with water/alcoholic plant extract
- ripening several months in oak barrels

- MALTOFERROCHIN (Herbadent)
  - natural malt wine with a high content of iron, suitable for the treatment of anaemia.
  - contains also Cinchonae bark extract

- CONDURANGO WINE
  - malt wine enriched with water-alcoholic extract of *Marsdenia condurango* bark
  - suitable for the treatment of digestive disorders, in case of loss of appetite

Other application forms

- instant/granular teas
- tablets, sugar coated tablets, capsules, effervescent tablets
- lozenges (pastilles), medicinal gums
- preparations for inhalation
- ointments, creams, lotions, aero-dispersions (sprays)
- adhesive plasters (emplastra)
- etc.