Development of digital learning materials for renewable pharmaceutical practice-oriented skills in English and Hungarian. Preparing university lecturers for educational challenges of the 21st century.

Pharmacognosy 2

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Introduction

Short description of the digital learning material:
Pharmacognosy covers general aspects of medicinal plants (such as industrial applications, research, cultivation and cultivars, gene technology, critical evaluation of holistic medicine and homeopathy, possibilities of phytotherapy) and discusses the chemical composition and other qualitative characteristics, as well as the most important areas of usage and pharmacology of herbal drugs and drug fractions such as essential oils.

Today many people purchase medicinal plants and herbal products to prevent or cure diseases. Therefore specialists (physicians and pharmacists) should become acquainted with medicinal plants and drugs that are used in pharmacotherapy (especially in phytotherapy) both in Hungary and abroad. Our pharmacy students are required to recognize the most important drugs that are traded and/or imported in Hungary and are official in the Hungarian and European Pharmacopoeias. Pharmacognosy 2 digital learning material contains the most important medicinal plants and their drugs which are characterized according to their active compounds, usage, dosage, interactions with other drugs and side-effects. Drugs containing sugars and/or mucilage and fatty oils are introduced in the Pharmacognosy 1 digital learning material. Hopefully, this teaching supplement will be a useful reference text for medical doctors, pharmacists, students and teachers of pharmacognosy, herbalists, botanists, natural product chemists and pharmacologists who require information on medicinal plants.

Notice: Medicines or products containing medicinal plants should only be taken under medical supervision or according to the manufacturer’s direction. The authors and the publisher cannot accept any liability for any adverse effects caused by applying the plants, drugs or products mentioned in this teaching supplement.

Keywords:
pharmacognosy, medicinal plant, secondary metabolites, herbal drugs, phytotherapy

Photos:
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Chapter 1

Drugs containing monoterpenes, essential oils

1.1 Terpenoids

- They are secondary metabolites, approx. 20,000 terpenoids are known.
- They are made up by isoprene units (Figure 1.1), which have \( \text{C}_5\text{H}_8 \) molecular formula.
- The isoprene units may be linked together head to tail or tail to tail.
- The different terpenoid groups can be seen in Table 1.1.

![Head Tail]

2-methyl-1,3-butadiene
(Isoprene)

**Figure 1.1**
The chemical structure of isoprene

<table>
<thead>
<tr>
<th>Name</th>
<th>Number of isoprene units</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>MONOTERPENES</td>
<td>2</td>
<td>( 2 \times \text{C}_5\text{H}_8 )</td>
</tr>
<tr>
<td>SESQUITERPENES</td>
<td>3</td>
<td>( 3 \times \text{C}_5\text{H}_8 )</td>
</tr>
<tr>
<td>DITERPENOIDS</td>
<td>4</td>
<td>( 4 \times \text{C}_5\text{H}_8 )</td>
</tr>
<tr>
<td>TRITERPENES</td>
<td>6</td>
<td>( 6 \times \text{C}_5\text{H}_8 )</td>
</tr>
<tr>
<td>TETRATERPENES, CAROTENOIDS *</td>
<td>8</td>
<td>( 8 \times \text{C}_5\text{H}_8 )</td>
</tr>
<tr>
<td>POLYTERPENOIDS</td>
<td>n</td>
<td>( n \times \text{C}_5\text{H}_8 )</td>
</tr>
</tbody>
</table>

* \( \text{C}_{40}\text{H}_{56} \)

In essential oils terpenes may occur as alcohols (menthol), ethers (cineole), ketones (carvone), etc. The most characteristic compounds of essential oils can be found in Table 1.2.
### Table 1.2 Composition of essential oils

<table>
<thead>
<tr>
<th>Common name</th>
<th>Botanical name</th>
<th>Important constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monoterpenes or sesquiterpenes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Juniper</td>
<td><em>Juniperus communis</em></td>
<td>Terpenes (pinene); sesquiterpene (cadinene)</td>
</tr>
<tr>
<td>Coriander</td>
<td><em>Coriandrum sativum</em></td>
<td>Linalool (65-80%)</td>
</tr>
<tr>
<td>Sandalwood</td>
<td><em>Santalum album</em></td>
<td>Santalol (sesquiterpene alcohol)</td>
</tr>
<tr>
<td><strong>Alcohols</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lavender</td>
<td><em>Lavandula officinalis</em></td>
<td>Linalyl acetate</td>
</tr>
<tr>
<td>Peppermint</td>
<td><em>Mentha piperita</em></td>
<td>Menthol acetate (4-9%)</td>
</tr>
<tr>
<td><strong>Esters</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cinnamon bark</td>
<td><em>Cinnamomum verum</em></td>
<td>Cinnamic aldehyde (60-75%)</td>
</tr>
<tr>
<td>Lemon</td>
<td><em>Citrus limon</em></td>
<td>Citral (3.5%)</td>
</tr>
<tr>
<td><strong>Aldehydes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caraway</td>
<td><em>Carum carvi</em></td>
<td>Carvone (60%)</td>
</tr>
<tr>
<td>Sage</td>
<td><em>Salvia officinalis</em></td>
<td>Thujone (50%)</td>
</tr>
<tr>
<td><strong>Ketones</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyme</td>
<td><em>Thymus vulgaris</em></td>
<td>Thymol (30%)</td>
</tr>
<tr>
<td><strong>Phenols</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ethers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anise and Star-anise</td>
<td><em>Pimpinella anisum and Illicium verum</em></td>
<td>Anethole (80%)</td>
</tr>
<tr>
<td>Eucalyptus</td>
<td><em>Eucalyptus globulus</em></td>
<td>Cineole (70%)</td>
</tr>
<tr>
<td>Parsley</td>
<td><em>Petroselinum sativum</em></td>
<td>Apiole (dimethoxysafrole)</td>
</tr>
<tr>
<td>Nutmeg</td>
<td><em>Myristica fragrans</em></td>
<td>Myristicin (methoxysafrole)</td>
</tr>
<tr>
<td><strong>Peroxides</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chenopodium</td>
<td><em>Chenopodium ambrosioides var. anthelmintica</em></td>
<td>Ascaridole (60-70%)</td>
</tr>
</tbody>
</table>

Monoterpenes can be classified into three groups: 1. acyclic monoterpenes (e.g. geraniol, nerol, linalool, citronellol), 2. monocyclic monoterpenes (e.g. menthol, thymol), 3. bicyclic monoterpenes (e.g. \( \alpha \)- and \( \beta \)-pinene, \( \alpha \)-thujone).

Monoterpenes are mostly produced in different essential oils. Volatile compounds are secreted by special glandular cells located within the tissues or at the surface of leaves, flowers, fruits, and seeds. Terpenes of resins (when dissolved in essential oils they are
Drugs containing monoterpenes, essential oils

called balsams) or oils are located in excretion or resin channels of the bark or wood of stems or roots.

Properties of essential oils

- Essential oils are mixtures of monoterpenes, sesquiterpenes, and/or phenylpropane derivatives. Their components are mostly liquids. The odour and taste of volatile oils is mainly determined by their oxygenated compounds, which are to some extent soluble in water (e.g. rose water, orange-flower water), but more soluble in alcohol. Many oils are terpenoid in origin. Fewer oils such as those of cinnamon or clove contain principally aromatic (benzene) derivatives together with the terpenes.
- The boiling points vary from 140 °C – 180 °C (monoterpenes) to 240 °C (sesquiterpenes).
- They consist of 5-200 components. The most characteristic compounds in the oil are called the main components), while additional components are present in lower amounts.
- They have characteristic smell and colour (colourless, yellow, green, blue).
- They are secreted in oil cells, in secretion ducts or cavities or in glandular hairs. They are often associated with other substances such as gums and resins.
- They can become oxidized (if exposed to light and O₂ – resinification); they cannot be dissolved in water but are soluble in organic solvents (chloroform, toluol, hexane).
- The most important plant families with plants accumulating essential oil: Lamiaceae, Apiaceae, Myrtaceae, Rutaceae, Asteraceae, Lauraceae
- Chemotypes: the same plant species can produce essential oils with different chemical components when grown in various conditions. For example, the common herb Thymus vulgaris L. produces several oils for medicinal use, depending upon the soil, climate and altitude in which it is cultivated. The environmental factors (climate, type of soil, etc.) and genetic factors can influence the composition of essential oils.
- Storage: Essential oils should be stored in a well-filled, airtight container, protected from light at a temperature not exceeding 25 °C. They are inflammable materials.
- Nomenclature: in the Ph. Eur. – e.g. Anisi aetheroleum, Anise oil
1.2 Drugs

Menthae piperitae folium and Menthae piperitae aetheroleum

Plant

*Mentha x piperita* (L.) Huds. - Peppermint (Lamiaceae)

*Mentha x piperita* is, as implied by its botanical name, a hybrid species from two parents, *M. spicata* (2n = 36 or 48) and *M. aquatica* (2n = 96). The European and American oil are derived to a large extent from the two varieties *M. piperita* var. *vulgaris* Sole (‘black mint’) and *M. piperita* var. *officinalis* Sole (‘white mint’), respectively. The plant is cultivated all over the world.

![Peppermint](image)

**Figure 1.2**

Peppermint (*Mentha x piperita* (L.) Huds.)

Drugs

Menthae piperitae folium (Peppermint leaf, Ph. Eur.), Menthae piperitae aetheroleum (Peppermint oil, Ph. Eur.)

Peppermint leaf consists of the whole or cut dried leaves of *Mentha x piperita* L. The whole drug contains not less than 12 ml/kg of essential oil. The cut drug contains not less than 9 ml/kg of essential oil. Peppermint oil is obtained by steam distillation from the fresh overground parts of the flowering plant of *Mentha x piperita*. 
Drugs containing monoterpenes, essential oils

Constituents

The main active component is essential oil (1-3 %), of which the principal constituent is usually menthol (35-55%) (Figure 1.4), together with menthon (10-35%) and menthyl acetate. Small amounts of sesquiterpenes occur in the oil, notably viridoflorol. Various flavonoids are present including luteolin and its 7-glycoside, rutin, hesperidin and highly oxygenated flavones. Other constituents include phenolic acids and small amounts of triterpenes.
**Uses**

Peppermint leaf is used in the symptomatic treatment of digestive disorders such as dyspepsia, flatulence and gastritis, although no clinical data are available in support of these indications. It has spasmolytic, cholangogue, carminative (in tea) and mild antiemetic (apply on sugar cube) effects. Peppermint leaf extract and the essential oil are used in external products, e.g. in ointment against itching and in toothpaste. Other uses: in food industry (spice, liqueur, soft drink).

**Dosage**

*Adults*: As an infusion 1.5-3 g of the drug in 150-200 ml of water, three times daily. Tincture (1:5, 45% ethanol), 2-3 ml, three times daily. As a cholangogue: 2-4 drop essential oil (EO) on sugar cube. For external use: in ointment - 1-2 % EO content.

*Elderly*: Dose as for adults.

*Children from 4 years of age*, daily dose as infusion only: 4-10 years – 3-5 g, 10-16 years – 3-6 g.

**Special warnings and precautions for use**

Do not use both the drug and EO in infants, babies and little children (until 7 years) because apnoea, collapse of lung and cardiac arrest may occur.
Drugs containing monoterpenes, essential oils

**Lavandulae flos and Lavandulae aetheroleum**

**Plant**

Lavandula angustifolia Mill. – Lavender (Lamiaceae)

The plant is native to South-Europe, in Hungary it is cultivated (Tihany, Pannonhalma). France is the principal producer.

![Figure 1.8](image)

Lavender (*Lavandula angustifolia* Mill.)

**Drugs**

*Lavandulae flos* (Lavender flower, Ph. Eur.), *Lavandulae aetheroleum* (Lavender oil, Ph. Eur.)

Lavender flower consists of the dried flowers of *Lavandula angustifolia* Mill. (syn. *L. officinalis* Chaix). It contains not less than 13 ml/kg of essential oil, calculated with reference to the dried drug. Lavender oil is obtained by steam distillation from the fresh flowers of *L. angustifolia*. 
Constituents
The characteristic constituents include 1-3% of essential oil, the main components of which are linalool (20-45%), linalyl acetate (25-46%), while other components include terpinene-4-ol, limonene, cineole, camphor, lavandulyl acetate and lavandulol. The flower contains other constituents such as coumarin derivatives, flavonoids, triterpenes and “Labiatae tannin” (rosmarinic acid).

![linalool and linalyl acetate](image)

**Figure 1.10-11**
The structure of linalool and linalyl acetate

Uses
Lavender flower can treat the symptoms of mood disturbances such as restlessness, agitation, insomnia and functional abdominal complaints. The flower and oil have mild sedative effect. Topically the oil is used for treating rheumatic pain, in ointments to mask disagreeable odors. Other uses: perfumery, aromatherapy, inhalation, insect repellent (moth).
Dosage

**Internal use**

*Adults and children over 12 years of age*: As an infusion 0.8-1.6 g of the drug in 150-200 ml of water, three times daily. Tincture (1:5, 50% ethanol), 60 drops daily. Oil: 1-4 drops (approx. 20-80 mg) on a sugar cube. *Elderly*: Dose as for adults.

*Children up to 12 years of age*: An infusion of approx. 0.4-1.6 g of the flower.

**External use**

*Adults and children over 12 years of age*: As a bath additive – lavender flower, 20-100 g to 20 litres of water; lavender oil, 6 drops per bath. For inhalation – several drops of the oil or 2-20% of the oil in a nebulizer. *Elderly*: Dose as for adults.

*Children up to 12 years of age*: As a bath additive – lavender flower, 10-100 g to 20 litres of water. As inhalation – 3 drops of a 1:10 dilution of the oil. The flowers are also used traditionally in bags for inhalation by children.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

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**Melissae folium**

**Plant**

*Melissa officinalis* L. – Lemon balm/Melissa (Lamiaceae)

Plant is native to Europe (South-West part), and it is cultivated in Hungary.

---

**Figure 1.12**

Melissa (*Melissa officinalis* L.)

---

**Drug**

*Melissae folium* (Melissa leaf, Ph. Eur.)

Melissa leaf consists of the dried leaves of *Melissa officinalis* L. It contains not less than 4.0% of total hydroxycinnamic derivatives expressed as rosmarinic acid, calculated with
reference to the dried drug. Fresh material may be used provided that when dried it complies with the monograph of the European Pharmacopoeia.

**Figure 1.13**

Melissa (*Melissa officinalis* L.)

Constituents

The main constituents are: essential oil (0.05-0.3%) containing monoterpenoid aldehydes, mainly geranial (citral a), neral (citral b), citronellal, citronellol and an alcohol (geraniol); flavonoids including glycosides of luteolin, quercetin, apigenin and kaempferol, “Labiatae tannin” (rosmarinic acid), caffeic acid, chlorogenic acid, triterpenoids (ursolic and oleanolic acids). Because of the low amount of the essential oil content, the oil is adulterated with cheaper lemon-type oils.

![Chemical structures](image)

- **citronellal**
- **geranial = citral a**
- **neral = citral b**
- **citronellol**

*E*-isomer of citral

*Z*-isomer of citral

**Figure 1.14-17**

The structure of geranial (citral a), neral (citral b), citronellal and citronellol

Uses

Therapeutic indications of Melissa leaf are: restlessness and irritability; symptomatic treatment of digestive disorders such as minor spasms. It has sedative, spasmolytic and antiviral activity. The drug can be used in pediatrics. Externaly Melissa is used for treating *Herpes labialis* (cold sores). The essential oil is insect repellent.
Drugs containing monoterpenes, essential oils

Dosage

Internal use

2-3 g of the drug as an infusion, two to three times daily. Tincture (1:5 in 45% ethanol), 2-6 ml three times daily.

External use

Cream containing 1% of an aqueous extract (70:1) two to four times daily.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Thymi herba

Plants

*Thymus vulgaris* L. and *T. zygis* L. – Thyme and Spanish thyme (Lamiaceae)

Thyme is native to the Mediterranean countries, and it is cultivated in Hungary.

![Figure 1.18](image)

**Figure 1.18**

Thyme (*Thymus vulgaris* L.)

Drug

*Thymi herba* (Thyme, Ph. Eur.), *Thymi aetheroleum* (Thyme oil, Ph. Eur.)

Thyme consists of the whole leaves and flowers separated from the previously dried stems of *Thymus vulgaris* L. or *T. zygis* L. or a mixture of both species. It contains not less than 12 ml/kg of essential oil, of which not less than 40% is thymol and carvacrol, calculated with reference to the anhydrous drug.
Constituents

Essential oil (1.5%) contains phenols (thymol, carvacrol) and terpenoids (p-cymene). Other constituents include flavonoids (e.g. thymonin, cirsilineol and 8-methoxy-cirsilineol), „Labiatae tannin“ (rosmarinic acid), caffeic acid, triterpenoids, long-chain saturated hydrocarbons and aliphatic aldehydes, and an arabinogalactan.

![Thymi herba](image)

**Figure 1.19**

*Thymi herba* (Thyme)

**Uses**

Thyme can be used for treating catarrhs of the upper respiratory tract, bronchial catarrh and in the supportive treatment of pertussis. It has expectorant, antitussive, antibacterial, antiseptic and appetizer activity. Other uses: spice, perfumery, liqueur industry.

**Dosage**

**Internal use**

*Adults and children from 1 year:* 1-2 g of dried herb, or the equivalent amount of fresh herb, as an infusion several times a day. Tincture (1:10, 70% ethanol) – 40 drops up to
Drugs containing monoterpenes, essential oils

three times daily. Topical use: A 5% infusion as a gargle or mouth-wash. The essential oil is a dermal and mucous membrane irritant, therefore, hypersensitivity reactions may develop.

Children up to 1 year: 0.5-1 g.

Undesirable effects
In very rare cases hypersensitivity reactions have been reported.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Serpylli herba**

**Plant**

*Thymus serpyllum* L. – Wild thyme (Lamiaceae)

The plant is native to Europe and North Africa. In Hungary it grows wild (on rocky ground).

![Wild thyme](image)

**Figure 1.23**

Wild thyme (*Thymus serpyllum* L.)

**Drug**

*Serpylli herba* (Wild thyme, Ph. Eur.)

Wild thyme consists of the whole or cut, dried, flowering aerial parts of *Thymus serpyllum* L. s.l. It contains minimum 3.0 ml/kg of essential oil, calculated with reference to the dried drug.
Constituents
The characteristic constituents of the drug include 0.1-0.6% of essential oil containing thymol, carvacrol and linalool, flavonoids, “Labiatae tannin” (rosmarinic acid) and caffeic acid. The volatile oil of *T. serpyllum* contains more linalool and *p*-cymene than *T. vulgaris*.

![Chemical structures of thymol, carvacrol, and linalool](image)

**Figure 1.24**
*Serpylli herba* (Wild thyme)

**Constituents**

**Uses and Dosage**

See Thyme
Origani herba

Plants

*Origanum onites* L. (Cyprian), *O. vulgare* subsp. *hirtum* (Link) Ietsw. (Greek) - Oregano (Lamiaceae)

Plants are native to Mediterranean countries, including Cyprus.

Figure 1.28

Oregano (*O. vulgare* L.)

Drug

*Origani herba* (Oregano, Ph. Eur.)

Oregano consists of the dried leaves and flowers separated from the stems of *Origanum onites* L. or *Origanum vulgare* L. subsp. *hirtum* (Link) Ietsw., or a mixture of both species. It contains minimum 25 ml/kg of essential oil and minimum 1.5 per cent of carvacrol and thymol, calculated with reference to the dried drug.
Constituents

The characteristic constituents include 1.0% essential oil, the main components of which are thymol, carvacrol and p-cymene. Other constituents are: flavonoids, “Labiatae tannin” (rosmarinic acid), ursolic acid.

Figure 1.30-32

The structure of thymol, carvacrol and p-cymene

Uses

Oregano can be used internally for treating acute bronchitis and laryngitis. It has expectorant, antitussive, antibacterial, antiseptic and appetizer effects. Externally the drug combined with chamomille can be used for treating wounds. Oregano is a popular spice.
Dosage

**Internal use**

*Adults:* As an infusion 3-6 g of the drug in 150-200 ml of water, three times daily.

**Contra-indication**

Thymol is a skin and mucous membrane irritant, therefore hypersensitivity reactions may develop (its essential oil must not be used in children under 2 years of age).

**Saturejae herba and Saturejae aetheroleum**

**Plant**

*Satureja hortensis* L. – Savory (Lamiaceae)

Plant is native to Mediterranean countries and in Hungary it is cultivated.

**Drug**

*Saturejae herba (= folium) (Savory), Saturejae aetheroleum (Savory oil)*

*Saturejae herba* consists of the dried leaves and flowers of *Satureja hortensis* L. It contains essential oil, which is obtained by steam distillation.

![Saturejae herba](image)

**Figure 1.33**

*Saturejae herba* (Savory)

** Constituents**

Savory contains approx. 0.3-2 % essential oil, the main components of which are carvacrol and *p*-cymene. Other constituents are „Labiatae tannin” (rosmarinic acid) and ursolic acid.
Uses
Savory can be used internally in case of gastrointestinal problems. The drug has appetizer, expectorant, stomachic and carminative effects. Other uses: spice, perfumery.

Dosage
Internal use
Adults: As an infusion 1-2 g of the drug in 150-200 ml of water, three times daily.

Majoranae herba
Plant
Origanum majorana L. - Sweet marjoram (Lamiaceae)
Plant is native to Mediterranean countries and in Hungary it is cultivated.

Drug
Majoranae herba (Sweet marjoram), Majoranae aetheroleum (Sweet marjoram oil)
Sweet marjoram consists of the dried leaves and flowers of Origanum majorana L. It contains essential oil, which is obtained by steam distillation from the leaves.
Drugs containing monoterpenes, essential oils

Majoranae herba (Sweet marjoram)

Constituents

The characteristic constituents include 0.5-1.3 % essential oil, which contains \( \alpha \)- and \( \gamma \)-terpinene and sabinene as the main components. Other constituents are: „Labiatae tannin” (rosmarinic acid), chlorogenic acid, caffeic acid and flavonoids.

\[
\begin{align*}
\text{sabinene} & \quad \alpha\text{-terpinene} & \quad \gamma\text{-terpinene}
\end{align*}
\]

Uses

Sweet marjoram can be used both internally and externally. It has appetizer and carminative effects. It can increase the gastric juice secretion. In ointment the drug and its essential oil can be used for treating obstructed nose (in case of cold). Other uses: spice, perfumery

Dosage

**Internal use**

*Adults and children over 12 years of age:* As an infusion 1-2 g of the drug in 150-200 ml of water, two times a day.
External use

Adults and children over 12 years of age: In ointment 5% EO content must be applied. Do not use internally for prolonged time (because of sabinene content), and do not use the ointment externally for infants and babies.

In addition to being commonly used in cooking, marjoram has a long history of medicinal use, by the Greeks as an antidote to poisoning and snake venom, by the Romans for stomach disorders and more recently for digestive and sedative properties. However, the oil is not suitable for use by pregnant women.

Hyssopi herba

Plant

Hyssopus officinalis L. – Hyssop (Lamiaceae)

Plant is native to Mediterranean countries and in Hungary it is cultivated.

Figure 1.40

Hyssop (Hyssopus officinalis L.)

Drugs

Hyssopi herba (Hyssop), Hyssopi aetheroleum (Hyssop oil)

Hyssop consists of the dried leaves and flowers of Hyssopus officinalis L. It contains essential oil, which is obtained by steam distillation.
Constituents

The characteristic constituents include 0.3-1.0% essential oil, which contains α- and β-pinene as the main components. Other constituents are: „Labiatae tannin” (rosmarinic acid), triterpenoids, flavonoids and diterpene (marrubiin).

\[ \alpha\text{-pinene} \quad \beta\text{-pinene} \]

Uses

Hyssop can be used both internally and externally. It has appetizer, diuretic and expectorant effects. It can increase the gastric juice secretion. The drug extract has anti-perspirant activity in case of external use. Other uses: spice, perfumery.

Dosage

Internal use

*Adults and children over 12 years of age:* As an infusion 1-2 g of the drug in 150-200 ml of water, three times a day.

Special warnings and precautions for use

Hyssop essential oil: it readily causes epileptiform convulsions, increases blood pressure, therefore, it should be used with caution.
Salvia officinalis folium

Plant
Salvia officinalis L. – Sage (Lamiaceae)
Sage is native to Mediterranean areas and cultivated world-wide.

Figure 1.44
Sage (*Salvia officinalis* L.)

Drug
Salviae officinalis folium (Sage leaf, Ph. Eur.)
Sage leaf consists of the whole or cut dried leaves of *Salvia officinalis* L. The whole drug contains not less than 15 ml/kg of essential oil and the cut drug not less than 10 ml/kg of essential oil, both calculated with reference to the anhydrous drug.

Figure 1.45
*Salviae officinalis folium* (Sage leaf)
Constituents

The characteristic constituents include 1.5–2.5 % essential oil containing monoterpenes such as α- and β-thujone (up to 63%), camphor, borneol and 1,8-cineole. Other constituents are: „Labiatae tannins” (rosmarinic acid), diterpenes (carnosol), flavonoids (e.g. 5-methoxysalvigenin) and triterpenoids (ursolic and oleanolic acids and their derivatives).

![Figure 1.46-49](image)

The structure of α- and β-thujone, camphor and borneol

Uses

Sage can be used for treating inflammations and infections of the mouth and throat such as stomatitis, gingivitis and pharyngitis; as well as hyperhidrosis.

Dosage

**Topical use**

An infusion of 3 g of the drug in 150 ml of water as a mouthwash or gargle.

**Oral use (in hyperhidrosis)**

Tincture: (1:10) in 55% ethanol, 75 drops daily

Infusion: 1-1.5 g of dried herb in 150 ml of water, once or several times daily

Dry extract: 160 mg of dry aqueous extract corresponding to 880 mg of drug three times daily.

In hyperhidrosis, treatment for 2-4 weeks is recommended, using an aqueous preparation.

Caution is required with the use of alcoholic preparations because of the presence of thujone.

Sage essential oil readily causes epileptiform convulsions, increases blood pressure, therefore, it must be used with caution.

**Pregnancy and lactation**

Given the potential toxicity of some constituents of the essential oil, the use of sage leaf is not recommended during pregnancy or lactation.
Rosmarini folium and Rosmarini aetheroleum

Plant
Rosmarinus officinalis L. – Rosemary (Lamiaceae)
Rosemary is native to Mediterranean areas and cultivated world-wide. The oil is produced principally in Spain and North Africa.

Drug
Rosmarini folium (Rosemary leaf, Ph. Eur.), Rosmarini aetheroleum (Rosemary oil, Ph. Eur.)
Rosemary leaf consists of the whole, dried leaves of Rosmarinus officinalis L. It contains not less than 12 ml/kg of essential oil, and not less than 3% of total hydroxycinnamic derivatives expressed as rosmarinic acid, both calculated with respect to the anhydrous drug.
Drugs containing monoterpenes, essential oils

Constituents

The characteristic constituents include 1.0-2.5% essential oil containing 1,8-cineole, borneol, camphor, α-pinene, bornyl acetate. The composition of the oil may vary according to the chemotype or other factors. Further constituents are phenolic diterpenes such as carnosol (up to 4.6%), carnosolic acid, rosmanol, isorosmanol, „Labiatae tannin” (rosmarinic acid), triterpene alcohols (α- and β-amyrin), and flavonoids (e.g. nepetin, nepitrin).

Figure 1.51
Rosmarini folium (Rosemary leaf)

Uses

Rosemary can be used both internally and externally. The internal therapeutic indication of the herb includes the improvement of hepatic and biliary function. It can be used in case of dyspeptic complaints. The herb has cholagogue, stomachic, carminative and spasmolytic effects. The drugs can be used externally in rheumatic conditions and peripheral circulatory disorders. It can promote wound healing. The plant and its oil have insect repellent activity. Other uses: spice, perfumery, liqueur industry.

Figure 1.52-55
The structure of 1,8-cineole, borneol, camphor and α-pinene
Dosage

**Internal use**

*Adults:* Infusion - 2-4 g of rosemary leaf daily.
Fluid extract – 1:1, 45% ethanol V/V, 1.5-3 ml daily
Tincture – 1:5, 70% ethanol, 3-8.5 ml daily

**External use**

*Adults:* Ethanolic extract (1:20)
Essential oil (2% V/V) in ethanol, as an antiseptic
1 litre of a decoction (1:20, 50 g) added to bath water (twice weekly)
In ointment: 1-2% essential oil content

Special warnings and precautions for use

Rosemary essential oil readily causes epileptiform convulsions, increases blood pressure, therefore it should be used with caution. Hot baths containing rosemary preparations should be avoided by patients with large open wounds, skin lesions, feverish conditions or acute inflammation, severe circulatory disorders or hypertension. Contact dermatitis of the hands, forearms and face was reported in a man working with an extract made from rosemary leaf. The diterpene carnosol was identified as the irritant by patch testing. Rosemary essential oil contains camphor, therefore it is not used in children under 7 years of age. Camphor can pass freely through the placenta.

Pregnancy and lactation

No data available. In accordance with general medical practice, rosemary leaf and essential oil should not be used medicinally during pregnancy and lactation without medical advice.
Rosae flos and Rosae aetheroleum

Plants
Rosa species (Rose), e.g. R. damascena, R. gallica, R. alba, R. centifolia (Rosaceae)
Rose species are widely cultivated all over the world, principally in Bulgaria, Turkey and Morocco.

![Rose Flower Image](image-url)

**Figure 1.56**
Rose (*Rosa* species)

Drugs
Rosae flos (= petalam) (Rose flower), Rosae aetheroleum (Rose oil)
Oil of rose is a volatile oil obtained by distillation from the fresh flowers of different *Rosa* species. The chief producing countries are Bulgaria, Turkey and Morocco, but smaller quantities are prepared elsewhere. Approximately 3000 parts of flowers yield only one part of oil. The oil is very expensive and very liable to adulteration.

Constituents
Rose petals contain approx. 0.2 % *essential oil* containing geraniol, citronellol and nerol. Although the monoterpane alcohols form about 70-75% of the oil, the odour is characteristically modified by the other constituents, such as sulphur containing compounds, thus no artificial mixture of the known constituents can be made to reproduce the odour of the natural oil. Other constituents are: tannins and flavonoids.
Uses
The rose extract has adstringent activity, and in floral water it is cleanser and has anti-inflammatory effect. Oil of rose is of great importance in perfumery and cosmetics.

Juniperi pseudo-fructus and Juniperi aetheroleum

Plant
Juniperus communis L. – Juniper (Cupressaceae)
Juniper is a circumpolar species. It can grow on chalky ground and sandy soil. The berries are collected in former Yugoslavia, Italy, Hungary, Poland, Sweden and other countries.
Drugs containing monoterpenes, essential oils

Figure 1.60
Juniper (Juniperus communis L.)

Drug

*Juniperi pseudo-fructus* (Juniper berry, Ph. Eur.), *Juniperi aetheroleum* (Juniper oil, Ph. Eur.)

Juniper berry consists of the dried ripe cone berry of *Juniperus communis* L. It contains not less than 10 ml/kg of essential oil, calculated with reference to the anhydrous drug. The essential oil can be obtained by steam distillation from the ripe cone berries.
Constituents
Essential oil (0.8-2%) of very variable composition depending on the source but consisting mainly of monoterpenes, principally α-pinene (24.1-55.4%). Other compounds of the essential oil are: sabinen, terpinen-4-ol, β-caryophyllene. Other constituents of the drug include condensed tannins, flavonoids, diterpene acids, aldehydes and alcohols, fatty alcohols and about 30% of glucose and fructose.

![Chemical structures](image)

α-pinene  terpinen-4-ol  sabinene  β-caryophyllene

Uses
Juniper has widely documented uses as a remedy to enhance the renal elimination of water and for dyspeptic complaints. It has strong diuretic and antiseptic effects. The ointment made from juniper extract can be used for treating rheumatic pain. In Slovenia an alcoholic drink (gin) is prepared from the berries.
Drugs containing monoterpenes, essential oils

Dosage

**Internal use**

*Adults:* 2-3 g of dried berries as an infusion in 150 ml of hot water, 3-4 times daily. Tincture (1:5 in ethanol 45%), 1-2 ml, 3 times daily.

**External use**

In bath: 30-50 g drug in 1.5 L hot water (filtrate can be used)

**Special warnings, interactions**

Juniper should not be used for more than 4 weeks without consulting a doctor. Acute or chronic inflammation of the kidney may occur. Juniper may influence glucose levels in patients with diabetes.

**Pregnancy and lactation**

Juniper should not be used during pregnancy and lactation. Abortifacient activity of juniper has been observed in rats after oral administration of a 50% ethanolic extract at 300 mg/kg bodyweight.

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**Camphor and Camphorae aetheroleum**

**Plant**

*Cinnamomum camphora* (L.) Sieb. et Presl. – Camphor (Lauraceae)

The plant is widely grown in Taiwan, Japan and South China.

**Drug**

Camphorae aetheroleum (Camphor oil), Camphor (= prepared from the steam distillation of the wood)

The best yield of camphor is obtained from old trees. The wood is cut into chips and treated with steam, when a solid sublimate of camphor and liquid volatile oil pass into the receiver. Camphor can also be prepared from the leaves.
Constituents

The wood contains essential oil with a high amount of camphor. In China 5 chemotypes can be distinguished: camphor-type, linalool-type, cineol-type, borneol-type and iso-nerolidol-type. Camphor has a characteristic odour and a pungent, aromatic taste, which is followed by a cold sensation.

![Chemical structure of camphor](image)

**Figure 1.66**
Camphor

**Figure 1.67**
The structure of camphor

Uses

Camphor is used externally as a rubefacient, and internally as a mild antiseptic and carminative. Oil of camphor tree is of great importance in perfumery and cosmetics.

Special warnings

Camphor should not be used in children under 7 years of age, because it can cause epileptiform convulsions, and passes freely through the placenta.
Drugs containing monoterpenes, essential oils

Eucalypti folium and Eucalypti aetheroleum

Plant

Eucalyptus globulus Labill. – Eucalyptus (Myrtaceae)

Eucalyptus is native to Australia, and is cultivated world-wide. Oil is produced in Portugal, South Africa, Spain, China, Brazil, Australia, India and Paraguay.

Drug

_Eucalypti folium_ (Eucalyptus leaf, Ph. Eur.), _Eucalypti aetheroleum_ (Eucalyptus oil, Ph. Eur.)

Eucalyptus leaf consists of the whole or cut dried leaves from older branches of _Eucalyptus globulus_ Labill. The whole drug contains not less than 20 ml/kg of essential oil and the cut drug not less than 15 ml/kg of essential oil, both calculated with reference to the anhydrous drug. Eucalyptus oil is obtained by steam distillation and rectification from the fresh leaves or the fresh terminal branchlets of various species of _Eucalyptus_ rich in 1,8-cineole. The species mainly used are _Eucalyptus globulus_ Labill., _Eucalyptus polybractea_ R.T. Baker and _Eucalyptus smithii_ R.T. Baker.
Constituents

Eucalyptus leaf contains 1-3.5% essential oil. The rectified oil contains 70-90% of 1,8-cineole. Other components of the oil are α- and β-pinene, γ-terpinene, p-cymene. The leaf contains tannins, flavonoids and triterpenes.

Uses

Eucalyptus leaf and oil can be used both internally and externally. In case of internal use the therapeutic indications include adjuvant treatment of chronic obstructive respiratory complaints (bronchitis) and bronchial asthma. It can be used for treating colds and catarrhs of the upper respiratory tract. It has expectorant and antiseptic activity.

It is taken internally in the form of mixtures, lozenges and pastilles, and by inhalation; while externally it is applied in ointments. Externally it can relieve the rheumatic complaints.
Dosage (of the oil)

**Internal use**
0.05-0.2 ml per dose; in capsules: 100-200 mg, 2-5 times daily

**External use**
By inhalation: 12 drops per 150 ml of boiling water, or a 1.5% V/V solution prepared from 1 tablespoon (15 ml) per litre of warm water, treatment may be repeated up to three times daily.

As a liniment: containing 25% V/V of oil.

As an ointment: containing 1.3% V/m, for adults and children over 12 years: to be applied as a thick layer, up to three times daily.

As a lozenge: 0.2-15 mg dissolved slowly in the mouth, repeated every 0.5-1 hour.

As a mouthwash: containing 0.9 mg/ml; 20 ml as a gargle twice daily.

**Contra-indications, special warnings, interactions**
Eucalyptus must not be used internally in cases of inflammation of the gastrointestinal tract or gall bladder, or when liver function is impaired. Eucalyptus oil and its preparations should not be applied to the face, especially the nose, of babies and little children. The oil induced hepatic microsomal enzyme activity in both *in vitro* and *in vivo* tests.

**Pregnancy and lactation**
Since human data are not available, eucalyptus should not be used during pregnancy and lactation without medical advice.

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**Carvi fructus**

**Plant**
*Carum carvi* L. - Caraway (Apiaceae)
It occurs both wild and cultivated in central and northern Europe.

**Drug**
*Carvi fructus* (Caraway fruit, Ph. Eur.)
Caraway fruit consists of the whole, dry mericarp of *Carum carvi* L. It contains not less than 30 ml/kg of essential oil, calculated with reference to the anhydrous drug.
Constituents
The characteristic constituent of caraway is essential oil (3-7 %). It consists of the ketone carvone and the monoterpenic limonene with small quantities of dihydrocarvone, carveol and dihydrocarveol. It also contains 10-18% of fixed oil, of which the main components are petroselinic (30-43%), linoleic (34-37%), oleic (15-25%) and palmitic (4-5%) acids. Other constituents include about 20% of protein, 15% carbohydrates, phenolic acids, mainly caffèic acid, and traces of flavonoids (quercetin, kaempferol and their glycosides).

Uses
Caraway has carminative and antispasmodic effects, therefore it can be used for treating gastrointestinal problems, such as flatulence, bloating. The carminative and antispasmodic properties have been experimentally verified. It is a culinary herb, spice and liqueur-aroma. Caraway can also treat the flatulent colic of infants.
Dosage

**Dried fruits – Internal use**

*Adults and children over 10 years of age:* 1.5-6 g of caraway fruit daily. 1-5 g of caraway fruit, crushed directly before use, covered with 150 ml of boiling water and allowed to stand for 10-15 min. A cup of warm tea is taken 1-3 times daily.

*Children from 4 to 10 years:* 1-4 g daily
*Children from 1 to 4 years:* 1-2 g daily
*Children up to 1 year:* 1 g daily

Caraway oil for children – Internal use

*Children above 4 years:* 3-6 drops daily
*Children from 1 to 4 years:* 2-4 drops daily
*Children up to 1 year:* 1-2 drops daily

**Caraway oil for children – External use (in case of flatulent colic)**

10% in a carrier oil, for example olive oil

**Contra-indication**

Sensitivity to Apiaceae (Umbelliferae).

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

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**Coriandri fructus and Coriandri aetheroleum**

**Plant**

Coriandrum sativum L. var. vulgare Alef.  -Coriander (Apiaceae)

It is indigenous to Italy, but is widely cultivated in the Netherlands, Central and Eastern Europe, the Mediterranean region (Morocco, Malta, Egypt), India, China and Bangladesh.

**Drug**

*Coriandri fructus* (Coriander fruit, Ph. Eur.), *Coriandri aetheroleum* (Coriander oil, Ph. Eur.)

Coriander consists of the dried cremocarp of *Coriandrum sativum* L. It contains not less than 3 ml/kg of essential oil, calculated with reference to the dried drug. Essential oil can be obtained by steam distillation from the fruits of *Coriandrum sativum* L. During ordinary storage of the fruits, the oil composition undergoes considerable alteration.
Constituents

The fruits contain 1.5-2.5% of essential oil. The main component of the oil is linalool (65-70%, depending on the source), and other components include α-pinene and limonene. Other constituents isolated from the fruits are coumarins, flavonoids and phenolic acids. The high content of fats (16-28%) and protein (11-17%) in the fruits make distillation residues suitable for animal feed.

Uses

Pharmacologically coriander and its oil are used as a flavouring agent (muscat taste), carminative and spasmylytic. It is a culinary herb. The oil is also used in perfumery industry.

Dosage

Dried fruits – Internal use

Adults: 1 g in 200 ml hot water, 3 times daily.
Aurantii amari epicarpium et mesocarpium

Plant

*Citrus aurantium* L. subsp. *amara* Engl. – Bitter orange (Rutaceae)

Bitter orange is native to North India, South China, but is cultivated elsewhere. Sweet orange is more widely cultivated, than bitter orange.

![Orange tree](image)

**Figure 1.81**
Orange (*Citrus aurantium* L.)

Drugs

(in the Ph. Eur.)

1 *Aurantii amari epicarpium et mesocarpium* - Bitter-orange epicarp and mesocarp

Dried epicarp and mesocarp of the ripe fruit of *Citrus aurantium* L. ssp. *aurantium* (*C. aurantium* L. ssp. *amara* Engl.) partly freed from the white spongy tissue of the mesocarp and endocarp. **Content**: minimum 20 ml/kg of essential oil (anhydrous drug).

2 *Aurantii amari epicarpii et mesocarpii tinctura* - Bitter-orange-epicarp and mesocarp tincture

The tincture is produced from 1 part of the freshly powdered drug and 5 parts of *alcohol (70 per cent V/V)* by an appropriate procedure.

3 *Aurantii amari flos* - Bitter-orange flower

It consists of the whole, dried, unopened flower of *Citrus aurantium* L. ssp. *aurantium* (*C. aurantium* L. ssp. *amara* Engl.). **Content**: minimum 8.0 per cent of total flavonoids, expressed as naringin (dried drug).

4 *Aurantii amari floris aetheroleum* - Bitter-orange-flower oil (Neroli oil)

Bitter-orange-flower oil is obtained by steam distillation from the fresh flowers of *Citrus aurantium* L. subsp. *aurantium* (*C. aurantium* L. subsp. *amara* Engl.).
Petitgrain aetheroleum (Paraguay) – from the fruits (is not official)

Constituents
Dried bitter orange peel contains not less than 2.5% of essential oil (linalyl acetate is the main component), vitamin C and flavonoid glycosides (hesperidin, neohesperidin).

\[
\begin{align*}
&\text{linalyl acetate} \\
&\text{(Bitter-orange epicarp and mesocarp)}
\end{align*}
\]

Uses
Bitter orange peel is used as a flavouring agent and as a bitter tonic. Its essential oil is used in the perfume industry (perfume, soaps).
Hesperidin in the soluble form functions as “vitamin P” (P = permeability). This molecule can reduce the permeability of capillary vessels.
Dr. Albert Szent-Györgyi had an important role in the discovery of Vitamin P.

Dosage
Single dose: 2 g

Contra-indications, special warnings
Patients with stomach and duodenal ulcer must not use the drug and its oil!
Drugs containing monoterpenes, essential oils

Coumarins have photosensitising effect in case of external use!

**Aurantii dulcis aetheroleum**

**Plant**

Citrus aurantium L. subsp. sinensis Engl. – Sweet orange (Rutaceae), (syn.: C. sinensis (L.) Osbeck., C. aurantium L. var. dulcis L.)

Sweet orange is native to India, China, the Mediterranean, and it is cultivated.

**Drug**

*Aurantii dulcis aetheroleum* (Sweet orange oil, Ph. Eur.)

Essential oil obtained without heating, by suitable mechanical squeezing from the fresh peel of the fruit of *Citrus sinensis* (L.) Osbeck (*Citrus aurantium* L. var. dulcis L.). A suitable antioxidant may be added. The peel of sweet orange is thinner than that of the bitter variety, its yellow colour is more pronounced and the taste is aromatic. As studied in Valencia orange peel, the colour originates from a complex mixture of carotenoids, the principal components being violeoxanthin (9-cis-violaxanthin), di-cis-violaxanthin and all-trans-violaxanthin together with a number of other carotenoids.

**Constituents**

Sweet orange peel contains 0.4-0.9 % essential oil. The main components of the oil are limonene, citral, neral, α-terpinene and sinensal. Other constituents include flavonoids (mainly naringenin) and carotenoids (e.g. 9-cis-violaxanthin).

![Chemical structures](image)

**Figure 1.84-87**

The structure of limonene, citral, neral and α-terpinene

**Uses**

Sweet orange oil is used in the perfumery industry and as a seasoning material in the food industry. Brazil and USA are the largest producers of sweet orange oil.

**Cardamom fruit and oil**

**Plant**

*Elettaria cardamomum* White et Maton - Cardamom (Zingiberaceae)
Principal producers are Sri Lanka, southern India, Guatemala. Although wild plants are found in India and Sri Lanka, cardamoms are mainly obtained from cultivated plants.

**Drug**

*Cardamomi fructus* (Cardamom fruit, Hungarian Pharmacopoeia VII.), *Cardamomi aetheroleum* (Cardamom oil)

Cardamom consists of the dried, nearly ripe fruits of *Elettaria cardamomum*. The seeds should be kept in the fruits until required for use. This prevents loss of essential oil and helps one to distinguish the fruits from those of *E. cardamomum var. major* (unofficial long wild native cardamom).

![Cardamom fruit](image)

**Figure 1.88**

*Cardamomi fructus* (Cardamom fruit)

**Constituents**

Cardamom contains 1-4% essential oil. 1,8-cineole and terpinyl acetate are the main components of the essential oil. The essential oil composition varies according to the *Elettaria* species and varieties. Other constituents include starch (50%), fixed oil (1-10%) and calcium oxalate.
Uses
Cardamom is used as a flavouring agent in curries and cakes and as a spice. The oil is applied in perfumery industry and in the manufacture of liqueurs. Pharmaceutically it has carminative effect and is used in tinctures.

Dosage
0.6-2 g seed/daily, 25 drops from the tincture to one glass of water.

Tanaceti herba

Plant
Tanacetum vulgare L. - Tansy (Asteraceae) (syn.: Chrysanthemum vulgare (L.) Bernh.)
Tansy is native to Europe and Asia. Tansy is used as an anthelminhtic in herbal medicine but its poisonous properties are also appreciated.

Figure 1.89-90
The structure of 1,8-cineole and terpinyl acetate

1,8-cineole
(= eucalyptol)

α-terpinyl acetate

Figure 1.91
Tansy (Tanacetum vulgare L.)
Pharmacognosy 2

Drug
Tanaceti herba (Tansy), Tanaceti aetheroleum (= Chrysanthemi aetheroleum, Tansy oil)

Constituents
It contains 0.5-1 % essential oil. Thujones are the main components of the oil. Several sesquiterpene lactones have been isolated from the flowers and shoot together with flavones. Numerous chemical races (originating from different geographical areas) are known.

![Figure 1.92-93](image)
The structure of α- and β-thujone

Uses
Anthelminthic (consultation with doctor!)

Dosage

Pregnancy and lactation
Tansy and its essential oil must not be used during pregnancy or lactation.

Myrrha

Plant
Commiphora molmol (Nees) Engl. - Myrrh (Burseraceae)
The plant is native to north-east Africa and Arabia.

Drug
Myrrha (Myrrh, Ph. Eur.), Myrrhae tinctura (Myrrh tincture, Ph. Eur.)
Myrrh consists of a gum-resin, which hardens in air, obtained by incision or produced by spontaneous exudation from the stem and branches of Commiphora molmol Engler and/or other species of Commiphora. Species other than C. molmol which may be acceptable sources of medicinal myrrh include C. abyssinica (Berg) Eng., and C. schimperi (Berg) Engl. The tincture is produced from 1 part of the drug and 5 parts of ethanol (90 per cent V/V) by a suitable procedure.

Constituents
Myrrh can be separated into three components: essential oil (6-7%), resin (25-40%) and gum (30-60%). The main constituents of the essential oil are furanosesquiterpenes of various structural types including furanoeudesma-1,3-diene, furanoeudesma-1,4-diene-
Drugs containing monoterpenes, essential oils

6-one, curzerenone, furanodiene, together with sesquiterpenes such as α-copaene and elemene and monoterpen (α-pinene). Characteristic constituents of the resin are α-, β- and γ-commiphoric acids. The gum consists mainly of a proteoglycan, in which chains of alternating galactose and 4-O-methyl-glucuronic acid, and separate chains of arabinose, are attached to the protein through hydroxyproline links.

![Chemical structures](image)

**Figure 1.94-98**
The structure of furanoeudesma-1,4-diene-6-one, curzerenone, furanodiene, α-copaene and α-pinene

**Uses**

Therapeutic indications of myrrh include topical treatment of gingivitis, stomatitis (aphthous ulcers), minor skin inflammations, minor wounds, supportive treatment for pharyngitis, tonsillitis.

**Dosage**

*Adults and elderly*: As a gargle or mouthwash, 1-5 ml of tincture (1:5, ethanol 90% V/V) in a glass of water several times daily. For use on skin, dab 2-3 times daily with diluted or undiluted tincture.

*Children*: as for adults except using only diluted tincture on skin.

**Special warnings, undesirable effects**

Because of alcohol content, a transient burning sensation on the skin may be experienced depending on the level of dilution of the tincture. Very rare cases of allergic contact dermatitis have been reported.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.
Orthosiphonis folium

Plant
Orthosiphon aristatus (Blume) Miq. – Java tea (Lamiaceae) (syn.: O. stamineus Benth., O. spicatus (Thunb.) Bak.)
The plant is native to China, east-Asia, Malaysia and Australia. In Java the native people use this plant against hypertension and as an antirheumatic drug.

Drug
Orthosiphonis folium (Java Tea, Ph. Eur.)
Java tea consists of the fragmented, dried leaves and tops of stems of Orthosiphon stamineus Benth. (O. aristatus Miq.; O. spicatus Bak.). Content: minimum 0.05 per cent of sinensetin (dried drug).

Figure 1.99
Orthosiphonis folium (Java tea)

Constituents
Java tea contains 0.02-0.7% essential oil (the main component is β-caryophyllene). Other characteristic constituents include diterpenes, flavonoids (sinensetin), rosmarinic acid, up to 12% of minerals with a high proportion of potassium.
Uses
Therapeutic indications of the drug include the irrigation of the urinary tract, especially in cases of inflammation and renal gravel, and as an adjuvant in the treatment of bacterial infections of the urinary tract.

Dosage
*Adults:* An infusion of 2-3 g of dried material in 150 ml of water 2-3 times daily.

Special warnings
Java tea should not be used in patients with oedema due to impaired heart and kidney function.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.
Chapter 2

Essential oils

2.1 Description of essential oils

Definition of essential oils
Essential oils are extracted from plants through steam distillation or expression. They have complex composition. They evaporate completely at room temperature.

Uses of essential oils
1. Pharmaceutical industry: scenting of ointments, creams, seasoning materials
2. Holistic medicine/natural healing, phytotherapy, aromatherapy: in herbal medicines, dietary supplements, massage oils, bath oils
3. Cosmetic and perfumery industry
4. Food industry: flavours and essences (confectionery, liqueurs)
5. Plant protection: natural pesticides (against infections), preserving materials
6. Veterinary medicine: massage oils, products against respiratory diseases (in horses)

Fields of their safe applications/uses
- Treatment of infections caused by bacteria and fungi
- Odour control of hospital-wards, prevention of the spread of infections
- Treatment of inflammations in the mouth
- Treatment of respiratory diseases (e.g. pharyngitis, asthma, bronchitis, COPD)
- Treatment of gastrointestinal problems (cramps in the stomach and intestines)
- Treatment of locomotor disorders (e.g. rheuma)
- Treatment of diseases of the skin (e.g. acne, wounds)
- Treatment of respiratory symptoms of smokers
- Treatment of mild depression, anxiety, insomnia, irritability
- To increase the ability to concentrate, to pay attention to something
- To decrease the symptoms of migraine
- To decrease the complaints before or after giving birth/delivery (pain, anxiety, treatment/cleaning of perineal wounds)
- Palliative treatment of patients suffering from a tumor, and long-stay patients (against abscess, decubital ulcer)
For therapeutic purposes essential oils are administered by inhalation (e.g. eucalyptus oil), orally (e.g. peppermint oil), as gargles and mouthwashes (e.g. thyme oil) and transdermally (e.g. lavender oil, rosemary oil).

**Definition of aromatherapy**

Aromatherapy is a form of alternative medicine that uses volatile plant materials, known as essential oils, and other aromatic compounds for the purpose of altering a person's mind, mood, cognitive function or health.

Essential oils containing a high amount (25 -30%) of ketones, e.g. peppermint oil, and phenols, e.g. thymol, in the thyme oil, **must be used in low dose and for a short period only!**

**Extraction techniques of essential oils**

The most important extraction techniques of essential oils include distillation (steam or water), expression, solvent extraction, enfleurage and maceration.

**Distillation**

Distillation is the most commonly used method for the extraction of essential oils. There are two techniques of distillation: *water* and *steam*.

**Water distillation**

The distillation apparatus, commonly called a ‘still’, consists of a vessel for plant material and water, a condenser to cool and condense the vapour produced and a vessel for collection, or ‘receiver’.

Material from the appropriate part of the plant for extraction is immersed in water in the distillation vessel. This is then heated to boiling point and the steam (water vapour) carries the volatile oils. The water safeguards some components by preventing overheating as the temperature will not exceed 100 °C (the boiling point of water at normal pressure). However, distillation can be a long process and water may damage some other compounds.

**Essential oils with a high percentage of esters can become hydrolyzed** (hydrolysis is a chemical reaction of a substance with water) **by contact with the hot water, which breaks them down to their constituent alcohols and carboxylic acids. E.g. in lavender, linalyl acetate can break down into linalool and acetic acid, so a short distillation time is favourable.**

**Steam distillation**

In steam distillation, steam – which is water vapour – is passed through the plant material at high pressure. Constituents that are insoluble in the water but volatile enough to be driven off by the steam come over and are cooled, condensed and collected in the receiving vessel.

The resultant liquid is a mixture of immiscible oil and water, which separate.

Steam distillation is economical in processing large amounts of material, requiring little labour or complex extraction apparatus.
The aqueous (water) portions left over from initial distillation are called hydrosols or floral waters, e.g. lavender, rose. They have many uses alongside essential oils and are utilized in the skin care and perfumery industries.

Essential oils extracted by water or steam distillation need further purification, especially drying to remove water. Essential oils produced by distillation are limited to compounds with a maximum molecular weight of 225–250.

**Expression**

Expression is the use of a crushing, mechanically applied pressure to squeeze oils from plant material. It was originally done by hand but is now mechanized, with use of centrifugal separators. Expression is used almost exclusively for citrus fruits with oil glands in the outer rind of the fruit. E.g. bergamot and lemon essential oils, which are very volatile owing to being rich in monoterpenes. Many of these would be lost in distillation because of the high temperatures. It is also a cheap method, using by-products from the juice industry.

**Solvent extraction**

Aromatic plant material is placed into organic solvents such as acetone or hexane, which dissolve the oils. Other solvents used are methanol, ethanol, toluene and petroleum ether.

The materials that become dissolved include not only the essential oil but also natural waxes, resinous materials, chlorophyll and other pigments. Solvent is then recovered in a still at reduced pressure, which lowers the solvent’s boiling point and permits the use of gentle heat. The concentrated extract is not distilled but is retained in the vessel in a liquid state. When it is removed and cooled, the concentrated extract solidifies to a waxy consistency called a concrete, which is made up of approximately 50% odourless wax. The unwanted wax is removed by washing with alcohol, which extracts the essential oil. The alcohol mixture is then filtered and alcohol is removed by vacuum distillation. The final residue is called the absolute.

**Enfleurage**

Enfleurage is a method that has long tradition, producing a rather impure product. Thin layers of cold, odourless fat such as lard (from pig) are coated onto glass plates and the plant material is spread in layers onto the top of the fat.

When the fat is saturated, it is washed with hexane to dissolve the essential oil.

After removal of hexane, the residue is washed with alcohol and the resultant solution is evaporated to give purer essential oil, or more strictly an absolute.

The true pomades are products of enfleurage as they are the fragrance-saturated fat.

Enfleurage was used to extract oils from delicate petals. It is very labour intensive and can last up to three months.
Pharmacological effects and ways of administration of essential oils (with some examples)

1. **Expectorant, antibacterial**: anise, sweet fennel, thyme, peppermint, sweet orange, lemon, sage, pine, chamomile, cinnamon, eucalyptus

2. **Anti-inflammatory, inhalation, treating of mouth**: chamomile, sage, eucalyptus, cinnamon, thyme

3. **Appetizer**: anise, sweet flag (*Acorus*), sweet fennel, bitter orange, peppermint, cinnamon

4. **Cholagogue**: Acorus, fennel, lavender, peppermint

5. **Carminative**: anise, sweet fennel, fennel, coriander, basil

6. **Spasmolytic**: chamomile, fennel, peppermint, cinnamon, yarrow (*Achillea*)

7. **Diuretic**: lovage, parsley, juniper

8. **Increase local circulation**: rosemary, lavender, pine, lemon, juniper

9. **Against headache (in compress)**: lemon, orange, pine, lavender

10. **Treatment of pollen allergy (dry inhalation)**: peppermint, chamomile

11. **Air freshener**: lavender, cinnamon, eucalyptus, pine

When essential oils are used externally, they should be diluted in vegetable oils e.g. in sweet almond oil, avocado oil, jojoba or olive oil.

**Special warnings, contra-indications**

The following essential oils may not be used for medicinal purposes or are used with some restriction after medical advice. These oils are not safe in case of aromatherapeutic application.

**Peppermint oil**

It should not be used in infants, babies and little children (until 7 years of age), because apnoea and collapse of lung or cardiac arrest may occur.

**Thyme oil**

It should not be used in little children (under 5 years of age) and patients with epilepsy or disease of the thyroid gland. Thyme oil is a dermal and mucous membrane irritant (thymol content).

**Oregano oil**

Because of thymol content this oil is a skin and mucous membrane irritant. It should not be used in children under 2 years of age.

**Rosemary oil**

This oil contains camphor, which can readily cause epileptiform convulsions. It should be used with caution (in oral dose).

**Juniper oil**

It should not be used during pregnancy and in patients with kidney disease. It has abortifacient activity and can enhance the inflammation in the kidney.
Camphor
It should not be used in children under 7 years of age, see peppermint. Epileptiform convulsions may occur. It can pass freely through the placenta.

Bitter orange oil
It should not be used orally in patients with gastric and duodenal ulcer. It has moderate phototoxic effect – if this oil is applied to the skin at a concentration over max. use level (1.4%), skin must not be exposed to sunlight or sunbed rays for 12 h.

Melissa oil
Skin sensitisation reaction possible; citral can cause a rise in ocular tension (oral use should be avoided in patients with glaucoma).

Lemon, Sweet orange oil
See bitter orange.

Eucalyptus oil
See camphor.

Cinnamon bark oil
Moderate dermal irritant, strong dermal sensitiser, moderate mucous membrane irritant; externally max. use level 0.1%!

Essential oils increasing blood pressure
- Rosemary
- Hyssop
- Cedar
- Common Sage (Dalmatian)
- Thyme

Essential oils causing epileptiform convulsions
- Sweet fennel
- Hyssop
- Camphor
- Common Sage (Dalmatian)
- Rosemary

Safe essential oils during pregnancy
In the first trimester essential oils must not be used! After the first trimester the following essential oils may be used after medical consultation: chamomile, roman chamomile, clary sage, ginger, lavender, neroli, rose, sandalwood.
Safe essential oils in babies and children
Chamomile, roman chamomile, lavender, clary sage. These oils may be used after medical consultation.

Essential oil (in the case of external use)
1-6 month: maximum 1%
6-24 month: 2%
2-10 years: 3%
over 10 years: 5%

Drugs

Melaleucae aetheroleum

Plant
Melaleuca alternifolia (Maiden et Betch) Cheel – Tea tree (Myrtaceae)
The plant is native to Australia. 3-6 m high shrub or tree. Australians use the oil against insect bites.

Drug
Melaleucae aetheroleum (Tea tree oil, Ph. Eur.)
Essential oil obtained by steam distillation from the foliage and terminal branchlets of Melaleuca alternifolia (Maiden and Betch) Cheel, M. linariifolia Smith, M. dissitiflora F. Mueller and/or other species of Melaleuca.

Appearance of the essential oil
Clear, mobile, colourless to pale yellow liquid with a characteristic odour.

Constituents
2% essential oil. The major components of tea tree oil are the monoterpenes terpinen-4-ol (minimum 30%), γ-terpinene (10-28%) and 1,8-cineole (less than 15%).

\[
\begin{align*}
\text{terpinen-4-ol} & \quad \text{(= eucalyptol)} \\
\end{align*}
\]

\[
\begin{align*}
\text{1,8-cineole} \\
\end{align*}
\]

Figure 2.1-2
The structure of terpinen-4-ol and 1,8-cineole
Characteristics
Antiseptic, antibacterial, antifungal, antiviral

Uses

Primary use
Skin care (mycosis of the legs, *Candida* infection, acne, tinea pedis, dandruff)

Other uses
Respiratory infections (cold, influenza, bronchitis), vaginal infections (trichomonal vaginitis, vaginal candidiasis and related cervicitis), cosmetic- and perfumery industry.

Dosage
External application: liquid or semi-solid preparations containing 5-10% m/m of tea tree oil. Higher concentrations have been used for certain conditions, e.g. tinea pedis (25-50% m/m). Female genital tract: depending on the indication, pessaries containing 200 mg of tea tree oil (approx. 10% in an oily vehicle) or tampons/douches containing solutions of 0.4-20% of the oil. Rarely it can cause allergy (contact dermatitis).

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Anisi aetheroleum (1) and Anisi stellati aetheroleum (2)

Plants
(1) *Pimpinella anisum* L. – Anise (Apiaceae), (2) *Illicium verum* Hook. – Star Anise (Illiciaceae)

*P. anisum* is native to the East-Mediterranean, and in Hungary it is cultivated. *I. verum* is native to China and Vietnam.

Drugs
(1) *Anisi aetheroleum* (Anise oil), (2) *Anisi stellati aetheroleum* (Star anise oil, Ph. Eur.)

(1) Essential oil obtained by steam distillation from the dry ripe fruits of *Pimpinella anisum* L. (2) Essential oil obtained by steam distillation from the dry ripe fruits of *Illicium verum* Hook.
Figure 2.3-4
Anisi fructus (Anise fruit) and Anisi stellati fructus (Star anise fruit)

Appearance of the essential oil
Clear, colourless or pale yellow liquid. The oil can be jellified at 14-16 °C because of trans-anethole content.

Constituents
2-6 % essential oil of anise. The major components of anise oil are trans-anethole (80-95%) and anisaldehyde. 5-8% essential oil of star anise. The major components of star anise oil are trans-anethole and methyl-cavicol.

\[
\begin{align*}
\text{trans-anethole} & \quad \text{anisaldehyde} & \quad \text{methyl chavicol} (= \text{estragole}) \\
\end{align*}
\]

Figure 2.5-7
The structure of trans-anethole, anisaldehyde and methyl-cavicol

Characteristics
Antiseptic, antibacterial, antifungal, spasmolytic, carminative.

Uses
Primary use
Gastrointestinal problems (flatulence, cramps), respiratory complaints (bronchitis, cough).

Other uses
Food industry (in lozenge, liqueur), soap- and toothpaste-scenting.

Contra-indications
Persons with known sensitivity to anethole should avoid aniseed and its oil.
Essential oils

Dosage
0.3 g (12 drops): daily dose (drop on sugar cube). Do not use under 2 years of age.

Pregnancy and lactation
Preparations containing the essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

**Aurantii dulcis aetheroleum**

Plant
*Citrus aurantium* L. subsp. *sinensis* Engl. – Sweet orange (Rutaceae)
Sweet orange is native to India, China and Mediterranean countries. Elsewhere it is cultivated.

Drug
*Aurantii dulcis aetheroleum* (Sweet orange oil, Ph. Eur.)
Essential oil obtained without heating, by suitable mechanical treatment from the fresh peel of the fruit of *Citrus sinensis* (L.) Osbeck (*Citrus aurantium* L. var. *dulcis* L.). A suitable antioxidant may be added.

Appearance of the essential oil
Clear, pale yellow to orange, mobile liquid, which may become cloudy when chilled. It has a characteristic odour of fresh orange peel.

Constituents
0.4-0.9 % essential oil. The major components of sweet orange oil are limonene and nerol. Coumarine is found in the peel of sweet orange.

Characteristics
Antiseptic, regenerating of the skin, increase digestion, sedative.

Uses
**Primary use**
In cosmetics (acne, cellulitis), for oily and combined skin.

**Other uses**
Aroma bath, oral hygiene. The tincture of the oil is a seasoning material in the food industry.

Special warning
Externally the oil may be phototoxic because of the coumarin content.

**Aurantii amari floris aetheroleum**

Plant
*Citrus aurantium* L. subsp. *amara* Engl. – Bitter orange (Rutaceae)
Pharmacognosy

Bitter orange is native to North-east India, South-China and it is also cultivated. The flowers are usually collected from older trees. 1 kg essential oil can be extracted from approx. 1000 kg flowers.

**Drug**

*Aurantii amari floris aetheroleum* (Bitter orange flower oil, Ph. Eur.) = *Neroli aetheroleum*

Bitter-orange-flower oil is obtained by steam distillation from the fresh flowers of *Citrus aurantium* L. subsp. *aurantium* (*C. aurantium* L. subsp. *amara* Engl.).

**Appearance of the essential oil**

A clear, pale-yellow or dark-yellow liquid, with a characteristic odour reminiscent of bitter-orange flowers, miscible with alcohol, with light petroleum, with fatty oils and with liquid paraffin.

** Constituents**

1-2 % essential oil. The main components of the oil are limonene and citronellol.

**Characteristics**

Improves digestion, sedative, regenerates the skin.

**Uses**

**Primary use**

Appetizer, skin care.

**Other uses**

In aromatherapy (bath, sedative).

**Special warning**

Externally the oil may be phototoxic because of the coumarin content.

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**Carvi aetheroleum**

**Plant**

*Carum carvi* L. – Caraway (Apiaceae)

The plant is native to Europe and Asia, and can also be cultivated.

**Drug**

*Carvi aetheroleum* (Caraway oil, Ph. Hg. VII.)

Caraway oil is obtained by steam distillation from the dried, ripe fruits of *Carum carvi* L.

**Appearance of the essential oil**

A clear colourless or yellow liquid with characteristic „caraway smell“.

** Constituents**

3-7% essential oil. The oil consists of the ketone carvone and the terpene limonene with small quantities of dihydrocarvone, carveol and dihydrocarveol.
Essential oils

Characteristics
Improves digestion, spasmolytic, carminative, antifungal.

Uses
Primary use
Gastrointestinal problems. Tea (infusion) made from the fruits can be used in pediatrics.

Dosage
3-6 drops daily

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Caryophylli floris aetheroleum

Plant
Syzygium aromaticum (L.) Merill et L.M. Perry – Clove (Myrtaceae)
The plant is indigenous to Madagascar, Mauritius and Molucca Islands. It is cultivated in Zanzibar and in the neighbouring island of Pemba.

Drug
Caryophylli floris aetheroleum (Clove oil, Ph. Eur.)
Clove oil is obtained by steam distillation from the dried flower buds of Syzygium aromaticum (L.) Merill et L. M. Perry (Eugenia caryophyllus C. Spreng. Bull. et Harr.).
Appearance of the essential oil

A clear, yellow liquid which becomes brown when exposed to air, miscible with methylene chloride, toluene and fatty oils. Its density is higher than that of water. Clove oil, like other essential oils, should be stored in well-filled, airtight containers, protected from light and heat.

 Constituents

15-25% essential oil. Clove oil contains 84-95% of phenols (eugenol), sesquiterpenes (α-, β-caryophyllenes) and small quantities of esters, ketones and alcohols.

Characteristics

Local anaesthetic, anti-inflammatory, antibacterial, antifungal.

Uses

Primary use

Dentistry, in mouth-wash (1-5% solution).

Other uses

Stimulant, aromatic, flavouring agent. Clove stem oil is produced in Tanzania and in Madagascar. It is used mainly in the flavouring and perfumery industries. Clove leaf oil is distilled in Madagascar, Tanzania and in Indonesia, and is used for the isolation of eugenol.

Special warning

Externally clove oil can cause allergy (oil must be diluted). Do not use in children.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Cinnamomi zeylanici corticis aetheroleum

 Plant

Cinnamomum zeylanicum Blume – Cinnamon (Lauraceae)

The plant is native to China, Ceylon, and it is cultivated elsewhere.
Drug

*Cinnamomi zeylanici corticis aetheroleum* (Cinnamon bark oil, Ceylon, Ph. Eur.)

Ceylon cinnamon bark oil is obtained by steam distillation of the bark of the shoots of *Cinnamomum zeylanicum* Nees (*C. verum* J.S. Presl.).

![Cinnamomi zeylanici cortex](image)

**Figure 2.11**
*Cinnamomi zeylanici cortex* (Cinnamon bark, Ceylon)

**Appearance of the essential oil**

A clear, mobile, light yellow liquid becoming reddish over time, with a characteristic odour reminiscent of cinnamic aldehyde.

**Constituents**

0.5-4% essential oil. The main components of cinnamon bark oil are cinnamic aldehyde and eugenol. The oil is liable to adulteration with cinnamon leaf oil and with oil of cassia. (Cinnamon leaf oil contains 70-95% of eugenol. Oil of cassia contains approx. 80% of aldehydes.).
Characteristics
Antibacterial, antifungal, appetizer, sedative, carminative.

Uses
Primary use
Antiseptic, gastrointestinal problems.

Other use
Aromatherapy.

Dosage
0.05-0.2 g daily dose

Special warning
Cinnamon bark oil can cause allergy (because of cinnamic aldehyde) when used externally. Do not use the oil in children.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Citronellae aetheroleum
Plant
*Cymbopogon winterianus* Jowitt – Citronella (Poaceae)
The plant is native to Java, and it can be cultivated.

Drug
*Citronellae aetheroleum* (Citronella oil, Ph. Eur.)
Oil obtained by steam distillation from the fresh or partially dried aerial parts of *Cymbopogon winterianus* Jowitt.

Appearance of the essential oil
Pale yellow to brown-yellow liquid, with a very strong odour of citronellal.
Constituents

0.5% essential oil. The main components of the citronella oil are geranial and citronellal.

\[
\begin{align*}
\text{citronellal} & \\
\text{geranial} & = \text{citral a} \\
& = E\text{-isomer of citral}
\end{align*}
\]

**Figure 2.14-15**
The structure of geranial and citronellal

Characteristics

Bactericide.

Uses

**Primary use**
Aromatheraphy (in aroma lamp – to sterilize air).

**Other uses**
Cosmetic and perfumery industry, repellent (cats do not like it).

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

**Coriandri aetheroleum**

Plant
*Coriandrum sativum* L. var. *vulgare* Alef. – Coriander (Apiaceae)

It is indigenous to Italy, but is widely cultivated in the Netherlands, Central and Eastern Europe, East-Mediterranean.

Drug
*Coriandri aetheroleum* (Coriander oil, Ph. Eur.)

Essential oil obtained by steam distillation from the fruits of *Coriandrum sativum* L.

Appearance of the essential oil
Clear, colourless or pale yellow liquid. It has a characteristic spicy odour.
Constituents
1.5-2.5% essential oil. The oil contains 65-70% of linalool depending on the plant source, and smaller amounts of α-pinene, γ-terpinene and limonene.

Characteristics
Sedative, carminative, flavouring agent, painkiller.

Uses
Primary use
Gastrointestinal problems, muscle relaxation (in liniments).

Other uses
Appetizer.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Eucalypti aetheroleum
Plant
Eucalyptus globulus Labill. – Eucalyptus (Myrtaceae)
Eucalyptus species are native to Australia, but they are also cultivated. “Citron-scented” eucalyptus oil, which is obtained from E. citriodora, is used in perfumery and contains a high proportion of the aldehyde citronellal.

Drug
Eucalypti aetheroleum (Eucalyptus oil, Ph. Eur.)
Eucalyptus oil is obtained by steam distillation and rectification from the fresh leaves or the fresh terminal branchlets of various species of Eucalyptus rich in 1,8-cineole. The most frequently used species are Eucalyptus globulus Labill., Eucalyptus polybractea R.T. Baker and Eucalyptus smithii R.T. Baker.

Appearance of the essential oil
A colourless or pale yellow liquid with an aromatic and camphoraceous odour and a pungent and camphoraceous taste.

Constituents
0.5-3.5% essential oil. The main component of eucalyptus oil is 1,8-cineole (not less than 70%), while minor components include α-pinene (2-8%) and camphor (less than 0.1%). To achieve these parameters and to minimise less desirable substances such as aldehydes, the oil obtained from initial steam distillation is rectified by alkaline treatment and fractional distillation.

Characteristics
Antiseptic, anticatarrhal.
Essential oils

Uses

**Primary use**
Cough, cold, bronchitis, other respiratory disorders.

**Other use**
Muscle pain, sauna.

Dosage

**Internal use**
0.05-0.2 ml per dose; in capsules: 100-200 mg, 2-5 times daily

**External use**

*By inhalation:* 12 drops per 150 ml of boiling water, or a 1.5% V/V solution prepared from 1 tablespoon (15 ml) per litre of warm water, treatment may be repeated up to three times daily.

*As a liniment:* containing 25% V/V of oil.

*As an ointment:* containing 1.3% V/m, for adults and children over 12 years: to be applied as a thick layer, up to three times daily.

*As a lozenge:* 0.2-15 mg dissolved slowly in the mouth, repeated every 0.5-1 hour.

*As a mouthwash:* containing 0.9 mg/ml; 20 ml as a gargle twice daily.

Contra-indications, special warnings, interactions

Eucalyptus oil and its preparations should not be applied to the face, especially the nose, of babies and little children. The oil induced hepatic microsomal enzyme activity in both *in vitro* and *in vivo* tests.

Pregnancy and lactation

Since human data are not available, eucalyptus should not be used during pregnancy and lactation without medical advice.

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**Foeniculi amari fructus aetheroleum**

**Plant**

*Foeniculum vulgare* Mill. subsp. *vulgare* var. *vulgare* – Bitter fennel (Apiaceae)

The plant is native to Mediterranean, and it can also be cultivated in West-Europe, Asia and America.

**Drug**

*Foeniculi amari fructus aetheroleum* (Bitter fennel fruit oil, Ph. Eur.)

Essential oil obtained by steam distillation from the ripe fruits of *Foeniculum vulgare* Miller, ssp. *vulgare* var. *vulgare*. 
Appearance of the essential oil
Clear, colourless or pale yellow liquid. It has a characteristic odour.

Constituents
2-6% essential oil. The oil contains predominantly trans-anethole (not less than 60%) and fenchone (not less than 15%) with not more than 5% estragole. (Trans-anethole can change into anisealdehyde during storage).

The structure of trans-anethole, fenchone, estragole and anisaldehyde
**Essential oils**

**Characteristics**
Spasmolytic, carminative.

**Uses**

**Primary use**
Gastrointestinal problems (flatulence, cramps).

**Dosage**
0.1-0.6 ml daily dose

**Contra-indications**
Persons with known sensitivity to anethole should avoid the use of fennel. The oil can cause epileptic convulsions, therefore patients with epilepsy should not use fennel oil.

**Pregnancy and lactation**
Preparations containing the essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

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**Juniperi aetheroleum**

**Plant**
*Juniperus communis* L. – Juniper (Cupressaceae)

Juniper is found from the Scandinavian Peninsula to the Mediterranean Sea.

**Drug**
*Juniperi aetheroleum* (Juniper oil, Ph. Eur.)

Essential oil obtained by steam distillation from the ripe, non-fermented berry cones of *Juniperus communis* L. A suitable antioxidant may be added.

**Appearance of the essential oil**
Mobile, colourless to yellowish liquid, with a characteristic odour (pine smell).

**Constituents**
2-3% essential oil. Essential oil (0.8-2 %) of very variable composition depending on the source, consisting mainly of monoterpenic hydrocarbons, principally α-pinene (24.1-55.4%). Other compounds of the essential oil are: sabinen, terpinen-4-ol, β-caryophyllene.

**Characteristics**
Spasmolytic, diuretic, improves blood circulation.

**Uses**

**Primary use**
Muscle pain, muscle cramps.
Other uses
Treatment of common cold, antiseptic. In French hospitals juniper oil is used as an antiseptic to sterilize air.

Dosage
20-100 mg daily dose (in capsules)

Contra-indication, Special warnings
Patients with inflammation of renal pelvis or sensitive skin should not use juniper oil.

Pregnancy and lactation
Juniper should not be used during pregnancy and lactation. Abortifacient activity of juniper has been observed in rats after oral administration of a 50% ethanolic extract at 300 mg/kg bodyweight.

Lavandulae aetheroleum
Plant
_Lavandula angustifolia_ Mill. – Lavender (Lamiaceae)
It is native to the Mediterranean, and can also be cultivated in South France and South Europe.

Drug
_Lavandulae aetheroleum_ (Lavender oil, Ph. Eur.)
Essential oil obtained by steam distillation from the flowering tops of _Lavandula angustifolia_ Miller (_Lavandula officinalis_ Chaix).

Appearance of the essential oil
Colourless or pale yellow, clear liquid. It has a characteristic odour (flower-scented).

Constituents
1.5% essential oil. The main components of the oil are linalool (20-45%) and linalyl acetate (25-46%). Others include terpinene-4-ol, limonene, cineole, camphor, lavandulol.

Characteristics
Sedative, anti-inflammatory, antiseptic.

Uses
**Primary use**
Skin care (burning, cuts, acne).

**Other use**
Aromatherapy (bath, ointment, inhalation), against insect bites.

Dosage
1-4 drops (approx. 20-80 mg), e.g. on a sugar cube. For children (up to 12 years of age): by inhalation – 3 drops of a 1:10 dilution of lavender oil. Children over 12 years of age:
as a bath additive – 6 drops per bath or 3 ml of a 20% solution. By inhalation – several drops of the oil or 2-20% of the oil in a nebulizer.

Contra-indication
Allergic reactions to lavender oil or one of its constituents.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Limonis aetheroleum

Plant
Citrus limon (L.) Burm. – Lemon (Rutaceae)
Lemons are widely cultivated and the essential oil is prepared around the Mediterranean, North and South America, in Australia and in parts of Africa. Other producing countries are: China, Israel and Turkey.

Drug
Limonis aetheroleum (Lemon oil, Ph. Eur.)
Essential oil obtained by suitable mechanical means, without the aid of heat, from the fresh peel of Citrus limon (L.) Burman fil.
Once the oil has been separated from the peel, it can be distilled without deterioration in quality, and some expressed oil of lemon is fractionally distilled to make terpeneless oil of lemon. Distilled oil of lemon is cheaper than that prepared by expression and large quantities of it are made and used for nonpharmaceutical purposes.

Appearance of the essential oil
Clear, mobile, pale yellow to greenish-yellow liquid with a characteristic odour. It may become cloudy at low temperatures.

 Constituents
0.5-1.5% essential oil. Lemon oil contains terpenes (limonene), pinene, aldehydes [(geranial = citral A), (neral = citral B] and esters (geranyl acetate). Lemon oil shows a marked tendency to resinify and should be protected from air and light as much as possible. During storage chemical alteration may occur in the oil.
Characteristics
Antiseptic, antidepressant.

Uses

Primary use
Treating of respiratory diseases (cold, influenza, sinusitis).

Other uses
Treating of oily skin, air-freshener, perfumery, flavouring agent.

Special warning
Lemon oil may have phototoxic effect in case of external use.

Matricariae aetheroleum

Plant
Matricaria recutita L. – Chamomile (Asteraceae)
The plant is native to and cultivated in southern and eastern Europe, in Asia and in North America.

Drug
Matricariae aetheroleum (Matricaria oil, Ph. Eur.)
Blue essential oil obtained by steam distillation from the fresh or dried flower-heads or flowering tops of Matricaria recutita L. (Chamomilla recutita L. Rauschert). There are 2 types of matricaria oil which are characterised as rich in bisabolol oxides, or rich in levomenol.
Essential oils

Figure 2.25

Matricariae flos (Chamomile flower)

Appearance of the essential oil
Clear, intensely blue, viscous liquid. It has an intense characteristic odour (bitterish smell).

Constituents
0.5-1.5% essential oil. The oil contains approx. 50% of the sesquiterpenes (chamazulene, and α-bisabolol and its oxides A, B, C), bisabolonoxide A, up to 25% of cis-and trans-en-yn-dicycloethers and β-farnesene. Chamazulene itself does not occur in the plant but is formed from matricin (sesquiterpene lactone) during steam distillation. Chemical alteration may occur during storage.

![Chemical structures](image)

Figure 2.26-28

The structure of α-bisabolol, bisabolol oxide A and chamazulene

Characteristics
Antiseptic, anti-inflammatory, pain killer, spasmolytic.

Uses
Primary use
Gastrointestinal problems (ulcer-protective), respiratory complaints (cold, influenza, sinusitis).
Other use

Dermatology.

Contra-indication

Sensitivity to *Matricaria* or other members of the Asteraceae.

Undesirable effects

Rare cases of contact allergy have been reported. *Matricaria* flower of the bisabolol oxide B-type can contain traces of the contact allergen anthecotulide. Most of the described allergic reactions to matricaria were due to contamination with *Anthemis cotula* or related species, which contain high amounts of anthecotulide. However, in cases where matricaria contact allergy has been acquired, cross-reactions to other sesquiterpene lactone-containing plants are common.

**Menthae piperitae aetheroleum**

Plant

*Mentha x piperita* (L.) Huds – Peppermint (Lamiaceae)

The plant is cultivated worldwide.

Drug

*Menthae piperitae aetheroleum* (Peppermint oil, Ph Eur.)

Essential oil obtained by steam distillation from the fresh aerial parts of the flowering plant of *Mentha × piperita* L.

Appearance of the essential oil

A colourless, pale yellow or pale greenish-yellow liquid. It has a characteristic odour and taste followed by a sensation of cold.

Constituents

1.2-3% essential oil. The oil must contain menthol (30-55%), menthon (14-32%), isomenthone (1.5-10%), methyl acetate (2.8-10%), menthofuran (1-9%), cineole (3.5-14%), limonene (1-5%), not more than 3% of pulegone and not more than 1% of carvone, with a higher ratio of cineole compared to that of limonene.

Characteristics

Pain killer, spasmolytic, antiseptic.

Uses

**Primary use**

Symptomatic treatment of digestive disorders (e.g. flatulence, irritable bowel syndrome), symptomatic treatment of coughs and colds.

**Other uses**

Symptomatic relief of tension-type headache, pruritus, urticaria and pain in irritable skin conditions.
Dosage

**Internal use**

*Adults:* For digestive disorders: 0.02-0.08 ml (1-4 drops) up to 3 times daily in dilute aqueous preparation (e.g. peppermint water or emulsion), or as drops on a lump of sugar.

For irritable bowel syndrome: 0.2-0.4 ml 3 times daily in enteric-coated capsules

*Children from 4-16 years of age:* For digestive disorders: proportion of adult dose according to body weight

**External use**

*Adults:* By inhalation: 3-4 drops added to hot water

In dilute liquid or semi-solid preparations, as an anaesthetic or antipruritic (equivalent to 0.1-1.0% m/m menthol) or as a counter-irritant and analgesic (equivalent to 1.25-16% m/m menthol), rubbed on to the affected area.

Tension-type headache: as a 10% solution rubbed on to the skin of forehead and temples.

*Children from 4-16 years of age*

Semi-solid preparations: 4-10 years: 2-10%, 10-16 years: 5-15%

Hydroethanolic preparations: 4-10 years: 2-4%, 10-16 years: 3-6%

**Contra-indication**

Contact sensitivity to peppermint oil or menthol.

**Special warnings**

Direct application of peppermint oil preparations to the nasal area or chest of babies and small children must be avoided because of the risk of laryngeal and bronchial spasms. Inhalation of menthol can cause apnoea and laryngoconstriction in susceptible individuals. Menthol can cause jaundice in newborn babies (glucose-6-phosphate dehydrogenase deficiency).

**Interaction**

Patients with achlorhydria (caused, e.g. by medication with H₂ receptor blockers) should use peppermint oil only in enteric-coated capsules.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, peppermint oil should not be used during pregnancy without medical advice.

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**Myristicae fragrantis aetheroleum**

**Plant**

*Myristica fragrans* Houtt. – Nutmeg (Myristicaceae)

Nutmeg is native to Malaysia, Maluccu Island (Indonesia), but it can also be cultivated.
Drug

*Myristicae fragrantis aetheroleum* (Nutmeg oil, Ph. Eur.)

Nutmeg oil is obtained by steam distillation of the dried and crushed kernels of *Myristica fragrans* Houtt.

**Figure 2.29**
Myristicae semen (Nutmeg)

**Appearance of the essential oil**
A colourless or pale yellow liquid, with a spicy odour.

**Constituents**
Nutmeg oil contains myristicin (4%) and elemicin (2%). Myristicin is 4-allyl-6-methoxy-1,2-methylenedioxybenzene. It is toxic to human beings and large doses of nutmeg oil may cause convulsions. Other compounds include pinene, sabinene, camphene (60-80%). Myristicin and elemicin have hallucinogenic effect.

**Figure 2.30-31**
The structure of myristicin and elemicin
Uses

Primary use
Food industry, liqueurs, perfumery.
In Ajurvedic medicine: the name of the plant is „mada shaunda” = „narcotic fruit”.

Terebinthini aetheroleum ab pinum pinastrum

Plant
Pinus pinaster Aiton – Turpentine tree (Pinaceae)
The plant is native to France, Italy, Portugal and Spain.

Drug
Terebinthini aetheroleum ab pinum pinastrum (Turpentine oil, Pinus pinaster type, Ph. Eur.)

Essential oil obtained by steam distillation, followed by rectification at a temperature below 180 °C, from the oleoresin obtained by tapping Pinus pinaster Aiton. A suitable antioxidant may be added. The purification consists of treatment with aqueous alkali to remove traces of phenols, resin acids, etc., and may be followed by redistillation.

Appearance of the essential oil
Clear, colourless or pale yellow liquid. It has a characteristic odour.

 Constituents
15-30% essential oil. Turpentine oil consists of the terpenes (+)- and (-)- α-pinene, (-)- β-pinene and camphene. During storage the oil becomes more allergenic.

 Characteristics
Pain killer, antibacterial, rubefacient.

Uses

Primary use
Treatment of common cold, rheumatic pain.

 Other use
Inhalation.

 Contra-indication
Allergy is possible.

Terebene is prepared from the oil of turpentine by the action of cold sulphuric acid, which converts the pinene into the optically inactive (±)-limonene (dipentene). Today, most turpentine is produced to provide its various constituents which find use in the manufacture of fragrances, insecticides, flavours.
### Rosmarini aetheroleum

**Plant**

*Rosmarinus officinalis* L. – Rosemary (Lamiaceae)

The plant is native to the Mediterranean, in Hungary it can be cultivated.

**Drug**

*Rosmarini aetheroleum* (Rosemary oil, Ph. Eur.)

Essential oil obtained by steam distillation from the flowering aerial parts of *Rosmarinus officinalis* L.

**Appearance of the essential oil**

Clear, mobile, colourless to pale yellow liquid with a characteristic odour.

**Constituents**

1-2.5% essential oil. Characteristic components of the oil are 1,8-cineole (= eucalyptol, 20-50%), α-pinene (15-26%), camphor (10-25%) and borneol (1-6%).

**Characteristics**

Spasmolytic, pain killer, antiseptic, improves blood circulation.

**Uses**

**Primary use**

Reduce muscle pain, in case of hypotension, backpain. The oil is used in preparations with 6-10% EO contain.

**Other use**

Treating respiratory complaints (e.g. cough).

**Contra-indication**

Hypersensitivity to rosemary.

**Special warnings**

Hot bath containing rosemary preparations should be avoided by patients with large open wounds, large skin lesions, feverish conditions or acute inflammation, severe circulatory disorders or hypertension, epilepsy.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, rosemary oil should not be used during pregnancy without medical advice.

### Salviae sclareae aetheroleum

**Plant**

*Salvia sclarea* L. – Clary sage (Lamiaceae)

The plant can be found from the Mediterranean Sea to Iran, it is cultivated in Russia, Turkey, Spain and Hungary.
Essential oils

Figure 2.32
Clary sage (*Salvia sclarea* L.)

Drug

*Salviae sclareae aetheroleum* (Clary sage oil, Ph. Eur.)

Essential oil obtained by steam distillation from the fresh or dried flowering stems of *Salvia sclarea* L.

Appearance of the essential oil

Colourless to brownish-yellow liquid, usually pale yellow, with a characteristic odour.

Constituents

0.2-1% essential oil. The oil contains linalool, linalyl acetate and sclareol as the main compounds.
Characteristics
Spasmolytic, sedative.

Uses

Primary use
Decrease the symptoms of menses (headache, cramps), against delivery pain.

Other use
Aromatherapy, skin care, perfumery industry.

Thymi aetheroleum

Plants

*Thymus vulgaris* L. and *T. zygis* Loefl. ex. L. – Thyme and Spanish thyme (Lamiaceae)
The plants are native to the Mediterranean, in Hungary they can also be cultivated.

Drug

*Thymi aetheroleum* (Thyme oil, Ph. Eur.)

Essential oil obtained by steam distillation from the fresh flowering aerial parts of *Thymus vulgaris* L., *T. zygis* Loefl. ex L. or a mixture of both species.

Appearance of the essential oil

Clear, yellow or very dark reddish-brown, mobile liquid with a characteristic, aromatic, spicy odour, reminiscent of thymol.

Constituents

1-3% essential oil. The thyme oil contains phenols, mainly thymol and/or carvacrol, and terpenoids.

Characteristics

Antibacterial, antifungal, expectorant, cough-reliever.
Essential oils

Uses

**Primary use**
Respiratory disorders (bronchial catarrh, supportive treatment of pertussis).

**Other use**
Dermatology (mycosis of the legs).

**Special warnings**
Children under 5 years of age and patients with epilepsy or disease of the thyroid gland should not use thyme oil.

**Pregnancy and lactation**
No data available. In accordance with general medical practice, thyme oil should not be used during pregnancy without medical advice.

**Menthae arvensis aetheroleum partim mentholi privum**

**Plant**
*Mentha canadensis* L. – Lamiaceae (syn: *Mentha arvensis* L. var. *piperascens* Malinv.)
The plant is native to East-Asia, China, Malaysia and Canada.

**Drug**
*Menthae arvensis aetheroleum partim mentholi privum* (Mint oil, partly dementholised, Ph. Eur.)
Essential oil obtained by steam distillation from the fresh, flowering aerial parts, recently gathered from *Mentha canadensis* L. (syn. *M. arvensis* L. var. *glabrata* (Benth) Fern., *M. arvensis* var. *piperascens* Malinv. ex Holmes), followed by partial separation of menthol by crystallisation.

**Appearance of the essential oil**
Colourless or pale yellow to greenish-yellow liquid with a characteristic odour.

**Constituents**
1-3 % essential oil. The main components of the oil are menthol and menthon.

**Use**
It has carminative effect. The plant can be used for essential oil production („Japanese peppermint oil“).
Chapter 3

Iridoid-containing drugs

3.1 Iridoids – Biosynthesis

Properties of iridoids

Iridoids are cyclopentan-[c]-pyran monoterpenoids. Most occur as glycosides; some occur free and as bis compounds. The number of these compounds is constantly increasing (several hundred iridoids are known). There are many seco-iridoids in which the pyran ring is open, and in a few the pyran ring oxygen is replaced by nitrogen. Iridoids are less stable compounds, they are easily decomposed by enzymes and are oxidised too. They can be dissolved in water and alcohol. Their name derives from *Iridomyrmex* (ant genus), which produces these compounds as a defensive secretion. Loganin is one of the most important iridoids, which is a precursor of the nonindole portion of some alkaloids. The most important plant families containing iridoid-producing species are: *Apocynaceae, Cornaceae, Ericaceae, Gentianaceae, Lamiaceae, Menyathaceae, Valerianaceae, Plantaginaceae*. Their pharmacological effects include: antibacterial, anti-inflammatory, sedative, pain killer, appetizer (secoiridoids). They are used as a bitter tonic. Because iridoids are not stable compounds, fast drying (at low temperature, at 40 °C) of the drugs is necessary during the primary processing and after careful packing, these drugs have to be stored protected from light.
Bitterness value in the European Pharmacopoeia 5.0

- The bitterness value is the reciprocal of the dilution of a compound, a liquid or an extract that still has a bitter taste.
- It is determined by comparison with quinine hydrochloride, the bitterness value of which is set at 200 000.
- Determination of the correction factor: A taste panel comprising at least 6 persons is recommended. The mouth must be rinsed with water R before tasting. To correct for individual differences in tasting bitterness amongst the panel members it is necessary to determine a correction factor for each panel member.
- Stock solution: Dissolve 0.100 g of quinine hydrochloride R in water R and dilute to 100.0 ml with the same solvent. Dilute 1.0 ml of this solution to 100.0 ml with water R.
- Reference solutions. Prepare a series of dilutions by placing in a first tube 3.6 ml of the stock solution and increasing the volume by 0.2 ml in each subsequent tube to a total of 5.8 ml; dilute the contents of each tube to 10.0 ml with water R.
- Determine as follows the dilution with the lowest concentration that still has a bitter taste.

Bitters

- Bitters are extensively used in liquid medicaments to stimulate appetite. Bitter constituents stimulate the gustatory nerves in the mouth and give rise to an increase in the psychic secretion of gastric juice.
- Causes of the lack of appetite: infections (caused by bacteria or viruses), psychosomatic diseases (anorexia nervosa, stress), consumption of medicines (e.g. antibiotics), decrease of sensation of taste (in the elderly) and smoking. Other causes: inappropriate production of gastric juice and bile, lack of enzymes produced by pancreas.
- Bitter compounds show a great chemical variation. Iridoids, seco-iridoids, sesquiterpene lactones and diterpenes have bitter taste. But bitter compounds with strong effect, e.g. cardioactive glycosides from Digitalis species, or alkaloids (strychnine) must not be used as a bitter tonic.
- Types of drugs containing bitters:
  1 amara pura – only bitters, e.g. Gentian, Centaury
  2 amara aromatica – aromatic bitters, e.g. Bitter orange
  3 amara acria – hot bitters, e.g. Ginger
  4 amara adstringentia – adstringent bitters, e.g. Condurango
  5 amara mucilaginosa – mucous bitters, e.g. Iceland moss
- Tinctures or hydroalcoholic extracts are usually produced from plants containing bitter compounds. Liquids and tinctures are in touch with taste buds on a bigger
Iridoid-containing drugs

surface, therefore the products can act very fast. Application: 20-30 min. before meal, the effect lasts for 2-3 hours.

- Drugs containing bitters must not be used for a long time, because adverse effects may develop (loss of appetite).

Drugs

Plantaginis lanceolatae folium

Plant

*Plantago lanceolata* L. – Ribwort plantain (Plantaginaceae)

The plant is native to Eurasia.

![Ribwort plantain (Plantago lanceolata L.)](image)

**Figure 3.2**

Ribwort plantain (*Plantago lanceolata* L.)
Drug

*Plantaginis lanceolatae folium* (Ribwort plantain leaf, Ph. Eur.)

Ribwort plantain leaf consists of the whole or fragmented, dried leaf and scape of *Plantago lanceolata* L. s. l. It contains not less than 1.5% of total ortho-dihydroxycinnamic acid derivatives, expressed as acteoside and calculated with respect to the dried drug.

![Plantaginis lanceolatae folium](image)

**Figure 3.3**

*Plantaginis lanceolatae folium* (Ribwort plantain leaf)

Constituents

The characteristic constituents are 2-6.5% mucilage-heteropolysaccharide, iridoid glycosides (aucubin, catalpol), phenylethanoids (acteoside, isoacteoside), flavonoids and silicic acid.
Iridoid-containing drugs

Figure 3.4-6
The structure of aucubin, catalpol and acteoside

Uses
Therapeutic indications include catarrhs of the respiratory tract, bronchitis, temporary, mild inflammations of the oral and pharyngeal mucosa. The drug has anti-inflammatory, antibacterial and cough suppressant activities. In ethnomedicine the leaves are used externally to cure the wounds and haemorrhoids.

Dosage

Internal use

Adults, elderly: average daily dose, 3-6 g of the drug or equivalent preparations.

Children: average daily dose: >1-4 years of age: 1-2 g, 4-10 years: 2-4 g, 10-16 years: 3-6 g.

Black colour of the leaves indicates that the drug must not be used for making preparations.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Other Plantago species in the European Pharmacopoeia

Psyllium seed; Psyllii semen (Plantago afra, P. indica)

Ispaghula seed; Plantaginis ovatae semen (Plantago ovata)

Plantago afra and P. indica are native to the Mediterranean, Asia and USA; P. ovata: India, Pakistan, Africa.
Figure 3.7-8
Psyllii semen (Psyllium seed) and Plantaginis ovatae semen (Ispaghula seed)

**Uses**
Mild laxative (due to mucilage content), against constipation, Crohn-disease, increases fibre-intake.

**Dosage**
(After 12 years of age): 10-30 g

**Special warnings**
It is worth calling the patients’ attention to the proper application of the drugs. Drugs containing mucilage can cause obstruction of the bowels, if the patient does not drink appropriate amount of water (or other liquid). Mucilage may prevent the absorption of other medicines, vitamins, glucose in the bowels.

**Euphrasiae herba**

**Plant**
*Euphrasia rostkoviana* Hayne. – Eyebright (Scrophulariaceae)
The plant is native to Europe. In Hungary it can be found in Transdanubia.

**Drug**
*Euphrasiae herba* (Eyebright, DAC)
Eyebright consists of the dried flowering aerial parts of *Euphrasia rostkoviana* Hayne.

**Constituents**
The characteristic constituents of the drug include iridoids (eufroside and aucubin), tannins and flavonoids.
Uses
It has antibacterial and anti-inflammatory activity. It can be used for treating conjunctivitis (in the form of sterile infusion).

Dosage
Daily dose 2 g, 2 % infusion – application form: in compress.

Lamii albi flos

Plant
*Lamium album* L. – White deadnettle (Lamiaceae)

The plant is native to Europe and Asia. It is a ruderal weed.
Figure 3.10
White deadnettle (*Lamium album* L.)

Drug

*Lamii albi flos* (White deadnettle flower), *Lamii albi herba* (White deadnettle, DAC)

*Lamii albi flos* consists of the dried flowers of *L. album*. *Lamii albi herba* consists of the dried flowering aerial parts of the plant.

Constituents

Flowers contain iridoids (lamalbid and 6-desoxylamalbid) and flavonoids. The characteristic constituents of the herb are tannins, mucilage and saponins.
Uses
The drugs of white deadnettle can be used for treating diseases of the upper respiratory system. Because of tannin content, it has an astringent effect. In ethnomedicine, the plant is used to treat benign prostate hypertrophy, leucorrhea and irregular menstruation. External use: treating of ulcer cruris, haemorrhoids.

Dosage
Daily dose 6-9 g, as an infusion.

Harpagophyti radix

Plant
_Harpagophytum procumbens_ (Burch.) DC., _H. zeyheri_ – Devil’s claw (Pedaliaceae)

These plants are native to Southern and Eastern Africa. It is collected in regions bordering on the Kalahari desert. It derives its trivial name from the characteristic appearance of the fruit.

Drug
_Harpagophyti radix_ (Devil’s claw root, Ph. Eur.)

Devil’s claw root consists of the cut and dried tuberous, secondary roots of _Harpagophytum procumbens_ D.C. and/or _H. zeyheri_ L. Decne. It contains not less than 1.2% of harpagoside, calculated with reference to the dried drug. Devil’s claw root is greyish-brown to dark brown and it has a bitter taste.
Constituents

The characteristic constituents are iridoid glycosides (harpagoside, harpagide, procumbide) (1-3% in *H. procumbens*, 0.7-1.7% in *H. zeyheri*). The phenolic glycosides acteoside (verbascoside) and sugars, mainly the tetrasaccharide stachyose (up to 46%) can also be found in the drug. The acylated phenolic glycoside 6-acetylacteoside has been found in *H. procumbens* but not in *H. zeyheri*.

![Structure of harpagoside, harpagide and procumbide](image)

**Figure 3.14-16**
The structure of harpagoside, harpagide and procumbide

Uses

The drug has anti-inflammatory and analgesic effect, therefore it can be used in the treatment of painful osteoarthritis and low back pain. On the basis of its bitter tonic properties, the drug is also widely documented as a remedy for loss of appetite and dyspepsia.
Dosage

Symptomatic treatment of painful osteoarthritis

*Adults, elderly:* 2-5 g (daily dose) of the drug or equivalent dry extract prepared with water or ethanol (max. 60% V/V)/water

Treatment for at least 2-3 months is recommended in cases of painful osteoarthritis.

Relief of low back pain

*Adults, elderly:* 4.5-9 g (daily dose) of the drug as dry extract prepared with water or ethanol (max. 60% V/V)/water

Loss of appetite or dyspeptic complaints

*Adults, elderly:* 0.5 g of the drug in decoction, 3 times daily, tincture (1:10, 25% ethanol) 3 ml

Not recommended for children.

Contra-indications

As with other drugs containing bitter substances, patients with gastric ulcers should consult their doctor before use.

Undesirable effects

Mild gastro-intestinal disturbances (e.g. diarrhoea, stomach upset, nausea) may occur in sensitive individuals especially at higher dosage level.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Agni casti fructus

Plant

*Vitex agnus castus* L. – Agnus castus (Verbenaceae)

The plant is native to Europe, North-Africa and Asia.

Drug

*Agni casti fructus* (Agnus castus fruit, Ph. Eur. 6.0)

Agnus castus consists of the whole, ripe, dried fruits of *Vitex agnus castus* L. It contains not less than 0.08% of casticin, calculated with reference to the dried drug.
Constituents
The characteristic constituents of the drug are iridoid glycosides such as agnuside (0.02-0.4%) and aucubin; bicyclic diterpenes of the labdane and clerodane types (e.g. rotundifuran); lipophilic flavonoids such as casticin (3’',5-dihydroxy-3,6,7,4’'-tetramethoxyflavone, 0.02-0.2%), hydrophilic flavones of O- or C-glycosidic types (e.g. orientin, isovitexin, luteolin-7-glucoside), essential oil (containing monoterpenes) and fatty oil.

![Structure of agnuside and aucubin](image)

**Figure 3.18-19**
The structure of agnuside and aucubin

Uses
Agnus castus can treat the PMS (premenstrual syndrome) including symptoms such as mastodynia or mastalgia. It is also used for treating menstrual cycle disorders such as polymenorrhea, oligomenorrhea or amenorrhea.
Dosage
Preparations equivalent to 30-40 mg of the drug daily or up to 240 mg of the drug daily in patients suffering from PMS.

Treatment for a minimum of 3 months may be appropriate, and seeking medical advice is recommended. Patients with tumors in breast or thyroid gland must not use the drug or its preparations.

Interaction
Mutual attenuation of effects might occur in patients under concomitant treatment with dopamine receptor antagonists.

Undesirable effects
Cases of allergic skin reactions have been reported.

Pregnancy and lactation
No data available. Agnus castus should not be taken during pregnancy. Lactation was inhibited in rats after subcutaneous administration of an agnus castus extract twice daily at about 100 times the human daily dose level. A human study showed an increase in lactation. Agnus castus should not be taken during lactation.
**Verbenae herba**

**Plant**

*Verbena officinalis* L. – Vervain (Verbenaceae)

The plant is native to Europe and Asia.

**Figure 3.20**

Vervain (*Verbena officinalis* L.)

**Drug**

*Verbenae herba* (Vervain, DAC)

Vervain consists of the dried, aerial flowering parts of *Verbena officinalis* L.

**Constituents**

The characteristic constituents of the drug are iridoid glycosides such as verbenalin; flavonoids and triterpenes.
Iridoid-containing drugs

![verbenalin structure](image)

**Figure 3.21**
The structure of verbenalin

**Uses**
It has expectorant, cough-suppressant activity, therefore it can be used for treating respiratory disorders and the inflammation of the throat. In ethnomedicine vervain can heal the wounds.

**Dosage**
2-4 g/daily dose.

**Pregnancy and lactation**
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

**Valerianae radix**

**Plant**
*Valeriana officinalis* L. – Valerian (Valerianaceae)

Valerian is native to Europe and Asia. It is obtained from wild and cultivated plants in Britain, the Netherlands, Belgium, France, Germany, Hungary and Japan. It is also cultivated in the USA. Polyploidy occurs in *V. officinalis* and there are diploid, tetraploid and octoploid types. Central European valerian is usually tetraploid. Other *Valeriana* species, for example, Indian valerian (*V. wallichii*) may not substitute the drug of *V. officinalis*, because of the risk of the cytotoxicity (higher valepotriate content).
Valerian (Valeriana officinalis L.)

Valerian root consists of the dried, whole or fragmented underground parts of *Valeriana officinalis* L. s.l., including the rhizome surrounded by the roots and stolons. It contains not less than 5 ml/kg of essential oil for the whole drug and not less than 3 ml/kg of essential oil for the cut drug, both calculated with reference to the dried drug and not less than 0.17 per cent of sesquiterpenic acids expressed as valerenic acid, calculated with reference to the dried drug. Valerian root has a characteristic odour.
Constituents

The drug contains 0.5-2% epoxy-iridoids: valepotriates (valtrate, isovaltrate, didrovaltrate, acevaltrate). They are unstable constituents and unlikely to be present in finished products. Similarly, baldrinals, the decomposition products of valepotriates, are not detected in valerian root preparations. Other characteristic constituents include essential oil containing monoterpenes such as bornyl esters, pinenes; sesquiterpenes (valerenal, valeranone); and less volatile sesquiterpenic acids (valerenic acid). Valerenic acid is responsible for the characteristic odour of the drug. Other constituents are monoterpane-alkaloids, GABA (gamma-aminobutyric acid) and flavonoids (6-methylapigenin).
Figure 3.24-27
The structure of valtrate, isovaltrate, didrovaltrate and acevaltrate

Uses
Valerian has a sedative and antispasmodic effect. Therapeutic indication includes the relief of temporary mild nervous tension and/or difficulty in falling asleep (insomnia). Valerian can reduce intestinal cramps.

Dosage
*Adult and elderly single dose*: 1-3 g of the drug (e.g. as a tea infusion) or equivalent extracts prepared with water or ethanol (max. 70%). For tenseness, restlessness and irritability, up to 3 times daily. As an aid to sleep, a single dose half to one hour before bedtime, with an earlier dose during the evening if necessary.

*Children from 3 to 12 years under medical supervision*: proportion of adult dose according to body weight, as non-alcoholic preparations. The use of valerian products should not be recommended under 3 years of age.

Neither dependence nor withdrawal symptoms have been reported.

Effect on ability to drive and use machines
Taking valerian root preparations immediately (up to 2 hours) before driving a car or operating hazardous machinery is not recommended. The effect of valerian preparations may be strengthened by consumption of alcohol.

Pregnancy and lactation
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.
Gentianae radix and Gentianae tinctura

Plant

*Gentiana lutea* L. – Gentian (Gentianaceae)

Gentian is native to mountainous districts of central and southern Europe and Turkey. As it is now a protected plant in some areas (e.g. in Hungary), attempts are being made to cultivate it in some EU countries (Germany, France, Italy).

Drug

*Gentianae radix* (Gentian root, Ph. Eur.), *Gentianae tinctura* (Gentian tincture, Ph. Eur.)

Gentian root consists of the dried, fragmented underground organs of *Gentiana lutea* L. Gentian root occurs as single or branched subcylindrical pieces of various lengths and usually 10 mm to 40 mm thick but occasionally up to 80 mm thick at the crown. Tincture produced from *Gentian root*, from 1 part of the comminuted drug and 5 parts of ethanol (70 per cent *V/V*) by a suitable procedure. It is a yellowish-brown or reddish-brown liquid. It has a strong bitter taste.

Constituents

The characteristic constituents of gentian root are secoiridoids (gentiopicroside, 1-4%, gentiamarin, amarogentin, amarosverin, amaropanin), oligosaccharides (bitter tasting...
gentianose and gentiobiose), xanthones (e.g. gentisin, a yellow colouring matter), alkaloids and traces of essential oil.

Bitter value of gentiopicroside is: 12 000; amaropanin: 20 000 000; amarogentin: 58 000 000.

![Chemical structures](image)

The structure of gentiopicroside, amarogentin, amarosverin and amaropanin

**Figure 3.29-32**

The structure of gentiopicroside, amarogentin, amarosverin and amaropanin

**Uses**

Gentian is a bitter tonic, appetizer (in case of anorexia too). It has cholagogue effect. It is also used in liqueur industry. The drug can reduce dyspeptic complaints.

**Dosage**

*Adult and elderly single dose:* 0.1-2 g of the drug in 150 ml of water in infusion, decoction or maceration, up to 3 times daily. Tincture (1:5, ethanol 45-70% V/V): average single dose of 1 ml, up to 3 times daily. Hydroethanolic extracts of equivalent bitterness value.

*Children, average daily dose:* 4-10 years of age: 1-2 g of the drug, 10-16 years of age: 2-4 g; in ethanol-free dosage forms.

For oral use in liquid preparations: in anorexia a single dose administered half to one hour before a meal, in dyspeptic complaints a single dose after the meal.

Overdose may lead to nausea or even vomiting.

**Contra-indication**

Patients with gastric or duodenal ulcer or hyperacidity should not consume gentian products.
Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation. Gentisin, a xanthone component, was proven to be a mutagen in vitro.

**Centaurii herba**

**Plant**

_Centaurium erythraea_ Rafn. – Centaury (Gentianaceae)

The plant is native to Europe and Asia.

![Centaurii herba](image)

**Figure 3.33**

Centaury (_Centaurium erythraea_ Rafn.)

**Drug**

_Centaurii herba_ (Centaury, Ph. Eur.)

Centaury consists of the whole or cut dried flowering aerial parts of _Centaurium erythraea_ Rafn (_C. minus_ Moench, _C. umbellatum_ Gilib., _Erythraea centaurium_ (L.) Pers.). Centaury has a very bitter taste.
Figure 3.34  
*Centaurii herba* (Centaury)

**Constituents**

Bitter-tasting constituents are secoiridoids, principally swertiamarin, gentiopicrin and sweroside, with bitterness values of about 12,000. Another secoiridoid, centapicrin, has a bitterness value of 4,000,000. Other iridoids include centauros ide (a dimeric secoiridoid), secologanin, 6'-m-hydroxy-benzoyl-loganin, dihydrocornin (a cyclopentane iridoid) and the secoiridoid alkaloid gentianine. Various methoxylated xanthones are also present. Other constituents are flavonoids, triterpenes, phenolic acids (*p*-coumaric, ferulic).
Uses
Therapeutic indications of the drug include dyspeptic complaints and lack of appetite. It can be used as a bitter tonic, cholagogue and appetizer.

Dosage
Adults: 1-4 g of the drug as a maceration, infusion or decoction in 150 ml of water, up to 3 times daily. 2-4 ml of liquid extract (1:1, ethanol 25% V/V), up to 3 times daily. Tincture (1:5, ethanol 70% V/V): 2-5 g daily.

Children: proportion of adult dose according to age or body weight, in ethanol-free dosage form.

For oral use in liquid preparations: for lack of appetite a single dose administered half to one hour before a meal, in dyspeptic complaints a single dose after the meal.

Overdose may lead to nausea or even vomiting.

Contra-indication
Patients with gastric or duodenal ulcer or hyperacidity should not consume centaury products.

Pregnancy and lactation
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.
Menyanthidis trifoliatae folium

Plant

*Menyanthes trifoliata* L. – Bogbean (Menyanthaceae)

The plant is native to Middle- and North-America, Europe, Asia. In Hungary it is protected.

![Bogbean (Menyanthes trifoliata L.)](image)

**Figure 3.39**

Bogbean (*Menyanthes trifoliata* L.)

Drug

*Menyanthidis trifoliatae folium* (Bogbean leaf, Ph. Eur.)

Bogbean consists of the dried, entire or fragmented leaf of *Menyanthes trifoliata* L. It has very bitter and persistent taste.
Constituents

The bitter-tasting constituents are secoiridoids such as foliamenthin and dihidrofoliamenthin, and the iridoid loganin. Other constituents include a monoterpene-alkaloid, flavonoids, triterpenes and coumarins.

![Chemical structures of foliamenthin, dihidrofoliamenthin, and loganin.]

Uses

It is a stomachic and bitter tonic. It has antibacterial activity.

Dosage

Single dose: 0.5-1 g as an infusion.

Overdose of the drug may lead to diarrhoea and vomiting.
Contra-indication
Patients with gastric or duodenal ulcer, hyperacidity or appendicitis should not consume bogbean products.

Pregnancy and lactation
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Oleae folium
Plant
Olea europea L. – Olive tree (Oleaceae)
The plant is native to the Mediterranean countries.

Drug
Oleae folium (Olive tree leaf)
The drug consists of the dried, entire or fragmented leaf of Olea europea L.
Constituents
The main constituents are secoiridoids such as oleuropein, flavonoids and triterpenes.

Figure 3.45
The structure of oleuropein

Uses
The leaf extract has spasmolytic effect, it can reduce blood pressure. It is used against atherosclerosis. The fatty oil (olive oil) extracted from the seeds is principally used.

Dosage
Single dose: 7-8 g as an infusion, 3 times daily.
Chapter 4

Drugs containing sesquiterpenes, diterpenes and terpenophenols

4.1 Sesquiterpenes

Sesquiterpenes are compounds containing 15 C-atoms. They are biogenetically derived from farnesyl pyrophosphate and may be linear, monocyclic or bicyclic in structure. They constitute a very large group of secondary metabolites, some having been shown to be „stress compounds” formed as a result of disease or injury. More than 100 different types of sesquiterpene skeletons and thousands of sesquiterpenes are known: some of them are components of volatile oils (sesquiterpene hydrocarbons and alcohols). Sesquiterpenes containing strongly oxidized functional groups (hydroxy, epoxy, aldehyde, carbonyl, carboxyl, ester, lactone) are solid, crystalline compounds and sesquiterpene-glycosides are crystalline compounds, too. They are characteristic compounds, first of all, in the plant family Asteraceae (= Compositae). Their proven pharmacological effects include: stomachic, anti-inflammatory, sedative, analgesic and antispasmodic to smooth muscle. However, a number of sesquiterpenes can cause allergy: e.g. pollen of Ambrosia artemisiifolia (ragweed, incorrectly wild hemp).

Sesquiterpene Lactones

They are particularly characteristic of the Asteraceae, but also occur in other plant families. Not only have they received attention from chemical and chemotaxonomic viewpoints, but may also possess antitumor, cytotoxic and antimicrobial activities, as well. They can be responsible for skin allergies in humans and they also act as insect deterrents. Chemically the compounds can be classified according to their carbocyclic skeletons, thus from the germacranolides can be derived the guaianolides, eudesmanolides, xanthanolides (Figure 4.1), etc. A structural feature of all these compounds, which appears to be associated with much of the biological activity, is the \(\alpha,\beta\)-unsaturated-\(\gamma\)-lactone. Species of Asteraceae containing sesquiterpene lactones include Taraxacum officinale (dandelion), Artemisia absinthium, Cichorium spp., Eupatorium spp. Sesquiterpene lactones of Umbelliferae are interesting in that the usual skeletal types (germacranolides, guaianolides, etc.) are found but all differ in their stereochemistry from the analogous compounds of the Compositae.
Drugs

Matricariae flos

Plant

*Matricaria recutita* L. – Chamomile (Asteraceae)

The plant is native to and cultivated in southern and eastern Europe. The flowers bloom in early to midsummer, and have a strong, aromatic smell. The flowers are collected in dry weather and are carefully dried.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Drug

*M. flos* (Matricaria flower, Ph. Eur.). **Other drugs:** *M. aetheroleum* (Matricaria oil, Ph.Eur.), *M. extractum fluidum* (Matricaria liquid extract, Ph. Eur.)

Matricaria flower consists of the dried flower-heads of *M. recutita* L. (syn.: *C. recutita* (L.) Rausch). It contains not less than 4 ml/kg of blue essential oil. Matricaria liquid extract is produced from *M. recutita*. It contains not less than 0.30% of blue residual oil. It is a brownish, clear liquid with an intense characteristic odour and characteristic bitter taste; miscible with water and with alcohol with development of turbidity, soluble in alcohol (50% *V/V*).
Matricariae flos (Matricaria flower)

Matricaria oil is a blue essential oil obtained by steam distillation from the fresh or dried flower-heads or flowering tops of *Matricaria recutita* L. (*Chamomilla recutita* L. Rauschert). There are 2 types of matricaria oil which are characterised as rich in bisabolol oxides, or rich in levomenol. Matricaria oil is a clear, intensely blue, viscous liquid. It has an intense characteristic odour.

Matricaria liquid extract is produced from *Matricaria flower*. It contains not less than 0.30% of blue residual oil. The extract is produced from the drug and a mixture of 2.5 parts of a 10% *m/m* solution of ammonia (NH₃), 47.5 parts of water and 50 parts of alcohol with an appropriate procedure for liquid extracts. Matricaria liquid extract is a brownish, clear liquid with an intense characteristic odour and characteristic bitter taste; miscible with water and with alcohol with development of turbidity, soluble in alcohol (50% *V/V*).

**Constituents**

The main active constituent of matricaria flower is essential oil (0.5-1.5%). The essential oil contains approximately 50% of the sesquiterpenes (–)-α-bisabolol and its oxides A, B and C, bisabolonoxide A, up to 25% of cis-and trans-en-yn-dicycloethers (or spiroethers) and chamazulene (up to 15%). A number of chemotypes depending on the proportions of bisabolol, bisabolol oxides and farnesene in the oil have been described. Other constituents of matricaria flower include coumarins, flavone derivatives (apigenin-7-glucoside, 0.5%), phenolic acids and polysaccharides (10%).
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Figure 4.4-10
The structure of matricin, chamazulene, α-bisabolol, bisabolol oxide A, cis-spiroether, trans-spiroether and spatulenol

Uses
Matricaria flower is used in the symptomatic treatment of gastrointestinal complaints such as minor spasms, flatulence and belching. It has spasmolytic, anti-inflammatory, antibacterial and immunostimulant effects. The ulcer protective properties of German chamomile have been ascribed to bisabolol-type constituents. The drug can also be used for treating minor inflammations of skin and mucosa, including the oral cavity, the gums, the respiratory tract and the anal and genital area.

Dosage

Internal use
Adults: As a tea infusion 3 g of the drug in 150-200 ml of water, three to four times daily.
Fluid extract (1:2, 50% ethanol): 3-6 ml daily. Dry extract: 50-300 mg three times daily.
Elderly: Dose as for adults.
Children: proportion of adult dose according to age or body weight.

External use
For compresses, rinses, gargles: 3-10% m/V infusion or 1% V/V fluid extract or 5% V/V tincture.
For bath: 5 g of the drug, or 0.8 g of alcoholic extract, per litre of water.
For vapour inhalation: 10-20 ml of alcoholic extract per litre of hot water.

Undesirable effects
Rare cases of contact allergy have been reported. Matricaria flower of the bisabolol oxide B-type can contain traces of the contact allergen anthecotulide. Most of the described allergic reactions to matricaria were due to contamination with *Anthemis cotula* or related species, which contain high amounts of anthecotulide. However, in
cases where matricaria contact allergy has been acquired, cross-reactions to other sesquiterpene lactone-containing plants are common.

**Chamomillae romanæ flos**

**Plant**

*Chamaemelum nobile* (L.) All. – Roman chamomile (Asteraceae)

The plant is cultivated in the south part of England, and in Belgium, France, Germany, Hungary, Poland, former Yugoslavia, Bulgaria, Egypt and Argentina. As a result of long cultivation most of the tubular florets present in the wild plant have become ligulate, and it is these ‘double’ flower-heads which form the commercial drug.

**Drug**

*Chamomillae romanæ flos* (Chamomile flower, Roman, Ph. Eur.)

Roman chamomile flower consists of the dried flower-heads of the cultivated double variety of *Chamaemelum nobile* (L.) All. (*Anthemis nobilis* L.). It contains not less than 7 ml/kg of essential oil.

![Chamomillae romanæ flos](image)

**Figure 4.11**

*Chamomillae romanæ flos* (Chamomile flower, Roman)

**Constituents**

Roman chamomile flowers contain essential oil (0.4-2.4%) which is blue when freshly distilled owing to the presence of azulene. The amount of chamazulene depends on the age and place of origin of the plant. Other components of the oil are *n*-butyl angelate and the esters of iso-butyric acid and tiglic acid. The drug also contains sesquiterpene lactones of the germacranoïd type (nobilin, 3-epinobilin), coumarins, flavonoids and phenolic acids (caffeic acid).
Uses
The medicinal use of roman chamomile flower is similar to that of matricaria flower. It is used in the symptomatic treatment of gastrointestinal complaints such as spasms and flatulence. It has spasmolytic, anti-inflammatory and carminative effects.

Dosage

Internal use
Adults: 3-12 g (daily dose) of the drug for making tea infusion.

Contra-indication
Sensitivity to Chamaemelum or other members of the Compositae.

Millefolii herba

Plant
Achillea millefolium s.l. (L.) – Yarrow (Asteraceae)

Yarrow is native to Europe and Western Asia but is widespread in most temperate regions including North America. It is an extremely diverse aggregate species with varying chromosome numbers and differences in oil composition.
Drug

*Millefolii herba* (Yarrow, Ph. Eur.)

Yarrow consists of the whole or cut, dried flowering tops of *Achillea millefolium* L. It contains not less than 2 ml/kg of essential oil and not less than 0.02% of proazulenes, expressed as chamazulene, both calculated with reference to the dried drug.

![Millefolii herba](image)

**Figure 4.17**

Yarrow [*Achillea millefolium* s.l. (L.)]

**Constituents**

The main active constituent of yarrow is essential oil (0.1-0.4%). The tetraploid form of the plant produces higher amounts of chamazulene in the oil than the hexaploid species. Germacranolide- and eudesmanolide-type sequiterpenes are also constituents of the oil together with caryophyllene, sabinene and borneol. Other constituents include sesquiterpene lactones (e.g. achillin), flavonoids (apigenin, luteolin), alkaloids (betonicine), triterpenes and sterols.

![achillin](image)

**Figure 4.18**

The structure of achillin

**Uses**

Yarrow is used, as is chamomile and matricaria, to treat various skin conditions and gastrointestinal problems (lack of appetite, dyspepsia). Female patients with the inflammation of the lesser pelvis can also use the drug infusion as a bath. The drug can
Drugs containing sesquiterpenes, diterpenes and terpenophenols

be used for the symptomatic treatment of minor spasm associated with menstrual periods.

**Dosage**

**Internal use**

*Adults*: As a tea infusion 4 g of the drug in 150-200 ml of water, three times daily.

**External use**

*For bath*: 100 g of the drug to 20 litre of water.

**Undesirable effects**

Contact allergy may occur. Thujone present in the essential oil may cause abortion, therefore the drug is not recommended during pregnancy (and lactation).

**Absinthii herba**

**Plant**

*Artemisia absinthium* L. – Wormwood (Asteraceae)

It is native to temperate regions of Eurasia and northern Africa, and it can be cultivated, too.

![Figure 4.19](image)

*Figure 4.19*  
Wormwood (*Artemisia absinthium* L.)

**Drug**

*Absinthii herba* (Wormwood, Ph. Eur.)

Wormwood consists of the basal leaves or slightly leafy, flowering tops, or of a mixture of these dried, whole or cut organs of *Artemisia absinthium* L. It contains not less than 2 ml/kg of essential oil, calculated with reference to the dried drug.
Constituents

The main active constituents of wormwood are sesquiterpene lactones (0.15-0.4%) (principally the guaianolides absinthin and artabsin), which are responsible for the bitter taste of the drug. The essential oil composition is very different according to the source of the plant. The most important components are cis-epoxyocimene (40%), β-thujone, spatulenol, trans-sabinyl acetate. Other constituents include flavonol glycosides, phenolic acids and tannins.

Uses

Wormwood is used to treat dyspeptic complaints, gastritis and gastrointestinal problems. It is an appetizer.

Dosage

Internal use

Adult single dose: As a tea infusion 1-1.5 g of the drug in 150 ml of water, up to three times daily. Elderly: dose as for adults. Children: proportional of adult dose according
Drugs containing sesquiterpenes, diterpenes and terpenophenols

to body weight. The dosage may be adjusted according to the bitterness sensitivity of
the individual.

Wormwood should not be taken continuously for periods of more than 3-4 weeks.

Overdose: excessive doses of wormwood preparations may cause vomiting, severe
diarrhoea, retention of urine or dazed feelings. Overdose of alcoholic preparations or the
use of the essential oil may cause central nervous system disturbances, which can lead
to convulsions and ultimately to unconsciousness and death.

Contra-indications

In the case of gastric and duodenal ulcers.

Pregnancy and lactation

The drug and its preparations should not be used during these periods.

**Cardui benedicti herba**

Plant

*Cnicus benedictus* L. - St. Benedict's thistle or Holy thistle (*Asteraceae*)

It is native to the Mediterranean region, from northern Portugal to southern France and
east to Iran. It is known in other parts of the world, including parts of North America, as
an introduced species.

![Figure 4.23](image)

St. Benedict's thistle or Holy thistle (*Cnicus benedictus* L.)

Drug

*Cardui benedicti herba* (St. Benedict's thistle flowering shoot)

Holy thistle consists of the whole or cut, dried flowering tops of *Cnicus benedictus* L.
Constituents
The main active constituents of the drug are sesquiterpene lactones (e.g. cnicin, artemisiifolin). Other constituents include essential oil (\(\pi\)-cymene, fenchone, cinnamic aldehyde), lignans (e.g. arctigenin) and flavonoids.

\[
\begin{align*}
\text{cnicin} & \\
\text{artemisiifolin}
\end{align*}
\]

Uses
Holy thistle is used to treat gastrointestinal problems. It is an appetizer and can induce the production of gastric juice.

Dosage

**Internal use**

*Adult single dose:* As a tea infusion 1-1.5 g of the drug in 150 ml of water, up to three times daily. *Elderly:* dose as for adults.
**Inulae radix**

**Plant**

*Inula helenium* L. – Elecampane (Asteraceae)

It is a perennial plant common in many parts of Great Britain, and ranges throughout central and Southern Europe, and in Asia as far eastwards as the Himalayas. It is naturalized in North America. The plant is protected in Hungary.

![Elecampane (Inula helenium L.)](image)

**Figure 4.27**

Elecampane (*Inula helenium* L.)

**Drug**

*Inulae radix* (Elecampane root)

The root is thick, branching and mucilaginous, and has a warm, bitter taste and a camphoraceous odor.
Constituents
The main active constituents of the drug are sesquiterpene lactones (alantolactone, isoalantolactone). Other constituents include inulin (44%), essential oil and triterpenes.

![Diagram of alantolactone and isoalantolactone](image)

Uses
The drug is used to treat respiratory problems because of its expectorant and antibacterial effects. It has diuretic activity.

Dosage

**Internal use**

*Adult single dose:* As a tea infusion 1 g of the drug in 150 ml of water, up to three times daily. *Elderly:* dose as for adults.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Arnicae flos

Plant

_Arnica montana_ L. – Arnica (Asteraceae)

_Arnica montana_ is endemic to Europe, from southern Iberia to southern Scandinavia and the Carpathians. It is absent from the British Isles and the Italian and Balkan Peninsulas. _A. montana_ grows in nutrient-poor siliceous meadows up to nearly 3,000 metres.

Drug

_Arnicae flos_ (Arnica flower, Ph. Eur.)

Arnica flower consists of the whole or partially broken, dried flower-heads of _Arnica montana_ L. It contains not less than 0.40% _m/m_ of total sesquiterpene lactones expressed as dihydrohelenalin tiglate, calculated with reference to the dried drug.

![Arnica flower](image)

Figure 4.31

_Arnicae flos_ (Arnica flower)

Constituents

The main active constituents of the drug are sesquiterpene lactones (pseudoguaianolide type, 0.2-0.8%), principally helenalin and its esters with acetic, tiglic and other carboxylic acids. Other constituents include diterpenes, flavonoids, pyrrolizidine alkaloids (tussilagine), essential oil containing fatty acids, and carotenoids.
Figure 4.32-33
The structure of helenalin and 11,13-dihydrohelenalin.

Uses
The drug is used to treat bruises, sprains, inflammation caused by insect bites and rheumatic complaints. The best herbal medicine for treatment of wounds and injuries.

Dosage
Only External use
Ointments, creams, gels or compresses made with 5-25% V/V tinctures or 5-25% V/V fluid extracts, diluted tincture (1:3 to 1:10), diluted fluid extracts or a decoction of 2.0 g of dried Arnica flower in 100 ml of water. Not to be used on open wounds.

Contra-indications
Allergy to Arnica or other members of the Asteraceae may occur.

Undesirable effects
Skin irritation has been reported. Contact dermatitis may develop in susceptible individuals.

Pregnancy and lactation
There is no restriction for external use, no harmful effects have been reported.

Cichorii radix
Plant
Cichorium intybus L. - Chicory (Asteraceae)
It is indigenous to Europe and is now widespread in northern states of the USA, Canada and parts of Asia. It is widely cultivated.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Figure 4.34
Chicory (*Cichorium intybus* L.)

Drug
Cichorii radix (Chicory root)
The root consists of the dried roots of *Cichorium intybus* L.

Figure 4.35
*Cichorii radix* (Chicory root)

Constituents
The dried roots contain a high proportion (up to 58%) of inulin together with other sugars. Other important constituents include various sesquiterpene lactones and glycosides, e.g. lactucin, lactucopicrin, cichorioside B (eudesmane type), 8-deoxylactucin (guaiane type) and picriside B (germacrane type).
Uses
Decoction of the root is used as a diuretic and to treat liver ailments. The root is also used as a tonic and laxative. The roasted roots are well-known for their use in coffee mixtures and as a coffee substitute.

Dosage
*Adults*: one dose is 1.5-2 g in 150 ml of water, decoction can be used.

**Taraxaci radix**

Plant
Taraxacum officinale Weber s.l. - Dandelion (Asteraceae)

It is indigenous to Europe and Asia.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Figure 4.41
Dandelion (*Taraxacum officinale* Weber s.l.)

Drug

*Taraxaci radix* (Dandelion root)

Dandelion root consists of the dried roots and rhizomes of *Taraxacum officinale* Weber s.l.

This drug is official in the Österreichisches Arzneibuch.

Figure 4.42
*Taraxaci radix* (Dandelion root)

Constituents

The dried roots contain sesquiterpene lactones including taraxacolide-β-D-glucoside, taraxinic acid-β-D-glucoside, and 11,13-dihydro-taraxinic acid-β-D-glucoside. Other constituents are triterpenes, phytosterols (e.g. taraxasterol), γ-butyrolactone glucoside
ester (taraxacose), chlorogenic acid, caffeic acid, potassium and amino acids. In autumn the dried root contains up to 40% of inulin, in spring about 2%.

![Chemical structures](image)

taraxacolide-O-β-D-glucoside  
taraxinic acid-β-D-glucoside  
11,13-dihydro-taraxinic acid-β-D-glucoside

**Figure 4.43-45**
The structure of taraxacolide-O-β-D-glucoside, taraxinic acid-β-D-glucoside, and 11,13-dihydro-taraxinic acid-β-D-glucoside.

**Uses**
The most relevant therapeutic indications of the drug include the restoration of hepatic and biliary function, treatment of dyspepsia and loss of appetite. The plant extract has a bitter taste. It has choleretic effect.

**Dosage**
Adults: 3-5 g of the drug or 5-10 ml of tincture (1:5, ethanol 25% V/V), three times daily.

**Contra-indications**
The drug and its preparation should not be used in case of occlusion of the bile ducts, gall-bladder empyema and obstructive ileus.

**Undesirable effects**
The drug can produce allergic contact dermatitis due to the presence of the sesquiterpene lactone taraxinic acid β-glucopyranosyl ester.

**Pregnancy and lactation**
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Tanaceti parthenii herba

Plant

*Tanacetum parthenium* (L.) Schulz Bip. – Feverfew (Asteraceae)

The plant is indigenous to South-East-Europe, the Caucasus, and Hungary, too.

Figure 4.46
Feverfew (*Tanacetum parthenium* (L.) Schulz Bip.)

Drug

Tanaceti parthenii herba (Feverfew, Ph. Eur.)

Feverfew consists of the dried, whole or fragmented aerial parts of *Tanacetum parthenium* (L.) Schultz Bip. It contains not less than 0.20% of parthenolide, calculated with reference to the dried drug. Fewerfew has a camphoraceous odour.

Figure 4.47
Tanaceti parthenii herba (Feverfew)
Constituents

The characteristic constituents are sesquiterpene lactones with germacranolide structure, e.g. parthenolide, 3-hydroxypartenolide and artemorine. Quaianolide-type components (canin) occur in significantly smaller amounts. Other constituents include essential oil (its components: camphor, chrysanthemol, p-cimene, borneol) and flavonoids.

![Chemical structures](image)

**Figure 4.48-50**
The structure of parthenolide, 3-hydroxypartenolide and artemorine.

Uses

The most relevant therapeutic indications of the drug include the prophylaxis of migraine.

Dosage

*Adults daily dose:* 50-120 mg of powdered drug or equivalent preparations. Treatment for at least a few months is recommended.

Contra-indications

The drug and its preparation should not be used in case of hypersensitivity to feverfew or other members of the *Asteraceae* family.

Undesirable effects

Allergic contact dermatitis, tongue irritation and inflammation may occur. Cases of abdominal pain and indigestion in patients who have taken the drug for long periods have been reported. Rare cases of diarrhoea, flatulence, nausea or vomiting have been noted.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

*Cynarae folium*

Plant

*Cynara scolymus* L. – Artichoke (Asteraceae)

It is a cultivated plant, but native to Mediterranean countries. It is an important plant of food industry.
Figure 4.51
Artichoke (Cynara scolymus L.)

Drug

*Cynarae folium* (Artichoke leaf, Ph. Eur.)

Artichoke leaf consists of the whole or cut, dried leaves of *Cynara scolymus* L. (C. *cardunculus* L. subsp. *flavescens* Wiklund.). It contains not less than 0.8% of chlorogenic acid calculated with reference to the dried drug.
Constituents

The main characteristic constituents are phenolic derivatives including caffeoylquinic acids, e.g. chlorogenic acid and 1,5-dicaffeoylquinic acids, and flavonoids, e.g. luteolin 7-glucoside (cynaroside), 7-rutinoside (scolymoside). Bitter-tasting sesquiterpene lactones, e.g. cynaropicrin, and various aliphatic acids, especially hydroxy acids, e.g. malic, lactic acids, also present. Cynarin (1,3-dicaffeoylquinic acids) found only in traces in the fresh or dried leaf, is generated from 1,5-dicaffeoylquinic acids during processing with hot water.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Figure 4.53-55
The structure of cynaropicrin, dehydrocynaropicrin and chlorogenic acid.

Uses
The most relevant therapeutic indications of the drug include digestive complaints (e.g. stomach ache, nausea, vomiting, feeling of fullness, flatulence) and hepatobiliary disturbances. Adjuvant to a low fat diet in the treatment of mild to moderate hyperlipidaemia.

Dosage
Adults and elderly daily dose: 5-10 g of dried leaf as an aqueous dry extract or infusion or other equivalent preparations.

Children over 4 years: proportion of adult dose according to age or body weight.

Contra-indications
The drug and its preparations should not be used in case of obstruction of the bile duct or known allergy to artichoke or other species of the Asteraceae.

Special warnings
Patients with cholelithiasis should take artichoke leaf only after consulting a physician.

Undesirable effects
Mild gastro-intestinal disturbances may occur in rare cases, allergic reactions might occur in sensitized patients.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
4.2 Diterpenes

Diterpenes are terpenoids with 20 C-atoms. The general formula of diterpene hydrocarbons is: \(4 \times (C_5H_8) = C_{20}H_{32}\). They contain 4 isoprene units. The fundamental compound, gerano-geranyl-pyrophosphate is formed from two molecules of geranyl-pyrophosphate or from one molecule of pharnesyl-pyrophosphate and from one molecule of dimethylallyl-pyrophosphate. The number of diterpenes with known structure is more than 600 to date. They may be open chained or cyclic. The most important representative of the open-chained diterpenes is phytol (Figure 4.56), which can be found in the structure of chlorophyll-A, chlorophyll-B, and vitamin K1. The most important diterpenes having cyclic structure are cembrane, labdane and pymarane (Figure 4.57-59). Diterpenes possess cytotoxic, antibacterial, antifungal, antiviral, anti-inflammatory, spasmyloytic and cardioactive effects.

![Figure 4.56](image1)

**Figure 4.56**
The structure of phytol.

![Figure 4.57-59](image2)

**Figure 4.57-59**
The most important types of diterpenes.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Drugs

Colophonium

Plant

*Pinus* sp. – Pine (Pinaceae)

*Pinus* species are native to most of the Northern Hemisphere and they live throughout most temperate and subtropical regions of the world. They are cultivated as ornamental plants in parks and gardens.

![Figure 4.60](image)

**Figure 4.60**
Scots pine (*Pinus sylvestris* L.)

Drug

*Colophonium* (Colophony, Ph. Eur.)

The drug is the residue remaining after distillation of the volatile oil from the oleoresin obtained from various species of *Pinus*. 
Constiuents
The resin contains 90% of diterpene resin acids, especially abietic acid.

Uses
Colophony can be used for preparation of rubefacient plasters and ointments. It has also been used to formulate microcapsules and nanoparticles.

Contra-indications
The drug and its preparations should not be used in case of known allergy to the resin.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
Marrubii herba

Plant

*Marrubium vulgare* L. – White horehound (Lamiaceae)

This perennial plant is native to Europe, temperate zone of Asia, North-Africa and India. It may be cultivated.

![Figure 4.63](image1)

White horehound (*Marrubium vulgare* L.)

Drug

*Marrubii herba* (White horehound, Ph. Eur.)

The drug consists of the whole or cut, dried flowering part of *Marrubium vulgare* L.

![Figure 4.64](image2)

*Marrubii herba* (White horehound)
Constituents

The main characteristic constituents of the drug are diterpenes (e.g. premarrubiin and marrubiin). Other characteristic constituents include essential oil (with \(p\)-cymene, limonene, \(\alpha\)-pinene), triterpenes and flavonoids.

![Chemical structures of marrubiin and premarrubiin](image)

**Figure 4.65-66**

The structure of premarrubiin and marrubiin.

Uses

The drug and its products can be used as expectorant in cough associated with cold. It is also used for symptomatic treatment of mild dyspeptic complaints such as bloating and flatulence and in the treatment of temporary loss of appetite.

Dosage

*Adults and elderly daily dose:* Herbal tea: 1-2 g of the comminuted herbal substance in 250 ml of boiling water as a herbal infusion, 3 times daily. Daily dose: 3-6g.

Liquid extract (1:1; 20-30% V/V ethanol): Single dose: 1.5-4 ml, 3 times daily. Daily dose: 4.5-12 ml.

Contra-indications

The drug and its preparations should not be used in case of hypersensitivity to the active substance and to other plants of the Lamiaceae family and obstruction of the bile duct, cholangitis, liver disease and ileus.

Special warnings

Patients with active peptic ulcer, gallstones and any other biliary disorders should consult a doctor before using *Marrubii herba* preparations. The use in children under 12 years of age has not been established due to lack of adequate data.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Ballotae nigrae herba**

Plant

*Ballota nigra* L. – Black horehound (Lamiaceae)
This perennial plant is native to Europe (Mediterranean region), central Asia and the eastern part of United States.

![Black horehound](image)

**Figure 4.67**
Black horehound (*Ballota nigra* L.)

Drug

*Ballo*tae *nigrae herba* (Black horehound, Ph. Eur.)

The drug consists of the dried flowering tops of *Ballota nigra* L. It contains minimum 1.5% of total *ortho*-dihydroxycinnamic acid derivatives, expressed as acteoside and calculated with reference to the dried drug.
The main characteristic constituents of the drug are phenylpropanoids [e.g. the ortho-dihydroxycinnamic acid glucoside acteoside (or verbascoside)] and diterpenes (e.g. marrubiin, 7-acetoxymarrubiin, ballotinone, ballotenol and ballonigrin). Other characteristic constituents include flavonoids (mainly derivatives of apigenin and luteolin), chlorogenic and caffeic acids.
The structure of marrubiin, 7-acetoxymarrubiin, ballotinone, ballotenol, ballonigrin and verbascoside.

Uses
The therapeutic indications of the drug include the tenseness, restlessness and irritability with difficulty in falling asleep. It has also been documented for the relief of mild spasmodic gastric complaints.

Dosage
*Adults and elderly single dose:* Herbal tea: 1.5-5 g of the drug in 250 ml of hot water.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Taxi baccatae folium**

Plant
*Taxus baccata* L. – European yew (Taxaceae)

This plant is a conifer and native to western, central and southern Europe, northwest Africa and southwest Asia. Most parts of the tree are toxic, except the bright red aril surrounding the seeds.
Figure 4.75
European yew (Taxus baccata L.)

Drug
Taxi baccatae folium (European yew leaf)
The drug consists of the dried leaves of Taxus baccata L.

 Constituents
The main characteristic constituents of the drug are diterpenes containing N-atom (e.g. taxol A and B, taxin A and B). Other constituents include biflavonoids and catechin.

Figure 4.76-79
The structure of taxol A and B, taxin A and B.
Drugs containing sesquiterpenes, diterpenes and terpenophenols

Uses

The diterpene alkaloids of the drug are highly toxic compounds with antimitotic activity, therefore their semi-synthetic derivatives are used in cancer therapy. Paclitaxel, a mitotic inhibitor used in chemotherapy, was developed from taxol. Taxol can be isolated in higher amounts from the bark of Taxus brevifolia L.

4.3 Terpenophenols

Cannabinoids are the most important group of the terpenophenols, and can be isolated from hemp (Cannabis sativa). Cannabinoids are synthetised from geranyl pyrophosphate and a phenol compound (olivetol) (Figure 4.80). In the course of biosynthesis first cannabigerol is produced, then cannabidiol, cannabinol and finally tetrahydrocannabinol (THC). THC is a psychoactive constituent of the cannabis plant. Cannabis sativa contains it only in traces but Cannabis sativa subspecies indica is a good source of this compound. Marihuana containing 2-6% of THC and hashish containing 5-20% of THC are dangerous drugs. Hop (Humulus lupulus L.), also belonging to the family of Cannabaceae, contains the terpenophenol derivatives humulone and lupulone. Humulone (α-lupulic acid), a phloroglucinol derivative with three isoprenoid side-chains, is a bitter-tasting chemical compound found in the resin of mature hops. Two side-chains are prenyl groups and one is an isovaleryl group. Further details about hop can be found in Chapter 10.

Figure 4.80
Biosynthesis of the terpenophenol tetrahydrocannabinol (THC).
Drugs

Cannabis indicae herba

Plant

*Cannabis sativa* L. ssp. *indica* (Lam.) E. Smallet Cronquist – Indian hemp (Cannabaceae)

This dioecious plant is native to the Indian subcontinent. Despite being illegal, it is widely cultivated. The leaves, the flowering tops or the resin of the female plants are collected. The finely chopped and dried leaf is marijuana, the resin of the plant is hashish. Hash oil is a resinous matrix of cannabinoids produced by a solvent (chloroform) extraction of cannabis and the evaporation of the solvent.

Drug

Cannabis indicae herba (Indian hemp)

The drug consists of the dried leaves and flowering parts of *Cannabis sativa* L. ssp. *indica* (Lam.) E. Smallet Croquist.

Constituents

The drug contains terpenophenols such as Δ⁹-THC, Δ⁹-tetrahydrocannabinol, cannabinol, cannabidiol, cannabidiolic acid, tetrahydrocannabinolic acid. A further constituent is about 0.1% of essential oil (with *p*-cymene, humulene).

\[
\text{Δ}^9\text{-tetrahydrocannabinol} \quad \text{cannabinol} \quad \text{cannabidiol}
\]

\[
\text{Δ}^9\text{-tetrahydrocannabinolic acid}
\]

Figure 4.81-84

The structure of Δ⁹-tetrahydrocannabinol, cannabinol, cannabidiol and Δ⁹-tetrahydrocannabinolic acid.

Uses

The drug has sedative, antineuralgic and spasmolytic effects. Therefore in the therapy the drug and its products (e.g. Marinol) can be used for decreasing nausea following chemotherapy, relieving muscle cramps and pains of patients with multiple sclerosis and as an appetizer for patients infected with HIV. Other uses of the plant are illegal.
5.1 Triterpenes and saponins

Triterpenes contain 30 C-atoms. They are synthetised from 6 mol isopentenyl-pyrophosphate (IPP) or 2 mol pharnesyl-pyrophosphate (FPP; C15). They may be open-chained or cyclic (tetra- or pentacyclic) compounds. The fundamental compound of triterpene hydrocarbons is squalene: $C_{30}H_{48}$ (Figure 5.1). The interlocking of isoprene units is head-foot (tail); but in the middle of the molecule is foot (tail)-foot (tail). Squalene is the fundamental compound of the biosynthesis of steroids. To the skeleton of cyclic triterpenes different functional groups can be attached (-OCH$_3$; -CHO; -COOH; -OH; -O-C-R), therefore a large degree of structural variability is possible. If the –OH and –COOH groups are present in glycosídic form, the compounds are called saponins. In the case of the presence of more than two sugar-molecules, the chain of the sugar units is mostly branched. Various types and structures of triterpenes can characterize plant taxonomic categories, and they can also cause differences in their pharmacological action and solubility. Saponins have a high molecular weight and a high polarity. As glycosides they can be hydrolysed by acids to yield an aglycone (sapogenin), various sugars and related uronic acids. Based on the structure of the aglycone, two kinds of saponins can be distinguished: 1) the steroidal (commonly tetracyclic) triterpenoids and 2) the pentacyclic triterpenoid types (Figure 5.2-5). Both of these have a glycosidic linkage at C-3. Steroidal alkaloids occur in the Solanaceae family. These constituents possess a heterocyclic nitrogen-containing ring, giving the compounds basic properties (e.g. solasodine, Figure 5.6). Triterpenes are wide-spread in various plants, they occur first of all in the dicotyledonous plants. Mainly triterpene glycosides (saponins) have important pharmaceutical role. Triterpene saponins are used as expectorant, diuretics, antibacterial, antifungal, antiviral agents and to treat venous insufficiency. Saponins often prevent the absorption of other materials (e.g. drugs). Saponins hemolyse red blood cells (erythrocytes), therefore they are strongly toxic compounds if they enter into the blood vessels. Their aqueous solutions are frothy, similarly to soap-solutions.

Figure 5.1
The structure of squalene.
Two main types of triterpenoids: tetracyclic triterpenoids and pentacyclic triterpenoids.

The structure of solasodine.

**Drugs**

*Liquiritiae radix*

Plant

Glycyrrhiza glabra L. – Liquorice (Fabaceae)

This perennial plant is native to Europe and temperate zone of Asia. It can be cultivated.
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.7
Liquorice (Glycyrrhiza glabra L.)

Drug

*Liquiritiae radix* (Liquorice root, Ph. Eur.). **Other Drug**

*Liquiritiae extractum fluidum ethanolicum normatum* (Liquorice ethanolic liquid extract, standardized, Ph. Eur.)

Liquorice root consists of the dried unpeeled or peeled, whole or cut root and stolons of *Glycyrrhiza glabra* L. It contains not less than 4.0% of glycyrrhizic acid, calculated with reference to the dried drug.

Standardised liquorice ethanolic liquid extract is produced from Liquorice root. It contains not less than 3.0% and not more than 5.0% of glycyrrhizic acid. The extract is produced from the drug and alcohol (70% *V/V*), with an appropriate procedure for liquid extracts. It is a dark brown, clear liquid with a faint characteristic odour and a sweet taste.
Constituents

The main characteristic constituents of the drug are triterpene glycosides (saponins, 2-15%), principally glycyrrhizic acid, the 3β-diglucuronide of glycyrrhetic acid, which occurs as a mixture of potassium and calcium salts known as glycyrrhizin. Other constituents include flavonoids (e.g. liquiritin, glabrol), isoflavonoids (e.g. glabrene), chalcones (e.g. isoliquiritin), sterols, coumarins (e.g. umbelliferone, herniarin), sugars (glucose, saccharose) and essential oil (approx. 0.05%).

![Figure 5.8](image)

Liquiritiae radix (Liquorice root)

![Figure 5.9-14](image)

The structure of glycyrrhizic acid, glycyrrhetic acid, liquiritin, isoliquiritin, glabrol and glabrene.
Drugs containing triterpenes, steroids, saponins and cardenolides

Uses

The therapeutic indications of the drug include the adjuvant therapy of gastric and duodenal ulcers and gastritis. Moreover the drug and its products can be used as expectorant in the case of coughs and bronchial catarrh. Liquorice root has a sweet taste due to its glycyrrhizin content (this constituent is 50 times sweeter than saccharose).

Dosage

Gastric and duodenal ulcers and gastritis

*Adults and elderly daily dose*: 5-15 g of liquorice root (equivalent to 200-600 mg of glycyrrhizic acid) taken in divided doses or 5-15 ml of standardized liquorice ethanolic liquid extract.

Coughs and bronchial catarrh

*Adults and elderly daily dose*: 1.5-5 g of liquorice root (equivalent to 60-200 mg of glycyrrhizic acid) taken in divided doses or 1.5-5 ml of standardized liquorice ethanolic liquid extract.

*Children 4 years of age and older*: as an expectorant only, in aqueous preparations; portion of adult dose according to age or body weight.

Products of liquorice root should not be taken for more than 4-6 weeks without medical advice.

Contra-indications

The drug and its preparations should not be used in case of cardiovascular-related disorders (e.g. hypertension), renal disorders, cholestatic or inflammatory liver disorders, hypokalaemia and severe obesity.

Special warnings

The maximum daily dose (15 g) of the drug (or a content of 600 mg of glycyrrhizin) should never be exceeded. Consumption of glycyrrhizin as a taste modifier should be limited to 100 mg/day. Overdose of the drug may cause adverse effects in more sensitive patients.

Interaction with other medicaments and other forms of interaction: Hypokalaemia may enhance the action of cardiac glycosides and interact with antiarrhythmic drugs or with drugs which induce reversion to sinus rhythm (e.g. quinidine). Concomitant use with other drugs inducing hypokalaemia may aggravate electrolyte imbalance. Glycyrrhizic acid has been reported to decrease plasma clearance and increase the AUC of prednisolone, and to potentiate hydrocortisone activity in human skin.

Pregnancy and lactation

Liquorice root and its preparations should not be used during pregnancy or lactation.

Quillajae cortex

Plant

*Quillaja saponaria* Mollina. – Soap bark tree (Rosaceae)

The evergreen, 15-18 m high tree is indigenous in Chile, Peru and Bolivia. In pharmacies it is available in chopped or powdered (pulverized) form. It irritates the
throat, the eyes and the nose during the process of pulverizing: it causes watery eyes and sneezing.

Drug

*Quillajae cortex* (Quillaja bark, ÖAB, Ph. Helv., DAC).

The drug consists of the dried peeled secondary roots of *Quillaja saponaria* Mollina.

**Figure 5.15**

*Quillajae cortex* (Quillaja bark)

**Constituents**

The drug contains a mixture of triterpene-saponin-glycosides (8.5-16.5%), in which the main sapogenine is quillaic acid. It contains tannins (derivatives of gallic acid; 10-15%) and Ca-oxalate.

**Figure 5.16**

The structure of quillaic acid.
Drugs containing triterpenes, steroids, saponins and cardenolides

Uses
The drug has expectorant, antifungal, antibacterial and immunostimulant actions. It is a cough-reliever and expectorant. It is used in the case of scalp diseases, against dandruff, oily hair and hair loss (alopecia).

Dosage

Coughs
Adults and elderly daily dose: 0.2 g of the drug (2 times a day) in 200 ml of hot water as a tea.

Scalp diseases
Adults and elderly daily dose: 1 g of the drug with 200 ml of hot water as an aqueous extract for rubbing.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Verbasci flos

Plants
Verbascum phlomoides L. (Orange mullein), V. densiflorum Bertol. (Dense-flowered mullein) - (Scrophulariaceae)

Verbascum species are native to Europe and Asia, and they possess the highest species diversity in the Mediterranean.

![Figure 5.17-18](image)

Orange mullein (*Verbascum phlomoides* L.), Dense-flowered mullein (*V. densiflorum* Bertol.)

Drug
Verbasci flos (Mullein flower, Ph. Eur.).
Verbasci flos consists of the dried flower, reduced to the corolla and the androecium of Verbascum thapsus L., V. densiflorum Bertol. (V. thapsiforme Schrad), and V. phlomoides L.

Figure 5.19
Verbasci flos (Mullein flower)

Constituents
The main characteristic constituents of the drug are triterpene glycosides (saponins), principally verbascosaponin. Other constituents of the drug are iridoids (e.g. aucubin, catalpol), flavonoids (e.g. apigenin, quercetin), cinnamic acid derivatives (e.g. protocatechu acid, caffeic acid, ferulic acid) and mucilage.

Figure 5.20
The structure of verbascosaponin.

Uses
The therapeutic indications of the drug include the adjuvant therapy of coughs and bronchial catarrh. The infusion of the drug has expectorant, diuretic and antibacterial activities. Verbasci flos is used as a component of tea-mixtures.
Drugs containing triterpenes, steroids, saponins and cardenolides

Dosage

*Adults and elderly daily dose:* 1.5 g of the drug in 200 ml of hot water used as an infusion, 2-3 times daily.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Saponariae albae radix**

Plant

*Gypsophila paniculata* L. – Baby’s breath (Caryophyllaceae)

This herbaceous perennial plant is native to central and eastern Europe. It can grow on the steppes in dry, sandy and stony places, often on calcareous soils.

![Figure 5.21](image)

**Figure 5.21**

Baby’s breath (*Gypsophila paniculata* L.)

Drug

*Saponariae albae radix* (White soapwort root)

The drug consists of the dried, peeled roots of *Gypsophila paniculata* L.
Constituents

The main characteristic constituents of the drug are triterpene saponins (6-20%). The main aglycons are gypsogenin and quillaic acid.

Uses

The therapeutic indications of the drug include the adjuvant therapy of coughs and bronchial catarrh. The decoction of the drug has expectorant effect.

Dosage

*Adults and elderly daily dose*: 30-150 mg of the pulverized drug in 200 ml of hot water used as a decoction.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
Drugs containing triterpenes, steroids, saponins and cardenolides

Primulae radix

Plants

*Primula veris* L. (Common cowslip), *P. elatior* (L.) Hill. (True oxlip) – (Primulaceae)

*Primula* species are perennial, herbaceous plants, native to Europe, North-Africa, West-Asia and the Caucasus; deserving protection.

![Common cowslip](image)

**Figure 5.25**
Common cowslip (*Primula veris* L.)

Drug

*Primulae radix* (Primula root, Ph. Eur.)

Primula root consists of the whole or cut, dried rhizome and root of *Primula veris* L. or *P. elatior* (L.) Hill. Primula root has a bitter taste.
Constituents

The main characteristic constituents are triterpene saponins (3-10%). The principal saponins have a branched chain of at least four sugars (glucuronic acid, glucose, galactose and rhamnose) at C-3. The main saponin of the drug is protoprimulagenin A. Other important constituents include phenolic glycosides. The main compounds of the essential oil in the root are primverin and primulaverin, which occur in both species, in highly variable amounts up to 2.3%. These compounds are the 2-primeverosides of 4-methoxy- and 5-methoxysalicylic acid methyl esters, respectively. Primula root has a characteristic odour due to its phenolic glycoside content.
Drugs containing triterpenes, steroids, saponins and cardenolides

Uses
The therapeutic indications of the drug include productive cough, catarrh of the respiratory system and chronic bronchitis.

Dosage

**Adults and elderly dose:** 0.5-1.5 g of the drug as a decoction or equivalent preparations. Maximum daily dose of the drug is 5-10 g. Overdose of the drug may lead to stomach upset, vomiting or diarrhoea.

**Children:** 4-10 years/0.5-1 g daily; 10-16 years/0.5-1.5 g daily.

Contra-indications
Patients with gastritis or gastric ulcer should not use the drug.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Hederae helicis folium**

Plant
*Hedera helix* L. – Ivy (Araliaceae)

This climbing evergreen plant is native to Europe, West-Asia, Caucasus and North-Africa.

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**Figure 5.27-29**
The structure of protoprimulagenin A, primverin and primulaverin.
Drug

Hederae helicis folium (Ivy leaf, Ph. Eur.)

Ivy leaf consists of the dried leaves of *Hedera helix* L. It contains three main saponins: hederasaponin C (hederacoside C), hederasaponin B and hederasaponin D, with not less than 2.5% of hederasaponin C.
Constituents

The main characteristic constituents are triterpene saponins (2.5-6%), principally hederasaponin C (hederacoside C), hederasaponin B and α-hederin. The aglycone part is hederagenin. Other constituents include phytosterols (cholesterol, stigmasterol, β-sitosterol), polyines (e.g. falcarinol, didehydrofalcarinol), flavonoids (e.g. rutin), cinnamic acid derivatives (e.g. caffeic acid, chlorogenic acid) and essential oil.

![Chemical structures of hederasaponin C (hederacoside C), hederasaponin B, falcarinol and didehydrofalcarinol.](image)

**Figure 5.32-35**

The structure of hederasaponin C (hederacoside C), hederasaponin B, falcarinol and didehydrofalcarinol.

Uses

The therapeutic indications of the drug include productive cough (when associated with hypersecretion of viscous mucus). The drug and its products can be used as an adjuvant treatment of inflammatory bronchial diseases. The drug can be used in suppositories.

Dosage

**Oral use**

Adults and elderly daily dose of ethanol-containing preparations: 250-420 mg; for children of 4-12 years: 150-210 mg; for children of 1-4 years: 50-150 mg; for children <1 year: 20-50 mg.

Adults and elderly daily dose of ethanol-free preparations: 300-945 mg; for children of 4-12 years: 200-630 mg; for children of 1-4 years: 150-300 mg; for children <1 year: 50-200 mg.

Overdose: it can provoke nausea and vomiting.

**Rectal use**

In suppositories: for children of 4-10 years: 960 mg.
Undesirable effects

Fresh leaves can cause allergic contact dermatitis. Polyines of the drug have been reported to be allergenic.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Betulae folium

Plants

*Betula pendula* Roth. (Silver birch), *B. pubescens* Ehrh. (Downy birch) – (Betulaceae)

Betula species are widespread in the Northern Hemisphere, particularly in northern temperate and boreal climates.

![Figure 5.36](Silver birch) (*Betula pendula* Roth.)

Drug

*Betulae folium* (Birch leaf, Ph. Eur.)

Birch leaf consists of the whole or fragmented dried leaves of *Betula pendula* Roth and/or *Betula pubescens* Ehrh., as well as hybrids of both species. It contains not less than 1.5% of flavonoids, calculated as hyperoside with reference to the dried drug.
Drugs containing triterpenes, steroids, saponins and cardenolides

**Betulae folium** (Birch leaf)

**Constituents**

The main characteristic constituents are flavonoids (1-3%), principally hyperoside and other quercetin glycosides, myricetin and kaempferol glycosides. The drug also contains triterpene saponins (e.g. triterpenesaponin 1, 2, 3). Other constituents include chlorogenic acid, monoterpenes, sesquiterpenes, potassium and traces of essential oil.

**Figure 5.37**

**Betulae folium** (Birch leaf)

**Figure 5.38-40**

The structure of triterpenesaponin 1, 2 and 3.
Uses

The therapeutic indications of the drug include the rinsing of the urinary tract, especially in cases of inflammation and kidney stones, and as an adjuvant in the treatment of bacterial infections of the urinary tract.

Dosage

*Adults and elderly dose:* 2-3 g of the drug as an infusion, 2-3 times daily. Tincture (1:10): 2 ml, 3 times daily. Fresh juice: 15 ml, 3 times daily.

Special warnings and precautions for use

Patients with impaired heart and kidney function should not use the drug and its preparations.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Veronicae herba

Plant

*Veronica officinalis* L. – Common speedwell (Scrophulariaceae)

This herbaceous plant is native to Europe, West-Asia and Caucasus. In Hungary it is widespread in the mountains and in the oak forests of Transdanubia.
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.41
(Common speedwell) (*Veronica officinalis* L.)

Drug

*Veronicae herba* (Common speadwell flowering shoot, Veronica herb)
The drug consists of the dried flowering shoot of *Veronica officinalis* L.
Figure 5.42
*Veronicae herba* (Common spreadwell flowering shoot, Veronica herb)

**Constituents**

The drug contains triterpenes, iridoid glycosides (0.5-1%, e.g.: catalpol, veronicoside, verproside), flavonoids (e.g. luteolin), caffeic acid, chlorogenic acid, D-mannitol, tannins and β-sitosterol.

![Chemical structures of veronicoside and verproside](image)

**Uses**

The drug has expectorant, antibacterial and anti-inflammatory activities. It can be used for the treatment of asthma bronchiale and rheumatic conditions.

**Dosage**

*Adults and elderly daily dose:* 2-3 g of the drug as an infusion, 2-3 times daily.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
Ononidis radix

Plant

*Ononis spinosa* L. – Restharrow (Fabaceae)

The plant is an approx. 0.8 m high perennial semi-shrub. It is native to Europe, North-Africa, West-Asia and India. It often occurs on meadows and pastures.

Drug

*Ononis radix* (Restharrow root, Ph. Eur.)

The drug consists of the whole or cut, dried root of *Ononis spinosa* L.

![Ononidis radix](image)

**Figure 5.45**

*Ononidis radix* (Restharrow root)

Constituents

The drug contains triterpenes, principally α-onocerin (onocol), isoflavonoids (e.g. formononetin, ononin, biochanin A 7-O-glucoside-6″-malonate), phytosterols (e.g. β-sitosterol), phenolic acids, tannins, minerals and essential oil (containing mainly trans-anethole, carvone, menthol).
The structure of α-onocerin (onocol), formononetin, ononin and biochanin A 7-O-glucoside-6′-malonate.

**Figure 5.46–49**
The structure of α-onocerin (onocol), formononetin, ononin and biochanin A 7-O-glucoside-6′-malonate.

**Uses**
The therapeutic indications include the rinsing the urinary tract, especially in cases of inflammation and kidney stones, and as an adjuvant in the treatment of bacterial infections of the urinary tract. The drug and its preparations have diuretic effect.

**Dosage**
*Adults and elderly daily dose:* 2-3 g of the drug as a decoction, 2-3 times daily.

**Pregnancy and lactation**
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Solidaginis virgaureae herba**

**Plant**
*Solidago virgaurea* L. – European goldenrod (Asteraceae)

This plant is native to Europe, North-Africa, temperate zones of Asia and India.
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.50
European goldenrod (*Solidago virgaurea* L.)

Drug

*Solidaginis virgaureae herba* (European goldenrod, Ph. Eur.)

It consists of the whole or cut, dried, flowering aerial parts of *Solidago virgaurea* L. It contains minimum 1.0% of flavonoids, expressed as hyperoside and calculated with reference to the dried drug.

Figure 5.51
*Solidaginis virgaureae herba* (European goldenrod)
Constituents

The drug contains triterpene saponins (up to 2%) which are derived from virgaureagenin (e.g. virgaureasaponin 1), polygalacic acid (e.g. polygalacic acid-3-β-D-glucoside) and other sapogenins. Other constituents include flavonoids (minimum 1.0%), phenol glycosides (e.g. virgaureoside A), phenolic acids such as chlorogenic and caffeic acids and a small amount of essential oil.

![virgaureasaponin 1](image1)

![virgaureoside A](image2)

![polygalacic acid-3-β-D-glucoside](image3)

**Figure 5.52-54**

The structure of virgaureasaponin 1, polygalacic acid-3-β-D-glucoside and virgaureoside A.

Uses

The therapeutic indications include the rinsing of the urinary tract, especially in cases of inflammation and kidney stones, and as an adjuvant in the treatment of bacterial infections of the urinary tract. The drug and its preparations have diuretic effect.

Dosage

*Adults and elderly dose*: 3-4 g of the drug as an infusion in 150 ml water, 2-3 times daily. *Children*: 1-4 years of age: 1-2 g; 4-10 years of age: 2-5 g; 10-16 years of age: 4-8 g.

Contra-indications

The drug should not be used in patients with oedema due to impaired heart or kidney function.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
Hippocastani semen

Plant

Aesculus hippocastanum L. – Horse-chestnut (Hippocastanaceae)

This tree is native to Europe. It is widely cultivated in streets and parks.

Figure 5.55

Horse-chestnut (*Aesculus hippocastanum* L.)

Drug

*Hippocastani semen* (Horse-chestnut seed, DAB)

The drug consists of the dried seeds of *Aesculus hippocastanum* L. containing not less than 3.0% of triterpene glycosides, expressed as anhydrous aescin and calculated with reference to the dried drug.
Constituents

The characteristic constituents, collectively known as aescin (3-10%), are a mixture of acylated triterpene saponins based on two main aglycones, protoaescigenin and barringtogenol C. All the saponins have a trisaccharide group at C-3 (comprising glucuronic acid with substituent sugars such as glucose, galactose or xylose at the 2- and 4-positions. The two major saponins, both arising from protoaescigenin, are esterified at the 21β-position, one with angelic acid, the other with tiglic acid, and with acetic acid at the 22α-position. Other constituents include flavonoids (mostly di- and triglycosides of quercetin and kaempferol), sterols, essential oil and a high proportion of starch (30-60%).

Figure 5.57-60
The structure of protoaescigenin, barringtogenol C, tiglic acid and angelic acid.
Uses
The therapeutic indications include the treatment of chronic venous insufficiency and varicosis. The saponin-mixture of the drug regulates the permeability of blood vessels and increases capillary resistency and the tone of veins.

Dosage
Adults and elderly daily dose: drug or hydroalcoholic extract containing 50-150 mg of triterpene glycosides (calculated as aescin), usually in divided doses. The drug is not recommended for children.

Pregnancy and lactation
The seed extracts have been used in clinical studies involving pregnant women, with some studies excluding those in the third trimester. No adverse effects have been reported, but in accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Calendulae flos
Plant
Calendula officinalis L. – Common marigold (Asteraceae)
The plant can be cultivated in warm temperate regions of the world.
Figure 5.61
Common marigold (*Calendula officinalis* L.)

**Drug**

*Calendulae flos* (Calendula flower, Ph. Eur.)

Calendula flower consists of the whole or cut, dried, and fully opened flowers which have been detached from the receptacle of the cultivated, double-flowered varieties of *Calendula officinalis* L. It contains not less than 0.4% of flavonoids, calculated as hyperoside with reference to the dried drug.
Drugs containing triterpenes, steroids, saponins and cardenolides

Constituents

The characteristic constituents are triterpene saponins (mainly oleanolic acid glycosides, e.g. calendulaglycoside A), triterpenes in free state (e.g. faradiol, α-amirin, lupeol). Other constituents include flavonoids, carotenoids (e.g. β-carotene, lycopene, zeaxanthin, violaxanthin), polysaccharides, sterols, sesquiterpenoids and essential oil.

Figure 5.62
*Calendulae flos* (Calendula flower)

![Constituents](image)

**calendulaglycoside A**

**faradiol**

**α-amirin**

**lupeol**

Figure 5.63-66
The structure of calendulaglycoside A, faradiol, α-amirin and lupeol.
Uses

The therapeutic indications include the symptomatic treatment of minor inflammations of the skin and mucosa. The drug and its preparations aid the healing of minor wounds, leg ulcer and burns.

Dosage

*Infusion for topical application:* 1-2 g of dried flower per 150 ml of water. *Fluid extract* 1:1 in 40% ethanol or tincture 1:5 in 90% ethanol. For the treatment of wounds the tincture is applied undiluted; for compresses the tincture is usually diluted at least 1:3 with freshly boiled water. *Semi-solid preparations* containing 2-10% of fluid extract 1:1.

Pregnancy and lactation

No data available. However, there are no objections to external use during pregnancy and lactation.

**Polygalae radix**

Plant

*Polygala senega* L. – Seneca snakeroot (Polygalaceae)

This plant is native to the eastern part of Canada and USA.

Drug

*Polygalae radix* (Senega root, Ph. Eur.)

Senega root consists of the dried and usually fragmented root and root crown of *Polygala senega* L. or of certain other closely related species or of a mixture of these *Polygala* species. Senega root has a faint, sweet odour, slightly rancid or reminiscent of methyl salicylate. Reduced to a powder, it is irritant and sternutatory (causes sneezing). When shaken with water, the powder produces a copious froth.
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.67
*Polygalae radix* (Senega root)

Constituents
The drug contains triterpene saponins (6-16%), for example senegasaponin A and B, senegin II and III. Other constituents include methyl salicylate, sugars and traces of essential oil.

Figure 5.68-70
The structure of senegasaponin A, senegin II and methyl salicylate.
Uses
Because of the saponin content the drug can be used as an expectorant in the treatment of bronchitis and the inflammation of the upper respiratory tract.

Dosage

*Adults and elderly daily dose*: 1.5-3 g of the drug (divided into 2 or 3 parts) with 250 ml of water, as a decoction. **Overdose**: nausea, vomiting, diarrhoea may occur!

The use of the drug is not recommended in children under 12 years of age

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Pruni africanae cortex**

Plant

*Prunus africana* Kalkm. – Red stinkwood (Rosaceae)

This evergreen tree is native to the montane regions of Sub-Saharan Africa.

Drug

*Pruni africanae cortex* (Pygeum africanum bark, Ph. Eur.)

The drug consists of the whole or cut, dried bark of the stems and branches of *Prunus africana* (Hook f.) Kalkm. (syn. *Pygeum africanum* Hook f.).

Constituents

The main constituents are phytosterols, e.g. β-sitosterol, β-sitosterol 3-glycoside, free C_{12}-C_{24} fatty acids, pentacyclic triterpenic acids (e.g. ursolic and oleanolic acid derivatives) and long chain apiphatic alcohols (*n*-docosanol, *n*-tetracosanol and their trans-ferulic acid esters).
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.71-74
The structure of β-sitosterol, ursolic acid, oleanolic acid and ferulic acid n-tetracosanol ester.

Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stage I and II of benign prostatic hyperplasia as defined by Alken

Stage I: Dysuria, pollakisuria, possibly nocturia, reduction in projection of the urine stream, no residual urine (stage of compensation of the bladder musculature)

Stage II: Same symptoms as at stage I, except with residual urine (incipient decompensation of the bladder musculature)

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck

Stage II: intermittent micturition problems (frequency, calibre of urine stream), more or less marked BPH, urine stream: between 10 and 15 ml/s maximal flow, no or low (< 50 ml) residual urine, no or incipient bladder trabeculation

Stage III: permanent micturition problems (frequency, calibre of urine stream), more or less marked BPH, urine stream: less than 10 ml/s maximal flow, residual urine more than 50 ml, trabeculated bladder

Dosage

Adults and elderly daily dose: 100-200 mg of the lipophilic extract of the drug.

Special warnings and precautions for use

All cases of difficulty urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.
Pregnancy and lactation
Not applicable.

Cimicifugae rhizoma

Plant
*Cimicifuga racemosa* (L.) Nutt. – Black cohosh (Ranunculaceae)
This plant is native to North-America.

Drug
*Cimicifugae rhizoma* (Black cohosh rhizome)
The drug consists of the dried rhizomes and roots of *Cimicifuga racemosa* (L.) Nutt.

![Cimicifugae rhizoma](image)

**Figure 5.75**
*Cimicifugae rhizoma* (Black cohosh rhizome)

Constituents
The main constituents are triterpene glycosides, e.g. cimicifugoside (cimigenol-3-O-\(\beta\)-D-xyloside), actein (formerly known 27-deoxyactein) and cimiracemoside F and G. All these glycosides are 3-O-xylosides or 3-O-arabinosides of aglycones of the cycloartane type. Other constituents include fukiik and piscidic acid and their esters, e.g. fukinolic acid, aromatic acids (caffeic, ferulic and isoferulic acids) and cimiracemates A-D (phenylpropanoid ester dimers).
Drugs containing triterpenes, steroids, saponins and cardenolides

![Chemical structures of cimicifugoside (cimigenol-3-O-β-D-xyloside), actein, cimiracemoside F and G, fukiik acid, piscidic acid, fukinolic acid and cimiracemates A-D.]

**Figure 5.76-86**
The structure of cimicifugoside (cimigenol-3-O-β-D-xyloside), actein, cimiracemoside F and G, fukiik acid, piscidic acid, fukinolic acid and cimiracemates A-D.

**Uses**
Therapeutic indications of the drug include climacteric symptoms such as hot flushes, profuse sweating, sleep disorders and nervous irritability.

**Dosage**
*Adult daily dose:* isopropanolic (40% V/V) or ethanolic (40-60% V/V) extracts corresponding to 40-140 mg of the drug or equivalent preparations.

Onset of action can be expected within 2-4 weeks. For further improvement medication should be taken for at least 6-8 weeks, maximum effects are seen within 3 months.

**Special warnings and precautions for use**
The use of the drug in patients with existing oestrogen-dependent tumors should be approached with caution. Clinical experience suggests a lack of risk, but relevant human toxicological data are unavailable.

**Pregnancy and lactation**
The drug and its preparations should not be taken during pregnancy and lactation.

**Centellae asiaticae herba**

**Plant**
*Centella asiatica* (L.) Urban. – Centella (Apiaceae)

This plant is native to the tropical and subtropical parts of Asia, Australia, Africa and America.
Drug

*Centellae asiaticae herba* (Centella)

Centella consists of the dried, fragmented aerial parts of *Centella asiatica* (L.) Urban. It contains not less than 6.0% of total triterpenoid derivatives, expressed as asiaticoside, calculated with reference to the dried drug.

![Centellae asiaticae herba](image)

**Figure 5.87**

Centellae asiaticae herba (Centella)

Constituents

The main characteristic constituents are triterpene acids, e.g. asiatic and madecassic acids, and their sugar esters, principally asiaticoside with small amounts of asiaticoside A and B. Depending on the source of the plant material, the amount of triterpenoids may vary from 1% to 8%. Other constituents include essential oil (with compounds of β-farnesene, β-caryophyllene, α-pinene, β-pinene), flavonoids (mainly quercetin and kaempferol glycosides) and phytosterols.
Drugs containing triterpenes, steroids, saponins and cardenolides

![Chemical structures of asiatic acid, madecassic acid, asiaticoside A, asiaticoside, asiaticoside B](image)

Figure 5.88-92
The structure of asiatic acid, madecassic acid, asiaticoside, asiaticoside A and B.

**Uses**
Therapeutic indications of the drug include the treatment of chronic venous insufficiency, varicosis and wound healing.

**Dosage**

**Internal use**
*Adult dose:* 0.6 g of the dried drug as an infusion, tincture or extract, up to four times daily.

**External use**
Semi-solid preparations containing 1% of extract or tincture.

**Undesirable effects**
A few cases of contact allergy have been reported after topical application.

**Pregnancy and lactation**
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

**5.2 Triterpenes in adaptogens**
Adaptogenic drugs:
- are not toxic; intervene as mild disturbing factors into the physiological processes
- they increase the resistance of organisms against different physical, chemical, biological actions and against stress
- they act as regulators in order to normalize the altered functions of organisms; decrease hyperfunctions, increase hypofunctions
• act as a tonic; improve the physical productivity, stimulate the central nervous system, act against premature exhaustion, increase the non-specific resistance of organisms, and the rate of protein- and RNA-synthesis

The drug of *Eleutherococcus senticosus* (Eleutheroococci radix) will be introduced in the Chapter 10 because its lignan compounds.

**Drugs**

**Ginseng radix**

**Plant**

*Panax ginseng* C.A. Meyer – Ginseng (Araliaceae)

This plant is native to China, Japan, Korea and Russia; and is cultivated in China, Japan and Korea. Korean ginseng is the most valuable. The root of *Panax quinquefolius*, which is native to North-America, can also be used as ginseng radix, but this drug is less valuable than the radix of *Panax ginseng*.

**Drug**

*Ginseng radix* (Ginseng, Ph. Eur.)

Ginseng consists of the whole or cut dried root of *Panax ginseng* C.A. Meyer. It contains not less than 0.40% of combined ginsenosides Rg1 and Rb1, calculated with reference to the dried drug.

![Ginseng radix](image)

**Figure 5.93**

*Ginseng radix* (Ginseng)
Constituents

The main characteristic constituents are triterpene saponins of the dammarane type, as derivatives of either protopanaxadiol or protopanaxatriol. Protopanaxadiol saponins are: ginsenosides Ra1, Ra2 and Ra3, ginsenosides Rb1, Rb2 and Rb3, ginsenosides Rc and Rd. Protopanaxatriol saponins are: ginsenosides Re and Rf, ginsenosides Rg1, Rg2 and Rh1. The total ginsenoside content of a 6-year-old main root varies between 0.7-3%. The lateral roots can contain two or three times more saponins than the main root. Other constituents include peptidoglycans called panaxans, acetylenic compounds (e.g. panaxinol), oligo- and polysaccharides, phenolic compounds such as vanillic acid and salicylic acid and traces of essential oil containing mainly sesquiterpenes.

![Chemical structures](image)

Figure 5.94-98
The structure of protopanaxadiol, protopanaxatriol, ginsenoside Rb1, ginsenoisde Re and panaxinol.

Uses

Therapeutic indications of the drug include the treatment of decreased mental and physical capacities such as weakness, exhaustion, tiredness and loss of concentration, as well as during convalescence.

Dosage

*Adult daily dose:* 0.5 g up to a maximum of 2 g of dried root or equivalent preparations.

Interaction with other medicaments

Ginseng may slightly reduce blood glucose level. A case of possible interaction of ginseng with warfarin anticoagulant therapy has been reported, but the mechanism remains unknown.

Undesirable effects

The excessive and uncontrolled intake of ginseng products should be avoided.
Pharmacognosy 2

Pregnancy and lactation
No human data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

5.3 Steroids

Similarly to terpenes, steroids are compounds with isoprene-skeleton.

Their most important groups in plants:

- sterols (with 27-29 C-atoms)
- spirostanols, furostanols, steroid-alkaloids (with 27 C-atoms)
- ekdisteroids (with 27 C-atoms)
- bufadienolids (with 24 C-atoms)
- cardenolides (with 23 C-atoms)
- pregnane-derivatives (with 21 C-atoms)
- oestrone (with 18 C-atoms)

The biosynthesis of steroids starts from squalene. From this compound squalene-2,3-oxide and cycloartenol will be formed (Figure 5.99).

![Figure 5.99](image)

**Figure 5.99**
The formation of cholesterol in higher plants.

**Sterols:** These compounds frequently occur in higher plants, but in small amounts and typically in glycosidic form. In the latter case the sugar part is attached to the OH-group
Drugs containing triterpenes, steroids, saponins and cardenolides

at C3-atom. The most well-known sterols are: β-sitosterol, stigmasterol, campesterol and cholesterol, having important role in the stabilization of membranes. They possess various pharmacological effects such as anti-inflammatory, antibacterial, antifungal and they can inhibit the growth of tumors.

Drugs

Urticae radix

Plants

_Urtica dioica_ L., (Great nettle), _U. urens_ L. (Small nettle) (Urticaceae)

These plants are native to Europe.

![Figure 5.100](image)

_Urtica sp._ (Nettle)

Drug

_Urticae radix_ (Nettle root, Ph. Eur.). **Other Drug**
Urtica dioica ad praeparationes homoeopathicas (Common stinging nettle for homoeopathic preparations, Ph. Eur.)

The drug consists of the whole, cut or powdered dried roots and rhizomes of *Urtica dioica* L., *Urtica urens* L., their hybrids or mixture of these plants.

Common stinging nettle for homoeopathic preparations: It is produced from the whole, fresh, flowering plant of *Urtica dioica* L.

![Urticae radix](image)

**Figure 5.101**

*Urticae radix* (Nettle root)

**Constituents**

The main characteristic constituents are sterols, e.g. β-sitosterol, β-sitosterol-3-O-glucoside, 7β-hydroxy-β-sitosterol. Other constituents include lignans such as (+)-neo-olivil, (-)-secoisolariciresinol, fatty acids, monoterpene diols, polysaccharides and coumarins (scopoletin).
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.102-104
The structure of β-sitosterol, β-sitosterol-3-O-glucoside and 7β-hidroxy-β-sitosterol.

Uses
Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stages I and II of benign prostatic hyperplasia as defined by Alken
See: Pruni africanae cortex

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck
See: Pruni africanae cortex

Dosage
Adult daily dose: 4-6 g of the drug as an infusion; 378-756 mg of dried extract (12-16:1, 70% V/V ethanol); 4.5-7.5 ml of fluid extract (1:1, 45% ethanol).

Special warnings and precautions for use
All cases of difficult urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation
Not applicable.
Epilobii herba

Plants

*Epilobium parviflorum* Schreb. (Small-flowered willowherb), *E. roseum* Schreb. (Pale willowherb), *E. montanum* L. (Broad-leaved willowherb) (Onagraceae)

Epilobium species are native to Europe.

![Figure 5.105 Pale willowherb (*Epilobium roseum* Schreb.)](image)

Drug

Epilobii herba (Epilobium)

The drug consists of the dried aerial flowering parts of *Epilobium parviflorum* Schreb., *E. roseum* Schreb., *E. montanum* L. or other *Epilobium* species.
Drugs containing triterpenes, steroids, saponins and cardenolides

Constituents

The main characteristic constituents are sterols, e.g. β-sitosterol, β-sitosterol-3-O-glucoside and esters of β-sitosterol (e.g. β-sitosterol-3-O-(6’-O-palmitil)-β-D-glucoside). Other constituents include flavonoids (mainly quercetin and kaempferol glycosides) and tannins (gallic acid and ellagic acid derivatives).

**Figure 5.106**
*Epilobii herba* (Epilobium)

**β-sitosterol**

**β-sitosterol-3-O-glucoside**

**β-sitosterol-3-O-(6’-O-palmitil)-β-D-glucoside**

**Figure 5.107-109**
The structure of β-sitosterol, β-sitosterol-3-O-glucoside and β-sitosterol-3-O-(6’-O-palmitil)-β-D-glucoside.
Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

*Stages I and II of benign prostatic hyperplasia as defined by Alken*

See: Pruni africanae cortex

*Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck*

See: Pruni africanae cortex

Dosage

*Adult daily dose:* 3-4 g of the drug as an infusion with 200 ml of water.

Special warnings and precautions for use

All cases of difficult urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

**Cucurbitae semen**

Plant

*Cucurbita pepo* L. – Pumpkin (Cucurbitaceae)

Pumpkin is a cultivated plant.

**Figure 5.110**

Pumpkin (*Cucurbita pepo* L.)

Drug

Cucurbitae semen (Pumpkin seed)

The drug consists of the whole, dried, ripe seeds of *Cucurbita pepo* L. and/or certain cultivars.
Constituents

The main characteristic constituents are phytosterols, principally Δ7-sterols such as stigmasta-7,22-dien-3β-ol (spinasterol), spinasterol-3β-D-glucoside, peposterol. β-sitosterol is present to a lesser extent. Other constituents include triglycerides, free fatty acids, amino acids, selenium, carotenoids and β- and γ-tocopherols.

Figure 5.111
*Cucurbitae semen* (Pumpkin seed)

Figure 5.112-114
The structure of spinasterol, spinasterol-3β-D-glucoside and peposterol.
Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

*Stages I and II of benign prostatic hyperplasia as defined by Alken*

See: Pruni africanae cortex

*Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck*

See: Pruni africanae cortex

Dosage

*Adult daily dose:* 10-20 g of the seeds or a corresponding amount of an extract.

Special warnings and precautions for use

All cases of difficulty urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

**Sabalis serrulatae fructus**

Plant

*Serenoa repens* (Bartram) Small. – Saw palmetto (Arecaceae)

This palm is native to USA.

Drug

*Sabalis serrulatae fructus* (Saw palmetto fruit, Ph. Eur.)

The drug consists of the dried ripe fruit of *Serenoa repens* (Bartram) Small. (*Sabal serrulata* (Michaux) Nichols). It contains minimum 11.0% of total fatty acids, calculated with reference to the dried drug. It has characteristic, strong, unpleasant but not rancid odour.
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.115
_Sabalis serrulatae fructus_ (Saw palmetto fruit)

**Constituents**

The main characteristic constituents are sterols, e.g. β-sitosterol and its 3-glucoside (and fatty acid derivatives of these, e.g. β-sitosterol-3-O-miristate), campesterol and stigmasterol. Other constituents include free fatty acids such as capric, caproic, caprylic, lauric, myristic, oleic, linoleic, stearic and palmitic acids; triglycerides, flavonoids, polysaccharides and essential oil.

![β-sitosterol](image1)

![β-sitosterol-3-O-miristate](image2)

![campesterol](image3)

![stigmasterol](image4)

**Figure 5.116-119**

The structure of β-sitosterol, β-sitosterol-3-O-miristate, campesterol and stigmasterol.
Pharmacognosy 2

Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stages I and II of benign prostatic hyperplasia as defined by Alken

See: Pruni africanae cortex

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck

See: Pruni africanae cortex

Dosage

Adult daily dose: 1-2 g of the drug or 320 mg of lipophilic extract or other equivalent preparation.

Special warnings and precautions for use

All cases of difficult urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

5.4 Spirostanes, furostanes and steroidal saponins

Spirostanes and furostanes are steroids containing 27 C-atoms; they are formed from sterols (e.g. cholesterol).

Furostanes: a furan- (tetrahydro-furan)-ring (E-ring) is formed from the side-chain attached to the C-17-atom of the steroid-skeleton. Spirostanes: they contain a tetrahydro-furan (E-ring) and a tetrahydro-piran ring (F-ring), e.g. diosgenin. Sometimes the 6-membered ring is a piperidin-ring containing N-atom (e.g. solasodine). These constituents are steroidglycoalkaloids and occur principally in the family of Solanaceae. In the group of spirostanes there may be differences in the configuration of C-5 and C-25 carbon atoms. The configuration of the C-5-atom depends on the cis-trans position of A/B-rings. In the case of trans-configuration the H-atom being on the C-5-atom has α-position (5α), but in the case of cis-configuration this H-atom has β-position (5β) (see Figure 5.120-127). Between carbon atoms C-5-6 a double bond is also possible (Δ₂-type). According to the configuration of the C-25 carbon atom we distinguish two main groups of spirostanes: 25D (25α) and 25L (25β).
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.120-122
The most important types of spirostanes.

Furostanes and spirostanes occur both in free and glycosidic form in various plants. If there is a sugar moiety in the molecule, the resulting compounds are called steroidal saponins. Similarly to triterpene saponins, their aqueous solutions can produce a soap-like froth and they hemolyze red blood cells.

They occur mainly in monocotyledons (Liliaceae, Agavaceae, Dioscoreaceae, Poaceae) and sporadically in dicotyledons (e.g.: Digitalis species). Drugs containing steroid-saponins have expectorant effect, they can be used for the treatment of purulent wounds, furuncles and different dermatological diseases. However, their main pharmaceutical significance lies in the fact that they are excellent raw materials for the pharmaceutical industry. Some are used as starting materials for the synthesis of sex hormones, cortisone or vitamin D.

Drugs

Dioscoreae tuber

Plant

Dioscorea mexicana, D. composita, D. floribunda, other Dioscorea species – Yams (Dioscoreaceae)

These plants are native to tropical and warm temperate regions of the world.

Drug

Dioscoreae tuber (Yam root)

The drug consists of the succulent, tuberous rhizome and branches (secondary roots) of Dioscorea mexicana, D. composita, D. floribunda or other Dioscorea species.
Constituents

The main characteristic constituents are steroidal saponins (1-8%), e.g. diosgenin aglycon and dioscin, gracillin. The root also contains starch and proteins.

![diosgenin](diosgenin.png) ![dioscin](dioscin.png) ![gracillin](gracillin.png)

**Figure 5.123-125**

The structure of diosgenin, dioscin and gracillin.

Uses

The aqueous extract of *D. villosa* is used as a spasmolytic, antiphlogistic and antirheumatic drug in the USA. In the pharmaceutical industry diosgenin is used as a raw material for producing pregnadienolon-acetate. This compound is a starting material of steroid drugs.

Avenae herba

Plant

*Avena sativa* L. – Common oat (Poaceae)

It is an annual plant and native to Europe, the Mediterranean region, Middle East and China. It can be cultivated.

Drug

*Avenae herba* (Oat herb)

Avenae herba consists of the fresh or dried aerial parts of *Avena sativa* L.
Drugs containing triterpenes, steroids, saponins and cardenolides

Constituents
The drug contains silicic acid, oligosaccharides, special amino acids, flavonoids (e.g. apigenin, vitexin, isovitexin, luteolin) and steroidal saponins (e.g. avenacoside A and B).

Uses
The therapeutic indications include the symptomatic treatment of minor inflammations of the skin and mucosa and the relief of mild symptoms of mental stress and help falling asleep. The drug and its preparations aid the healing of minor wounds, leg ulcers and burns.
Dosage

Adults and elderly dose:

Comminuted herbal substance (single dose): 3 g for the preparation of an infusion. Liquid extract (1:4-6 ethanol 15-50% v/v): up to 5 ml up to 3 times daily. Liquid extract (1:4-6 water): up to 5 ml up to 3 times daily.

The use of the drug is not recommended in children under 12 years of age.

Special warnings and precautions for use

Caution is advised when used in patients with coeliac disease because data on the protein content are not available.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Trigonellae foenugraeci semen

Plant

*Trigonella foenum-graecum* L. – Fenugreek (Fabaceae)

It is an annual plant and native to Europe, Mediterranean region, Middle East, China. It can be cultivated.
Fenugreek consists of the dried, ripe seeds of *Trigonella foenum-graecum* L. It has a strong characteristic aromatic odour.

**Figure 5.129**
Fenugreek (*Trigonella foenum-graecum* L.)

**Drug**

*Trigonellae foenugraeci semen* (Fenugreek, Ph. Eur.)

Fenugreek consists of the dried, ripe seeds of *Trigonella foenum-graecum* L. It has a strong characteristic aromatic odour.
Constituents

The characteristic constituents are steroidal saponins, occurring mainly as furostanol 3,26-diglycosides such as trigofenosides A-G. On hydrolysis the saponins yield 0.6-1.7% of spirostanol sapogenins consisting mainly (approx. 95%) of diosgenin and its $25\beta$-epimer yamogenin in a 3:2 ratio, together with tigogenin. Steroidal sapogenin-peptide esters such as fenugreekine are also present. Other constituents include mucilage galactomannane polysaccharides, trigonelline (= coffearine, N-methylbetaine of nicotinic acid), protein, amino acids, enzymes, flavonoids, sterols, lecithin and choline. The characteristic aroma compound of the drug is 3-hydroxy-4,5-dimethyl-2-(5H)-furanone (sotolone).
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.131-136
The structure of trigofoenoside A and B, diosgenin, yamogenin, trigonelline and 3-hydroxy-4,5-dimethyl-2-(5H)-furanone (sotolone).

Uses
Internally the drug can be used in the adjuvant therapy of diabetes mellitus, in the case of anorexia, as an adjunct to a low fat diet in the treatment of mild to moderate hypercholesterolaemia. Externally the drug and its products are used to treat furunculosis, ulcers and eczema.

Dosage
Internal use
Adults:
Diabetes mellitus or hypercholesterolaemia: 25 g of powdered seeds or equivalent preparations daily.
Lack of appetite: 1-6 g of powdered seeds up to three times daily with water, before meals.
Overdose: 100 g of the drug taken daily can cause minor gastrointestinal symptoms such as diarrhoea and flatulence.

External use
It can be used as an emollient. 50 g of powdered seeds boiled in 250 ml of water for 5 min, then applied as a warm moist poultice.

Interactions with other medicaments
Because of mucilage content fenugreek may affect the absorption of drugs taken simultaneously.
Pregnancy and lactation

Fenugreek should not be used during pregnancy and lactation.

**Rusci rhizoma**

**Plant**

*Ruscus aculeatus* L. – Butcher’s broom (Liliaceae)

This plant is native to Europe.

![Butcher’s broom (Ruscus aculeatus L.)](image)

**Figure 5.137**

Butcher’s broom (*Ruscus aculeatus* L.)

**Drug**

*Rusci rhizoma* (Butcher’s broom, Ph. Eur.)

The drug consists of the dried, whole or fragmented underground parts of *Ruscus aculeatus* L. It contains minimum 1.0% of total sapogenins, expressed as ruscogenins (mixture of neoruscogenin and ruscogenin), calculated with reference to the dried drug.

**Constituents**

The characteristic constituents of the drug are steroidal saponins based upon (25R)-spirost-5-ene-1β,3β-diol (ruscogenin) and spirosta-5,25(27)-diene,10,3β-diol (neoruscogenin), such as ruscoside, ruscin, deglucoruscoside and deglucoruscin. Other constituents are flavonoids, anthraquinones, essential oil and sterols.
Drugs containing triterpenes, steroids, saponins and cardenolides

![Chemical structures of ruscogenin, neoruscogenin, ruscoside and ruscin.]

**Figure 5.138-141**
The structure of ruscogenin, neoruscogenin, ruscoside and ruscin.

**Uses**
The therapeutic indications include the supportive therapy for relieving the symptoms of chronic venous insufficiency, such as painful and heavy legs, tingling and swelling. Supportive therapy for symptoms of haemorrhoids, such as itching and burning.

**Dosage**

*Adult and elderly daily dose:* Solid or liquid extracts in amounts corresponding to 7-11 mg of total ruscogenins.

**Pregnancy and lactation**

In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice. No adverse effects have been reported in mothers or newborn babies when used in late pregnancy.

### 5.5 Cardenolides and bufadienolides

Cardioactive glycosides are a kind of steroid glycosides, which act on the human heart. We can distinguish two main aglycone types of the cardioactive glycosides: cardenolides and bufadienolides. Medicinally the cardenolide group is more important. Cardenolides have a steroid skeleton with 23 C-atoms and contain γ-lacton (butenolide) ring, e.g. digitoxygenin.

Bufadienolides with 24 C-atoms contain, on the C-17 carbon atom, a δ-lacton ring (α, β - γ, δ doubly unsaturated), e.g. scillarenin (**Figure 5.142-148**).
Figure 5.142-143
The structure of cardenolides and bufadienolides.

In both types of aglycones, a sugar molecule or a side chain containing sugar molecules is connected to the β-OH group of C-3 carbon atom. The sugar components of cardioactive glycosides are mainly deoxy-sugars and glucose. If glucose is present in the chain, it can always be found at the end of the chain. The deoxy-sugars are 6-deoxy-sugars (e.g. L-rhamnose, D-fucose, D-digitalose, L-tevetose) or 2,6-deoxy-sugars (e.g. D-digitoxose, D-cymarose, L-oleandrose) (Figure 5.144). Recently, 2-O-methyl and 2-O-acetyl sugars have also been discovered.

The biosynthesis of cardenolides and bufadienolides starts from cholesterol (C27) through pregnane derivatives [(by side-chain shortening (C21); e.g. progesterone)] (Figure 5.145). In the formation of these compounds the incorporation of the active acetyl group of acetyl-CoA plays an important role. Cardenolides dissolve in alcohols (eg. methanol, ethanol). Cardioactive glycosides occur rarely in higher plants, their occurrence is not characteristic even at the level of plant families, they are associated rather with some genera or species. Some families with cardiac glycoside-containing taxa are: Apocynaceae, Liliaceae, Ranunculaceae, Fabaceae, Moraceae, Scrophulariaceae, Euphorbiaceae. Cardioactive glycosides exert their pharmacological effect on the heart muscles. In therapeutic dose they improve cardiac output by increasing the force of heart muscle contraction and increasing the volume of blood pumped into the vascular system (positive inotropic action). They can decrease heart rate (negative chronotropic action) and venous pressure, while diuresis shows an upward tendency. The action of cardenolic glycosides is always greater than the action of the corresponding aglycones. Cardenolide glycosides are employed in the case of heart insufficiency, which occurs as a consequence of atherosclerosis, hypertonia, asthma cardiale or problems with a cardiac valve (valvular or cardiac insufficiency).
Drugs containing triterpenes, steroids, saponins and cardenolides

**Figure 5.144**
The structure of D-digitoxose and D-cymarose.

**Figure 5.145**
The formation of cardenolides from cholesterol.
Drugs

Digitalis purpureae folium

Plant

*Digitalis purpurea* L. – Purple foxglove (Scrophulariaceae)

This biennial or short-lived perennial plant is native to most of temperate-Europe and North-Africa. It is cultivated as an ornamental and medicinal plant.

![Purple foxglove](image)

**Figure 5.146**

Purple foxglove (*Digitalis purpurea* L.)

Drug

*Digitalis purpureae folium* (Purple foxglove leaf)

The drug consists of the dried first- or second-year leaves of *Digitalis purpurea* L. It contains not less than 0.3% of total cardenolides calculated as digitoxin.
Drugs containing triterpenes, steroids, saponins and cardenolides

Constituents

The characteristic constituents of the drug are cardenolide glycosides (0.15-0.4%). Their aglycones are: digitoxigenin, gitoxigenin and gitaloxigenin. The main glycosides include purpurea glycoside A, purpurea glycoside B and purpurea glycoside C, digitoxin, gitoxin and gitalotoxin. Other constituents are steroidal saponins, flavonoids (e.g. apigenin, luteolin), derivatives of cinnamic acid such as caffeic acid and chlorogenic acid and anthraquinone-derivatives.

Uses

The isolated constituents act on the heart. They have positive inotropic effects. The fine powder of the dried leaves is used in pharmaceutical technology for preparing pellets. Digitoxin prepared in a pure crystalline form is used to make tablets.

The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.

Digitalis lanatae folium

Plant

Digitalis lanata Ehrh. – Woolly foxglove (Scrophulariaceae)

This perennial or biennial plant is native to central and south-eastern Europe. It can be cultivated. This plant is protected in Hungary.
Drug

*Digitalis lanatae folium* (Woolly foxglove leaf)

The drug consists of the dried first-year leaves of *Digitalis lanata* Ehrh.

**Figure 5.157**

*Digitalis lanatae folium* (Woolly foxglove leaf)
Constituents

The characteristic constituents of the drug are cardenolide glycosides (1%). Their aglycones are: digitoxigenin, gitoxigenin, digoxigenin, diginatigenin and gitaloxigenin. The main glycosides include lanatoside A, lanatoside B, lanatoside C, lanatoside D, lanatoside E, digitoxin, digoxin, acetyldigoxin and glucoverodoxin. Other constituents are steroidal saponins, flavonoids (e.g. apigenin, luteolin), caffeic acid and $p$-coumaric acid and anthraquinone-derivatives.

![Chemical structures](image)

**Figure 5.158-164**

The structure of digitoxigenin, gitoxigenin, digoxigenin, diginatigenin, gitaloxigenin, digoxin and lanatoside C.

Uses

The isolated constituents act on the heart. They have positive inotropic effects. The leaves are used principally for the preparation of lanatosides and digoxin. Digoxin has become the most widely used drug in the treatment of congestive heart failure. Digoxin is more rapidly absorbed from the gastrointestinal tract than the purpurea glycosides. Lanatoside C is less well absorbed than digitoxin but it is less cumulative.

Overall the pharmacological effects of the *Digitalis* glycosides start approx. 6 to 12 hours after administration, but the constituents break down completely after 10 to 20 days.

The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.

Strophanthi semen

Plant

*Strophanthus kombe* Oliver – Strophanthus (Apocynaceae)

This plant is a climbing shrub and native to tropical East-Africa.
Drug

*Strophanthi semen* (Strophanthus seed)

The drug consists of the seeds without their feathery hairs of *Strophanthus kombe* Oliver.

**Constituents**

The characteristic constituents of the drug are cardenolide glycosides (8-10%). The main glycosides are K-strophanthoside, K-strophanthin-β and cymarin, all based on the aglycone of strophanthidin. The other constituents of the seeds include 30% of fatty oil, trigonelline, choline and mucilage.

![K-strophanthoside](image1)

![K-strophanthin-β](image2)

![strophanthidin](image3)

![G-strophanthin (= ouabain)](image4)

**Figure 5.165-168**

The structure of K-strophanthoside, K-strophanthin-β, strophanthidin and G- strophanthin (= ouabain).

**Uses**

The cardioactive constituents of the drug in a pure crystalline form are used for the preparation of injections. Cardioactive glycosides of the drug administered in intravenous injections act within a few minutes, and their effect lasts for approx. 36 hours. Their pharmacological activity is similar to that of *Digitalis* glycosides, but *Strophanthus* glycosides do not accumulate, therefore these cardenolides are used in the case of acute cardiac insufficiency as life-saving medicines. *Strophanthus gratus* seeds (*Strophanthi grati semen*) contain 4-8% cardioactive glycosides with G-strophanthin (= ouabain), which can also be used in injections. *Strophanthus gratus* is native to West-Africa.

The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.
Convallariae herba

Plant

Convallaria majalis L. – Lily of the valley (Liliaceae)

This perennial plant is native to Europe and in the temperate zones of Asia. It occurs in oak-woods and other deciduous forests.

Figure 5.169
Lily of the valley (Convallaria majalis L.)

Drug

Convallariae herba (Lily of the valley)

The drug consists of the dried aerial parts (collected when the flowers are beginning to open) of Convallaria majalis L.

Figure 5.170
Convallariae herba (Lily of the valley)
**Constituents**

The characteristic constituents of the drug are cardenolide glycosides (0.2-0.5%). The principal glycoside is convallatoxin which on hydrolysis yields strophanthidin and (-)-rhamnose. The plant contains several minor cardenolides (about 40 glycosides associated with nine different aglycones). Other constituents are steroidal saponins, flavonoids (mainly apigenin, luteolin, kaempferol, quercetine and their derivatives) and azetidin-2-carboxylic acid.

**Figure 5.171-173**

The structure of strophanthidin, convallatoxin and azetidin-2-carboxylic acid.

**Uses**

The therapeutic indications include the treatment of cardiac insufficiency, cor pulmonale and cardiac failures associated with oedema formation. It has diuretic effect. The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.

**Adonidis herba**

**Plant**

*Adonis vernalis* L. – Spring pheasant’s eye (Ranunculaceae)

This perennial plant is native to Europe, Caucasus and Siberia. In Hungary it is protected because of its rare occurrence. It occurs in Mecsek and Bakony mountains.
Drugs containing triterpenes, steroids, saponins and cardenolides

Figure 5.174
Spring pheasant’s eye (*Adonis vernalis* L.)

Drug

*Adonidis herba* (Spring pheasant’s eye)

The drug consists of the dried aerial flowering parts of *Adonis vernalis* L.

Constituents

The characteristic constituents of the drug are cardenolide glycosides (0.25-0.5%). The principal glycoside is adonitoxin which is the glycoside of adonitoxigenin. The drug also contains strophanthidin-type cardenolides. Other constituents are flavonoid-glycosides, ascorbic acid (vitamin C) and sugar alcohols.

![Figure 5.175-176](image)

The structure of adonitoxigenin and adonitoxin.

Uses

The cardenolides of the drug are poorly absorbed from the gastrointestinal tract, but they are broken down more quickly than *Digitalis* cardenolides, therefore they cannot accumulate. The therapeutic indications include nervous cardiac troubles, angina pectoris, cardiac failures associated with oedema formation. It has diuretic effect. The
drug or its extracts and pure constituents are very toxic, therefore they should not be used without medical advice.

**Nerii folium**

**Plant**

*Nerium oleander* L. – Oleander (Apocynaceae)

This perennial woody shrub (or small tree) is native to South-Europe and West-Asia. It is cultivated as ornamental plant.

*Figure 5.177*

Oleander (*Nerium oleander* L.)

**Drug**

*Nerii folium* (Oleander leaf)

The drug consists of the dried leaves (collected during flowering period) of *Nerium oleander* L.
Constituents

The characteristic constituents of the drug are cardenolide glycosides (1-2%). The principal glycosides are oleandrin, adynerin, odoroside A and oleasides A-F. The main aglycones include oleandrogenin (=16-acetylgitoxigenin), adynerigenin (= 3-hydroxy-8,14-epoxycardenolide), digitoxigenin, oleagenin and uzarigenin (= 5α-digitoxigenin). The drug also contains flavonoids such as rutin and kaempferol-3-O-rhamnoglucoside; as well as ursolic and oleanolic acids.

Figure 5.178

_Nerii folium_ (Oleander leaf)

The structure of oleandrogenin, oleandrin, adynerigenin, adynerin, digitoxigenin, oleagenin and oleaside A.

Figure 5.179-185
Uses

The cardenolides of the drug act similarly to the Digitalis cardenolides. The industrial preparations of the drug can be used for the treatment of arrhythmia and circulatory disorders, as well as other cardiac complaints associated with changes in the weather. The drug or its extracts and pure constituents are very toxic, therefore they should not be used without medical advice.

Erysimi herba et semen

Plant

Erysimum diffusum Ehrh. – Gray diffuse wallflower (Brassicaceae)

This perennial, overwintering, herbaceous plant is native to Europe and Asia.

Drug

Erysimi herba et semen (Gray diffuse wallflower flowering shoot and seed)

The drug consists of the dried aerial flowering parts and seeds of Erysimum diffusum Ehrh.

 Constituents

The characteristic constituents are cardenolides based on strophanthidin aglycone. The principal cardenolides include helveticoside and erizimoside (= glucohelveticoside). The seeds contain glucosinolates, sterols and fatty oil. Flavonoids occur mostly in the aerial parts of the plant.

Figure 5.186-188

The structure of strophanthidin, helveticoside and erizimoside (= glucohelveticoside).
Drugs containing triterpenes, steroids, saponins and cardenolides

Uses
Formerly the drug was used for the treatment of mild cardiac insufficiency. At present the plant is not frequently used.

**Leonuri cardiaeae herba**

Plant

*Leonurus cardiaca* L. – Motherwort (Lamiaceae)

This perennial plant is native to Mediterranean countries, Europe and Asia.

![Figure 5.189](image)

**Figure 5.189**

Motherwort (*Leonurus cardiaca* L.)

Drug

*Leonuri cardiaeae herba* (Motherwort, Ph. Eur.)
The drug consists of the whole or cut, dried flowering aerial parts of *Leonurus cardiaca* L. It contains minimum 0.2% of flavonoids, expressed as hyperoside, and calculated with reference to the dried drug.

**Figure 5.190**
*Leonuri cardiaecae herba* (Motherwort)

**Constituents**

The characteristic constituents of the drug are bufadienolides. They are glycosides of scillarenin and 5,6-dehydro-scillarenin. Other constituents include diterpenes (e.g. marrubiin), iridoids (e.g. ajugoside), flavonoids, stachidrin (dimethyl-pirrolidinium-2-carboxilate) and triterpenes such as ursolic and oleanolic acid.

**Figure 5.191-192**
The structure of scillarenin and 5,6-dehydro-scillarenin.

**Uses**

The drug can be used for the treatment of mild cardiac insufficiency and nervous heart complaints. *Leonuri cardiaecae herba* may be combined with *Cratægi folium cum flore* (hawthorn leaf and flower) in herbal teas.

**Dosage**

*Adult and elderly daily dose:* 4 g of the drug as an infusion.
Drugs containing triterpenes, steroids, saponins and cardenolides

**Scillae bulbus**

**Plant**

*Urginea maritima* (L.) Baker – Squill (Liliaceae)

Squill occurs wild as an aggregate of at least six species of varying chromosome number. The plant is native to Mediterranean countries and West Asia. White squill can be found in Spain, Portugal, Sardinia, Malta, Cyprus and Greece; red squill is native to Algeria and Morocco.

**Drug**

*Scillae bulbus* (Squill bulb)

The drug consists of the dried sliced bulbs of *Urginea maritima* (L.) Baker, from which the membranous outer scales have been removed.

**Constituents**

The characteristic constituents of the drug are bufadienolides. In white squill there is a mixture of 15 bufadienolides: the aglycone is scillarenin and the principal glycosides are scillaren A, glucoscillaren A and proscillaridin A. In red squill the principal glucosides are scillirozide and glucoscillirozide, their aglycone part is scillirosidine.

![Chemical structures](image)

**Figure 5.193-198**

The structure of scillarenin, scillaren A, glucoscillaren A, proscillaridin A, scillirozide and scillirosidine.

**Uses**

In pharmaceutical industry white squill is used principally. Scillaren A and proscillaridin A can be absorbed from the gastrointestinal tract (almost in 25%), therefore these compounds are administered orally. The therapeutic indications include aorta-insufficiency, angina pectoris, oedema associated with nephritis. In small doses the drug provokes mild gastric irritation causing a reflex secretion from the bronchioles, therefore it can be used as an expectorant, but in large doses it causes vomiting.
The drug should not be used without medical advice.

**Hellebori radix (et rhizoma)**

**Plant**

*Helleborus niger* L. – Black hellebore (Ranunculaceae)

This perennial plant is indigenous to Central Europe. In Hungary *Helleborus* species are protected.

![Image of Black hellebore](image)

**Figure 5.199**

Black hellebore (*Helleborus niger* L.)

**Drug**

*Hellebori radix (et rhizoma)* (Black hellebore root et rhizome)

The drug consists of the whole or cut, dried roots and rhizomes of *Helleborus niger* L.
Drugs containing triterpenes, steroids, saponins and cardenolides

Constituents
The characteristic constituents of the drug are bufadienolides. The principal constituent is hellebrin which is the glycoside of the aglycone hellebrigenin. The drug also contains steroidal saponins, but their structure has not been identified yet.

Uses
The bufadienolides of the drug have a digitalis-like action. The aglycone hellebrigenin is the bufadienolide analogue of strophanthidin. The drug which has cardiotonic as well as abortifacient properties is considered dangerous and is now obsolete in ordinary medicine. The drug is used principally in veterinary medicine: *Hellebori rhizoma* is placed into the ears of pigs, sheep or in the chest of cows, where the drug causes inflammation, and it increases the resistance of these animals against different infections (so called stimulus therapy).
Chapter 6

Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Definition of alkaloids

Old definition: Alkaloids are the end products of plant metabolism; they are organic heterocyclic bases containing N-atom and having strong physiological action.

In the meantime it has been justified that alkaloids occur also in animals (e.g. salamanders, frogs, insects, sea animals, etc.), as well as fungi and bacteria.

New definition: Alkaloids are cyclic organic compounds, which contain the N-atom in the state of negative oxydation grade; and occur in various living organisms in limited quantities.

Classification of alkaloids

Compared with most other classes of natural compounds, alkaloids are characterized by a great structural diversity and there is no uniform classification for alkaloids. They are often divided into the following major groups:

- “True alkaloids”, which contain N-atom in a heterocycle and originate from amino acids. Their characteristic examples are atropine, nicotine and morphine. This group also includes some alkaloids which beside nitrogen containing heterocycle contain terpene (e.g. evonine) or peptide fragments (e.g. ergotamine). This group also includes piperidine alkaloids (e.g. coniine), although they do not originate from amino acids.
- “Protoalkaloids”, which contain N-atom outside the heterocycle, but in the form of amino group; they also originate from amino acids (e.g. mescaline, ephedrine).
- Polyamine alkaloids: they are derivatives of putrescin, spermidine and spermine.
- Peptide and cyclopeptide alkaloids.
- Pseudoalkaloids. Their biosynthesis does not start from amino acids:
  - Terpene alkaloids (e.g. aconitine);
  - Steroid alkaloids (tomatidine, solanidine).

Another possibility for classification

One of the well-established classifications is based on the chemical structures of alkaloids. According to this classification there are two main classes:

- Nonheterocyclic or atypical alkaloids, sometimes called „protoalkaloids” or biological amines.
- Heterocyclic or typical alkaloids, divided into 14 groups according to their ring structure.
Alkaloids occur in both plants and animals. The plant species in the following plant families can produce alkaloids with various structures: Magnoliaceae, Lauraceae, Menispermaceae, Berberidaceae, Ranunculaceae, Papaveraceae, Fabaceae, Rutaceae, Loganinaceae, Apocynaceae, Gentianaceae, Rubiaceae, Boraginaceae, Solanaceae, Asteraceae, Liliaceae, Amaryllidaceae, Orchidaceae, etc.

**Most important properties of alkaloids**

Most alkaloids are crystalline substances which form salts with various acids, such as malic acid, succinic acid, fumaric acid, meconic acid and citric acid. In plants alkaloids may exist in the free state, as salts or as N-oxides. A few, for example nicotine and conine are oxygen-free and are liquids. There are some coloured alkaloids such as berberine (yellow) or sanguinarine (copper-red), but alkaloids are generally colourless. Usually the free bases cannot be dissolved in water but are readily dissolved in organic solvents. Salts are soluble in water but sparingly soluble in organic solvents. Of course there are some exceptions (e.g. caffeine, colchicine). They have a variety of applications and medicinal uses, which will be detailed at the description of each plant drug.

**Extraction:** Extraction methods of alkaloids vary depending on the scale and purpose of the process, as well as the nature of the raw material. Most alkaloids are present in the form of salts formed with organic acids in the source plants. Generally, drugs are soaked with the mixture of ammonia and 70% alcohol (3:7). Base extraction is achieved by processing the raw material with alkaline solutions (e.g. ammonia) and extracting the alkaloid bases with organic solvents, such as 1,2-dichloroethane, chloroform, diethyl ether or benzene. The most frequent extraction techniques are: Soxhlet, extraction with shaker, extraction with ultrasonic water-bath and extraction with acid progress.

**Tests for alkaloids:** Most alkaloids are precipitated from neutral or slightly acidic solutions by Mayer’s reagent (potassiomercuric iodide solution), by Wagner’s reagent.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

(solution of iodine in potassium iodide), by solution of tannic acid, by Hager’s reagent (a saturated solution of picric acid) and by Dragendorff’s reagent (solution of potassium bismuth iodide). Purine-derivative alkaloids (e.g. caffeine) can be detected by murexide test.

6.2 Alkaloids formed from ornithine

Alkaloids formed from ornithine (Figure 6.2) can be found in species belonging to the plant families of Solanaceae, Convolvulaceae, Boraginaceae, Asteraceae, Fabaceae and Erythroxylaceae.

Biosynthesis starting from ornithine can result in the formation of two main types of alkaloids, the group of tropane- and ecgonine-alkaloids, and the group of pyrrolizidine-alkaloids (Figure 6.3).

Another biosynthesis pathway from ornithine (through the formation of putrescine and other intermediers) can lead to the formation of alkaloids with pyrrolizidine-skeleton. Farfarae folium (Tussilago farfara), Echinaceae radix (Echinacea purpurea) and Petasitidis folium (Petasites hybridus) also contain pyrrolizidine alkaloids, but their use in phytotherapy is not attributed to their alkaloid content.

![Figure 6.2](https://example.com/figure62.png)

The structure of ornithine (α,δ-diamino-valerianic acid)
Figure 6.3
Some ornithine-derived alkaloids

Drugs

Belladonnae folium

Plant
Atropa belladonna L. – Belladonna (Deadly nightshade) (Solanaceae)

This perennial herbaceous shrub is native to Europe, West-Asia, Caucasus and North-Africa.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Figure 6.4
Belladonna /Deadly nightshade (Atropa belladonna L.)

Drug

*Belladonae folium* (Belladonna leaf, Ph. Eur.). **Other drugs:** *Belladonae folii extractum siccum normatum* (Belladonna leaf dry extract, standardized, Ph. Eur.), *Belladonae pulvis normatus* (Belladonna, prepared, Ph. Eur.), *Belladonae folii tinctura normata* (Belladonna leaf tincture, standardised, Ph. Eur.)

Belladonna leaf consists of the dried leaf or of the dried leaf and flowering, and occasionally fruit-bearing tops of *Atropa belladonna* L. It contains not less than 0.30% of total alkaloids, calculated as hyoscyamine with reference to the drug dried at 100°C to 105°C. The alkaloids consist mainly of hyoscyamine together with small quantities of hyoscine (scopolamine).

Belladonna leaf has a slightly nauseous odour.

Standardised belladonna leaf dry extract is produced from Belladonna leaf. It contains not less than 0.95% and not more than 1.05% of total alkaloids, calculated as hyoscyamine, with reference to the dried extract. The extract is produced from the drug and ethanol (70% *V/V*) using an appropriate procedure. The drug is a hygroscopic brown or greenish powder.

Prepared belladonna is belladonna leaf powder adjusted if necessary by adding powdered lactose or belladonna leaf powder with a lower alkaloid content to contain 0.28% to 0.32% of total alkaloids, calculated as hyoscyamine with reference to the dried drug. It has slightly nauseous odour.

Tincture is produced from Belladonna leaf. It contains 0.027% to 0.033% of total alkaloids, calculated as hyoscyamine. The alkaloids consist mainly of hyoscyamine together with small quantities of hyoscine. The tincture is produced from 1 part of the powdered drug and 10 parts of ethanol (70% *V/V*) by a suitable procedure.

Constituents

The characteristic constituents of the leaves are tropane alkaloids (0.3-0.6%), e.g. atropine, L-hyoscyamine, apoatropine, L-scopolamine and cuscohygrine. [Atropine = ester of tropine (3α-hydroxy-tropane) formed with racemic tropic acid (α-phenyl-β-
hydroxy-propionic acid). These alkaloids can also be found in the root of the plant (in amount of 0.3-0.9%). Other constituents of the leaves are flavonoids (quercetin, kaempferol) and coumarins such as scopoletin.

**Figure 6.5-8**

The structure of atropine (DL-hyoscyamine), apoatropine, L-scopolamine and scopoletin.

**Uses**

In pharmaceutical industry pure crystalline atropine and its derivatives are used. Atropine and its preparations such as *Tinctura belladonnae* and *Extractum belladonnae siccum* are used in the case of hyperacidity and stomach ulcer. Atropine (and the diluted aqueous solution of atropine-sulphate) is used in ophthalmology as a mydriatic drug because it can dilate the pupils of the eyes. Its application is strictly prohibited in the case of glaucoma. Atropin is used in tablets as spasmyloytic, in injections against bile stones (cholelithiasis) and kidney stones (nephrolithiasis). It is an analgesic drug in the case of painful menstruation (accompanied with cramps). The drug acts on the central nervous system in the case of neurovegetative dystony and neurastheny. Its overdosage causes psychomotoric restlessness, excitement and hallucination. Side effects include xerostomia, hoarseness, visual disorders. Overdose of atropin can lead to death, therefore the drug and its products should not be used without medical advice!

**Hyoscyami folium**

**Plant**

*Hyoscyamus niger* L. – Hyoscyamus (Henbane) (Solanaceae)

This annual or biennial plant is native to Europe, but it is also cultivated.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Figure 6.9
Hyoscyamus/Henbane (*Hyoscyamus niger* L.)

Drug

*Hyoscyami folium* (Hyoscyamus leaf).

Hyoscyamus leaf consists of the dried leaves or the dried leaves and flowering tops of *Hyoscyamus niger* L. It is required to contain not less than 0.05% of total alkaloids calculated as hyoscyamine. The British Pharmacopoeia description refers to petiolate as well as sessile leaves, the first-year biennial leaves being thus admitted.

Figure 6.10
*Hyoscyami folium* (Hyoscyamus leaf)
Constituents

The main characteristic constituents of the leaves are tropane alkaloids (0.03-0.25%), with L-hyoscyamine and L-scopolamine (ratio 1.2:1), atropine, apoatropine and cuscohygrine. L-hyoscyamine is the principal alkaloid in the seeds. Other constituents of the leaves are flavonoids (e.g. rutin) and coumarins in traces.

![Structure of L-hyoscyamine, L-scopolamine and cuscohygrine.](image)

**Figure 6.11-13**
The structure of L-hyoscyamine, L-scopolamine and cuscohygrine.

Uses

Hyoscyamus leaf is used similarly to Belladonna leaf, but its dose should be set higher, because of the lower alkaloid-content. Earlier the drug was used in asthma cigarettes. The drug and its products should not be used without medical advice!
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

**Stramonii folium**

**Plant**

*Datura stramonium* L. – Datura/Thornapple (Solanaceae)

This plant is native to Europe, but it is also cultivated.

![Datura/Thornapple](image)

**Figure 6.14**

Datura/Thornapple (*Datura stramonium* L.)

**Drug**

*Stramonii folium* (Stramonium leaf, Ph. Eur.). **Other Drug** *Stramonii pulvis normatus* (Stramonium, prepared, Ph. Eur.)

Stramonium leaf consists of the dried leaf or of the dried leaf, flowering tops and occasionally, fruit-bearing tops of *Datura stramonium* L. and its varieties. It contains not less than 0.25% of total alkaloids, calculated as hyoscyamine with reference to the drug dried at 100°C to 105°C. The alkaloids consist mainly of hyoscyamine with varying proportions of hyoscine (scopolamine). Stramonium leaf has an unpleasant odour.

Prepared stramonium is stramonium leaf powder adjusted, if necessary, by the addition of powdered lactose or stramonium leaf of lower alkaloid content to contain 0.23% to 0.27% of total alkaloids, calculated as hyoscyamine with reference to the dried drug. It is a greyish-green powder with an unpleasant odour.
Constituents
The main characteristic constituents of the leaves are tropane alkaloids (0.2-0.6%) with L-hyoscyamine and L-scopolamine. The ratio of these two compounds is variable, in the older leaves this ratio is 2:1, but in the younger leaves L-scopolamine content is higher. Other alkaloids include atropine, apoatropine and cuscohygrine. These alkaloids can be found in every part of the plant, therefore it is very toxic. Other constituents of the leaves are flavonoids (e.g. rutin) and coumarins (scopoletin and umbelliferon).

Uses
The drug has spasmolytic action, and can be used in the treatment of asthma, cough and chronic laryngitis. The powder of stramonium leaves mixed with the powder of henbane leaves and impregnated with KNO₃ was used earlier in asthma-cigarettes. The drug and its products should not be used without medical advice!
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Cocae folium

Plant
*Erythroxylum coca* Lam. – Coca (Erythroxylaceae)
The plant is a shrub cultivated in Bolivia, Peru, Columbia and Java.

Drug
*Cocae folium* (Coca leaf)
Coca leaf consists of the dried leaves of *Erythroxylum coca* Lam.

Constituents
The main characteristic constituents of the leaves are tropane alkaloids (0.7-2.5%) of which cocaine, cinnamylcocaine and α-truxilline are the most important. These alkaloids occur in different proportions in different commercial varieties. Other alkaloids include tropacocaine, benzoylecgonine and β-truxilline.

Figure 6.18-21
The structure of cocaine, cinnamylcocaine, benzoylecgonine and α-truxilline.

Uses
Pure cocaine was used earlier as a local anaesthetic, today its use is restricted to otolaryngology. Cocaine is a dangerous drug, its use without medical control is illegal and prohibited. It stimulates the central nervous system, decreases the sensation of hunger, increases the efficiency of muscles and causes euphoria. Its long term use causes dependence, its overdose causes somatic and senile insanity.
Nicotianae folium

Plant

Nicotiana tabacum L. – Tobacco (Solanaceae)

This plant is cultivated worldwide.

Figure 6.22
Tobacco (Nicotiana tabacum L.)

Drug

Nicotianae folium (Tobacco leaf)

Tobacco leaf consists of the dried leaves of Nicotiana tabacum L. or other cultivated species (e.g. N. rustica L.)

 Constituents

The main characteristic constituents of the leaves are alkaloids (0.05-10%). The principal tobacco alkaloids have a pyridine moiety associated with either a pyrrolidine ring (ornithine-derived) or a piperidine ring (lysine-derived). The former group is represented by nicotine and the latter by anabasine. Tobacco leaf contains nornicotine as well. Other constituents are flavonoids and coumarins.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Figure 6.23-25
The structure of nicotine, nornicotine and anabasine.

Uses
Since nicotine is strongly toxic (50-100 mg of pure nicotine causes death), tobacco and its alkaloids are not significant constituents for the pharmaceutical industry. However, nicotine is used for the synthesis of nicotinic acid and nicotinamide. A recent pharmaceutical introduction is that of nicotine chewing-gum, nasal spray or patch, intended to help smokers who want to give up smoking.

The health-deteriorating effect of smoking is well-known; 1 g of tobacco leaf contains 5-10 mg of nicotine, which can cause arrhythmia, atherosclerosis, gastritis, chronic bronchitis, stomach ulcer, vascular spasms, vasoconstriction in the limbs, necrosis of the limbs, cancer of throat, oesophagus, lung and stomach.
Pulmonariae herba

Plant

*Pulmonaria officinalis* L. – Pulmonaria (Boraginaceae)

This plant is native to Europe mainly in oak-forests.

---

Figure 6.26

Pulmonaria (*Pulmonaria officinalis* L.)

Drug

*Pulmonariae herba* (Pulmonaria)

The drug consists of the dried flowering aerial parts of *Pulmonaria officinalis* L.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Constituents
The drug contains pyrrolizidine alkaloids, mucilage, silicic acid, flavonoids, chlorogenic acid, rosmarinic acid and allantoin.

![allantoin](image)

Figure 6.27
Pulmonariae herba (Pulmonaria)

Uses
Today the drug is principally used in ethnomedicine. It has expectorant and cough-reliever effect. But it should be highlighted that the internal use of the drug does not recommended because of pyrrolizidine alkaloids.
**Symphyti radix**

**Plant**

*Symphytum officinale* L. – Comfrey (Boraginaceae)

The plant occurs in Europe in wet meadows and marshy areas.

![Figure 6.29](image)

*Figure 6.29*

Comfrey (*Symphytum officinale* L.)

**Drug**

*Symphytis radix* (Comfrey root)

The drug consists of the dried rhizomes and roots of *Symphytum officinale* L.

![Figure 6.30](image)

*Figure 6.30*

*Symphyti radix* (Comfrey root)
Constituents

The drug contains pyrrolizidine alkaloids (0.05-0.08%) with 1,2-unsaturated necine ring structures, almost entirely in the form of their N-oxides, e.g. 7-acetylintermedine, 7-acetyllycopsamine together with smaller amounts of intermedine, lycopsamine and symphytine. Comfrey root also contains allantoin (0.6-4.7%), mucilage, phenolic acids such as rosmarinic acid, salicylic acid and caffeic acid, triterpene saponins (based on the aglycon of hederagenin) such as symphytoxide A, and lithospermic acid.

![Chemical structures of alkaloids](image)

Figure 6.31-35

The structure of 7-acetylintermedine, 7-acetyllycopsamine, intermedine, lycopsamine and symphytine.

Uses

The therapeutic indications include the treatment of strains, contusions, distorsions, osteoarthritis, epicondylitis, tendovaginitis and periarthritis. The drug and its preparations can be used only externally.

Dosage

Ointments or other preparations containing up to 35% of root extract (1:2, ethanol 60% V/V), applied 3-4 times daily. Comfrey root preparations should be applied only to intact skin.

Its use is not recommended for more than 4-6 weeks per year (if the daily application contains between 10 μg and 100 μg of pyrrolizidine alkaloids).

Pregnancy and lactation

No human data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

### 6.3 Alkaloids formed from lysine

Lysine (Figure 6.36) and its associated compounds give rise to a number of alkaloids, some of which are analogous to the ornithine group. Although in some cases, such as the quinolizidine lupin alkaloids, lysine is incorporated via a symmetrical precursor, e.g. cadaverine; in the majority of examples (anabasine, sedamine) the incorporation is
asymmetric. In general, for the simple α-substituted piperidines, the C-2 of lysine becomes the point of attachment of the α-side-chain. Lysine-derived alkaloids occur in the plant families of Piperaceae, Crassulaceae, Fabaceae, Punicaceae, Apiaceae, Solanaceae, Lobeliaceae and Arecaceae.

Figure 6.36
The structure of lysine.

Figure 6.37
Biosynthesis of some lysine-derived alkaloids and nicotine.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Figure 6.38
Formation of quinolizidine alkaloids from lysine.
Drugs

Lobeliae herba

Plant

*Lobelia inflata* L. – Lobelia (Lobiaceae)

This annual plant is indigenous to the eastern USA and Canada. It is also cultivated in the USA and the Netherlands.

![Lobelia inflata](image)

**Figure 6.39**

Lobelia (*Lobelia inflata* L.)

Drug

*Lobelieae herba* (Lobelia)

The drug consists of the dried aerial parts of *Lobelia inflata* L.
**Constituents**

The drug contains a mixture of alkaloids (0.2-0.6%), the principal alkaloid being lobeline, while other related alkaloids include lobelanine, lobelanidine, lobinine and isolobinine.

![lobeline and lobelanine structures](image)

**Figure 6.40-43**
The structure of lobeline, lobelanine, lobelanidine and lobinine.

**Uses**

Lobelia or the pure constituent lobeline are used in spasmodic asthma and chronic bronchitis. Lobeline stimulates the respiratory system, and it is used in the case of gas-, CO- and narcotic-poisonings. It is also included in some antismoking preparations. In the form of injection lobeline hydrochloride is used in the resuscitation of new-born infants. The drug has a paralytic effect in toxic doses. The drug and its preparations should not be used without medical advice.
Laburni semen (Cytisi semen)

Plant

*Laburnum anagyroides* Medic. – Laburnum (Fabaceae)

This shrub or small tree is native to Europe.

*Figure 6.44*

Laburnum (*Laburnum anagyroides* Medic.)

Drug

*Laburni semen* (Laburnum seed)

The drug consists of the dried, ripe seeds of *Laburnum anagyroides* Medic.
Constituents

The drug contains a mixture of alkaloids, the principal quinolizidine alkaloid being cytosine, and additional alkaloids include N-methyl-cytisine, sparteine and the pyrrolizidine laburnine.
Uses
The drug is used for the isolation of cytisine, which stimulates the respiratory system; it is used against the paralysis of respiration. The drug and its preparations should not be used without medical advice.

**Sarothamni scoparii herba**
Plant
*Sarothamnus scoparius* (L.) Wimm. – Broom (Fabaceae)
Broom is a perennial shrub native to Europe.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

**Figure 6.50**
Broom [*Sarothamnus scoparius* (L.) Wimm.]

**Figure 6.51**
Sarothamni scoparii herba (Broom)

Drug

*Sarothamni scoparii herba* (Broom)

The drug consists of the dried flowering aerial parts of *Sarothamnus scoparius* (L.) Wimm.
Constituents

The drug contains a mixture of alkaloids (0.8-1.5%), the principal quinolizidine alkaloid is sparteine and additional alkaloids are lupanine, 4-hydroxylupanine, 13-hydroxylupanine and 17-oxosparteine. Other constituents include amines such as dopamine, flavonoids, e.g. scoparin and kaempferol, coumarins and small amounts of essential oil.

![Chemical structures of alkaloids](image_url)

**Figure 6.52-56**

The structure of sparteine, lupanine, 4-hydroxylupanine, 13-hydroxylupanine and 17-oxosparteine.

Uses

The drug is used for the isolation of sparteine, which has antiarrhythmic action. It decreases the excitability of the stimulus-leader system in the heart, decreases or stops ventricle-fibrillation. It increases blood pressure and has diuretic activity. Spartein or the drugs containing this compound can only be used under medical supervision. The usage of this drug is not recommended for pregnant women, and for patients suffering from high blood pressure.

6.4 Alkaloids formed from phenylalanine

Phenylalanine (**Figure 6.57**) with tyrosine and dihydrophenylalanine and their corresponding decarboxylation products are the precursors of a large number of alkaloids, e.g. protoalkaloids, benzylisoquinolines, protoberberines, ipecacuanha alkaloids, as well as the morphine- and rhoeadine-type alkaloids. These alkaloids occur in the plant families of Berberidaceae, Ranunculaceae, Papaveraceae, Fumariaceae, Rubiaceae, Solanaceae and Liliaceae.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

**Figure 6.57**
The structure of phenylalanine.

![Chemical structure of phenylalanine](image)

phenylalanine
($\alpha$-amino-$\beta$-phenyl-propionic acid)

**Drugs**

**Capsici fructus**

**Plants**

*Capsicum annuum* L. *var. minimum* (Miller) Heiser or *Capsicum frutescens* L. – Paprika/Capsicum (Solanaceae)

Paprika is native to Middle-America, Mexico, but it is also widely cultivated, e.g. in Hungary.
Figure 6.58
Paprika (*Capsicum annuum* L.)

**Drug**

*Capsici fructus* (Capsicum, Ph.Eur.)

The drug consists of the dried ripe fruits of *Capsicum annuum* L. var. *minimum* (Miller) Heiser and small-fruited varieties of *Capsicum frutescens* L. It contains minimum 0.4% of total capsaicinoids expressed as capsaicin, and calculated with reference to the dried drug.

It has extremely pungent taste.
Constituents
The main active constituents are capsaicinoids, principally capsaicin (63-77%), dihydrocapsaicin (20-32%) and nordihydrocapsaicin and small amounts of homodihydrocapsaicin. The fruit also contains carotenoids such as capsanthin, capsorubin, β-cryptoxanthin, zeaxanthin, lutein and β-carotene, flavonoids and ascorbic acid (vitamin C).

Figure 6.59
Capsici fructus (Capsicum)

capsanthin

capsorubin

Figure 6.60-65
The structure of capsaicin, dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin, capsanthin and capsorubin.
Uses

The drug and its preparations are used medically for external purposes (not more than 10 days). The therapeutic indications are relief of muscle pain, e.g. backache, treatment of pain in osteoarthritis and rheumatoid arthritis, treatment of neuralgias such as the pain following herpes zoster and painful diabetic neuropathy and treatment of pruritus of varying aetiology, such as in prurigo nodularis or associated with psoriasis, haemodialysis or contact with water.

Dosage

Adults and children over 12 years of age: in liquid or semi-solid forms: preparations containing extracts corresponding to 0.025%-0.075% of capsaicinoids, 3-4 times daily. In plasters: extracts corresponding to 10-40 μg of capsaicinoids per cm².

Capsicum preparations should not be used on broken skin or wounds and in the case of known hypersensitivity to capsaicinoids.

Special warnings and precautions for use

The drug should not be applied to mucosa or near the eyes. It is recommended not to scratch the site of application to avoid damaging the skin. Treatment should be discontinued if excessive warmth is experienced. Hands should be washed with soap and water after handling products.

Interaction with other medicaments

Capsicum should not be used together with other external products, e.g. other rubefacient or pain relieving gels at the same application site.

Undesirable effects

Capsicum preparations usually cause hyperaemia with marked erythema. This reaction is part of the normal pharmacological effect and generally subsides within a short time. Skin hypersensitivity reactions such as urticaria and vesiculation may occur. In such cases treatment should be discontinued.

Pregnancy and lactation

No human data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.
Ephedrae herba

Plant

*Ephedra distachya* L. – Ephedra/Common horse-tail (Ephedraceae)

The plant is native to Europe. In Asia, mainly in China other *Ephedra* species occur (*E. sinica*, *E. equisetina*). In India and Pakistan the species of *E. intermedia* and *E. gerardina* can be found.

![Ephedra distachya L.](image)

**Figure 6.66**

*Ephedra (Ephedra distachya L.)*

Drug

*Ephedrae herba* (Ephedra)

The drug consists of slender, more or less broken aerial stems which are woody and usually branch only at the base.
Constituents

The main active constituents are protoalkaloids (0.5-2%) such as (-)-ephrine, (+)-pseudoephedrine, (+)-norpseudoephedrine, (-)-norephedrine, (-)-methylephedrine and (+)-methylpseudoephedrine. Other constituents include flavonoids and tannins.

Uses

The main effective substance of the drug is (-)-ephrine, which is a sympathomimetic, exerting spasmolytic effect on bronchus-muscles, therefore it can be used in the case of asthma bronchiale, in conditions resulting from allergy and bronchitis. Due to its vasoconstrictive action, it can be used in the case of cold as a component of nasal drops. The drug and its products should not be used without medical advice.

Papaveris fructus sine seminibus

Plant

Papaver somniferum L. – Poppy (Papaveraceae)
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Different varieties of the plant are widely cultivated, but in some countries permission is required for cultivation.

![Poppy](image)

**Figure 6.74**
Poppy (*Papaver somniferum* L.)

**Drug**

*Papaveris fructus sine seminibus* (Poppy capsule without seeds)

The drug consists of the dried, ripe fruits (capsules) without seeds of *Papaver somniferum* L.
Constituents
The main active constituents are the mixture of approx. 30 alkaloids; the main component is morphine (0.015-0.018%). The additional alkaloids (0.035-0.23%) include codeine, thebaine, papaverine, narcotine and narceine. The isolation of morphine from dried poppy straw was patented by a Hungarian pharmacist, János Kabay in 1930.

Figure 6.75
*Papaveris fructus sine seminibus* (Poppy capsule without seeds)
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

![Chemical structures of different alkaloids](image)

**Figure 6.76-81**

The structure of morphine, codeine, thebaine, papaverine, narcotine and narceine.

**Uses**

The drug is used for the extraction of morphine and the main additional alkaloids in the pharmaceutical industry.

**Opium crudum**

**Plant**

*Papaver somniferum* L. – Poppy (Papaveraceae)

Opium is produced after incision of the green, unripe capsules of poppy. The incision must not penetrate into the interior of the capsule. The latex, which is at first white, rapidly coagulates and turns brown. Each capsule is cut several times at intervals of 2 or 3 days. After collection the latex is placed in a tilted vessel so that the dark fluid which is not required may drain off. By exposure to air opium acquires a suitable consistency for packing.

**Drug**

*Opium crudum* (Opium, raw, Ph. Eur.). **Other Drug** *Opii pulvis normatus* (Opium, prepared, Ph. Eur.)

Raw opium is intended only as starting material for the manufacture of galenical preparations. It is not dispensed as such. Raw opium is the air-dried latex obtained by incision from the unripe capsules of *Papaver somniferum* L. It contains not less than 10.0% of morphine and not less than 2.0% of codeine, both calculated with reference to the drug dried at 100°C to 105°C. Raw opium has a characteristic odour and a blackish-brown colour. It consists of masses of various sizes, which tend to be soft and shiny and, after drying, become hard and brittle.
Opium is raw opium powdered, and dried at a temperature not exceeding 70°C. It contains:

- morphine: 9.8% to 10.2% (drug dried at 100-105°C for 4 h)
- codeine: minimum 1.0% (drug dried at 100-105°C for 4 h).

Content adjusted if necessary by adding a suitable excipient or raw opium powder.

Opium prepared is a yellowish-brown or dark brown powder.

Constituents

The main active constituents are the mixture of alkaloids; the main component is morphine. The additional alkaloids include codeine, thebaine, papaverine, narcotine and narceine. Other constituents are different organic acids, e.g. meconic acid, fumaric acid, malic acid and succinate acid, sugars, amino acids and water.

Uses

The drug is used for the extraction of morphine and the main additional alkaloids in the pharmaceutical industry. A number of pharmaceutical products contain opium or its extract, e.g. Tinctura opii, Pulvis opii et ipecacuanhae, Pulvis opii, Extractum opii, Opium concentratum. Tinctura and Pulvis opii can be used in the case of diarrhoea as consequence of acute infection. Pulvis opii et ipecacuanhae has expectorant, diaphoretic and cough-reliever effects in the case of cold. Extractum opii and Opium concentratum are substituting agents of morphine. Morphine can be used for the alleviation of strong pains (e.g. in the case of cancer) and as a narcotic drug, but it causes euphoria and dependency. It is one of the most dangerous drugs if used illegally. Codeine and narcotine are cough-relievers, papaverine has a spasmylytic action.

Chelidonium majus L. – Greater celandine (Papaveraceae)

The plant is native to Europe.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Figure 6.82
Greater celandine (*Chelidonium majus* L.)

Drug

*Chelidonii herba* (Greater celandine)

The drug consists of the dried, whole or cut aerial parts of *Chelidonium majus* L. collected during flowering. It contains minimum 0.6% of total alkaloids, expressed as chelidonine, calculated with reference to the dried drug.

Figure 6.83
*Chelidonii herba* (Greater celandine)
Constituents

The main active constituents are benzylisoquinoline alkaloids (0.01-1%) of the berberine, protoberberine, and benzophenanthridine types, the principal alkaloids being chelidonine together with protopine, sanquinarine, chelerythrine, etc. Over 20 alkaloids have been identified in the drug. Other substances include cholin, methylamin, thyramin, chelidonic acid, citric acid, malic acid, succinic acid, derivatives of caffeic acid and flavonoids.

![Chemical structures of berberine, chelidonine, protopine, sanquinarine, and chelidonic acid](image)

Uses

The therapeutic indications of the drug include the symptomatic treatment of mild to moderate spasms of the upper gastrointestinal tract, minor gall bladder disorders and dyspeptic complaints such as bloating and flatulence. The freshly obtained yellow latex of the plant can be employed for removal of warts, because alkaloids of this latex have strong antiviral, antibacterial action and they inhibit cell division.

Dosage

Daily dose for adults and children over 12 years: 1-4 g of the drug as a tea infusion. 125-700 mg of standardized hydroalcoholic extracts corresponding to 9-24 mg of total alkaloids, calculated as chelidonine. Tincture (1:10): 2-4 ml, 3 times daily. Fluid extract (1:1): 1-2 ml, 3 times daily. In long-term use for more than 4 weeks, checks on liver enzyme activity are recommended.

Overdose: Abdominal pain, gastrointestinal cramps, urinary urgency, drowsiness and haematuria may result due to the alkaloids. In this case, treatment must be stopped immediately.

For removal of warts the yellow latex flowing out of the freshly harvested plant can be used or the tincture (1:1, 96% V/V) prepared from the fresh or dried herb.
Contra-indications

Patients with biliary obstruction or existing or previous liver diseases should not use the drug and its preparations internally. In case of gallstones, the drug and its preparations should not be used without medical advice.

Undesirable effects

Mild gastrointestinal disturbances, such as nausea or diarrhoea, stomach upset sometimes occur. In rare cases, hepatic inflammation and an increased liver enzyme activity and serum bilirubin have been reported, but this is reversible on discontinuation of therapy.

Pregnancy and lactation

No data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

Fumariae herba

Plant

Fumaria officinalis L. – Fumitory (Fumariaceae)

The plant is native to Europe.
Drug

*Fumariae herba* (Fumitory, Ph. Eur.)

The drug consists of the whole or fragmented, dried aerial parts of *Fumaria officinalis* L. harvested in full bloom. It contains not less than 0.4% of total alkaloids, expressed as protopine and calculated with reference to the dried drug.
Constituents

The main active constituents are isoquinoline alkaloids (0.3-1.3%) of the protopine, spirobenzylisoquinoline and protoberberine types, the principal ones being protopine and fumarophycine together with cryptopine, sinactine and fumaritine. Over 20 alkaloids have been identified. Other constituents are flavonoids (e.g. rutin), aliphatic acids such as fumaric and malic acids and hydroxycinnamic acid derivatives (e.g. coumaric acid, caffeic acid and ferulic acid).
The therapeutic indications of the drug include the treatment of digestive complaints such as stomach ache, nausea, vomiting, feeling of fullness and flatulence due to hepatobiliary disturbance. The smooth muscle-relaxing effect of the drug extract has been demonstrated on isolated rat duodenum.

Dosage

*Daily dose for adults:* 4-6 g of the drug as an aqueous extract or infusion. Liquid extract (1:1, ethanol 25% V/V) or tincture (1:5, ethanol 45% V/V).

Contra-indications

Patients with biliary obstruction should not use the drug and its preparations internally. In case of gallstones, the drug and its preparations should not be used without medical advice.

Pregnancy and lactation

No data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

**Berberidis radicis cortex**

**Plant**

*Berberis vulgaris* L. – Barberry (Berberidaceae)

This shrub is native to Europe.

![Barberry](image1)

**Figure 6.96**

Barberry (*Berberis vulgaris* L.)

**Drug**

*Berberidis radicis cortex* (Barberry root-bark)

The drug consists of the whole or fragmented, dried root-bark or partly the roots of *Berberis vulgaris* L.
Constituents

The main active constituents are alkaloids (8%), the principal one being berberine. Additional alkaloids are oxyberberine, palmatine, jatrorrhizine, etc.

![Structures of berberine, oxyberberine, palmatine, jatrorrhizine](image)

**Figure 6.97**

*Berberidis radicis cortex* (Barberry root-bark)

**Figure 6.98-101**

The structure of berberine, oxyberberine, palmatine and jatrorrhizine.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Uses
The extract prepared from the drug has antibacterial, cholagogue and smooth muscle-relaxing effects. The drug is principally used in ethnomedicine and homoeopathy. It can be used in the treatment of digestive complaints such as stomach ache, nausea, vomiting, feeling of fullness and flatulence due to hepatobiliary disturbance, but these effects have not been proved by clinical studies.

Dosage

*Daily dose for adults:* 2 g of the drug as an infusion.

Contra-indications
Patients with biliary obstruction should not use the drug and its preparations internally. In case of gallstones, the drug and its preparations should not be used without medical advice.

Pregnancy and lactation
No data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

**Hydrastis rhizoma**

**Plant**
*Hydrastis canadensis* L. – Goldenseal (Ranunculaceae)

This small perennial plant is indigenous to the woods of eastern Canada and eastern USA. Today it can be cultivated, too, mainly in the USA and Europe.

**Drug**
*Hydrastis rhizoma* (Goldenseal rhizome, Ph. Eur.)

The drug consists of the whole or cut, dried rhizome and root of *Hydrastis canadensis* L.

It contains minimum 2.5% of hydrastine and minimum 3.0% of berberine, calculated with reference to the dried drug.

**Constituents**
The main active constituents are alkaloids (2.5-6%), e.g. hydrastine, berberine and canadine.
Figure 6.102-104
The structure of hydrastine, berberine and canadine.

Uses
The extract prepared from the drug has antibacterial, cholagogue, smooth muscle-relaxing and sedative effects. The drug is principally used for the treatment of digestive complaints such as dyspepsia, gastritis, feeling of fullness and flatulence. Hydrastine hydrochloride has been used in various forms to control uterine haemorrhage.

Dosage
Daily dose for adults: 0.5-1 g of the drug as an infusion.

Contra-indications
Patients with hypertonia should not use the drug and its preparations.

Pregnancy and lactation
The drug and its products must not be used during pregnancy and lactation.

Colchici tuber
Plant
*Colchicum autumnale* L. – Autumn crocus or meadow saffron (Liliaceae)
This perennial plant is native to Europe.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

**Figure 6.105**
Autumn crocus or meadow saffron (*Colchicum autumnale* L.)

**Drug**

*Colchici tuber* (Colchicum corm)

The drug consists of the dried corm collected during or directly after the flowering period of *Colchicum autumnale* L.

** Constituents**

The main active constituents are colchicine-type alkaloids (0.1-0.6%), the main alkaloids being colchicine (60%) and demecolcine. Further alkaloids are artefacts developed during drying and storage.
Uses

Pure colchicine has cytostatic effect, therefore it is used in biological experiments to produce polyploidy or multiplication of the chromosomes in a cell nucleus. Colchicum preparations are also used to relieve gout, but must be employed under medical supervision. **Pure colchicine is highly toxic!** The less toxic demecolcine can be used in cancer therapy (chemotherapy).

Dosage

*Daily dose for patients with gout:* 1 mg of colchicum preparations, maximum dose 4-8 mg.

Pregnancy and lactation

The drug and its products must not be used during pregnancy and lactation.

Ipecacuanhae radix

Plant

*Cephaelis ipecacuanha* (Brot.) Rich. and *C. acuminata* Karsten – Matto Grosso and Costa Rica Ipecacuanha (Rubiaceae)

*Cephaelis ipecacuanha* is a shrub found in Brazil, mainly in the moist and shady forests of Matto Grosso and Minas Geraes. It is also cultivated in Malaya and Burma. *C. acuminata* is found in Columbia, Nicaragua and Costa Rica.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Drug

*Ipecacuanhae radix* (Ipecacuanha root, Ph. Eur.). **Other drugs:** *Ipecacuanhae extractum fluidum normatum* (Ipecacuanha liquid extract, standardised, Ph. Eur.), *Ipecacuanhae tinctura normata* (Ipecacuanha tincture, standardised, Ph. Eur.), *Ipecacuanhae pulvis normatus* (Ipecacuanha, prepared, Ph. Eur.)

Ipecacuanha root consists of the fragmented and dried underground organs of *Cephaelis ipecacuanha* (Brot.) A.Rich., known as Matto Grosso ipecacuanha, or of *Cephaelis acuminata* Karsten, known as Costa Rica ipecacuanha, or of a mixture of both species. It contains not less than 2.0% of total alkaloids, calculated as emetine with reference to the dried drug. The principal alkaloids are emetine and cephaëline. Ipecacuanha root has a slight odour.

Standardised liquid extract produced from *Ipecacuanha root*. It contains minimum 1.80% and maximum 2.20% of total alkaloids, calculated as emetine. The extract is produced from the herbal drug and solvent of suitable strength by an appropriate procedure. It is a dark-brown liquid.

Tincture produced from *Ipecacuanha root*. It contains 0.18% (m/m) to 0.22% (m/m) of total alkaloids, calculated as emetine. The tincture is produced by a suitable procedure from the herbal drug and ethanol of suitable strength. It is a yellowish-brown liquid.

Prepared ipecacuanha is ipecacuanha root powder adjusted, if necessary, by the addition of powdered lactose or ipecacuanha root powder with a lower alkaloid content to contain 1.9% to 2.1% of total alkaloids, calculated as emetine with reference to the dried drug. It is a light grey to yellowish-brown powder with a slight odour.

Constituents

The main active constituents are isoquinoline derivative alkaloids (2-3.5%), principally with emetine and cephaëline. These alkaloids derive from the condensation of dopamine.
with loganin (an iridoid compound). Additional alkaloids are psychotrine, psychotrine methylether and emetamine. Other constituents include starch, iridoid glucoside and calcium oxalate.

**Figure 6.108**
The biosynthesis of emetine.

**Figure 6.109-111**
The structure of cephaëline, psychotrine and emetamine.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Uses

Ipecacuanha is used as an expectorant and emetic and in the treatment of amoebic dysentery. The action of emetine and cephaëline is dose-dependent. In low doses they have expectorant activity, but in higher doses they possess emetic effect. Psychotrine is a selective inhibitor of the human immunodeficiency virus. The drug and its preparations should not be used without medical advice.

Dosage

*Single dose:* for babies (from 3 months to 1 year): 0.01 g; from 1 year to 3 years: 0.015 g; from 3 years to 6 years: 0.02 g; from 6 years to 9 years: 0.025 g; from 9 years to 12 years: 0.03 g; for adults: 0.05 g.

Pregnancy and lactation

The drug and its products must not be used during pregnancy and lactation.

**Boldi folium**

Plant

*Peumus boldus* Mol. –Boldo (Monimiaceae)

*Peumus boldus* is a dioecious, evergreen shrub or a small tree, which is native to Chile, Peru and Marocco. It is cultivated in Italy.

![Figure 6.112](image)

**Figure 6.112**

Boldo (*Peumus boldus* Mol.)

Drug

*Boldi folium* (Boldo leaf, Ph. Eur.)

Boldo leaf consists of the whole or fragmented dried leaf of *Peumus boldus* Molina. The whole drug contains not less than 20.0 ml/kg and not more than 40.0 ml/kg and the fragmented drug not less than 15.0 ml/kg of essential oil. It contains not less than 0.1% of total alkaloids, expressed as boldine, calculated with reference to the anhydrous drug. Boldo leaf has an aromatic odour especially when rubbed.
Constituents

The main characteristic constituents are isoquinoline alkaloids of the aporphine and noraporphine types (0.25-0.5%), the major alkaloids being boldine and isoboldine. Other constituents are essential oil (2-3%) containing monoterpenes such as p-cymene, linalool, ascaridole, 1,8-cineole, etc. and flavonoids (especially glycosides of rhamnetin, isorhamnetin and kaempferol).

![Chemical structures of boldine and isoboldine]

Uses

The therapeutic indications of the drug include the treatment of minor hepatobiliary dysfunction and the symptomatic treatment of mild digestive disturbances.

Dosage

Adult daily dose: 2-5 g of the drug as a tea infusion. 0.2-0.6 g of the crude drug or equivalent hydroethanolic extract. Tincture (1:5, ethanol 80% V/V): 1-3 ml, fluid extract (1:1, ethanol 80% V/V): 0.5-1 ml.

The drug and its preparations should not be used for more than 4 weeks.
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Contra-indications

Patient with biliary obstruction should not use the drug. The essential oil of the plant must not be used in therapy due to its toxic ascaridole content.

Pregnancy and lactation

The drug and its products must not be used during pregnancy and lactation. Very high doses of a dry ethanolic boldo leaf extract (800 mg/kg/day) have been reported to cause abortifacient and teratogenic effects in rats.

Curare

Plants

*Chondrodendron tomentosum* Ruiz. et Pavon (Menispermaceae), *Strychnos toxifera* Schomburgk ex Bentham (Loganiaceae)

*Chondrodendron tomentosum* is a liana found in the rain forests by the river Amasonas. The drug used to be traded in the “tube” of bamboo-cane (*Bambusa sp.*), therefore it was called “Tube-curare”. Because of its botanical origin its synonym name is “Menispermaceae-curare”, too. *Strychnos toxifera* is also a liana found in Brazil, Peru, Ecuador, Venezuela and Columbia. The drug was packed in gourds, therefore it was called „Calabash-curare”.

Drug

*Curare* (Curare)

Curare is a brown or black, bitter paste. Tube-curare is the concentrated aqueous extract of the bark or leaves of *Chondrodendron tomentosum* Ruiz. et Pavon. Calabash-curare is prepared similarly from *Strychnos toxifera* Schomburgk ex Bentham.

Constituents

Tube-curare contains principally (+)-tubocurarine (dimer alkaloid, bisbenzylisoquinoline type), (-)-curine and (+)-chondrocurarine. Calabash-curare contains a mixture of approx. 40 alkaloids with principally C-toxiferine (dimer alkaloid).
Uses
Curare is now little used except as a source of alkaloids. Tubocurarine chloride is used to secure muscular relaxation in surgical operations and in certain neurological conditions. The action of C-toxiferine is 20-50 times stronger than that of (+)-tubocurarine. Curare was used as an arrow poison by the indigenous inhabitants.
Chapter 7

Drugs containing alkaloids of tryptophan and histidine origin

7.1 Alkaloids formed from tryptophan

With a few minor exceptions, tryptophan (Figure 7.1) and its decarboxylation product, tryptamine, give rise to the large class of indole alkaloids. The alkaloids biosynthesised from tryptophan occur not only in plants, but also in fungi. In the synthesis of these alkaloids terpenoids are often involved, as well.

![Figure 7.1](image-url)
The structure of tryptophan.

Drugs

Secale cornutum

Fungus

*Claviceps purpurea* (Fries) Tulasne (Clavicipitaceae)

Drug

*Secale cornutum* (Ergot)

The drug is the overwintering form of the fungus (*Claviceps purpurea*), which grows on the ears of cereals (e.g. rye). The drug is 1.5-4 cm long, 2-5 mm thick, dark-purple, or brownish-black, a slightly bent sclerotium.
Constituents

The drug contains a mixture of approx. 30 alkaloids (0.05-1%). Classification of ergot-alkaloids: amides, peptide-alkaloids, clavin-alkaloids. Besides the alkaloids, the drug contains amines, anthraquinone-derivatives and fatty oils in ~40%. The most important ergot-alkaloids are the derivatives of lysergic (D-lysergic) acid: ergometrine, ergotamine, ergocristine. Diethylamide of lysergic acid (LSD = Lisergsäure-diethylamide) can be prepared by partial synthesis from lysergic acid. It has hallucinogenic action and it is a dangerous illegal drug. In the molecule of ergocristine, an isopropyl-group is connected to the oxasolidin(one)-ring instead of CH$_3$-group.
Drugs containing alkaloids of tryptophan and histidine origin

Figure 7.3-7
The structure of lysergic acid, LSD, ergometrine, ergotamine and ergocristine.

Uses
The amide- and peptide alkaloids are used for pharmaceutical purposes. The action of ergometrine is similar to that of oxytocine; it has myometrium-contractive action; it can be used at delivery. The most important pharmacological effect of ergotamine is its vasoconstrictor action, therefore it is used for the alleviation of bleeding after delivery and for treatment of migraine. The dihydro-derivatives of ergotoxine-alkaloids (mixture of many alkaloids) can be used to decrease blood pressure.
**Rauwolfiae radix**

**Plant**

*Rauwolfia serpentina* (L.) Benth et Hook – Rauwolfia (Apocynaceae)

The plant is native to India, Pakistan and South-Vietnam.

![Figure 7.8 Rauwolfia [Rauwolfia serpentina (L.) Benth et Hook]](image)

**Drug**

*Rauwolfiae radix* (Rauwolfia root, DAB)

The drug consists of the dried roots and rhizomes of *Rauwolfia serpentina* (L.) Benth et Hook.
Drugs containing alkaloids of tryptophan and histidine origin

**Figure 7.9**
*Rauwolfiae radix* (Rauwolfia root)

**Constituents**
It contains a mixture of ~50 alkaloids (alkaloid content: 1.5-3%). The most important alkaloids of the drug are reserpine, yohimbine and aymalicine.

![Reserpine](image)

**Reserpine**

![Yohimbine](image)

**Yohimbine**

![Aymalicine](image)

**Aymalicine**

**Figure 7.10-12**
The structure of reserpine, yohimbine and aymalicine.
Pharmacognosy 2

Uses

Reserpine has sedative and hypotensive action; it can be used for reducing anxiety, stress, aggression and in the treatment of chronic schizophrenia. Aymalicine increases the blood supply of the brain. Yohimbine can be employed as an aphrodisiac.

**Vincae minoris herba**

**Plant**

*Vinca minor* L. – Lesser periwinkle (Apocynaceae)

The evergreen plant occurs in Europe and also in Hungary.

![Lesser periwinkle](image)

**Figure 7.13**

Lesser periwinkle (*Vinca minor* L.)

**Drug**

*Vinca minoris herba* (Lesser periwinkle)

The drug consists of the flowering part of *Vinca minor* L.
Drugs containing alkaloids of tryptophan and histidine origin

**Figure 7.14**  
*Vincae minoris herba* (Lesser periwinkle)

**Constituents**

The drug contains a mixture of ~40 alkaloids (0.25-1%); the main alkaloid is vincamine (25-65% of the total alkaloid content). Further characteristic substances include loganin, derivatives of benzoic acid and of cinnamic acid, glycosides of these compounds, flavonoids (kaempferol and quercetin) and ursolic acid.

**Figure 7.15-18**  
The structure of vincamine, 3,4-dihydroxy-benzoic acid, 2,3-dihydroxy-benzoic acid and ursolic acid
Uses

*Vinca minor* is an industrial medicinal plant, used for the preparation of vincamine. Vincamine exerts a hypotensive action, dilates the blood vessels of the brain, increases its blood and oxygen supply. From vincamine the ethylester of apovincaminic acid (Cavinton®) can be prepared by semisynthetic way. Cavinton® dilates the cerebral blood vessels; it can be used in the insufficiency of cerebral blood circulation.

In traditional medicine the drug is used in the case of the disorders of cerebral blood circulation, against amnesia, forgetfulness, decrease of the intellectual ability. In the case of hypertonia it can be used for lowering blood pressure.

**Catharanthi herba**

Plant

*Catharanthus roseus* (L.) G. Don – Madagascar periwinkle (Apocynaceae)

This plant is native to Madagascar, but it is also widespread in many tropical and subtropical countries.

![Madagascar periwinkle](image)

**Figure 7.19**

Madagascar periwinkle [*Catharanthus roseus* (L.) G. Don]

Drug

*Catharanthi herba* (Madagascar periwinkle)

The drug consists of the flowering part of the evergreen sub-shrub of *Catharanthus roseus* (L.) G. Don.

Constituents

The drug contains a mixture of ~ 90 alkaloids (alkaloid content is ~0.7%); the main alkaloids are vinblastine and vincristine.
Drugs containing alkaloids of tryptophan and histidine origin

Figure 7.20-21
The structure of vinblastine and vincristine.

Uses
The drug is used for the preparation of vinblastine and vincristine in the pharmaceutical industry. These compounds have mitosis inhibiting action; they can be used in cancer therapy as cytostatics, particularly in the case of leukemia and lymphogranulomatosis (Hodgkin-disease).

Strychni semen
Plant

*Strychnos nux-vomica* L. – Nux vomica (Loganiaceae)

The plant is native to India, Sri Lanka (Ceylon) and North-Australia.

Drug

*Strychni semen* (= Nux vomica) (Nux vomica seed, Ph. Hg. VII.)

The drug consists of the dried, ripe seeds of the small tree or shrub of *Strychnos nux-vomica* L.

Constituents
The drug contains a mixture of alkaloids (2.5-4%) such as strychnine, brucine (1:1) and several other alkaloids. Further effective substances include loganin and chlorogenic acid.
Figure 7.22-25
The structure of strychnine, brucine, loganin and chlorogenic acid.

Uses

Strychnine, which is a very bitter substance, increases the muscle tension. It can be used in the case of reconvalescence, exhaustion and after stroke to increase the sensibility of the sense organs, and for treatment of paralysis. The alkaloid content was formerly used as a circulatory stimulant in such cases as surgical shock, but its use is now limited to that of a respiratory stimulant in certain cases of poisoning.

Cinchonae cortex

Plant

_Cinchona pubescens_ Vahl (= _C. succirubra_ Pavon ex Klotzsch) – Red cinchona (Rubiaceae)

The plant is native to the eastern slopes of the Andes mountain at the height of 1500-2500 m: Venezuela, Bolivia; it can also be found in Zaire and in Malaysia.

Drug

_Cinchonae cortex_ (Cinchona bark, Ph. Eur.) = _Chinae succirubrae cortex_

The drug consists of the whole or cut, dried bark of _Cinchona pubescens_ Vahl (_Cinchona succirubra_ Pavon), of _C. calisaya_ (Weddell), of _C. ledgeriana_ (Moens ex Trimen) or of their varieties or hybrids. It contains minimum 6.5% of total alkaloids, of which 30% to 60% consists of quinine-type alkaloids calculated with reference to the dried drug. Cinchona bark has an intense bitter, somewhat astringent taste.
Constituents

The drug contains a mixture of different alkaloids (6-7% alkaloid-content); its main alkaloids are quinine, quinidine, cinchonine, cinchonidine. Further characteristic substances of the drug include tannins, triterpenes and quinic acid.

![Figure 7.26](image)

*Figure 7.26*

*Cinchonae cortex* (Cinchona bark)

**Uses**

The mentioned alkaloids are effective against malaria; quinine is antipyretic, chinidine has antiarrhythmic action. Pure quinine is used in the therapy against malaria and as
fever reducer, pure chinidin against disorders of cardiac rhythm. The tincture prepared from this drug is appetizing.

**Physostigmas semen**

**Plant**

*Physostigma venenosum* Balf. – Calabar bean (Fabaceae)

This plant is native to tropical West-Africa; it was newly introduced to India and Brasilia.

**Drug**

*Physostigmas semen = Calabar semen* (Calabar bean)

The drug consists of the seeds of *Physostigma venenosum* Balf.

** Constituents**

The drug contains a mixture of several alkaloids (alkaloid content is 0.1-0.5%); its main alkaloids are physostigmine and eseroline.

![Chemical structures of physostigmine and eseroline](image)

*Figure 7.30-31*

The structure of physostigmine and eseroline.

**Uses**

Physostigmine has a parasympathomimetic effect, it can be used in ophthalmology for constricting the pupil, and to treat glaucoma. Physostigmine salicylate is used for contracting the pupil of the eye, often to combat the effect of mydriatics. With Alzheimer’s disease it has shown some evidence of inducing a slight improvement in intellectual and cognitive performance. It is used in the veterinary medicine against flatulence.

**Uncariae tomentosae radix**

**Plant**

*Uncaria tomentosa* (Willd.) DC. – Cat’s claw (Rubiaceae)

The plant is native to Middle- and South-America (Peru).

**Drug**

*Uncariae tomentosae radix* (Cat’s claw root)
Drugs containing alkaloids of tryptophan and histidine origin

The drug consists of the dried roots of *Uncaria tomentosa* (Willd.) DC.

**Constituents**

The drug contains a mixture of different indole alkaloids (0.1-0.5%) (with tetra- and pentacyclic ring systems): pteropodin, rinchophylline, mitraphylline. Other constituents are saponins, oleanolic acid and ursolic acid.

![Figure 7.32-33](image)

**Figure 7.32-33**

The structure of pteropodin and rinchophylline.

**Uses**

The drug has antirheumatic, antiviral and immunostimulant actions, and is also used as a pharmaceutical raw material. It can be used in the treatment of joint diseases and rheuma. **The drug and its preparations should not be used during pregnancy and lactation!**

**Passiflorae herba**

**Plant**

*Passiflora incarnata* L. – Passion flower (Passifloraceae)

The plant is native to America and Europe (Italy, Greece).

**Drug**

*Passiflorae herba* (Passion flower, Ph. Eur.)

Passion flower consists of the fragmented or cut, dried aerial parts of *Passiflora incarnata* L. It may also contain flowers and/or fruits. It contains not less than 1.5 per cent of total flavonoids expressed as vitexin, calculated with reference to the dried drug.
Constituents
The drug contains traces of β-carboline alkaloids, e.g. harmol, harmalol and harman. Other characteristic constituents are flavonoids, mainly C-glycosides of apigenin and luteolin such as isovitexin, isoorientin and their 2”-β-D-glucosides, and maltol (possibly is an artefact) and traces of essential oil.

\[
\text{Figure 7.35-37}
\]

The structure of harmol, harmalol and harman.

Uses
The therapeutic indications include tenseness, restlessness and irritability with difficulty in falling asleep.
Dosage

*Adult single dose*: 0.5-2 g of the drug as an infusion, 3-4 times daily. The drug should not be recommended under 12 years of age.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

### 7.2 Alkaloids formed from histidine

Alkaloids biosynthesized from histidine (*Figure 7.38*) are not widely distributed in plants.

![Figure 7.38](image)

The structure of histidine.

Imidazole alkaloids can be formed from histidine. The most important pharmaceutical examples of this group are *Pilocarpus* alkaloids, pilocarpine being used as an ophthalmic cholinergic drug.

**Drug**

**Jaborandi folium**

**Plant**

*Pilocarpus jaborandi* Holmes, *P. microphyllus* Stapf, *P. pennatifolius* Lemaire (Rutaceae)

These plants are native to the neotropical region of South America, mainly in Brazil.

**Drug**

*Jaborandi folium* (Jaborandi leaf)

The drug consists of the dried leaves of *Pilocarpus* species.
Constituents

The drug contains a mixture of alkaloids (alkaloid content is 0.5-7%) having a lactone ring; its main alkaloid is pilocarpine. Further alkaloids include iso-pilocarpine, pilocarpidin, (+)-pilosine and (+)-iso-pilosine. It also contains essential oils (comprising mainly terpinene and dipentene) and tannins.

Figure 7.39-40
The structure of pilocarpine and pilosine.

Uses

The drug is used as an industrial drug. Pure pilocarpine is applied as a parasympathomimetic. It is used mostly in ophthalmology; it can cause contraction of the pupils (its action being antagonistic to that of atropine). In the case of glaucoma pilocarpine decreases the internal pressure of the eye and the pain.
Chapter 8

**Purine-containing drugs, drugs containing specific amino acid derivatives**

8.1 Alkaloids having purine skeleton

The fundamental compound of purine-alkaloids is: xanthine (2,6-dihydroxy-purine). It is formed from one molecule of glycine, one molecule of glutamine and one molecule of aspartic acid.

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glycine

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aspartic acid

Figure 8.1
The structure of glycine, glutamine, aspartic acid and xanthine.

```

```
O
\ |  |
\  |
1 2 3
4 5 6
7 8 9
H

N

xanthine (lactam-form)

```

```
O
\ |  |
\  |
1 2 3
4 5 6
7 8 9
H

N

xanthine (lactim-form)

```

Figure 8.2
The lactim and lactam form of xanthine.

The most important purine-alkaloids include caffeine (1,3,7-trimethyl-xanthine), theophylline (1,3-dimethyl-xanthine) and theobromine (3,7-dimethyl-xanthine).
Drugs

Coffeae semen

Plants

*Coffea arabica* L., *C. liberica* Buill. ex Hiern (Rubiaceae)

These plants are native to Ethiopia; and are cultivated in South-America (Brazil, Columbia), Middle-America, Angola, Liberia, South-Arabia, South-India, Ceylon (Sri-Lanka), Java and Sumatra.

Figure 8.3
Coffee shrub (*Coffea arabica* L.)

Drug

*Coffeae semen* (Coffee bean)

The drug consists of the roasted beans of the cultivated shrub of *Coffea arabica* L.
Constituents

The drug contains caffeine (0.3-2.5%), theophylline, theobromine and other additional alkaloids in traces. Other effective substances are the following: chlorogenic acid (3-5%); diterpenes, fatty oils, proteins and niacine. In roasted coffee ~300 compounds can be identified by gas chromatography (GC).

![Caffeine and Chlorogenic Acid](image)

**Figure 8.4-5**
The structure of caffeine and chlorogenic acid.

Uses

Caffeine stimulates the central nervous system, increases the pulse rate, the blood supply of the brain, the muscles, the heart, the kidney and the skin; it increases the mental capacity. Caffeine inhibits sleep, decreases the tiredness of striated muscles, increases blood pressure and the action of analgesics. It can be used as a component of analgesics, in sobering up intoxicated persons, in barbiturate-intoxications. Caffeine has diuretic effect. Its use is not recommended in the case of hypertonia, stomach ulcer and in patients with different heart diseases.

**Theae folium**

Plant

*Camellia sinensis* (L.) O. Kuntze – Tea shrub (Theaceae)

This plant is native to South-China, Cambodia, India; it is cultivated in Sri Lanka (Ceylon), Indonesia, Japan, Middle-Africa, Georgia, Pakistan, Argentina, Brazil and Peru.

Drug

*Theae (nigrae) folium* = black tea leaves; *Theae viridis folium* = green tea leaves

The drug consists of the young leaves of the cultivated shrub of *Camellia sinensis* (L.) O. Kuntze.
Constituents

The drug contains caffeine (2.5-4.5%), theophylline (0.02-0.04%) and theobromine (0.05%). Caffeine occurs in tea leaves in free state or partly connected to tannins (catechol, epicatechol, gallocatechol and epigallocatechol). Caffeine level is higher in green tea than in black tea. The drug’s volatile oil content is 0.5-1%. Further characteristic substances of the drug are flavonoids and saponins.

![Caffeine and Theophylline Structures](image)

**Figure 8.7-8**

The structure of theophylline and caffeine.

Uses

The drug acts as a stimulant; the caffeine-content of one cup of tea is ~20 mg.
Cacao semen

Plant

*Theobroma cacao* L. – Cocoa (Sterculiaceae)

The plant is native to Middle- and South-America. It is cultivated in Ghana, Kamerun, Brazil and in other countries.

Drug

*Cacao semen* (Cocoa seed)

The drug consists of the roasted seeds without seed-coat of *Theobroma cacao* L.

Constituents

The drug contains theobromine (1-2 %), caffeine (0.2-0.3 %), theophylline (in traces), tannins (5 %) and fats (50-60 %).
Uses
Cocoa powder is used for preparation of cacao (cocoa)-drink and chocolate. Cacao/cocoa-butter is also used for producing chocolate; in pharmacy it is the basic material of ointments, creams and suppositories.

Colae semen
Plant
Cola acuminata (Beauv.) Schott et Endl., C. nitida (Vent.) Schott et Endl., C. ballayi Cornu, C. verticillata (Schumach. Et Thunn.) Stapf (Sterculiaceae)
These plants are native to tropical West-Africa; they are cultivated in Brazil, the Caribic Islands and in India.

Drug
Colae semen (Cola, Ph. Eur.)
Cola consists of the whole or fragmented dried seeds, freed from the testa, of Cola nitida (Vent.) Schott et Endl. (C. vera K. Schum.) and its varieties, as well as of Cola acuminata (P. Beauv.) Schott et Endl. (Sterculia acuminata P. Beauv.). It contains not less than 1.5 per cent of caffeine, calculated with reference to the dried drug.
Constituents
The drug contains caffeine (0.6-3%), theobromine (0.1%) and tannins (2.4%). In the fresh drug caffeine is bound to tannins, but during drying and storing these compounds are decomposed, and caffeine will be present in its free state. 100 ml Coca-cola contains 0.01-0.03 g of caffeine.

![Caffeine structure](image)

**Figure 8.12**
The structure of caffeine.

Uses
The drug acts as a stimulant; it can be used as the raw material of cola drinks.

**Guarana**

Plant
*Paullinia cupana* H. B. Kunth (Sapindaceae)
The plant is native to Venezuela and Brazil.

Drug

_Guarana_ (Guarana)

The drug consists of the dry paste prepared from the seeds of the climbing shrub of _Paullinia cupana_ H. B. Kunth.

Constituents

The drug contains caffeine (2.5-8%), catechols and tannins (~ 25%).

Uses

A drink is prepared from this drug, which is a stimulant. The drug can be used in preparations against headache.

### Mate folium

Plant

_Ilex paraguariensis_ St. Hill. – Maté (Aquifoliaceae)

The plant is native to Paraguay, Uruguay, South-Brazil and North-Argentina.

Drug

_Mate folium_ (Maté leaf, DAC)

The drug consists of the dried and cured leaves of the tree of _Ilex paraguariensis_ St. Hill.

Constituents

The plant contains caffeine (0.5-1.5%), chlorogenic acid (12%), volatile oils (0.3%) and flavonoids.
Uses
In the above mentioned countries of South-America mate tea is a national tea drink.

8.2 Alkaloids having terpenoid skeleton
The skeletons of these alkaloids are of terpenoid origin, but the origin of the N-atom is often unknown.

Pseudoalkaloids
- monoterpenic alkaloids (*Valeriana* species)
- sesquiterpenic alkaloids (*Nuphar* species)
- diterpenic alkaloids (*Aconitum* species)
- steroid alkaloids (*Veratrum*- and *Solanum*-species)
**Drugs**

**Aconiti tuber**

Plant

*Aconitum napellus* L. – Aconite (Ranunculaceae)

The plant is native to the high mountains of Europe and Asia.

![Figure 8.14](image)

*Figure 8.14*

Aconite (*Aconitum napellus* L.)

Drug

*Aconiti tuber* (= radix)

The drug consists of the dried roots of the perennial plant of *Aconitum napellus* L.

Constituents

The drug contains a mixture of alkaloids (0.2-3%); its main alkaloid being aconitine, which is an easily hydrolizable diester (acetyl- and benzoylester) having a very complicated chemical structure.
Uses

The drug is only used in the case of neuralgia and chronic arthritis in homoeopathy. Aconitine is one of the strongest poisons of plant origin. Lethal dose: 2-5 mg. It causes respiratory paralysis and cardiac collapse.
Veratri rhizoma et radix

Plant

*Veratrum album* L. – Veratrum (Liliaceae)

The plant occurs in central and southern Europe and also in Hungary.

![Figure 8.16](image)

Veratrum (*Veratrum album* L.)

Drug

*Veratri rhizoma et radix* (Veratrum rhizome and root, Ph. Hg. VII.)

The drug consists of the dried rhizomes and roots of *Veratrum album* L.

Constituents

The drug contains protoveratrine A and B, as main alkaloids; it also contains several additional alkaloids and alkaloid-glycosides.
Purine-containing drugs, drugs containing specific amino acid derivatives

Figure 8.17
The structure of protoveratrine A.

Uses
The compounds mentioned above have hypotensive and vasodilator effect, similarly to cardenolides. The drug is used by the pharmaceutical industry to isolate the active alkaloids.

Dulcamarae fructus et stipes (= Solani herba)

Plant
*Solanum dulcamara* L. - Nightshade (Solanaceae)

The plant occurs in Asia, Europe and also in Hungary.
Drug

*Dulcamarae fructus et stipes* (Nightshade fruit and stalk)

The drug consists of the dried fruits together with fruit stalks of *Solanum dulcamara* L.

*Figure 8.18*

Nightshade (*Solanum dulcamara* L.)

*Figure 8.19*

*Dulcamarae fructus et stipes* (Nightshade fruit and stalk)
Constituents
The main constituents are steroid glycoalkaloids and steroid saponins.

![Solasodine structure](image)

**Figure 8.20**
The structure of solasodine.

Uses
In traditional medicine the drug is used in the case of rheuma, gout (arthritis), different dermatological diseases, e.g. eczema and psoriasis.

Today it is a basic material of the pharmaceutical industry, because pregnadienolone acetate can be prepared by partial synthesis from the aglycones, which can be formed after hydrolysis of steroid glycoalkaloids and of steroid saponins. Pregndienolone acetate is the starting material of all steroid hormones, contraceptives, corticosteroids (having anti-inflammatory action) and a number of other medicines.

### 8.3 Drugs containing specific amino acid derivatives

In plants, a variety of substances including alkaloids, different amines, betains, guanidin-derivatives, alliin-derivatives and glucosinolates can be derived from amino acids.

**Drugs**

**Allii sativi bulbus**

**Plant**

*Allium sativum* L. - Garlic (Alliaceae)

With a history of human use of over 7,000 years, garlic is native to central Asia, and has long been a staple in the Mediterranean region, as well as a frequent seasoning in Asia,
Africa, and Europe. It was known to the ancient Egyptians, and has been used for both culinary and medicinal purposes.

**Figure 8.21**
Garlic (*Allium sativum* L.)

**Drugs**

*Allii sativi bulbi pulvis* (Garlic powder, Ph. Eur.), *Allium sativum ad preparationes homoeopathicas* (Ph. Eur.)

Garlic powder is produced from the bulbs of *Allium sativum* L., cut, freeze-dried or dried at a temperature not exceeding 65°C and powdered. It contains not less than 0.45 per cent of allicin, calculated with reference to the dried drug. The mother tincture of *Allium sativum* L. is prepared by maceration of the cut drug using alcohol of a suitable concentration.
Constituents

The carefully dried, powdered material contains about 1% of alliin ([(+)-S-allyl-L-cysteine sulphoxide] as the main sulphur-containing amino acid. Other characteristic compounds include (+)-S-methyl-L-cysteine sulphoxide, S-allyl-cysteine, ubiquitous amino acids, steroids and adenosine. In the presence of the enzyme alliinase, alliin will be converted to allicin (1 mg of alliin is considered to be equivalent to 0.45 mg of allicin). Allicin is the precursor of different transformation products, including ajoenes, vinyldithiines, oligosulphides and polysulphides depending on the condition applied. Material derived from garlic by steam distillation or extraction in an oily medium containing various allicin transformation products.
Figure 8.23-30
The structures of alliin, allicin, dimethylsulphide, dimethyl-disulphide, diallyl-disulphide, allyl-methyl-sulphide, allyl-methyl-disulphide, diallyl-trisulphide.

Uses
Therapeutic indications of garlic include prophylaxis of atherosclerosis, treatment of elevated blood lipid levels insufficiently influenced by diet, treatment of high blood pressure and garlic also can be used in the case of upper respiratory tract infections.

Dosage
Prophylaxis of atherosclerosis or treatment of elevated blood lipid levels

*Adults*: The equivalent of 6-10 mg of alliin (approx. 3-5 mg of allicin) daily, typically contained in one clove of garlic or in 0.5-1.0 g of dried garlic powder.

Upper respiratory tract infections

*Adults*: 2-4 g of dried bulb or 2-4 ml of tincture (1:5, 45% ethanol), three times daily

Interaction with other medicaments
Garlic may have antiplatelet properties. It might therefore be expected to increase the risk of bleeding with conventional antiplatelet drugs and other drugs that have antiplatelet adverse effects. In two cases interactions have been observed in patients on warfarin who had used garlic products.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
Allii ursini folium

Plant

*Allium ursinum* L. – Wild Garlic/Ramson (Alliaceae)

This plant is native to Europe, North-Asia and Hungary (mostly in Transdanubia). In Hungary the plant is protected; leaves can be collected with official permission, but the bulbs should not be collected. The leaves of *A. ursinum* are easily mistaken for lily of the valley (*Convallaria majalis*), but the latter plant is toxic, and may cause fatal poisoning. A good means of positively identifying ramson is grinding the leaves between one's fingers, which should produce a garlic-like smell.

![Wild garlic](image)

**Figure 8.31**

Wild garlic (*Allium ursinum* L.)

Drug

*Allii ursini folium* (Wild garlic leaf)

The drug consists of the dried leaves of *Allium ursinum* L.
Constituents
The chemical composition of this plant is similar to that of garlic. The characteristic compounds include allicin (formed from alliin), sulphides, disulphides, ascorbic acid (vitamin C), \( \gamma \)-L-glutaminyl-peptides, flavonoids, prostaglandins (in traces) and lectins.

Uses
Wild garlic has antibacterial effect, mostly used in the treatment of intestinal infections; it has weak antihypertonic, antiarteriosclerotic action and cardioprotective action.

Dosage
see garlic

**Allii cepae bulbus**

Plant
*Allium cepa* L. - Onion (Alliaceae)
The plant is native to Iran, Egypt, Europe, Mexico and cultivated all over the world.
Drug

*Allii cepae bulbus* (Onion)

The drug is the fresh bulb of *Allium cepa* L.
Constituents
The bulb contains approx. 0.01% essential oil with alliin-derivatives (methyl and propyl alliin). Other constituents are cepaenes, quercetine (4%; mainly in the scale leaves), flavonoids (e.g. kaempferol glycosides), phloroglucine, sugars, oligosaccharides, glycosides of oleanolic acid, vitamins and selenium.

S-propyl-L-cysteine-sulfoxide  phloroglucine  protocatechu acid-methylester

Figure 8.35-37
The structure of S-propyl-L-cysteine-sulphoxide, phloroglucine and protocatechu acid-methylester.
Uses
Onion is an appetizer. The drug has antibacterial activity. It can be used particularly in the case of a runny nose, common cold and tracheitis.

Dosage
see garlic

**Bursae pastoris herba**

**Plant**
*Capsella bursa pastoris* (L.) Medic. - Shepherd’s-purse (Brassicaceae)

It is native to eastern Europe and Asia, but is naturalized and considered a common weed in many parts of the world.

![Image of Capsella bursa pastoris](image)

**Figure 8.38**
Shepherd’s-purse (*Capsella bursa pastoris* (L.) Medic.)

**Drug**
*Bursae pastoris herba* (Shepherd’s-purse)

The drug is the flowering shoot of *Capsella bursa pastoris* (L.) Medic.
Constituents

The characteristic compounds of the drug are cholin, acetylcholin, thyamine, flavonoids (luteolin, kaempferol, quercetin and their derivatives), polypeptides.

**Figure 8.40–42**

The structure of cholin, acetylcholin and thyamine (parahydroxyphenyl-ethylamine).
Uses
The drug exerts a haemostatic and diuretic action. It slightly decreases blood pressure, and can be used in the case of menorrhagia.

Dosage
5 g of the drug is used for preparing a tea infusion (150 ml). 10-15 g is the daily dose.

Galegae herba

Plant
*Galega officinalis* L. - Goat’s rue (Fabaceae)
It is native to Europe and Asia, but it can be cultivated, as well.

![Goat’s Rue](image)

**Figure 8.43**
Goat’s Rue (*Galega officinalis* L.)

Drug
*Galegae herba* (Goat’s rue)
The drug is the upper part of the flowering branches of the shrub of *Galega officinalis* L.
Constituents

The main active compounds of the drug are lysine, arginine, citrulline and derivatives of guanidine (e.g. galegin). Other relevant compounds are alkaloids (peganin), saponins, and flavonoids (kempferol, quercetin, luteolin).

Figure 8.44
Galegae herba (Goat’s rue)

arginine (α-amino-δ-guanidino-valerianic acid)  lysine (α,ε-diamino-caprionic acid)

citrulline (α-amino-δ-ureido-valerianic acid)  guanidine (imino-carbamide)  galegin

Figure 8.45-49
The structure of arginine, lysine, citrulline, guanidine and galegin.
Purine-containing drugs, drugs containing specific amino acid derivatives

Uses
The drug has been traditionally used in the treatment of mild diabetes (not severe cases, in old patients). From galegin anti-diabetic medicines were developed.

Dosage
2 g of the drug is used for preparing infusion (150 ml). 6 g is the recommended daily dose.

Phaseoli legumen

Plant
_Phaseolus vulgaris_ L. - Bean (Fabaceae)
It is cultivated all over the world.

Drug
_Phaseoli legumen_ (Bean pod)
The drug is the pod (without seeds) of the dried crop of the cultivated varieties.
Constituents

The main active compounds of the drug are amino acids, e.g. glutaminic acid, arginine, proline, asparaginic acid and methionin. Other characteristic compounds are flavonoids, e.g. kaempferol, quercetin and their glycosides (rutin), saponins, chromium salts, silicic acid ($H_2SiO_3$).

\[\text{glutaminic acid (}\alpha\text{-amino-glutaric acid)}\]
\[\text{arginine (}\alpha\text{-amino-}\delta\text{-guanidino-valerianic acid)}\]
\[\text{methionin (}\alpha\text{-amino-}\gamma\text{-methylmercapto-butyric acid)}\]

\[\text{proline (pyrrolidin-2-carboxylic acid = 2-carboxy-pyrrolidin)}\]
\[\text{asparaginic acid (amino-succinic acid)}\]

**Figure 8.51**

*Phaseoli legumen* (Bean pod)

**Figure 8.52-56**

The structure of glutaminic acid, arginine, proline, asparaginic acid and methionine.
Uses
The drug is used mainly in traditional medicine, due to its diuretic and antidiabetic activity.

Dosage
2.5-5 g of the drug is used for preparing infusion (150 ml). 5-10 g is the recommended daily dose.
Chapter 9

Drugs containing cyanogenic glycosides and glucosinolates

9.1 Cyanogenic glycosides

In 1830 the cyanogenic glycoside manihotoxin was isolated from *Manihot utilissima* (cassava). In the same year amygdalin was obtained from bitter almonds, linamarin from linseed and phaseolunatin from a bean, *Phaseolus lunatus*. Cyanogenic glycosides belong to the products of secondary plant metabolism. Over 2500 plant species involving about 110 families (e.g. Rosaceae, Fabaceae, Linaceae, Asteraceae) are estimated to be cyanogenic. The presence or absence of hydrogen cyanide (HCN) has taxonomic importance and is used as a character for separating the subfamilies of Rosaceae. The release of HCN is related to the cyanogenic glycoside content of the plants. Cyanogenic glycosides can be hydrolysed by enzymatic or spontaneous hydrolysis (this process is cyanogenesis). HCN can inactivate the cytochrome oxidase enzyme, therefore in high doses it can block the central nervous system (CNS).

The production of HCN depends on both the rate of biosynthesis of cyanogenic glycosides and on the existence (or absence) of its degrading enzymes. Amino acids are the precursors of the biosynthesis of cyanogenic glycosides. Amino acids are hydroxylated, then the N-hydroxylamino acids are converted to aldoximes, which are turned into nitriles. The latter compounds are hydroxylated to alpha-hydroxynitriles and then they are glycosilated to cyanogenic glycosides (Figure 9.1). The generation of HCN from cyanogenic glycosides (Figure 9.2) is a two-step process involving deglycosilation and the cleavage of the molecule (regulated by beta-glucosidase and alpha-hydroxynitrilase). The tissue level compartmentalisation of cyanogenic glycosides and their hydrolysing enzymes prevents large-scale hydrolysis in intact plant tissue. The actual level of cyanogenic glycosides is determined by various factors, including both developmental and ecological ones.

These compounds are composed of an alpha-hydroxynitrile type aglycone and of a sugar moiety (mostly D-glucose). The most well-known cyanogenic glycosides include linamarin, lotaustralin, prunasin and amygdalin (mandelonitrile-β-gentiobioside) (Figure 9.3). In plants they have defensive roles against pest insects.
Figure 9.1  
Biosynthetic pathway for cyanogenic glycosides.

Figure 9.2  
The generation of HCN from cyanogenic glycosides.

Figure 9.3  
The structures of some well-known cyanogenic glycosides.
Drugs

Amygdalae amarae semen

Plant

Prunus dulcis var. amara – Bitter almond (Rosaceae)

Bitter almond is native in subtropical regions of China, Asia Minor, the Mediterranean Basin, Europe and California.

Drugs

Amygdalae amarae semen, Amygdalae oleum virginale (Ph. Eur.), Amygdalae oleum raffinatum (Ph. Eur.)

Virgin almond oil is the fatty oil obtained by cold expression from the ripe seeds of Prunus dulcis (Miller) D.A. Webb var. dulcis or Prunus dulcis (Miller) D.A. Webb var. amara (D.C.) Buchheim or a mixture of both varieties. Refined almond oil is the fatty oil from the ripe seeds of the same varieties, obtained by cold expression, followed by rectification. A suitable antioxidant may be added. Almond oil is a yellow, clear, liquid, slightly soluble in alcohol, miscible with light petroleum. It solidifies at about −18°C and has a relative density of about 0.916.

Constituents

The main components of bitter almond are cyanogenic glycosides (amygdalin 1-8% and prunasin). The seeds contain essential oil, 30% protein and 35-60% fatty oils (fatty acids: palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid).

![Image of amygdalin and prunasin structures]

**Figure 9.4**

The structure of amygdalin and prunasin.

Uses

Bitter almond seeds are used for producing vegetable oil and aroma in food industry. Sweet almond oil is used in body lotions as emollient (softening effect on the skin).

Bitter almond oil can be used as a solvent for certain kinds of drugs, e.g. preparation of oily injections in pharmaceutical industry.

**Bitter almond seeds may be toxic because of their cyanogenic glycoside content. The consumption of 10 or 60 seeds may cause fatal poisoning in the case of children or adults, respectively.**
Lini semen

Plant

*Linum usitatissimum* L. - Flax (Linaceae)

Flax has long been cultivated for its fibres and seeds in a number of countries (South America, India, USA, Canada, Europe).

![Flax](image)

**Figure 9.5**

Flax (*Linum usitatissimum* L.)

Drugs

*Lini semen* (Linseed, Ph. Eur.), *Lini oleum virginale* (Linseed oil, virgin, Ph. Eur.)

Linseed consists of the dried ripe seeds of *Linum usitatissimum* L. Virgin oil is obtained by cold expression from ripe seeds of *Linum usitatissimum* L. A suitable antioxidant may be added. The oil is a clear, yellow or brownish-yellow liquid, on exposure to air turning dark and gradually thickening. When cooled, it becomes a soft mass at about −20 °C. It is very slightly soluble in alcohol, miscible with light petroleum. Relative density: about 0.931.
Constituents

The seeds contain 0.1-1.5% of cyanogenic glycosides such as linustatin and neolinustatin. Other relevant components include 3-9% of mucilage polysaccharides composed mainly of galacturonic acid, xylose, galactose and rhamnose units. The seeds contain 30-45% fatty oil mainly consisting of triglycerides of linolenic (40-60%), linoleic and oleic acids. Other constituents include 25% of protein, sterols, lignans (secoisolariciresinol) and a serine proteinase inhibitor.

Uses

Linseed has a mild laxative effect. Internally the seeds can be used in the management of constipation, irritable bowel syndrome (IBS), diverticular disease, and in the case of symptomatic short-term treatment of gastritis and enteritis.

Dosage

**Internal use**

*Adults and children over 12 years of age*

As a laxative: 5 g of whole, finely-cracked or freshly crushed seeds, soaked in water and taken with a glassful of liquid three times daily. The effect starts 18-24 hours later.
As a demulcent for gastritis and/or enteritis: for a mucilaginous preparation soak 5-10 g of whole linseed in 150 ml water and strain after 20-30 minutes.

**External use**

30-50 g of crushed or powdered seeds as a warm poultice or warm compress (for abscesses, furuncles, and in the case of eczema and psoriasis)

*Children from 6 to 12 years of age:* half the adult dose

*Children under 6 years of age:* to be treated under medical supervision only

Because of the gradual mode of action of bulk-forming laxatives, treatment should be continued for a minimum of 2-3 days to ensure optimum benefit. If abdominal pain occurs, or if there is no response after 48 hours, use of linseed should be discontinued and medical advice must be sought.

Linseed (whole, finely-cracked or freshly crushed) should be soaked and taken with at least 10-fold amounts of liquid, otherwise intestinal obstruction may occur.

**Contra-indications**

Atonic and obstructive ileus, subileus or conditions likely to lead to intestinal obstruction. Acute abdominal pain of any origin (e.g. appendicitis)

**Interaction with other medicaments**

The absorption of other medications taken at the same time may be delayed. Patients with diabetes should be aware of a potential delay in glucose absorption.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Overdose**

In spite of its cyanogenic glycoside content, single doses of up to 150-300 g of powdered linseed are not toxic.

### 9.2 Glucosinolates

Glucosinolates are a class of organic compounds that contain sulphur and nitrogen and are derived from glucose and an amino acid (Figure 9.11). They occur as secondary metabolites in almost all plants of the order Brassicales including the families Brassicaceae and Cappar(id)aceae; but also in some other orders, for example, in Violales and Euphorbiales. About 120 different glucosinolates are known to occur naturally in plants.

From this group of compounds sinigrin and sinalbin were isolated in crystalline form from black and white mustards. These and similar glycosides have since been isolated from many plants, particularly those used as condiments (e.g. horseradish) or in folk medicine. They are volatile compounds and have a characteristic smell and hot taste.

Glucosinolates are water-soluble anions and belong to the glucosides. Every glucosinolate contains a central carbon atom, which is bound via a sulphur atom to the thioglucoce group (making a sulphated aldoxime) and via a nitrogen atom to a sulphate...
Drugs containing cyanogenic glycosides and glucosinolates

In addition, the central carbon atom is bound to a side group; different glucosinolates have different side groups, and it is the variation in the side chain that is responsible for the variation in the biological activities of these plant compounds.

They are synthesized from certain amino acids: the so-called aliphatic glucosinolates are derived mainly from methionine, but also from alanine, leucine, isoleucine or valine. Aromatic glucosinolates include indolic glucosinolates, such as glucobrassicin, derived from tryptophan, and others derived from phenylalanine, its chain-elongated homologue homophenylalanine, and sinalbin derived from tyrosine.

Plants contain the enzyme myrosinase, which, in the presence of water, cleaves off the glucose group from a glucosinolate. The remaining molecule then quickly converts to an isothiocyanate, a nitrile, or a thiocyanate; these are the active substances that serve as defence for the plant. Glucosinolates are also called mustard oil glycosides. The standard product of the reaction is isothiocyanate (mustard oil); the other two products mainly occur in the presence of specialised plant proteins that alter the outcome of the reaction (Figure 9.12). To prevent damage to the plant itself, the myrosinase enzyme and glucosinolates are stored in separate compartments of the cell and occur together only in case of physical injury.

Mustard oil has a strong antibacterial activity against different microorganisms, and has rubefacient effect. Internally the drugs containing mustard oil can be used for treating respiratory diseases, e.g. hay fever. Externally this compound is used in the form of plasters to treat rheumatic complaints. The chemopreventive effects of the glucosinolates present in cruciferous vegetables (e.g. broccoli, cabbage) have already been reported. Glucosinolates are well known for their toxic effects in both humans and animals at high doses.
**Pharmacognosy 2**

**Drugs**

**Sinapis nigrae semen**

**Plant**

*Brassica nigra* (L.) Koch – Black mustard (Brassicaceae)

It is cultivated in Hungary, and native in Europe, North Africa, Caucasus and the Indian subcontinent.

**Drug**

*Sinapis nigrae semen* (Black mustard seed)

The drug consists of the dried ripe seeds of *Brassica nigra* (L.) Koch.

![Sinapis nigrae semen](image)

**Figure 9.13**

*Sinapis nigrae semen* (Black mustard seed)

** Constituents**

The seeds contain 1-5% of sinigrin (glucoside of allyl isothiocyanate), sinapin (pseudoalkaloid), 30% of fatty oil, small amounts of mucilage.
Drugs containing cyanogenic glycosides and glucosinolates

![Chemical structures of sinigrin, sinapin, and allyl isothiocyanate]

**Figure 9.14-16**
The structure of sinigrin, sinapin and allyl isothiocyanate.

**Uses**
Mustard has been traditionally used, particularly in the form of plasters, as a rubefacient, in the case of rheumatic pains. Allyl isothiocyanate (volatile mustard oil) can be used for preparation of liniments or ointments to treat rheuma. In an aqueous medium sinigrin will be converted to allyl isothiocyanate, which has strong antibacterial activity against e.g. *Staphylococcus aureus* and *Escherichia coli* in high dilution.

Mustard is a spice, and in this form can be used for treating digestive problems.

In veterinary medicine, mustard is applied as a stomachic and diuretic medicinal plant.

**Pregnancy and lactation**
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
Chapter 10

Drugs containing phenylpropanoid and phloroglucin derivatives

10.1 Phenylpropanoid derivatives

Phenolic compounds probably constitute the largest group of plant secondary metabolites. They are widespread in nature, and can be found in most classes of natural compounds having aromatic moieties. They range from simple structures with one aromatic ring to highly complex polymeric substances, for example tannins and lignins. Phenols are important compounds of some medicinal plants, which are used as coloring agents, antioxidants, flavourings and aromatizers. Phenylpropanoids are mostly derived from $p$-coumaric acid ($p$-hydroxycinnamic acid). These compounds are located in various essential oils. They have alcoholic, aldehyde and carboxylic acid groups, e.g. eugenol (= phenolic phenylpropane). Medicinal plants containing phenylpropanoid derivatives are widely used in phytotherapy. It should be noted that some compounds (e.g. trans-isoasarone, trans-isoeugenol methyl ether and trans-isoelemicin in the rhizome of Asarum europaeum L.) should not be used for medicinal purposes because of their toxic effect.
Figure 10.1
Biosynthesis of some cinnamic acid derivatives.

Figure 10.2
The structure of trans-isoasarone, trans-isoeugenol methyl ether and trans-isoelemicin.

Drugs

Cinnamomi cortex
Plant
Cinnamomum zeylanicum Nees. – Cinnamon (Lauraceae)
The plant is native to India, Ceylon and cultivated (Java, Sumatra, South America).

**Figure 10.3**
Cinnamon (*Cinnamomum zeylanicum* Nees.)

**Drug**
*Cinnamomi cortex* (Cinnamon bark, Ph. Eur.). **Other drugs:** *Cinnamomi zeylanici corticis aetheroleum* (Cinnamon bark oil, Ph. Eur.), *Cinnamomi corticis tinctura* (Cinnamon bark tincture, Ph. Eur.), *Cinnamomi zeylanici folii aetheroleum* (Cinnamon leaf oil, Ph. Eur.)

Cinnamon consists of the dried bark, freed from the outer cork and the underlying parenchyma, of the shoots grown on cut stock of *Cinnamomum zeylanicum* Nees. It contains not less than 12 ml/kg of essential oil. Cinnamon has a characteristic, aromatic odour.

**Figure 10.4**
*Cinnamomi cortex* (Cinnamon bark)
Ceylon cinnamon bark oil is obtained by steam distillation of the bark of the shoots of *Cinnamomum zeylanicum* Nees. A clear, mobile, light yellow liquid becoming reddish over time, with a characteristic odour reminiscent of cinnamaldehyde.

The tincture is produced from 1 part of the drug and 5 parts of ethanol (70 per cent *V/V*) by an appropriate procedure. *Appearance*: clear, brownish-red liquid, with a characteristic odour.

Cinnamon leaf oil is obtained by steam distillation of the leaves of *Cinnamomum zeylanicum* Nees. It is a clear, mobile, reddish-brown to dark brown liquid, with a characteristic odour reminiscent of eugenol.

**Constituents**

Cinnamon contains up to 4% of essential oil consisting principally of cinnamaldehyde (60-75%) together with cinnamyl acetate and eugenol. Other compounds of the oil are β-caryophyllene, linalool and 1,8-cineole. The essential oil of the leaf contains 70% of eugenol. Other constituents include pentacyclic diterpenes (the pesticide cinnzeylanol), oligomer procyanidins and phenolcarboxylic acids (caffeic acid, ferulic acid, sinapinic acid).

![Figure 10.5-7](image)
The structure of cinnamaldehyde, eugenol and *trans*-cinnamic acid.

**Uses**

The drug has antimicrobial effect. Therapeutic indications include dyspeptic complaints such as gastrointestinal spasm, bloating and flatulence; loss of appetite and diarrhoea. Cinnamon oil can be used by inhalation in case of respiratory mycoses. Externally the drug and its oil are used in foot bath (because of antiseptic property). *In vitro* and a few *in vivo* studies demonstrated the antidiabetic activity of cinnamon. The leaf essential oil is used in cosmetic industry (in soaps, creams, perfumes).

**Dosage**

*Adult and elderly daily dose*: 1.5-4 g of dried bark or as an infusion; 0.5-1.0 ml of fluid extract (1:1, 70% ethanol); 2-4 ml of tincture.

*Children*: for infantile diarrhoea, proportion of adult dose according to age and body weight in alcohol-free preparations.

*Overdose*: Cinnamon bark oil and cinnamaldehyde in doses over 0.2 g/day (equivalent to 15-20 g of crude drug) have irritant properties.

**Contra-indications**

Patients with known allergy to cinnamon, cinnamon bark oil or cinnamaldehyde, and in case of gastric and duodenal ulcers.
Pregnancy and lactation

Only limited data available. In accordance with general medical practice, cinnamon and its preparations should not be used internally during pregnancy and lactation without medical advice.

**Caryophylli flos**

**Plant**

*Syzygium aromaticum* (L.) Merill et Perry – Clove (Myrtaceae)

The plant is native to Indonesia, Madagascar, Mauritius and Maluku Islands.

**Drug**

*Caryophylli flos* (Clove, Ph. Eur.). **Other Drug** Caryophylli floris aetheroleum (Clove oil, Ph. Eur.)

Clove consists of the whole flower buds of *Syzygium aromaticum* (L.) Merill et L. M. Perry (*Eugenia caryophyllus* (C. Spreng.) Bull. et Harr.) dried until they become reddish-brown. It contains not less than 150 ml/kg of essential oil. Clove has a characteristic, aromatic odour.

![Caryophylli flos](image)

**Figure 10.8**

*Caryophylli flos* (Clove)

Clove oil is obtained by steam distillation from the dried flower buds of *Syzygium aromaticum* (L.) Merill et L. M. Perry (*Eugenia caryophyllus* C. Spreng. Bull. et Harr.). A clear, yellow liquid which becomes brown when exposed to air, miscible with methylene chloride, toluene and fatty oils.
Constituents

Clove contains up to 20% of essential oil consisting principally of eugenol (80-95%) together with approx. 3% acetyl-eugenol. The oil also contains sesquiterpenes (α- and β-caryophyllene) and small quantities of esters, ketones and alcohols. Other constituents include flavonoids (quercetin and kaempferol glycosides), tannins (e.g. gallotannin), syringic acid and triterpenes.

![Figure 10.9-10](image_url)
The structure of eugenol and acetyl-eugenol.

Uses

Clove has antibacterial, antifungal, antiviral, local anesthetic and spasmylytic activities. In dentistry it is used as a disinfectant and anaesthetization of the canal in teeth. The drug is applied in mouthwashes, in case of inflammation of the mouth and the throat. Internally clove can be used in case of digestive problems. It is a taste corrigent. The drug is used as a stimulant aromatic, as a spice and for the preparation of the volatile oil.

Clove stem oil is produced in Tanzania and in Madagascar; it is used mainly in the flavouring and perfumery industries. Clove leaf oil is distilled in Madagascar, Tanzania and in Indonesia, and is used for the isolation of eugenol.

Dosage

**Adult and elderly daily dose:** 3-5 g of dried drug or as an infusion.

_For the symptomatic treatment of minor inflammations in the mouth or the throat:_

Mouthwashes corresponding to 1-5% essential oil. Apply several times daily.

The use in children and adolescents under 18 years of age is not recommended. Not to be used for more than 1 week.

_For the temporary relief of toothache due to a dental cavity:_

Undiluted essential oil or solutions in a strength up to 50% or gels in a strength of 20%. Repeat administration after 20 minutes, then every 2 hours if necessary. Not to be used for more than 1 week. Application: A small piece of cotton wool should be soaked in the undiluted oil or in a diluted solution; semi-solid dosage forms should be placed on a cotton bud. Cotton bud or cotton wool should be accurately directed to the decayed part of the tooth.

The use in children and adolescents under 18 years of age is not recommended.

_Overdose:_ No case of overdose from oromucosal or dental use has been reported. However, after oral administration of 5-10 ml of clove oil in children below 2 years of age, life threatening conditions were observed. Overdose may lead to CNS depression, urinary abnormalities, anion gap acidosis, deterioration of liver function, coma, seizure...
and low blood glucose levels. Treatment should be supportive and symptomatic; there have been reports in the literature that N-acetylcysteine has been successfully used as an antidote.

Contra-indications

Patients with known allergy to clove, clove oil or cinnamaldehyde should not use these drugs.

Pregnancy and lactation

No data available. In accordance with general medical practice, clove and its preparations should not be used internally during pregnancy and lactation without medical advice.

**Zingiberis rhizoma**

Plant

*Zingiber officinale* Roscoe – Ginger (Zingiberaceae)

The plant is grown in many parts of the world, including Jamaica, China, India and Africa. Jamaica ginger, once the traditional pharmaceutical ginger, has been largely replaced by other sources. It was introduced into Europe by the Phoenician traders.

![Ginger](image)

*Figure 10.11*

Ginger (*Zingiber officinale* Roscoe)

Drug

*Zingiberis rhizoma* (Ginger, Ph. Eur.)

Ginger consists of the dried, whole or cut rhizome of *Zingiber officinale* Roscoe, with the cork removed, either completely or from the wide flat surfaces only. Whole or cut, it contains not less than 15 ml/kg of essential oil, calculated with reference to the
anhydrous drug. Ginger has a characteristic aromatic odour and a spicy and burning taste.

**Figure 10.12**
*Zingiberis rhizoma* (Ginger)

**Constituents**

Essential oil (0.25-3%) contains monoterpenes (mainly geranial), and sesquiterpenes (mainly β-sesquiphellandrene, *ar*-curcumene, α-zingiberene). Pungent principles (4-7.5% w/w) consist of the gingerols (e.g. 6-gingerol, zingerone), shogaols (e.g. 6-shogaol) and related phenolic ketone derivatives. Other constituents include diarylheptenones, diterpenes, 6-gingesulphonic acid, monoacyldigalactosyl glycerols, coumaric acid, ferulic acid, fatty acids and sterols. Gingerols: they will be converted into dehydro derivatives (shogaols) during storage. Their ratio (gingerols:shogaols) determines the freshness of the drug.
Drugs containing phenylpropanoid and phloroglucin derivatives

The structure of 6-gingerol, zingerone and 6-shogaol.

Figure 10.13-15
The structure of 6-gingerol, zingerone and 6-shogaol.

Uses
Therapeutic indications include the prophylaxis of nausea and vomiting in motion sickness, the management of digestive disorders and as a postoperative antiemetic for minor day-case surgical procedures. Ginger is used in food, liqueur and perfume industries.

Dosage
*Adult and children over 6 years*: 0.5-2 g of the powdered drug daily in single or divided doses; for the prophylaxis of motion sickness, 30 minutes before travel.

Undesirable effect
Heartburn has been reported in a few cases.

Contra-indications
The drug has anticholinergic effect. Ginger and its products must not be administered with anticoagulants at the same time. Ginger may enhance absorption of sulphaguanidine.

Pregnancy and lactation
No data available. In accordance with general medical practice, ginger and its preparations should not be used internally during pregnancy and lactation without medical advice.

Curcumae xanthorrhizae rhizoma

Plant
*Curcuma xanthorrhiza* Roxb. – Turmeric, javanese (Zingiberaceae)
The plant is cultivated in Indonesia.

Drug
*Curcumae xanthorrhizae rhizoma* (Turmeric, javanese; Ph. Eur.)
Javanese turmeric consists of the dried rhizome, cut in slices, of *Curcuma xanthorrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich). It contains not less than 50 ml/kg of essential oil and not less than 1.0% of dicinnamoyl methane derivatives expressed as curcumin, both calculated with reference to the anhydrous drug. Javanese turmeric has an aromatic odour.

![Figure 10.16](image)

*Curcumae xanthorrhizae rhizoma* (Turmeric, javanese)

**Constituents**

The major characteristic constituents are curcuminoids (1-2%) – a mixture of dicinnamoylmethane derivatives such as curcumin (diferuloylmethane), monodemethoxycurcumin (*p*-coumaroylferuloyl-methane) and other phenolic and non-phenolic diarylheptanoids, and essential oil (3-12%) containing bisabolane sesquiterpenes such as *ar*-curcumene, xanthorrhizol, β-curcumene and germacrone. The presence of xanthorrhizol and absence of bisdemethoxycurcumin (*di*-p-coumaroylmethane) are species-specific, distinguishing Javanese turmeric from turmeric (*Curcuma longa = C. domestica*).
Drugs containing phenylpropanoid and phloroglucin derivatives

Figure 10.17-18
The structure of curcumin (diferuloylmethane) and monodemethoxycurcumin (p-coumaroylferuloyl-methane).

Uses
Therapeutic indications include the symptomatic treatment of mild digestive disturbances and minor biliary dysfunction.

Dosage
Adult and elderly average daily dose: 2 g of the drug or corresponding extracts.
Patients with cholelithiasis should take Javanese turmeric only after consulting a physician.

Contra-indications
The drug is not recommended in case of biliary obstruction.

Pregnancy and lactation
No human data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

Anisi fructus
Plant
Pimpinella anisum L. – Anise (Apiaceae)
This annual plant is widely cultivated in Europe (Spain, Germany, Italy, Hungary, Bulgaria), Egypt and in America (Chile, Mexico). Spain and Egypt are the principal producers of the anise essential oil.

Drug
Anisi fructus (Aniseed, Ph. Eur.). Other Drug Anisi aetheroleum (Anise oil, Ph. Eur.).
Aniseed consists of the whole dry cremocarp of *Pimpinella anisum* L. It contains not less than 20 ml/kg of essential oil. Aniseed has an odour reminiscent of anethole. The fruit is a cremocarp and generally entire; a small fragment of the thin, rigid, slightly curved pedicel is frequently attached.

Essential oil is obtained by steam distillation from the dry ripe fruits of *Pimpinella anisum* L. It is a clear, colourless or pale yellow liquid.

**Figure 10.19**  
*Anisi fructus* (Aniseed)

### Constituents

The active constituent of the drug is the essential oil (2-6%). The essential oil contains predominantly *trans*-anethole (80-95%) with smaller amounts of estragole (methyl-cavicul), anisaldehyde, *cis*-anethole; sesquiterpene and monoterpene hydrocarbons are also present. Other constituents include coumarins (umbelliferone, scopoletin), furocoumarins, flavonoids, phenolic acids and fixed oil.

**Figure 10.20-22**  
The structure of *trans*-anethole, estragole and anisaldehyde.

### Uses

Therapeutic indications include dyspeptic complaints such as mild spasmodic gastrointestinal complaints, bloating, flatulence and catarrh of the upper respiratory
Drugs containing phenylpropanoid and phloroglucin derivatives

tract. The drug has expectorant, carminative, stomachic, spasmolytic (in case of urinary and gastrointestinal tract) and antibacterial activities. Aniseed is used as a component of herbal teas for stimulation of breast milk (because of lactiferous effect). Aniseed is a spice, it is also used in the food and liqueur industries.

Dosage

*Adult average daily dose:* 3 g of crushed fruits as an infusion or similar preparations.

*Children average daily dose:* up to 1 year of age, 0.5 g of crushed fruits as an infusion; 1-4 years of age, 1 g; 4-10 years of age, 2 g; 10-16 years of age, the adult dose (3 g).

The maximum daily dose of the essential oil is 0.3 g (greater doses are hepatotoxic and toxic for children).

Undesirable effect

Rare cases of contact dermatitis caused by anethole-containing toothpastes and cosmetic creams have been reported.

Contra-indications

Persons with known sensitivity to anethole should avoid aniseed.

Pregnancy and lactation

Aniseed may be used during pregnancy and lactation at the recommended dosage, as aqueous infusion only. It should be highlighted that preparations containing essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

**Anisi stellati fructus**

Plant

*Illicium verum* Hook. – Star anise (Illiciaceae)

Star anise is an evergreen tree, indigenous to the south-west provinces of China. The fruits are collected and the oil is distilled locally in China and Vietnam.

Drug

*Anisi stellati fructus* (Star anise, Ph. Eur.). **Other Drug** *Anisi stellati aetheroleum* (Star anise oil, Ph. Eur.).

The drug consists of the dried composite fruit (aggregate of follicles) of *Illicium verum* Hook. It contains minimum 70 ml/kg of essential oil (anhydrous drug). The fruit carpels are brown and emit the odour of anethole.

Essential oil is obtained by steam distillation from the dry ripe fruits of *Illicium verum* Hook. It is a clear, colourless or pale yellow liquid.
Constituents
The active constituent of the drug is the essential oil (2-8%), with similar chemical composition as we have seen in aniseed (*Pimpinella anisum* L.). See above.

It should be noted that another *Illicium* species, *Illicium anisatum* (Japanese star anise), can not substitute Chinese star anise. Japanese star anise is a poisonous species (with bitter taste) containing anisatin, a sesquiterpene lactone!

Uses
Therapeutic indications and other uses are similar to those of aniseed (*Pimpinella anisum* L.). See above.

Dosage
It is similar to that of aniseed (*Pimpinella anisum* L.). See above.

Undesirable effect
It is similar to aniseed (*Pimpinella anisum* L.). See above.

Contra-indications
It is similar to aniseed (*Pimpinella anisum* L.). See above.

Pregnancy and lactation
It is similar to aniseed (*Pimpinella anisum* L.). See above.
Drugs containing phenylpropanoid and phloroglucin derivatives

**Foeniculi dulcis fructus and Foeniculi amari fructus**

**Plants**

*Foeniculum vulgare* Miller subsp. *vulgare* var. *dulce* – Sweet fennel (Apiaceae),
*Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare* – Bitter fennel (Apiaceae)

Sweet fennel is mainly cultivated in Europe. Bitter fennel is also cultivated in many parts of Europe and substantial amounts are imported from India, China and Egypt.

![Sweet fennel and Bitter fennel](image)

**Figure 10.24**

Sweet fennel (*Foeniculum vulgare* Miller subsp. *vulgare* var. *dulce*)

**Drugs**

*Foeniculi dulcis fructus* (Sweet fennel, Ph. Eur.), *Foeniculi amari fructus* (Bitter fennel, Ph. Eur.). **Other Drug** *Foeniculi amari fructus aetheroleum* (Bitter fennel fruit oil, Ph. Eur.).

Sweet fennel consists of the dry cremocarps and mericarps of *Foeniculum vulgare* Miller sp. *vulgare* var. *dulce* (Miller) Thellung. It contains not less than 20 ml/kg of essential oil, calculated with reference to the anhydrous drug. The oil contains not less than 80.0 per cent of anethole. Sweet fennel is pale green or pale yellowish-brown.

Bitter fennel consists of the dry cremocarps and mericarps of *Foeniculum vulgare* Miller sp. *vulgare* var. *vulgare*. It contains not less than 40 ml/kg of essential oil, calculated with reference to the anhydrous drug. The oil contains not less than 60.0% of anethole and not less than 15.0% of fenchone. Bitter fennel is greenish-brown, brown or green.

Bitter fennel fruit oil is obtained by steam distillation from the ripe fruits of *Foeniculum vulgare* Miller, ssp. *vulgare* var. *vulgare*. It contains fenchone (12.0% to 25.0%) and *trans*-anethole (55.0% to 75.0%). Appearance: clear, colourless or pale yellow liquid. It has a characteristic odour.
Constituents

The active constituent of the drugs is the essential oil. The essential oil of sweet fennel contains predominantly \textit{trans}-anethole with not more than 10\% of estragole and not more than 7.5\% of fenchone. Other components of the oil are \(\alpha\)- and \(\beta\)-pinene, limonene and \(p\)-cymene. Bitter fennel fruit oil contains predominantly \textit{trans}-anethole and fenchone with not more than 5\% of estragole. The taste of the essential oil depends on the ratio of \textit{trans}-anethole (sweet compound) and fenchone (bitter compound).

It also contains pinenes, \(p\)-cymene, sabinene, \(\alpha\)-phellandrene and \(\gamma\)-terpinene. Other constituents of the fruits include water-soluble glycosides of monoterpenoid, alkyl and aromatic compounds, coumarins (scopoletin, bergapten) and flavonoids.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fenchone.png}
\caption{The structure of \textit{trans}-anethole, estragole and fenchone.}
\end{figure}
Drugs containing phenylpropanoid and phloroglucin derivatives

Uses
Therapeutic indications include dyspeptic complaints such as mild, spasmodic gastrointestinal ailments, bloating and flatulence and catarrh of the upper respiratory tract. The drugs have antibacterial, antifungal, expectorant (in case of upper respiratory catarrh), spasmolytic (especially in biliary and renal colic) and galactogogue activities. Due to children’s preference of sweet taste to bitter taste, sweet fennel fruit is predominantly used in paediatrics in case of gastrointestinal problems because of its carminative and stomachic effects, and in case of bronchitis as an expectorant and cough suppressant. It should be noted that the essential oil should not be recommended for children, because it may trigger epileptic seizures.

Dosage
*Adult daily dose:* 5-7 g of crushed fruits as an infusion or similar preparations.

*Children average daily dose: up to 1 year of age,* 1-2 g of crushed fruits as an infusion; *1-4 years of age,* 1.5-3 g; *4-10 years of age,* 3-5 g; *10-16 years of age,* the adult dose (5-7 g).

Undesirable effect
Rare cases of contact dermatitis caused by anethole-containing preparations have been reported.

Contra-indications
Persons with known sensitivity to anethole should avoid the use of fennel.

Pregnancy and lactation
Fennel may be used during pregnancy and lactation at the recommended dosage, as aqueous infusion only. It should be highlighted that preparations containing essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

Calami rhizoma
Plant
*Acorus calamus* L. – Calamus or Sweet flag (Araceae)
This perennial plant is common on the banks of streams. Originating in Asia, it is now widely distributed in Asia, Europe and North America. In Hungary, it can only be collected with the permission of the Inspectorate of Environment and Nature Protection, e.g. along the Drava river. The plant has different varieties according to ploidy level; *Acorus calamus* var. *calamus* (European, 3n), *A. calamus* var. *americanus* (2n) and *A. calamus* var. *angustata* (East Asian, 4n).
Figure 10.29  
Calamus (*Acorus calamus* L.)

Drug  
*Calami rhizoma* (Calamus, Ph. Helv.). **Other Drug** *Calami aetheroleum* (Calamus oil).  
The drug consists of the dried, cut rhizome of *Acorus calamus* L. 

Figure 10.30  
*Calami rhizoma* (Calamus)
Constituents

Calamus contains 1.7-9.3% of essential oil containing diketo-spirane mono- and sesquiterpenes (acorone, acorenone), which are responsible for the bitter taste. Another relevant component of the oil is asarone (phenylpropane derivative). The composition of the oil from 2n, 3n and 4n varieties differs and the $\beta$-asarone content increases with ploidy (in var. americanus: $\beta$-asarone (0-0.5%), var. calamus: $\beta$-asarone (3-13%), var. angustata: $\beta$-asarone (80%). The phenylpropane derivative cis-isoasarone (= $\beta$-asarone) is potentially carcinogenic. Therefore some researchers recommend the selection of races for pharmaceutical use. Other cinnamic acid derivatives of the drug are methyl eugenol and methyl isoeugenol. Other constituents include mucilages, starch and lignan derivatives.

![Chemical structures of asarone, $\beta$-asarone, methyl eugenol, methyl isoeugenol and acorone.]

**Figure 10.31-35**

The structure of asarone, $\beta$-asarone, methyl eugenol, methyl isoeugenol and acorone.

Uses

Therapeutic indications include digestive disorders and loss of appetite. The drug and its product have stomachic, appetizer and carminative effects. Calamus is also used in liqueur industry. The prolonged used of calamus is not recommended (mostly 3n and 4n varieties)!

Today the drug is mainly used as a source of calamus oil, which is applied in perfumery industry.

Dosage

*Adult daily dose:* 1 g of crushed drug as an infusion (200 ml).

For children the drug and its products are not recommended.
Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Petroselini fructus**

Plant

*Petroselinum crispum* (Mill.) Nym. var. *crispum* – Parsley (Apiaceae)

Parsley is a cultivated plant all over the world.

![Figure 10.36](image)

**Figure 10.36**

Parsley (*Petroselinum crispum* (Mill.) Nym. var. *crispum*)

Drug

*Petroselini fructus* (Parsley fruit). **Other drugs:** *Petroselini radix* (Parsley root), *Petroselini aetheroleum* (Parsley oil).

The drug consists of the dried fruits of *Petroselinum crispum* (Mill.) Nym. var. *crispum*. 
Drugs containing phenylpropanoid and phloroglucin derivatives

Figure 10.37
_Petroselini fructus_ (Parsley fruit)

Constituents

Parsley fruits contain 2-6% of essential oil containing phenylpropane derivatives (apiole, myristicin, elemicin, allyl tetramethoxy benzene) and monoterpenes (α- and β-pinene, myrcene). Other constituents include furocoumarins (bergapten).

![apiol, myristicin, elemicin](image)

Figure 10.38-40
The structure of apiol, myristicin and elemicin.

Uses

The drug has spasmolytic and strong diuretic effects. The essential oil is abortive in higher doses! Patients with nephritis should not use the drug.

Dosage

*Adult daily dose:* 1 g of crushed drug as an infusion (200 ml).

For children the drug and its products are not recommended.
Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice. Because of the abortive property of the essential oil it should not be used during pregnancy.

**Balsamum peruvianum**

**Plant**

Myroxylon balsamum (L.) Harms. var. pereirae (Royle) Harms. – Peru balsam (Fabaceae)

The plant is cultivated in Sri Lanka and Sumatra. Peru balsam is produced in Central America (San Salvador, Honduras and Guatemala).

**Drug**

Balsamum peruvianum (Peru balsam, Ph. Eur.)

Peru balsam is the balsam obtained from the scorched and wounded trunk of Myroxylon balsamum (L.) Harms var. pereirae (Royle) Harms. It contains not less than 45.0% m/m and not more than 70.0% m/m of esters, mainly benzyl benzoate and benzyl cinnamate. A dark brown, viscous liquid which is transparent and yellowish-brown when viewed in a thin layer; the liquid is not sticky, it is non-drying and does not form threads; practically insoluble in water, freely soluble in ethanol, not miscible with fatty oils, except for castor oil.
Constituents
The balsam contains vanillin, benzoic acid benzyl ester, cinnamic acid benzyl ester, methyl benzoate and methyl cinnamate.
Uses
Peru balsam is used as an antiseptic dressing for wounds, in case of freezing and ulcus cruris. Allergic skin reactions may occur.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Filipendulae ulmariae herba
Plant
*Filipendula ulmaria* (L.) Maxim. – Meadowsweet (Rosaceae)
The plant is native to Europe, and prefers wet habitats (e.g. meadows and slashes).
Drugs containing phenylpropanoid and phloroglucin derivatives

Figure 10.47
Meadowsweet [*Filipendula ulmaria* (L.) Maxim.]

Drugs

*Filipendulae ulmariae herba* (Meadowsweet, Ph. Eur.)

The drug consists of the whole or cut, dried flowering tops of *Filipendula ulmaria* (L.) Maxim. (= *Spiraea ulmaria* L.). It contains minimum 1 ml/kg of steam-volatile substances, calculated with reference to the dried drug. It has aromatic odour of methyl salicylate, after crushing.
**Constituents**

The drug contains glycosides of salicylaldehyde, of methyl salicylate (spiraein) and of salicyl alcohol. Steam distillation of the dried flowers yields a small amount (0.2%) of essential oil (arising from the phenolic glycosides during drying and storage), of which about 75% is salicylaldehyde. Other constituents are flavonoids (up to 6%) such as spiraeoside (quercetin-4’-glucoside), hyperoside and kaempferol-4’-glucoside. Ellagitannins (10-15%) are derived from galloyl-4,6-hexahydroxydiphenoyl-β-D-glucose units, the major one being the dimeric compound rugosin D.

**Figure 10.49-54**

The structure of salicylaldehyde, salicyl alcohol, salicin, salicylic acid methyl ester and spiraeoside.
Uses

The drug is used in the supportive therapy for common cold. Meadowsweet is also used to enhance the renal elimination of water, but this indication is not supported by scientific evidence.

Dosage

The daily dose of the drug as a tea infusion:

Adults: 2-6 g, children 1-4 years of age: 1-2 g, children 4-10 years of age: 2-3 g, children 10-16 years of age: adult dose.


Contra-indications

The drug should not be used in cases of hypersensitivity to salicylates.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Salicis cortex

Plant

Salix alba L. or other Salix species – Willow (Salicaceae)

The plant is native to Europe, with a preference of wet habitats.

Figure 10.55
Willow (Salix sp.)

Drug

Salicis cortex (Willow bark, Ph. Eur.)
Willow bark consists of the whole or fragmented dried bark of young branches or whole dried pieces of current year twigs of various species of genus *Salix* including *S. purpurea* L., *S. daphnoides* Vill. and *S. fragilis* L. The drug contains not less than 1.5% of total salicylic derivatives, expressed as salicin, calculated with reference to the dried drug. Willow bark is markedly bitter.

**Figure 10.56**
*Salicis cortex* (Willow bark)

**Constituents**

The characteristic constituents are derivatives of salicin, mainly salicortin, 2’-O-acetylsalicortin and/or tremulacin. *Salix purpurea* contains 4-8% of total salicin. It also contains the chalcone isosalipurpuroside, the flavanone eriodictyol-7-glucoside and tannins.
Drugs containing phenylpropanoid and phloroglucin derivatives

Figure 10.57-61
The structure of salicin, salicortin, 2'-O-acetylsalicortin, tremulacin and isosalipurpuroside.

Uses
Therapeutic indications of the drug include the relief of low back pain, symptomatic relief of mild osteoarthritic and rheumatic complaints.

Dosage
Adult daily dose: dried hydroalcoholic or aqueous extracts, tinctures or fluid extracts are recommended, equivalent to 120-240 mg of total salicin. The drug is not recommended for children.

Contra-indications
The drug should not be used in cases of hypersensitivity to salicylates.

Special warnings and precautions
The treatment of children with willow bark extracts is not recommended because of the structural similarity of salicylic derivatives in willow bark to acetylsalicylic acid. The use of synthetic acetylsalicylic acid (aspirin) in children is still associated with the so-called Reye’s syndrome.

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

10.2 Lignans
Lignans are dimeric compounds formed by the binding of two molecules of a phenylpropene derivative. About 300 lignans have been isolated and categorized into a number of groups according to their structural features (Figure 10.62). The lignans of
Podophyllum spp. are the most important pharmaceutical examples, which are formed from two molecules of coniferyl alcohol or the corresponding acid with subsequent modification. They are generally colourless, crystalline constituents. Neolignans are also derived from the same units as lignans but the C6-C3 moieties are linked head to tail or head to head and not through the β-β’ carbons. They can be found in the heart-woods of trees of the Magnoliaceae, Lauraceae and Piperaceae. The most important biological effects of the lignans are antibacterial, antifungal, cytotoxic and antimitotic. Neolignans have antirheumatic and antiallergic actions.

Figure 10.62
The most important types of lignans and neolignans in plants.
Drugs containing phenylpropanoid and phloroglucin derivatives

Drug

Podophylli rhizoma

Plant

*Podophyllum peltatum* L.– Podophyllum or May-apple (Berberidaceae)

The plant is native to North-America but it can be cultivated.

Figure 10.63

Podophyllum (*Podophyllum peltatum* L.)

Drug

*Podophylli rhizoma* (Podophyllum rhizome)

The drug consists of the whole or fragmented dried rhizomes of *Podophyllum peltatum* L. From the drug *Podophyllum resina* is also prepared by an alcoholic extraction followed by a precipitation with diluted hydrochloric acid and drying process.
Figure 10.64

*Podophyli rhizoma* (Podophyllum rhizome)

Constituents

The characteristic constituents are 3-6% of resin containing lignans such as podophyllotoxin, α- and β-peltatin and other lignans. Podophyllotoxin is a highly toxic compound, therefore its semi-synthetic derivatives such as etoposide and teniposide are used in cancer therapy.

![Chemical structures](image)

Figure 10.65-67

The structure of podophyllotoxin, α- and β-peltatin.

Uses

It was mentioned above that the semi-synthetic derivatives of podophyllotoxin are used in cancer therapy. Etoposide is currently available for the treatment of small-cell lung cancer and testicular cancer, and teniposide is used in paediatric cancers. Other podophyllotoxin-related analogues are also tested. Podophyllotoxin may be used
Drugs containing phenylpropanoid and phloroglucin derivatives
topically, and is most effective in the treatment of venereal warts, condylomas. In these cases suspensions prepared with 25% of paraffin oil can be used.

**Eleutherococci radix**

**Plant**

*Eleutherococcus senticosus* (Rupr. et Maxim.) Maxim. – Eleutherococcus (Araliaceae)

This plant is native to China, East-Asia and Siberia.

**Drug**

*Eleutherococci radix* (Eleutherococcus root, Ph. Eur.)

The drug consists of the dried, whole or cut underground organs of *Eleutherococcus senticosus* (Rupr. et Maxim.) Maxim. It contains minimum 0.08% for the sum of eleutheroside B and eleutheroside E.

![Image of Eleutherococci radix](image.jpg)

---

**Figure 10.68**

Fig. 5.99 *Eleutherococci radix* (Eleutherococcus root)

**Constituents**

The main characteristic constituents are lignans, e.g. eleutheroside E (syringaresinol diglucoside, 0.1%) and eleutheroside B<sub>4</sub> (sesamin, 0.023%). Other constituents include phenylpropanoids, e.g. eleutheroside B (syringin, 0.5%), sinapyl alcohol, chlorogenic acid; coumarins, saponins (e.g. protoprimulagenin A), sterols (β-sitosterol) and polysaccharides such as glucans.
The structure of eleutheroside E, eleutheroside B₄, eleutheroside B and protoprimulagenin A.

**Uses**

Therapeutic indications of the drug include the treatment of decreased mental and physical capacities such as weakness, exhaustion, tiredness and loss of concentration, as well as during convalescence.

**Dosage**

*Adults*: 1-2 ml of fluid extract (1:1, ethanol 40% V/V), 1-3 times daily. 65-195 mg of dry extract (14-25:1, ethanol 40% V/V), daily. Other preparations corresponding to 2-3 g of dried root and rhizome daily.

**Special warnings and precautions for use**

A few reports of blood pressure increase have been reported in hypertensive patients. A causal relationship to the use of the drug could not be established.

**Pregnancy and lactation**

No human data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

**10.3 Phloroglucin derivatives**

Phloroglucin derivatives rarely occur in higher plants, rather in ferns, (e.g. Polyopodiaceae family). Their molecules are built up of one or more (2-4) phloroglucin „core“. They can be extracted with organic solvents (mainly ethyl ether). They have anthelmintic or sedative effect. Male fern, hop and St. John’s Wort belong to this group. The latter medicinal plant will be introduced in Chapter 12.
Drugs containing phenylpropanoid and phloroglucin derivatives


drugs

Figure 10.73
The structure of phloroglucinol.

Drugs

Filicis maris rhizoma
Plant
Dryopteris filix-mas (L.) Schott – Male fern (Dryopteridaceae)
The vermifuge properties of ferns were known to the ancients, their use being mentioned in the works of Dioskurides and Theophrastus. The plant is common all over the world. Hybridization readily occurs and the plant may be derived from D. abbreviata and other ferns of unknown source.

Figure 10.74
Male fern (Dryopteris filix-mas (L.) Schott)

Drugs
Filicis maris rhizoma (Male fern rhizome), Filicis maris herba (Male fern aerial shoot)
The drug is the rhizome, the internal part of which is light green (yellowish-green). The rhizome should be dried quickly but carefully. On long-term storage the interior part becomes brown, and the amounts of active compounds decrease. The drug has slight odour and the taste is at first sweetish, afterwards becoming bitter and extremely nauseous.

Constituents

The active constituents of male fern are phloroglucinol derivatives which occur as mono-, bi-, tri- and tetracyclic compounds. Two or more molecules of the simple monocyclic derivatives such as aspidinol or filinicin acid may condense to give bicyclic compounds (e.g. albaspidin) and tricyclic ones such as filicic acid. In this compound the central phloroglucinol unit is apparently always a butyryl derivative but the other two units show great variability, and may not be identical even within a single molecule.

![filicic acid](image)

**Figure 10.75**
The structure of filicic acid.

Uses

Male fern, usually in the form of the oleoresin, is used as an anthelminthic drug. Its use requires care, as cases have occurred in which it has been absorbed and caused blindness. Today safer drugs are available. The etheric extract of the plant may irritate the stomach and can cause nausea, therefore gelatin capsules can be used.

Dosage

*Adults*: approx. 6-8 g daily. Children under 4 years and elderly should not use the drug and its products.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Lupuli flos

Plant

*Humulus lupulus* L. – Hop (Cannabaceae)

The plant is cultivated, mostly in England, Germany, Belgium, France, Russia and California. In the Early Middle Ages the German monks started to use wild hops for
Drugs containing phenylpropanoid and phloroglucin derivatives

brewing. Hop pillows were used to promote the onset of sleep. In Hungary the plant has been known since the 11th century.

![Hop plant images]

**Figure 10.76**
Hop (*Humulus lupulus* L.)

**Drug**

*Lupuli flos* (Hop strobile, Ph. Eur.)

The plant is dioecious. The drug is the female inflorescence and the multiple fruit of the cultivated hop species. Female inflorescence = the flowers located in the axil of the bracts in pairs. The inside of the bracts is covered with small, glossy, light yellow glandular scales, which contain hop bitter (e.g. lupulin).

The drug consists of the dried, generally whole, female inflorescences of *Humulus lupulus* L. The aromatic scent can become unpleasant during long-term storage.
Constituents
Bitter principles consisting mainly of prenylated phloroglucinol derivatives called α-acids or humulones (2-12% of dried strobile), principally humulone (35-70%), and β-acids or lupulones (1-10% of dried strobile), principally lupulone (30-55%). Other relevant constituent is essential oil (consisting mainly of myrcene, humulene and β-caryophyllene). Although only a trace of 2-methyl-3-buten-2-ol is found in the freshly-harvested drug, the amount is higher in stored material after 2 years due to degradation of humulones and lupulones. The most important flavonoids are quercetin and kaempferol glycosides, prenylated flavonoids, notably the chalcones xanthohumol (up to 1% of dried strobile and 80-90% of total flavonoids), and 8- and 6-prenylharnigenin. Other constituents include phenolic acids, tannins, polysaccharides and minerals.
Uses

The drug has sedative effect. The therapeutic indications include tenseness, restlessness and sleep disorders. It promotes the onset of sleep. Hop strobile is recommended by the Commission E for excitement, anxiety and sleep disorders. Because of the bitter taste the drug is an appetizer. The bactericidal effect of phloroglucin derivatives has been demonstrated. The potent phyto-oestrogen of the drug is 8-prenylnaringenin. Its oestrogenic activity has also been verified.

Dosage

**Internal use**

*Adults and children over 12 years of age*: 0.5 g of the drug as an infusion, 2-4 times daily; 0.5-2 ml of liquid extract (1:1, 45% ethanol) or 1-2 ml of tincture (1:5, 60% ethanol), up to 3 times daily or other equivalent preparations. Combination with other herbal sedatives may be beneficial.

**External use**

*Infants and young children*: up to 500 g of dry hop strobile (previously stored for 1-2 years) in a hop pillow.

Side effects, Contra-indications, Interactions

The drug can increase the effects of other CNS depressants, e.g. alcohol, sedatives. In extremely high doses oestrogen-like effects may occur. Interaction may develop with hormone-containing medicines taken simultaneously.

Pregnancy and lactation

No data available. In accordance with general medical practice, hop strobile preparations should not be used internally during pregnancy and lactation without medical advice.
Chapter 11

Drugs containing coumarin derivatives

11.1 Coumarins, furanocoumarins and pyranocoumarins

Derivatives of benzo-α-pyron such as coumarin (the lactone of O-hydroxycinnamic acid), umbelliferone and scopoletin are common in plants both in the free state and as glycosides. First coumarin was isolated from tonco bean (Dipteryx odorata) by Vogel in 1820. In coumarins an O atom (e.g. in the form of OH or CH$_3$OH) links to the 7th carbon atom (C-7) (Figure 11.1). Some 1100 natural coumarins have been isolated. Coumarin has been found in approx. 150 species belonging to over 30 different plant families. It occurs in the undamaged plant as trans-O-glucosyloxycinnamic acid, while in the damaged plant tissue an enzyme activity leads to a loss of glucose and trans→cis isomerization followed by ring closure. Coumarin emits a characteristic odour of new-mown hay. It occurs mostly in Fabaceae (e.g. sweet clover, melilot and tonco bean) family. In ammoniacal solution coumarins show blue fluorescence under UV-light.

- Furanocoumarins (e.g. marmesin, bergapten) and pyranocoumarins (e.g. visnadin) occur particularly in the Rutaceae and Apiaceae families. (Figure 11.2)

Coumarin derivatives can be classified as

- Non-condensed coumarins: substituted with OH or OCH$_3$ at positions C-6 and C-7, less commonly at C-5 and C-8. For example: umbelliferon (7-hydroxy-coumarin in Angelicae radix), scopoletin (6-methoxy-7-hydroxy-coumarin in Scopoliae radix), fraxin, izofraxidin and fraxetin in Fraxini cortex and herniarin (in Herniariae herba). C-prenylated coumarins: rutamarin (in Rutae herba), umbelliprenin (in Angelicae radix)
- Furanocoumarins: an additional furan ring is fused at C-6 and C-7 (psoralen-type) or C-7 and C-8 (angelicin-type). Some examples: imperatorin, bergapten, angelicin (in Angelicae, Imperatoriae, Pimpinellae radix), xanthotoxin (Ammi majoris fructus), psoralen (Rutae herba)
- Pyranocoumarins: an additional pyran ring is fused at C-7 and C-8 (seselin-type). For example: visnadin (Ammi majoris fructus)
- Dimeric coumarins, e.g. daphnoretin (Daphne mezerei cortex)

Coumarin and its derivatives have relevant pharmacological effects such as anticoagulant, spasmylic, photoprotective or inducing photosensibility, antibacterial and/or antifungal and diuretic.
Figure 11.1
The structure of coumarin and the biosynthesis of umbelliferone from trans-cinnamic acid.

Figure 11.2
Some coumarin derivatives
Meliloti herba

Plant

*Melilotus officinalis* (L.) Pall. – Melilot (Fabaceae)

The plant is native to Eurasia and introduced in North America, Africa and Australia. In Hungary it can be found at roadsides, railroads, abandoned fields and along rivers.

Figure 11.3

Melilot (*Melilotus officinalis* (L.) Pall.)

Drug

*Meliloti herba* (Melilot)

Melilot consists of the dried flowering tops of *Melilotus officinalis* (L.) Pall.
Constituents
The main characteristic constituents are coumarin, 3,4-dihydrocoumarin (melilotin), scopoletin and umbelliferone. Other constituents include flavonoids (mostly kaempferol and quercetin glycosides), triterpene saponins, phenolic acids (caffeic acid, melilotic acid = o-dihydrocoumaric acid) and essential oil.

![M. herba](image)

**Figure 11.4**
*Meliloti herba* (Melilot)

**Figure 11.5-8**
The structure of coumarin, 3,4-dihydrocoumarin (melilotin), scopoletin and umbelliferone.

Uses
The therapeutic indications include symptomatic treatment of problems related to varicose veins, such as painful and heavy legs, nocturnal cramps in the legs, itching and swelling. If the symptoms persist for more than 2 weeks, a doctor or a qualified health care practitioner should be consulted.
Dosage:

**Internal use**

*Adults:* Drug or preparation corresponding to 3-30 mg of coumarin daily.

**External use**

Extracts in semi-solid preparations.

**Side effects, Contra-indications, Interactions**

Hypersensitivity to the active substances may develop. If there is inflammation of the skin, thrombophlebitis, varicosis or subcutaneous induration, ulcers, sudden swelling of one or both legs, cardiac or renal insufficiency, a doctor should be consulted. Interactions between anticoagulants and Melilotus-containing medicinal products have been reported.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, melilot and its preparations should not be used internally during pregnancy and lactation without medical advice.

**Angelicae radix**

**Plant**

*Angelica archangelica* L. – Angelica (Apiaceae)

*Angelica archangelica* grows wild in Europe (Finland, Sweden, Norway, Denmark, Hungary). It is cultivated in France, Germany and in Asia. Its appearance is similar to several poisonous species of Apiaceae (*Conium, Heracleum*), and should not be consumed unless it has been identified with absolute certainty.

![Figure 11.9](image-url)

*Angelica (Angelica archangelica L.)*

**Drug**

*Angelicae radix* (Angelica root, Ph. Eur.)
Whole or cut, carefully dried rhizome and root of *Angelica archangelica* L. (*Archangelica officinalis* Haffm.). It contains minimum 2.0 ml/kg of essential oil, calculated with reference to the dried drug. It has bitter taste.

![Angelicae radix](image)

**Figure 11.10**

*Angelicae radix* (Angelica root)

**Constituents**

The characteristic constituents are coumarins, principally the prenylcoumarins ostheneol and osthol, and further 20 furanocoumarins including bergapten, angelicin, imperatorin, isoimperatorin, xanthotoxin, psoralen and isopimpinellin. Other relevant constituents of the drug include essential oil (0.3-1.3%) containing mainly monoterpenes with small amount of sesquiterpenes; phenolic acids (caffèic and chlorogenic acids), angelic acid, fatty acids, tannins and starch.
Drugs containing coumarin derivatives

Uses
The therapeutic indications include dyspeptic complaints such as mild gastrointestinal spasms, sluggish digestion, flatulence and feeling of fullness, lack of appetite, anorexia and bronchitis.

Dosage
*Adult and elderly daily dose:* 3-6 g of the drug, or as an infusion, 1-6 ml of liquid extract (1:1 in 25% ethanol), 1-6 ml of tincture (1:5 in 50% ethanol) divided into three doses.

*Children over 4 years, average daily dose:* 4-10 years of age, 2-3 g; 10-16 years of age, 3-4 g.

Special warnings and special precautions for use
Prolonged exposure to sunlight should be avoided during taking angelica root since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation
No data available. In accordance with general medical practice, angelica and its preparations should not be used internally during pregnancy and lactation without medical advice.

**Ammi visnagae fructus**

**Plant**
*Ammi visnaga* (L.) Lam. – Bisnaga (Apiaceae)
Pharmacognosy 2

The plant is native to the Mediterranean region, Asia, Argentina, Chile and Mexico.

![Figure 11.17](image)

**Figure 11.17**

Bisnaga (*Ammi visnaga* (L.) Lam.)

**Drug**

*Ammi visnagae fructus* (Bisnaga fruit)

The drug consists of the ripe, dried seeds of *Ammi visnaga* (L.) Lam.

** Constituents**

The characteristic constituents are 2-4% of furanocoumarins (khellin), 0.2-0.5% of pyranocoumarins (visnadin). Other constituents include flavonoids, essential oil, fatty oil and proteins.
**Uses**

Furano- and pyranocoumarins are used in the pharmaceutical industry as smooth muscle relaxant compounds. Visnadin is a coronary artery vasodilator. Khellin can be used in the treatment of asthma.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the drug should not be used internally during pregnancy and lactation without medical advice.

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**Ammi majoris fructus**

**Plant**

*Ammi majus* L.– Ammi (Apiaceae)

The plant is native to the Mediterranean region, West Asia and Caucasus.

**Drug**

*Ammi majoris fructus* (Ammi fruit)

The drug consists of the ripe, dried seeds of *Ammi majus* L.
Figure 11.20
_Ammi majoris fructus_ (Ammi fruit)

**Constituents**

The characteristic constituents are furanocoumarins (xanthotoxin, imperatorin, bergapten and isopimpinellin). Other constituents include flavonoids, essential oil, fatty oil and proteins.

![Diagrams of chemical structures](image)

**Figure 11.21-24**
The structure of xanthotoxin, imperatorin, bergapten and isopimpinellin.
Drugs containing coumarin derivatives

Uses
Furanocoumarins are used as smooth muscle relaxant compounds. In dermatology xanthotoxin can be used for treatment of vitiligo (leucoderma), psoriasis (consultation with medical doctor is recommended).

Special warnings and special precautions for use
Prolonged exposure to sunlight should be avoided since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation
No data available. In accordance with general medical practice, the drug should not be used internally during pregnancy and lactation without medical advice.

Levistici radix

Plant

*Levisticum officinale* Koch – Lovage (Apiaceae)

The plant is native to West Asia (Iran) and South Europe. In Hungary it can be cultivated.

![Lovage (Levisticum officinale Koch)](image)

**Figure 11.25**
Lovage (*Levisticum officinale* Koch)

Drug

*Levistici radix* (Lovage root, Ph. Eur.)

The drug consists of the whole or cut, dried rhizome and root of *Levisticum officinale* Koch. It contains minimum 4.0 ml/kg of essential oil for the whole drug and minimum 3.0 ml/kg of essential oil for the cut drug (dried drug).
Constituents
The characteristic constituents of the drug are coumarins (e.g. coumarin, umbelliferon) and furanocoumarins (bergapten and psoralen), and some essential oil (0.6-1%).

![Chemical structures of umbelliferon, coumarin, bergapten, and psoralen](image)

Uses
Traditional herbal medicinal product used to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints. The drug has diuretic effect.

Dosage
*Adults and elderly*
As a herbal tea
Single dose: 2-3 g of comminuted herbal substance in 150 ml of boiling water as a herbal infusion, twice daily. Average daily dose: 4-6 g.

The use in children and adolescents under 18 years of age is not recommended. Duration of use: not to be used for more than 2-4 weeks.

If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Contra-indication

Hypersensitivity to the active substance and to other plants of the Apiaceae family or to trans-anethole may develop.

Special warnings and special precautions for use

The use in children and adolescents under 18 years of age is not recommended because of concerns requiring medical advice. If complaints or symptoms such as fever, dysuria, spams, or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Prolonged exposure to sunlight should be avoided since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Apii fructus

Plant

*Apium graveolens* L. – Celery (Apiaceae)

The plant is cultivated all over the world.

![Figure 11.31](image_url)

Figure 11.31

Celery (*Apium graveolens* L.)

Drug

*Apii fructus* (Celery fruit)
The drug consists of the whole and ripe fruits of *Apium graveolens* L.

**Constituents**

The characteristic constituents of the drug are coumarins, furanocoumarins (e.g. bergapten, isopimpinellin) and prenyl-coumarins (e.g. ostenol, apigravin). Other constituents include essential oil (2-3%) and fatty oil.

![Figure 11.32-35](image)

**Figure 11.32-35**

The structure of bergapten, isopimpinellin, ostenol and apigravin.

**Uses**

Traditional herbal medicinal product used to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints. The drug has diuretic effect. The drug has long-standing use in the treatment of rheumatic diseases.

**Dosage**

**Adults and elderly**

As a herbal tea

Single dose: 2-3 g of comminuted herbal substance in 150 ml of boiling water as a herbal infusion, twice daily. Average daily dose: 4-6 g.

The use in children and adolescents under 18 years of age is not recommended. Duration of use: not to be used for more than 2-4 weeks.

If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

**Contra-indication**

Hypersensitivity to the active substance and to other plants of the Apiaceae family. Patients with nephritis must not use the drug and its preparations.
Special warnings and special precautions for use

The use in children and adolescents under 18 years of age is not recommended because of concerns requiring medical advice. If complaints or symptoms such as fever, dysuria, spams, or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Prolonged exposure to sunlight should be avoided since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.
Chapter 12

**Drugs containing anthraquinone and naphthoquinone derivatives**

In this chapter quinone, naphthoquinone, anthraquinone, dianthrone and naphthodianthrone derivatives will be introduced.

Quinones are a class of organic compounds that are formally derived from aromatic compounds (such as benzene or naphthalene) by conversion of an even number of \(-\text{CH}=\) groups into \(-\text{C}(=\text{O})–\) groups with any necessary rearrangement of double bonds, resulting in a fully conjugated cyclic dione structure. The class includes some heterocyclic compounds. The typical member of the class is 1,4-benzoquinone, often simply called quinone. Other important examples are 1,4-naphthoquinone and 9,10-anthraquinone (Figure 12.1). Quinones are oxidized derivatives of aromatic compounds and are often readily made from reactive aromatic compounds with electron-donating substituents such as phenols and catechols, which increase the nucleophilicity of the ring and contribute to the large redox potential needed to break aromaticity. (Quinones are conjugated but not aromatic). Quinones are electrophilic Michael acceptors stabilised by conjugation. Depending on the quinone and the site of reduction, reduction can either rearomatise the compound or break the conjugation. Conjugate addition nearly always breaks the conjugation.

![Figure 12.1](image)

The structure of quinone, 1,4-naphthoquinone and 9,10-anthraquinone.

### 12.1 Quinone derivatives

**Drugs**

**Uvae ursi folium**

*Plant*

*Arctostaphylos uva-ursi* (L.) Spreng. – Bearberry (Ericaceae)

The plant is a small evergreen shrub found in central and northern Europe and in North America.
Drug

_Uvae ursi folium_ (Bearberry leaf, Ph. Eur.)

Bearberry leaf consists of the whole or cut, dried leaf of _Arctostaphylos uva-ursi_ (L.) Spreng. It contains minimum 7.0% of anhydrous arbutin calculated with reference to the dried drug.
Constituents

The main characteristic constituents of the drug are arbutin (5-15%), methylarbutin (up to 4%), piceosid, small amounts of the free aglycones hydroquinone and methylhydroquinone. Other constituents include gallic acid and gallotannins (up to 20%), flavonoids and triterpenes (mainly ursolic acid and uvaol).

![Chemical structures](image_url)

**Figure 12.4-7**
The structure of arbutin, methylarbutin, piceosid and hydroquinone.

Uses

Therapeutic indications include the uncomplicated infections of the lower urinary tract such as cystitis, when antibiotic treatment is not considered essential.

Dosage

*Adults and elderly*: cold water maceration of the dried leaves corresponding to 400-800 mg of arbutin daily, divided into 2-3 doses or equivalent preparations. The daily dose of the drug is 3 g daily.

Patients should be advised to consume plenty of liquid during the treatment. Alkalinization of the urine may be beneficial. Treatment should be continued until complete disappearance of symptoms (up to a max. of 2 weeks). If the symptoms worsen during the first week of treatment medical advice should be sought.

Not recommended for children.

Contra-indication

Patients with kidney disorders must not use the drug and its preparations.

Special warnings and special precautions for use

The amount of free hydroquinone in bearberry leaf preparations should be controlled. Hydroquinone is a topical irritant and a hepatotoxin, oral ingestion of 5-12 g has been...
fatal. Long term external application of creams containing up to 10% of hydroquinone has caused skin colloid degeneration (ochronosis).

Undesirable effects
Nausea and vomiting may occur due to stomach irritation from the high tannin content of the drug.

Interaction
Concomitant acidification of the urine (by other remedies) may result in a reduction of efficacy.

Pregnancy and lactation
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

**Vitis idaeae folium**

Plant

*Vaccinium vitis-idaea* L. – Cowberry/Lingonberry (Ericaceae)

The plant is a short shrub and native to boreal forests and the Arctic tundra throughout the Northern Hemisphere from Eurasia to North America.

![Cowberry](image)

**Figure 12.8**

Cowberry (*Vaccinium vitis-idaea* L.)

Drug

*Vitis idaeae folium* (Cowberry leaf)

Cowberry leaf consists of the whole or cut, dried leaf of *Vaccinium vitis-idaea* L.
Drugs containing anthraquinone and naphthoquinone derivatives

Constituents
The main characteristic constituents of the drug are arbutin (3-8%), 6’-O-acetyl-arbutin, and small amounts of the free aglycone hydroquinone. Other constituents include tannins (catechins) and flavonoids.

![Arbutin and 6’-O-acetyl-arbutin structures](image)

Uses
Therapeutic indications include the uncomplicated infections of the lower urinary tract such as cystitis, when antibiotic treatment is not considered essential.

Dosage
Adults and elderly: cold water maceration of the dried leaves corresponding to 400-800 mg of arbutin daily, divided into 2-3 doses or equivalent preparations.
Patients should be advised to consume plenty of liquid during the treatment. This drug is safer than bearberry leaf because of lower amount of tannins.

Contra-indication
Patients with kidney disorders must not use the drug and its preparations.

Special warnings and special precautions for use
The amount of free hydroquinone in the leaf preparations should be controlled. Hydroquinone is a topical irritant and a hepatotoxin, oral ingestion of 5-12 g has been fatal.

Pregnancy and lactation
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

12.2 Naphthoquinone derivatives
Naphthoquinones are a class of organic compounds derived from naphthalene. Several isomeric naphthoquinones are known [1,2-naphthoquinone, 1,4-naphthoquinone (= para-naphthoquinone)]. 1,4-naphthoquinone forms volatile yellow triclinic crystals and has a sharp odor reminiscent of benzoquinone. It is almost insoluble in cold water, slightly soluble in petroleum ether, and more soluble in polar organic solvents. In alkaline solutions it produces a reddish-brown color. Vitamin K is a derivative of 1,4-naphthoquinone. Naphthoquinones are produced by higher plants, fungi and Actinomycetes bacteria and have significant biological actions including antibacterial, fungicidal, insecticidal, cytostatic and anticarcinogenic. They have been shown to be biosynthesized via a variety of pathways including acetate and malonate (e.g. plumbagin), shikimate/succinyl CoA combined pathway (e.g. lawsone) and shikimate/mevalonate combined pathway (e.g. alkannin) (Figure 12.12). In plants they occur in reduced or glycosidic form. Juglone (5-hydroxy-1,4-naphthalenedione) is one of the most relevant constituents in the group of naphthoquinones. It occurs naturally in the leaves, roots, husks, and bark of plants in the Juglandaceae family, particularly the black walnut (Juglans nigra), and is toxic or growth-stunting to many types of plants. It is sometimes used as a herbicide, as a dye for cloth and inks, and as a coloring agent in foods and cosmetics. Juglone is an example of allelopathic compounds, a substance that is synthesized by one type of plant and affects the growth of another.
Drugs containing anthraquinone and naphthoquinone derivatives

Figure 12.12
Biosynthesis of naphthoquinone.

Drugs

Juglandis folium

Plant

*Juglans regia* L. – Common walnut (Juglandaceae)

The plant is native to the region stretching from the Balkans eastward to the Himalayas and southwest China. *Juglans regia* is a large, deciduous tree attaining heights of 25–35 m, and a trunk up to 2 m diameter.
Figure 12.13
Common walnut (Juglans regia L.)

Drug

*Juglandis folium* (Walnut leaf)

Walnut leaf consists of the whole or cut, dried leaf of *Juglans regia* L. When the leaves become dark it means that the drug cannot be used for making preparations.

Figure 12.14

*Juglandis folium* (Walnut leaf)
Drugs containing anthraquinone and naphthoquinone derivatives

Constituents

The main characteristic constituents of the drug are the naphthoquinone derivatives juglone, hydrojuglone and hydrojuglone glycoside. Other constituents include 10% of tannins, mainly ellagitannins, flavonoids (hiperoside, quercetine and kaempferol glycosides), phenolcarboxylic acids (e.g. caffeic acid) and 0.01-0.03% of essential oil (with \( \beta \)-caryophyllene, germacrene D, ocimene).

![Diagram of juglone, hydrojuglone, and hydrojuglone glucoside]

Figure 12.15-17

The structure of juglone, hydrojuglone and hydrojuglone glycoside.

Uses

Its products are traditional herbal medicinal products for use in the specified indications exclusively based upon long-standing use. Therapeutic indications of walnut leaf include the relief of minor inflammatory conditions of the skin and its medicinal products are used in excessive perspiration of hands and feet.

Dosage

Relief of minor inflammatory conditions of the skin

Adults and elderly: 4-6 g of the comminuted herbal substance in 200 ml of boiling water as a decoction. Apply as an impregnated dressing to the affected areas of the skin 2-4 times daily.

In the case of excessive perspiration of hands and feet

Adults and elderly: 4-6 g of the comminuted herbal substance in 200 ml of boiling water as a decoction. Apply as an impregnated dressing to the affected areas of the skin up to 30 minutes twice daily. The use in children and adolescents under 18 years of age is not recommended because of lack of adequate data.

Duration of use: not to be used for more than 1 week.
Contra-indication

Hypersensitivity to the active substance may occur. Patients with open wounds and large skin injuries must not use the drug and its preparations.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Alkannae radix

Plant

*Alkanna tinctoria* (L.) Tausch. – Alkanet (Boraginaceae)

The plant is found in Hungary, southern Europe and Turkey. It can be found on calciferous ground and sandy soil. In Hungary it is a protected plant. The leaves have whitish, bristly hairs.

![Figure 12.18](image)

*Figure 12.18*

Alkanet (*Alkanna tinctoria* (L.) Tausch.)

Drug

*Alkannae radix* (Alkanet root)

It consists of reddish-purple roots about 10-15 cm long and 1-2 cm diameter. The surface is deeply fissured and readily exfoliates.

Constituents

The main characteristic constituents of the drug are naphthoquinone derivatives, 5-6% of alkannin (a natural red dye) and alkannin esters. Other constituents include pyrrolizidine alkaloids.
Drugs containing anthraquinone and naphthoquinone derivatives

Figure 12.19-21
The structure of alkannin, alkannin-β,β-dimethylacrylate and alkannin isovalerate.

Uses
Alkannin and its derivatives have antibacterial and antifungal effects. Therapeutic indications include the relief of inflammatory conditions of the skin, e.g. ulcus cruris. Cosmetic industry uses the drug as a natural dye in colouring oils and eye-shadow. In the form of a tincture it is used for the microscopical detection of oils and fats. Because of its pyrrolizidine alkaloid content the drug and its preparations can only be applied externally.

Dosage
Adults and elderly: 4-5 g of the comminuted herbal substance in 150 ml of boiling water as an infusion. Apply as an impregnated dressing to the affected areas of the skin 2-4 times daily. In ointment: 5-10 g of aqueous or ethanolic extract of the drug in 100 g.

Contra-indication
Hypersensitivity to the active substance may occur. Patients with open wounds and large skin injuries must not use the drug and its preparations.

Pregnancy and lactation
No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.
Droserae herba

Plants

*Drosera rotundifolia* L., *D. ramentacea* Burch. ex. Harv. et Sond, *Drosera* sp. – Drosera, Sundews (Droseraceae)

*Drosera*, commonly known as the sundews, comprise one of the largest genera of carnivorous plants, with at least 194 species. These members of the family Droseraceae attract, capture, and digest insects using stalked mucilaginous glands covering their leaf surfaces. The insects are used to supplement the poor mineral nutrition of the soil in which they grow. Various species, which vary greatly in size and form, can be found growing natively on every continent except Antarctica. Sundews generally grow in seasonally moist or more rarely constantly wet habitats with acidic soils and high levels of sunlight. Common habitats include bogs, fens, swamps and marshes. Many species grow in association with sphagnum moss, which absorbs much of the soil's nutrient supply and also acidifies the soil, making nutrients less available to other plants. The plant is found in Hungary, but it is strictly protected. It can also be cultivated (e.g. in Finland).

![Figure 12.22](image)

Sundew (*Drosera rotundifolia* L.)

Drug

*Droserae herba* (Sundew herb)

Sundew consists of the dried above- and below-ground parts of *Drosera rotundifolia* L., *D. ramentacea* Burch. ex. Harv. et Sond, *D. longifolia* L., *D. intermedia* Hayne and other *Drosera* species. The herb contains 0.1-0.2% of naphthoquinone derivatives calculated as juglone in respect to the dry mass of the herb.
Drugs containing anthraquinone and naphthoquinone derivatives

Constituents

The main characteristic constituents of the drug are naphthoquinone derivatives such as plumbagin, plumbagin-5-O-glucoside, ramenton, ramentaceon and rossoliside (7-methyl-hydrojuglone-4-O-β-D-glucoside). Other constituents include flavonoids, mucilage and proteolytic enzymes.
Figure 12.24-28

The structure of plumbagin, plumbagin-5-O-glucoside, ramenton, ramentaceon and rossoliside (7-methyl-hydrojuglone-4-O-β-D-glucoside).

Uses

The drug and its preparations have antibacterial, bronchoantispasmodic and antitussive activities. Therapeutic indications include the relief of inflammatory conditions of the respiratory tract, e.g. bronchitis, pharyngitis and laryngitis.

Dosage

Adults and elderly: 1 g of the comminuted herb in 200 ml of boiling water as an infusion, 2-3 times daily. 3 g is the daily dose.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Lawsoniae folium

Plant

Lawsonia inermis L. – Henna (Lythraceae)

Henna is a tall shrub or small tree, 2.6 m high. The henna plant is native to tropical and subtropical regions of Africa, southern Asia, and northern Australasia in semi-arid zones.

Drug

Lawsoniae folium (Henna leaf)
Henna consists of the dried leaves of *Lawsonia inermis* L. The leaves are greenish-brown to brown and about 2.5-5 cm long.

**Constituents**

The main characteristic constituents of the drug are naphthoquinone derivatives such as 1,4-naphthoquinone and 2-hydroxy-1,4-naphthoquinone (lawsone). Other constituents include phenolic glycosides, coumarins, xanthones, flavonoids (mainly luteolin and its 7-O-glucoside) and tannins.

![Structures of 1,4-naphthoquinone and 2-hydroxy-1,4-naphthoquinone (lawsone).](image)

**Uses**

Henna is commonly used as a dye for the hair, and wool washed in a dilute solution of ammonia and boiled in a decoction of the drug should be dyed Titian red. Because of tannin content, the drug can be used for treating burns, wounds and fungal infections of the skin.

The adstringent stem-bark of *L. inermis* is traditionally used in India for the treatment of jaundice, enlargement of the liver and spleen, and for various skin diseases.

**Dosage**

*Adults and elderly:* 1 g of the comminuted herb in 200 ml of boiling water as an infusion, 2-3 times daily. For External use 3 g of the drug, daily. Prolonged use of the drug is not recommended for internal purposes.

*Pregnancy and lactation:* No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

**12.3 Anthraquinone derivatives**

Substances of the anthraquinone type may occur both in free state and as glycosides. Natural compounds also contain reduced derivatives of the anthraquinones (oxanthrones, anthranols and anthrones) and compounds formed by the union of two anthrone molecules (*Figure 12.31*).
Anthraquinone glycosides are often easily hydrolysed. The following aglycones have long been established: chrysophanol (from rhubarb and cascara), aloe- emodin (from rhubarb and senna), rhein (from rhubarb and senna), emodin (from frangula and cascara) and physcion (from frangula and cascara) (Figure 12.32).

Figure 12.31
Interrelationship of anthraquinone derivatives.

Figure 12.32
The main anthraquinone aglycones.
In monocotyledons, anthraquinone derivatives are found only in the Liliaceae, in the form of C-glycosides (e.g. barbaloin). Among dicotyledons they occur in the Rubiaceae, Polygonaceae, Rhamnaceae, Ericaceae, Euphorbiaceae and Scrophulariaceae. Anthraquinones are either synthetized via the acetate-mevalonate pathway or they are derived from shikimate and mevalonate. The medicinally important purgative anthraquinones are formed by this way and all have 1,8-dihydroxy substitution. In their structure there is a –OH group at a C-6 position, and its oxylated forms (-CH2OH, -COOH) are at C-3 position.

Anthraquinone derivatives are often orange-red compounds. They are usually soluble in hot water or dilute alcohol. Bornträger’s test is often used for their detection (the free anthraquinone-derivatives (aglycones = 1,8-dihydroxy-anthraquinone derivatives) can be extracted with chloroform and separated with aqueous-base (ammonia) solution. The aqueous layer becomes reddish). Anthranol and anthrone derivatives are isomeric and one may be partially converted to the other in solution. Anthrone is a pale yellow, nonfluorescent substance, which is insoluble in alkali. Its isomer, anthranol, is a brownish-yellow compound and forms a strongly fluorescent solution in alkali. Anthranol derivatives, for example aloin, show green fluorescence in borax or other alkaline solutions (Schouteten reaction). Anthraquinones can be found in a variety of forms in plants. It depends on the plant species, the part of the plant (the drug), the developmental stage of the plant, the method of drying and storage.

Anthraquinone derivatives have laxative activity. Anthrones and dianthrones are the most effective substances. The action of the compounds is restricted to the large bowel (hence their effect is delayed up to 6 h or longer). It has been suggested that anthraquinone derivatives influence the ion transport across colon cells by inhibition of Cl- channels.

Drugs

Frangulae cortex

Plant

*Rhamnus frangula* L. – Frangula (Alder buckthorn) (Rhamnaceae)

The plant is a tall deciduous shrub. It is native to Europe, northernmost Africa, and western Asia, from Ireland and Great Britain north to Scandinavia, east to central Siberia and in western China, and south to northern Morocco, Turkey, and in the Caucasus Mountains. It is also introduced in eastern North America. Its ripe, black fruits and fresh bark are poisonous.

Drug

*Frangulae cortex* (Frangula bark, Ph. Eur.). **Other Drug** *Frangulae corticis extractum siccum normatum* (Frangula bark dry extract, standardised, Ph. Eur.)

Frangula bark consists of the dried, whole or fragmented bark of the stems and branches of *Rhamnus frangula* L. (*Frangula alnus* Miller). It contains not less than 7.0% of glucofrangulins, expressed as glucofrangulin A and calculated with reference to the dried drug. Bark for medicinal use is dried and stored for a year before use, as fresh
bark is violently purgative and its high amounts of anthrones and anthranoles are responsible for spasms in the bowel.

Standardised frangula bark dry extract is produced from *Frangula bark*. It contains not less than 15.0% and not more than 30.0% of glucofrangulins, expressed as glucofrangulin A and calculated with reference to the dried extract. The measured content should not deviate from that stated on the label by more than ± 10%. The extract is produced from the drug and ethanol (50 to 80 per cent *V/V*) by an appropriate procedure. It’s a yellowish-brown, fine powder.

![Frangulae cortex](image)

**Figure 12.33**

*Frangulae cortex* (Frangula bark)

**Constituents**

The main characteristic constituents of the dried bark are glucofrangulin A and B (emodin-6-O-α-L-rhamnosyl-8-O-β-D-glucoside and emodin-6-O-β-D-apiosyl-8-O-β-D-glucoside respectively), frangulin A, B and C (emodin-6-O-α-L-rhamnoside, emodin-6-O-β-D-apioside and emodin-6-O-β-D-xyloside) and emodin-8-O-β-D-glucoside, together with small amounts of other anthraquinone glycosides, dianthrones and aglycones (chrysophanol, physcion). Tannins can be found in frangula bark, as well.
Drugs containing anthraquinone and naphthoquinone derivatives

Figure 12.34-40
The structure of glucofrangulin A and B, frangulin A and B, frangulaemodin, chrysophanol and physcion.

Uses
Therapeutic indications include the short term treatment of occasional constipation.

Dosage
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

Adults, elderly and children over 10 years: preparations equivalent to 20-30 mg of glucofrangulins daily, calculated as glucofrangulin A. The drug and its preparations are not recommended for children under 10 years of age.

Overdose
The major symptoms are griping and severe diarrhoea with consequent loss of fluid and electrolytes, which should be replaced. Treatment should be supportive with generous amounts of fluid. Electrolytes, particularly potassium, should be monitored, this is especially important in the elderly and the young.

Contra-indication
The drug and its preparations should not be used in the following cases: intestinal obstruction and stenosis, atony, inflammatory colon diseases (e.g. ulcerative colitis, Crohn’s disease), appendicitis, abdominal pain of unkown origin, severe dehydration states with water and electrolyte depletion.
Special warnings and special precautions for use

As for all laxatives, frangula bark should not be given when any undiagnosed acute or persistent abdominal symptoms are present. If laxatives are needed every day the cause of the constipation should be investigated. Long term use of laxatives should be avoided. Use for more than 2 weeks requires medical supervision. Chronic use may cause pigmentation of the colon (pseudomelanosis coli) which is harmless and reversible after drug discontinuation. Abuse with diarrhoea and consequent fluid and electrolyte losses may cause: dependence with possible need for increased dosages, disturbance of the water and electrolyte (mainly hypokalaemia) balance, an atonic colon with impaired function. Intake of anthranoid-containing laxatives for more than a short period of time may result in aggravation of constipation. Hypokalaemia can result in cardiac and neuromuscular dysfunction, especially if cardiac glycosides, diuretics or corticosteroids are taken. Chronic use may result in albuminuria and haematuria. In chronic constipation stimulant laxatives are not an acceptable alternative to a changed diet.

Interactions with other medicaments and other forms of interactions

Hypokalaemia potentiates the action of cardiac glycosides and interacts with antiarrhythmic drugs or with drugs which induce reversion to sinus rhythm (e.g. quinidine). Concomitant use with other drugs inducing hypokalaemia (e.g. thiazide diuretics, adrenocorticosteroids and liquorice root) may aggravate electrolyte imbalance.

Undesirable effects

Abdominal spasm and pain and yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may develop.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice. Excretion of active principles in breast milk has not been investigated. However, small amounts of active metabolites (e.g. rhein) from other anthranoids are known to be excreted in breast milk.

Rhamni purshianae cortex

Plant

*Rhamnus purshiana* DC. – Cascara buckthorn (Rhamnaceae)

Cascara is a large shrub or small tree and it is native to western North America from southern British Columbia south to central California, and eastward to northwestern Montana.

Drug

*Rhamnus purshiana* cortex (Cascara, Ph. Eur.)

Cascara consists of the dried, whole or fragmented bark of *Rhamnus purshianus* D.C. (*Frangula purshiana* (D.C.) A. Gray ex J. C. Cooper). It contains not less than 8.0% of hydroxyanthracene glycosides of which not less than 60% consists of cascarosides, both expressed as cascaroside A and calculated with reference to the dried drug.
Constituents

The main active constituents of the dried bark are cascarosides A, B, C, D, E and F. Cascarosides A and B are mixed anthrone-\(\text{C}\) and O-glycosides, being the 8-O-\(\beta\)-D-glucosides of 10-(S)-deoxyglucosyl aloe-emodin anthrone and of 10-(R)-deoxyglucosyl aloe-emodin anthrone (aloins A and B) respectively. Cascarosides C and D are the 8-O-\(\beta\)-D-glucosides of 10-(R)(S)-deoxyglucosyl chrysophanol anthrone (chrysaloin A and B). Cascarosides E and F are 8-O-\(\beta\)-D-glucosides of 10-deoxyglucosyl emodin. The cascarosides comprise between 60-70% of the total hydroxyanthracene complex. Aloins A and B together with chrysaloin A and B account for 10-30% of the total hydroxyanthracene complex. The remaining 10-20% consists of a mixture of hydroxyanthracene O-glycosides including monoglycosides of chrysophanol, aloe-emodin, emodin and physcion together with the corresponding aglycones.
Figure 12.42-47
The structure of cascarosides A, B, C, D, E and F.

Uses
Therapeutic indications include the short term treatment of occasional constipation.

Dosage
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

Adults, elderly and children over 10 years: dried bark: 0.3-1 g in a single daily dose. Infusion: 1.5-2 g of dried bark in 150 ml of hot water. Preparations equivalent to 20-30 mg of hydroxyanthracene derivatives daily, calculated as cascaroside A. The drug and its preparations are not recommended for children under 10 years of age.

Overdose
The major symptoms are griping and severe diarrhoea with consequent loss of fluid and electrolytes, which should be replaced. Treatment should be supportive with generous amounts of fluid. Electrolytes, particularly potassium, should be monitored, this is especially important in the elderly and the young.

Contra-indication
The drug and its preparations should not be used in the following cases: intestinal obstruction and stenosis, atony, inflammatory colon diseases (e.g. ulcerative colitis, Crohn’s disease), appendicitis, abdominal pain of unkown origin, severe dehydration states with water and electrolyte depletion.
Special warnings and special precautions for use

As for all laxatives, cascara bark should not be given when any undiagnosed acute or persistent abdominal symptoms are present. If laxatives are needed every day the cause of the constipation should be investigated. Long term use of laxatives should be avoided. Use for more than 2 weeks requires medical supervision. Chronic use may cause pigmentation of the colon (pseudomelanosis coli) which is harmless and reversible after drug discontinuation. Abuse with diarrhoea and consequent fluid and electrolyte losses may cause: dependence with possible need for increased dosages, disturbance of the water and electrolyte (mainly hypokalaemia) balance, an atonic colon with impaired function. Intake of anthranoid-containing laxatives for more than a short period of time may result in aggravation of constipation. Hypokalaemia can result in cardiac and neuromuscular dysfunction, especially if cardiac glycosides, diuretics or corticosteroids are taken. Chronic use may result in albuminuria and haematuria. In chronic constipation stimulant laxatives are not an acceptable alternative to a changed diet.

Interactions with other medicaments and other forms of interactions

Hypokalaemia potentiates the action of cardiac glycosides and interacts with antiarrhythmic drugs or with drugs which induce reversion to sinus rhythm (e.g. quinidine). Concomitant use with other drugs inducing hypokalaemia (e.g. thiazide diuretics, adrenocorticosteroids and liquorice root) may aggravate electrolyte imbalance.

Undesirable effects

Abdominal spasm and pain and yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may develop.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice. Excretion of active principles in breast milk has not been investigated. However, small amounts of active metabolites (e.g. rhein) from other anthranoids are known to be excreted in breast milk.

Rhei radix

Plants

*Rheum palmatum* L. – Chinese rhubarb or *R. officinale* Baill. – Rhubarb (Polygonaceae)

Chinese rhubarb is native to North and Northwest China, and *R. officinale* can be found in South China and Indochina. It can be cultivated in Hungary. The 8-10-year-old plants are used.
Rhubarb consists of the whole or cut, dried underground parts of *Rheum palmatum* L. or of *Rheum officinale* Baillon or of hybrids of these two species or of a mixture. The underground parts are often divided; the stem and most of the bark with the rootlets are removed. It contains not less than 2.2% of hydroxyanthracene derivatives, expressed as rhein, calculated with reference to the dried drug. Rhubarb has a characteristic, aromatic odour.
Constituents

The main active constituents of the drug are hydroxyanthracene derivatives (3-12%) consisting mainly (60-80%) of mono- and diglucosides of rhein, chrysophanol, aloe-emodin, physcion and emodin, and only small amounts of the respective aglycones. Dianthrone glycosides (sennosides) are also present and small amounts of anthrone glycosides depending on the time of harvesting and the conditions of drying. Other constituents include gallotannins, pectin, flavonoids and oxalic acid.
Uses
Therapeutic indications include the short term treatment of occasional constipation.

Dosage
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

**Adults, elderly and children over 10 years:** dried bark: drug or its preparations are equivalent to 15-50 mg of hydroxyanthracene derivatives daily (calculated as rhein), preferably taken in one dose at night. The drug and its preparations are not recommended for children under 10 years of age. Because of its tannin content the drug can be used also against diarrhoea. With this indication, the recommended dose of the drug is 0.1-0.3 g daily.

Overdose
It is similar to the Frangula or Cascara drugs (see above these drugs).

Contra-indication
It is similar to the Frangula or Cascara drugs (see above these drugs). The drug is not recommended for long-term use. Due to oxalic acid content renal stones may develop.

Special warnings and special precautions for use
It is similar to the Frangula or Cascara drugs (see above these drugs).

Interactions with other medicaments and other forms of interactions
It is similar to the Frangula or Cascara drugs (see above).
Drugs containing anthraquinone and naphthoquinone derivatives

Undesirable effects

It is similar to the Frangula or Cascara drugs (see above).

Pregnancy and lactation

It is similar to the Frangula or Cascara drugs (see above).

**Aloe capensis**

Plant

*Alloë ferox* Mill. – Cape aloes (Liliaceae)

*Alloë ferox* is native to South and East Africa and Macaronesia. Its powder is extremely bitter. The plant can be cultivated. *Alloë ferox* prefers dry-tropical climates, open areas, sandy-loamy soils, full sun, and moderate watering with a good drainage system.

![Figure 12.55](image)

Cape aloes (*Alloë ferox* Mill.)

**Drug**

*Aloe capensis* (Cape aloes, Ph. Eur.). **Other Drug** *Aloes extractum siccum normatum* (Aloes dry extract, standardised, Ph. Eur.).

Cape aloes consists of the concentrated and dried juice of the leaves of various species of *Aloe*, mainly *Aloë ferox* Miller and its hybrids. It contains not less than 18.0% of hydroxyanthracene derivatives, expressed as barbaloin and calculated with reference to the dried drug. The drug comprises dark brown masses tinged with green and having a shiny conchooidal fracture, or a greenish-brown powder, soluble in hot alcohol, partly soluble in boiling water.

Standardised aloes dry extract is prepared from Barbados aloes or Cape aloes, or a mixture of the two, by treatment with boiling water. It is adjusted, if necessary, to
contain not less than 19.0% and not more than 21.0% of hydroxyanthracene derivatives, expressed as barbaloin and calculated with reference to the dried extract. A brown or yellowish-brown powder, sparingly soluble in boiling water.

**Figure 12.56**

*Aloe capensis* (Cape aloes)

**Constituents**

The main active constituents are aloin A and B (barbaloin) and 5-hydroxyaloin A, which are aloe-emodin anthrone-C-glycosides. Aloinosides A and B, which are anthrone-C and O-glycosides, are also considered as active constituents. Other compounds are 2-acetonyl-5-methyl-chromones (aloeresins) and small quantities of 1,8-dihydroxy-anthraquinones (e.g. aloe-emodin).
Drugs containing anthraquinone and naphthoquinone derivatives

**Figure 12.57-60**
The structure of aloin A and B, 5-hydroxyaloin and aloe-emodin.

**Uses**
Therapeutic indications include the short term treatment of occasional constipation. It should be highlighted that aloes are the most violent laxatives among drugs containing anthranoids.

**Dosage**
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

*Adults, elderly and children over 10 years:* preparations are equivalent to 10-30 mg of hydroxyanthracene derivatives, calculated as barbaloin, to be taken in one dose daily at night. The drug and its preparations are not recommended for children under 10 years of age.

**Overdose**
It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

**Contra-indication**
It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

**Special warnings and special precautions for use**
It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

**Interactions with other medicaments and other forms of interactions**
It is similar to the Frangula, Cascara and Rhubarb drugs (see above).
Undesirable effects
It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

Pregnancy and lactation
It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

**Aloe barbadensis**

**Plant**

*Aloë barbadensis* Mill. – Barbados aloes (syn.: *Aloë vera* (L.) Burm.) (Liliaceae)

*Aloë vera* is a succulent plant species that probably originated in northern Africa. It is widely cultivated throughout the world.

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**Drug**

*Aloe barbadensis* (Barbados aloes, Ph. Eur.)

Barbados aloes consists of the concentrated and dried juice of the leaves of *Aloe barbadensis* Miller. It contains not less than 28.0% of hydroxyanthracene derivatives, expressed as barbaloin and calculated with reference to the dried drug. The drug comprises dark brown masses, slightly shiny or opaque with a conchoidal fracture, or a brown powder, soluble in hot alcohol, partly soluble in boiling water.

**Constituents**

The main active constituents are 25-40% of barbaloin (mixture of aloein A and B), and their respective 6-O-p-coumaroyl esters, 3-4% of 7-hydroxyaloin A and B and their 6-O-p-coumaroyl esters (characteristic for Barbados aloes). All these compounds are aloe-emodin anthrone-C-glycosides. Small amounts of the aglycones aloe-emodin and
Drugs containing anthraquinone and naphthoquinone derivatives

Chrysophanol are also present. Other constituents are 5-methylchromone glycosides, mainly the 8-glucosyl derivative aloeresin B with smaller amounts of its coumaroyl and cinnamoyl esters.

![Chemical structures of aloin A and B, 7-hydroxyaloin A and B and aloe--emodin](image)

**Figure 12.62-66**
The structure of aloin A and B, 7-hydroxyaloin A and B and aloe-emodin.

**Uses**
Therapeutic indications include the short term treatment of occasional constipation. It should be highlighted that aloes are the most powerful laxatives among drugs containing anthranoids. Aloe gel is frequently used in dermatology. This is a liquid containing mucilage and obtained by mechanical pressure from the epidermic cells of *A. barbadensis*.

**Dosage**
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

*Adults, elderly and children over 10 years*: preparations are equivalent to 10-30 mg of hydroxyanthracene derivatives, calculated as barbaloin, to be taken in one dose daily at night. The drug and its preparations are not recommended for children under 10 years of age.

**Overdose**
It is similar to the other laxative drugs (see above).

**Contra-indication**
It is similar to the other laxative drugs (see above).
Special warnings and special precautions for use
It is similar to the other laxative drugs (see above).

Interactions with other medicaments and other forms of interactions
It is similar to the other laxative drugs (see above).

Undesirable effects
It is similar to the other laxative drugs (see above).

Pregnancy and lactation
It is similar to the other laxative drugs (see above).

12.4 Dianthrone derivatives
These are compounds derived from two anthrone molecules. They readily form as a result of mild oxidation of anthrone or mixed anthrones. They can be found in species of *Cassia*, *Rheum* and *Rhamnus*. In this group the sennidins, aglycones of the sennosides, are among the best-known compounds. It should be noted that two chiral centres (at C-10 and C-10') are present in the dianthrones, and for a compound having two identical anthrone moieties, e.g. sennidin A, two forms (the 10S, 10'S and 10R, 10'R) are possible together with the meso form (sennidin B) (Fig. 12.67-12.68).

![Structure of sennidin A and B](image-url)

**Figure 12.67-68**
The structure of sennidin A and B.

Drugs

*Sennae folium*

Plants
*Cassia angustifolia* Vahl. - Tinnevelly senna and/or *C. acutifolia* Delile - Alexandrian senna (Caesalpiniaceae)
The senna plants are small shrubs. *C. acutifolia* is indigenous to tropical Africa and is cultivated in Sudan. *C. angustifolia* is native to Somaliland, Arabia and is cultivated in South India (Tinnevelly).

**Drug**

*Sennae folium* (Senna leaf, Ph. Eur.). **Other Drug** *Sennae folii extractum siccum normatum* (Senna leaf dry extract, standardised, Ph. Eur.).

Senna leaf consists of the dried leaflets of *Cassia senna* L. (*C. acutifolia* Delile), known as Alexandrian or Khartoum senna, or *Cassia angustifolia* Vahl, known as Tinnevelly senna, or a mixture of the two species. It contains not less than 2.5% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried drug. Senna leaf has a slight characteristic odour.

Standardised senna leaf dry extract is produced from Senna leaf. It contains not less than 5.5% and not more than 8.0% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried extract. The measured content does not deviate from the value stated on the label by more than ± 10%. The extract is produced from the drug and ethanol 50 to 80% *V/V* with an appropriate procedure. Brownish or brown powder.
Constituents
The main active constituents are sennoside A and B (3%), which are rhein-dianthrone
diglucosides. Smaller amounts of other dianthrone diglucosides, monoanthraquinone
glicosides and aglycones are also present.

Figure 12.70-73
The structure of sennoside A, B, C and D.

Uses
Therapeutic indications include the short term treatment of occasional constipation.

Dosage
The correct individual dose is the smallest required to produce a comfortable soft-
formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 15-30 mg of
hydroxyanthracene derivatives, calculated as sennoside B, to be taken once daily at
night. The drug and its preparations are not recommended for children under 10 years of
age.

Overdose
It is similar to the other laxative drugs (see above).

Contra-indication
It is similar to the other laxative drugs (see above).

Special warnings and special precautions for use
It is similar to the other laxative drugs (see above).
Interactions with other medicaments and other forms of interactions
It is similar to the other laxative drugs (see above).

Undesirable effects
It is similar to the other laxative drugs (see above).

Pregnancy and lactation
It is similar to the other laxative drugs (see above).

**Sennae fructus acutifoliae**

**Plant**
*Cassia acutifolia* Delile – Alexandrian senna (Caesalpiniaceae)

**Drug**
*Sennae fructus acutifoliae* (Senna pods, Alexandrian, Ph. Eur.).

Alexandrian senna pods consist of the dried fruits of *Cassia senna* L. (*C. acutifolia* Delile). They contain not less than 3.4% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried drug. Alexandrian senna pods have a slight odour.

Constituents
The main active constituents are sennoside A and B (ca. 4%), which are rhein-dianthrone diglucosides. Smaller amounts of other dianthrone diglucosides, monoantraquinone glucosides and aglycones are also present.
Uses
Therapeutic indications include the short term treatment of occasional constipation.

Dosage
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 15-30 mg of hydroxyanthracene derivatives, calculated as sennoside B, to be taken once daily at night. The drug and its preparations are not recommended for children under 10 years of age.

Overdose
It is similar to the other laxative drugs (see above).

Contra-indication
It is similar to the other laxative drugs (see above).

Special warnings and special precautions for use
It is similar to the other laxative drugs (see above).

Interactions with other medicaments and other forms of interactions
It is similar to the other laxative drugs (see above).

Undesirable effects
It is similar to the other laxative drugs (see above).

Pregnancy and lactation
It is similar to the other laxative drugs (see above).

Sennae fructus angustifoliiæ

Plant
*Cassia angustifolia* Vahl. - Tinnevelly senna (Caesalpiniaceae)

Drug
*Sennae fructus angustifoliiæ* (Senna pods, Tinnevelly, Ph. Eur.).

Tinnevelly senna pods consist of the dried fruits of *Cassia angustifolia* Vahl. They contain not less than 2.2% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried drug. Tinnevelly senna pods have a slight odour.

Constituents
The main active constituents are sennoside A and B (ca. 3%), which are rhain-dianthrone diglucosides. Smaller amounts of other dianthrone diglucosides, monoantraquinone glucosides and aglycones are also present.

Uses
Therapeutic indications include the short term treatment of occasional constipation.
Drugs containing anthraquinone and naphthoquinone derivatives

Dosage
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 15-30 mg of hydroxyanthracene derivatives, calculated as sennoside B, to be taken once daily at night. The drug and its preparations are not recommended for children under 10 years of age.

Overdose
It is similar to the other laxative drugs (see above).

Contra-indication
It is similar to the other laxative drugs (see above).

Special warnings and special precautions for use
It is similar to the other laxative drugs (see above).

Interactions with other medicaments and other forms of interactions
It is similar to the other laxative drugs (see above).

Undesirable effects
It is similar to the other laxative drugs (see above).

Pregnancy and lactation
It is similar to the other laxative drugs (see above).

12.5 Naphthodianthrone derivatives
Hypericin is the most well-known example of naphthodianthrone derivatives. The large chromophore system in the molecule means that it can cause photosensitivity when ingested beyond threshold amounts. Photosensitivity is often seen in animals that have been allowed to graze on St. John's Wort. Because hypericin accumulates preferentially in cancerous tissues, it is also used as an indicator of cancerous cells. In addition, hypericin is under research as an agent in photodynamic therapy, whereby a biochemical is absorbed by an organism to be later activated with spectrum-specific light from specialized lamps or laser sources, for therapeutic purposes. The antibacterial and antiviral effects of hypericin are also believed to arise from its ability for photo-oxidation of cells and viral particles.

Drugs

Hyperici herba

Plant
Hypericum perforatum L. – St. John’s Wort (Hypericaceae)
The plant is abundant throughout Europe in grasslands, woodlands and hedges, extending to the Himalayas and Asia. It is an herbaceous perennial with bright yellow flowers.

Figure 12.75
St. John’s Wort (*Hypericum perforatum* L.)

**Drug**

*Hyperici herba* (St. John’s Wort, Ph. Eur.). **Other Drug** *Hypericum perforatum ad praeparationes homeopathicas* (Hypericum for homoeopathic preparations, Ph. Eur.).

St. John’s Wort consists of the whole or cut, dried flowering tops of *Hypericum perforatum* L., harvested during flowering. It contains not less than 0.08% of total flavonoids, expressed as hypericin and calculated with reference to the dried drug.

Figure 12.76
*Hyperici herba* (St. John’s Wort)
Constituents

The main active constituents are naphthodianthrones, phloroglucinols and flavonoids. Naphthodianthrones (0.05-0.3%), consisting mainly of hypericin and pseudohypericin, accumulate primarily in the flowers and buds. Protohypericin and protopseudohypericin are transformed into hypericin and pseudohypericin respectively on exposure to light. The principal phloroglucinols are hyperforin (2-4%) and adhyperforin. Both compounds have limited stability and their oxidated derivatives are also present. The main flavonoids (2-4%) include hyperoside, quercitrin, isoquercitrin and rutin (quercetin glycosides). Biflavonoids (e.g. amentoflavone) occur mainly in the flowers. Other constituents include chlorogenic acid, tannins and essential oil (0.1%) containing monoterpenes.

![Hypericin](image1)

**Figure 12.77-80**
The structure of hypericin, pseudohypericin, hyperforin and hyperoside.

Uses

Therapeutic indications include the treatment of mild or mild to moderate depressive episodes. Traditional herbal medicinal products of the drug are used for the symptomatic treatment of minor inflammations of the skin (such as sunburn) and as an aid in healing of minor wounds.

Dosage

Preparations based on hydroalcoholic extracts (50-60% ethanol):

*Adults, elderly and children over 12 years*: 450-1050 mg of hydroalcoholic dry extracts with drug-to-extract ratios of 2.5-5:1, 4-7:1, 5-7:1, daily.
Herbal tinctures and teas:
3-4.5 ml of tincture (1:5, ethanol 60% V/V), daily and 2-4 g of the drug as an infusion, daily.
Children from 6 to 12 years under medical supervision only: half the adult dose.

Overdose
Serious phototoxic reactions may occur at much higher dosages than used therapeutically (3600 mg of hydroalcoholic extract containing 11.25 mg of hypericin). Typical phototoxic symptoms include rash, pruritus and erythema. During treatment exposure to direct sunlight should be avoided.

Contra-indication
Hypersensitivity to the active substance may occur. Hypericum extracts must not be used concomitantly with cyclosporine, tacrolimus, digoxin, amprenavir, indinavir and other protease-inhibitors, irinotecan and other cytostatic agents.

Special warnings and special precautions for use
As with all antidepressant treatments, full manifestation of the therapeutic effect may take 3-4 weeks. There is a risk of suicide, particularly at the beginning of treatment, due to the delay between treatment and clinical improvement. If a significant treatment response in depressive disorders is not apparent after 4 weeks, the medication should be discontinued.

Interactions with other medicaments and other forms of interactions
A number of interactions with preparations of St. John’s wort have been reported. Induction of several subtypes of the enzyme cytochrome P450 has been discussed as a potential mechanism of the interactions, but increased expression of the P-glycoprotein drug transporter has also been reported. Documented and hypothetical interactions of St. John’s wort are introduced in the following table.

Table 12.1 Documented and hypothetical interactions of St. John’s Wort

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV protease inhibitors</td>
<td>1,2</td>
<td>Insufficient therapy</td>
</tr>
<tr>
<td>HIV reverse transcriptase inhibitors</td>
<td>1</td>
<td>Insufficient therapy</td>
</tr>
<tr>
<td>Warfarin</td>
<td>1</td>
<td>Reduced anticoagulant effect</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>1,2</td>
<td>Rejection of transplanted organs</td>
</tr>
<tr>
<td>Combined oral contraceptives</td>
<td>1</td>
<td>Spotting between periods, unwanted pregnancy</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>1</td>
<td>Increased risk of epileptic seizure</td>
</tr>
<tr>
<td>Digoxin</td>
<td>2</td>
<td>Heart failure, heart rhythm problems</td>
</tr>
<tr>
<td>Theophylline</td>
<td>1</td>
<td>Insufficient asthma therapy</td>
</tr>
<tr>
<td>Triptans</td>
<td>3</td>
<td>Serotonin syndrome</td>
</tr>
<tr>
<td>SSRIs</td>
<td>3</td>
<td>Serotonin syndrome</td>
</tr>
</tbody>
</table>
Drugs containing anthraquinone and naphthoquinone derivatives

**Mechanism:** 1 Hepatic enzyme induction; 2 Induction of the permeability glycoprotein; 3 Synergistic effects with serotonin reuptake inhibitors

**Undesirable effects**

Gastrointestinal disorders, allergic reactions of the skin, fatigue and restlessness may occur. The frequency is not known. Fair-skinned individuals may react with intensified sunburn-like symptoms under intense sunlight.

**Pregnancy and lactation**

In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
Chapter 13

Drugs containing flavonoids

Flavonoids are the largest group of naturally occurring phenols. Today more than 3000 of these compounds are known. Chemically they are diphenyl-propanes (C₆-C₃-C₆). Flavonoids are formed from three acetate units and a phenylpropane unit (Figure 13.1). They can be classified according to the binding site of C₆ part: flavonoids: α-binding site; isoflavonoids: β-binding site and neoflavonoids: γ-binding site (Figure 13.1). They are also classified according to the state of oxygenation of the C₃ unit (Figure 13.2). Dimeric compounds with e.g. 5’-8-carbon-carbon linkage are also known (isoflavonoids, e.g. amentoflavone, see Figure 13.3).

Most flavonoids have yellow colour, and they are more common in higher plants, where they are localised in the cell sap. Flavonoids are used as chemotaxonomic markers. They occur both in the free state and as glycosides (mostly in O-glycoside form, but a considerable number of C-glycosides are known). Flavonoid-glycosides are soluble in water and alcohol, but insoluble in organic solvents. In alkaline solution (NH₃ steam or NaOH) flavonoids produce intensive yellow colour (in the case of flavanon, isoflavon types this colour is pale; in the case of chalcones this colour is orange). With FeCl₃, flavonoids produce blue or green colour, if they have free -OH (hydroxyl) group on the fifth carbon atom. Flavonoids form a chelate complex (which shows orange fluorescence) with basic lead-(II)-acetate. 5-hydroxy-flavons and flavonols form yellow fluorescent chelate complex with zirconium oxychloride (ZrOCl₂). 5-hydroxy-flavons and flavonols form yellow chelate complex with aluminium-salts (AlCl₃) (Figure 13.4). This complex shows yellowish-green fluorescence under UV-light. This complex dissolves after treatment with hydrochloric acid. 5-hydroxy-flavons and flavonols form borine-complex with oxalic-boric acid solution, which shows yellow fluorescence under UV-light.

Flavonoids have many important physiological roles in plants:
- Attract insects – they provide the yellow colour of flowers (pollination)
- Repellents, insecticide materials
  - e.g. rotenoids (Figure 13.5) (Derris sp., Tephrosia sp., Amorpha sp.)
    - Phytoalexins – they protect plants from infections caused by fungi or bacteria (phytoalexins = „plant antibodies“)
  - e.g. pterocarpans (Figure 13.5) (Fabaceae)
    - Enzyme inhibitors, take part in oxidation-reduction processes (antioxidant, radical scavengers)
    - Influence plant growth
    - Colouring matters (e.g. haematoxilin in Hematoxylon sp.)

Plants containing flavonoids are used in medicine and phytotherapy for different purposes. They have different properties. Some flavonoids decrease the permeability of capillary vessels and increase the resistance of capillaries [e.g. Vitamin P (citrin = hesperidin + eriodictin) and rutin]. They have anti-inflammatory activity and prevent oedema formation, therefore they can be used for treating varicose veins [e.g. the product Rutascorbin, hydroxyethylrutoside (in the product Venoruton)]. Procyanidins are coronary artery dilators and cardiac tonics (e.g. Crataegus sp., Ginkgo sp.). They have
diuretic activity (e.g. *Betula, Solidago, Viola, Orthosiphon, Ononis* sp.). *Citrus* flavonoids (e.g. nobiletin, tangeretin) showed anti-allergic effect. Other effects include diaphoretic (e.g. *Tilia, Sambucus, Filipendula*), spasmylytic (apigenin in chamomile), isoliquiritigenin in liquorice root), anti-hepatotoxic and choleretic (*Silybum, Helichrysum*) and phytooestrogen (isoflavonoids in soy bean). Phytooestrogens, which are chemically isoflavonoids, are similar both functionally and structurally to oestradiol and related sex hormones and exert weak oestrogenic effects. Phytooestrogens may have positive effects in the prevention of cancer, heart diseases and postmenopausal symptoms.

![Diagram of flavonoids, isoflavonoids, and neoflavonoids](image)

**Figure 13.1**
The building units and main groups of flavonoids.
Drugs containing flavonoids

Figure 13.2
Structural types of flavonoids.

Figure 13.3
The structure of amentoflavone.
**Drugs**

**Tiliae flos**

*Plants*

*Tilia cordata* Mill. (Small-leaved lime), *T. platyphyllos* Scop. (Large-leaved lime), *Tilia x vulgaris* Heyne (Lime) - (Tiliaceae)

*Tilia* is a genus of about 30 species of trees native throughout most of the temperate Northern Hemisphere. The genus occurs in Europe and eastern North America, but the greatest species diversity is found in Asia.
Drugs containing flavonoids

Figure 13.6
Small-leaved lime (*Tilia cordata* Mill.)

Figure 13.7
Large-leaved lime (*T. platyphyllos* Scop.)

**Drug**

*Tiliae flos* (Lime flower, Ph. Eur.)

Lime flower consists of the whole, dried inflorescence of *Tilia cordata* Miller, of *Tilia platyphyllos* Scop., of *Tilia × vulgaris* Heyne or a mixture of these. Lime flower has a faint aromatic odour and a faint, sweet and mucilaginous taste. The drug has to be
checked for the presence of *T. argentea* (silver lime)! This plant contains stellate hairs on the abaxial surfaces of the leaves. Its drug has narcotic smell and unpleasant taste.

**Figure 13.8**
Silver lime (*Tilia argentea* L.)

**Figure 13.9**
*Tiliae argenteae flos* (Silver lime flower)
Drugs containing flavonoids

Constituents

Lime flower contains 1% of flavonoids. The most characteristic flavonoids include astragalin (kaempferol-3-O-glycoside), isoquercitrin (quercetin-3-O-glycoside), quercitrin (quercetin-3-O-rhamnoside), tiliroside [kaempferol-3-(6"-p-coumaroil-glucoside)] and hyperoside (quercetin-3-O-galactoside). The drug contains 0.01-0.02% of essential oil, which is responsible for the faint odour of the dried drug. Other constituents include phenolic acids (e.g. caffeic acid, chlorogenic acid and p-coumaric acid), proanthocyanidins, tannins and 10% of mucilage (galactomannans).

Figure 13.10

*Tiliae flos* (Lime flower)

Figure 13.11-15

The structure of tiliroside [kaempferol-3-(6"-p-coumaroil-glucoside)], quercitrin (quercetin-3-O-rhamnoside), isoquercitrin (quercetin-3-O-glycoside), kaempferol and quercetin.
**Pharmacognosy 2**

**Uses**

Lime flower has multiple applications. Therapeutic indications include the treatment of common cold, unproductive cough and sore throat. It has antimicrobial, expectorant and diaphoretic effect. Traditional use of the drug includes the relief of mild symptoms of mental stress.

**Dosage**

Relief of symptoms of common cold and mild symptoms of mental stress:

*Adult and elderly daily dose*: Herbal tea: 1.5 g of the comminuted herbal substance in 150 ml of boiling water as an herbal infusion 2-4 times daily. Daily dose: 3-6 g. In liquid extract: single dose is 2 ml, 1-2 times daily. Daily dose: 2-4 ml. In tincture: single dose is 1 ml, 1-2 times daily. Daily dose: 1-2 ml.

*Children between 4 and 12 years of age*: Herbal tea: 1 g of the comminuted herbal substance in 150 ml of boiling water as an herbal infusion 2-4 times daily. Daily dose: 2-4 g. In case of mild symptoms of mental stress: the use in children under 12 years of age is not recommended.

**Contra-indications**

Hypersensitivity to the active substance may occur.

**Pregnancy and lactation**

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

**Sambuci flos**

**Plant**

*Sambucus nigra* L. – Elder (Caprifoliaceae)

This shrub or small tree is native throughout Europe and Western and Central Asia. This plant should be distinguished from *Sambucus ebulus* (danewort/dwarf elder) (Figure 13.17). It has unpleasant odour, purple anthers in the flowers, erected fruits. The fruits and seeds contain cyanogenetic glycosides. The consumption of few seeds can cause severe nausea and vomiting at children. The root of danewort (Ebuli radix) is used as a diuretic.
Figure 13.16
Elder (*Sambucus nigra* L.)

Figure 13.17
Danewort/Dwarf elder (*Sambucus ebulus* L.)

Drug

*Sambuci flos* (Elder flower, Ph. Eur.).

Elder flower consists of the dried flowers of *Sambucus nigra* L. It contains not less than 0.80% of flavonoids, calculated as isoquercitroside with reference to the dried drug.
Constituents

Elder flower contains approx. 3% of flavonoids (astragalin, isoquercitrin, quercetin, kaempferol, rutin and hyperoside). Other constituents include triterpenes (e.g. ursolic acid and oleanolic acid), sterols (e.g. β-sitosterol and stigmasterol), approx. 3% of phenolic acids (e.g. chlorogenic acid, p-coumaric acid and ferulic acid), 0.15% of essential oil and mucilage.

Uses

Elder flower is administered mainly as an herbal tea for the treatment of feverish diseases and the common cold. It acts as a diaphoretic but the mechanism is unclear. The drug also has diuretic properties. In ethnomedicine the fruits of *S. nigra* (*Sambuci fructus*) are also used because of their mild laxative effect.
Dosage

*Adolescents over 12 years of age, adults, elderly:* 2-5 g of dried drug or as an infusion, 3 times daily. Liquid extract (1:1, 25% V/V ethanol): 3-5 ml, 3 times daily. Tincture (1:5, 25% V/V ethanol): 10-25 ml, 3 times daily. The use is not recommended in children under 12 years of age.

Contraindications

Hypersensitivity to the active substance may occur. Patients with cardiac problems should not use diaphoretic drugs (e.g. *Tiliae* and *Sambuci flos*).

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

**Equiseti herba**

Plant

*Equisetum arvense* L. – Field horsetail (Equisetaceae)

*Equisetum arvense* is a herbaceous perennial plant, native throughout the arctic and temperate regions of the northern hemisphere. It has separate sterile, photosynthesizing and fertile spore-bearing stems, growing from a perennial underground rhizomatous...
stem system. The fertile stems are produced in early spring and are non-photosynthetic, while the green sterile stems start to grow after the fertile stems have wilted, and persist through the summer until the first autumn frosts. Sterile, green stems are collected as the drug. The presence of other *Equisetum* species should be excluded, mainly *E. palustre* (marsh horsetail) (Figure 13.23), because this plant contains toxic palustrine and deoxypalustrine (Figure 13.24-25). The shoots of *E. palustre* are shorter and its sporangia appear on the sterile shoot in June.

![Field horsetail (*Equisetum arvense* L.)](image)

**Figure 13.22**
Field horsetail (*Equisetum arvense* L.)
Drug

*Equiseti herba* (Equisetum stem, Ph. Eur.)

The drug is the whole or cut, dried sterile aerial parts of *Equisetum arvense* L. It contains minimum 0.3% of total flavonoids expressed as isoquercitrinoside calculated with reference to the dried drug.
Constituents

The drug contains approx. 8-10% of silicic acid and 1% of flavonoids. The most characteristic flavonoids are astragalin (kaempferol-3-O-glucoside), isoquercitrin (quercetin-3-O-glucoside) and hyperoside (quercetin-3-O-galactoside). Other constituents include approx. 1% of phenolic acids (e.g. chlorogenic and caffeic acid).

Figure 13.27-29

The structure of astragalin (kaempferol-3-O-glucoside), isoquercitrin (quercetin-3-O-glucoside) and hyperoside (quercetin-3-O-galactoside).
Drugs containing flavonoids

Uses

The drug and its traditional herbal medicinal products can be used to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints. It has diuretic, antibacterial and anti-inflammatory activities.

Dosage

Adults and children over 12 years of age: 2-3 g of the powdered drug into 250 ml boiling water, prepared as tea infusion, 3 times daily.

Special warnings and precautions

The use is not recommended in children under 12 years of age because of the lack of available experience. If complaints or symptoms such as fever, dysuria, spasm or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Contra-indications

Conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal diseases).

Pregnancy and lactation

No data available. In accordance with general medical practice, horsetail and its preparations should not be used during pregnancy and lactation without medical advice.

Crataegi folium cum flore

Plants

*Crataegus monogyna* Jacq., *C. laevigata* DC. (syn. *C. oxyacantha* L.) – Common and Midland Hawthorn (Rosaceae)

*Crataegus monogyna* is a species of hawthorn native to Europe, northwest Africa and western Asia. It has been introduced to many other parts of the world where it is an invasive weed. *C. laevigata* is native to western and central Europe. In the flowers of *C. monogyna* there are yellow anthers and only one stigma can be found, while the flowers of *C. laevigata* contain deep purple anthers and two stigmas. *Crataegus* species have berry-like false fruits, but structurally they are pome fruits.
Drug

Crataegi folium cum flore (Hawthorn leaf and flower; Ph. Eur.). **Other Drug** Crataegi folii cum flore extractum siccum (Hawthorn leaf and flower dry extract; Ph. Eur.)

The drug consists of the whole or cut, dried flower-bearing branches of *Crataegus monogyna* Jacq. (Lindm.), *C. laevigata* (Poiret) D.C. (*C. oxyacanthoides* Thuill.) or their hybrids or, more rarely, other European *Crataegus* species including *C. pentagyna* Waldst. et Kit. exWilld., *C. nigra* Waldst. et Kit., *C. azarolus* L. It contains minimum 1.5% of flavonoids expressed as hyperoside and calculated with reference to the dried drug.

Crataegi folii cum flore extractum siccum: The extract is produced from *Hawthorn leaf and flower.*
Drugs containing flavonoids

Content:
- for aqueous extracts: minimum 2.5% of flavonoids, expressed as hyperoside (dried extract);
- for hydroalcoholic extracts: minimum 6.0% of flavonoids, expressed as hyperoside (dried extract).

The extract is produced from the drug by a suitable procedure using either water or a hydroalcoholic solvent equivalent in strength to a minimum of 45% \( V/V \) ethanol. It is a light brown or greenish-brown powder.

Constituents

The major characteristic constituents are flavonoids (approx. 2%) such as vitexin (apigenin-8-C-glucoside), isovitexin (apigenin-6-C-glucoside), orientin (luteolin-8-C-glucoside), isoorientin (luteolin-6-C-glucoside), hyperoside (quercetin-3-O-galactoside) and rutin (quercetin-3-O-rutinoside). The drug contains 2.5-3% of procyanidins. They are based on the condensation of catechin and/or epicatechin with varying degrees of polymerisation. The most relevant are oligomeric procyanidins containing 2 to 8 monomeric units. Other constituents include tannins, triterpenes and phenolic acids (e.g. chlorogenic and caffeic acids).
Uses

Therapeutic indications include nervous heart complaints. The drug preparations support the cardiac and circulatory functions. Hydroalcoholic extracts of the drug can be used in the case of declining cardiac performance corresponding to Functional Capacity Class II as defined by the New York Heart Association (NYHA).

Classification of Functional Capacity by the New York Heart Association:

Class II.: Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.

Dosage

Adult and elderly

Preparations based on hydroalcoholic extracts: these extracts (drug to extract ratio 4-7:1) with defined oligomeric procyanidin or flavonoid content, 160-900 mg daily

Herbal teas and other preparations: 1-1.5 g of comminuted drug as an infusion, 3-4 times daily. Tincture: 20 drops 2-3 times daily.

Special warnings and precautions for use

A doctor must be consulted in cases where symptoms continue unchanged for longer than 6 weeks, or when fluid accumulates in the legs. Medical intervention is absolutely necessary when pain occurs in the region of the heart, spreading out to the arms, upper abdomen or the area around the neck or in cases of respiratory distress (dyspnoea).
Pregnancy and lactation

No human data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

**Crataegi fructus**

**Plants**

*Crataegus monogyna* Jacq., *C. laevigata* DC. (syn. *C. oxyacantha* L.) – Common and Midland Hawthorn (Rosaceae)

**Drug**

*Crataegi fructus* (Hawthorn berries, Ph. Eur.).

Hawthorn berries consist of the dried false fruits of *Crataegus monogyna* Jacq. (Lindm.), or *Crataegus laevigata* (Poir.) D.C. (synonym: *Crataegus oxyacantha* L.) or their hybrids or a mixture of these false fruits. They contain not less than 1.0% of procyanidins, calculated as cyanidin chloride with reference to the dried drug. The false fruit has a sweet mucilaginous taste.

![Crataegi fructus](image)

**Figure 13.37**

*Crataegi fructus* (Hawthorn berries)

**Constituents**

The active constituents of the drug are similar to those of the leaf and flower: procyanidins, flavonoids, triterpenes, phenolic acids, and ascorbic acids.

**Uses**

Therapeutic indications include cardiac complaints. The drug and its preparations support the cardiac and circulatory functions.
Dosage

*Adults:* hydroalcoholic extracts (1:1.3-3), 2-2.5 ml daily. Powdered hawthorn berries, 0.3-1 g three times daily or as an infusion; liquid extract (1:1 in 25% ethanol), 0.5-1 ml three times daily; tincture (1:5 in 45% ethanol), 1-2 ml three times daily.

Special warnings and precautions for use

A doctor must be consulted in cases where symptoms continue unchanged for longer than 6 weeks, or when fluid accumulates in the legs. Medical intervention is absolutely necessary when pain occurs in the region of the heart, spreading out to the arms, upper abdomen or the area around the neck or in cases of respiratory distress (dyspnoea).

Pregnancy and lactation

No human data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

**Violae herba cum flore**

Plants

*Viola tricolor* L. - Wild pansy, *V. arvensis* Murray - Field pansy (Violaceae)

*Viola tricolor* is a common European plant, *V. arvensis* is native to Europe, western Asia and North Africa.

![Figure 13.38](https://example.com/image.png)

*Figure 13.38*

Wild pansy (*Viola tricolor* L.)
Drugs containing flavonoids

Figure 13.39
Field pansy (Viola arvensis Murray)

Drug

*Viola* *arvensis* Murray

The drug consists of the dried flowering aerial parts of *Viola arvensis* Murray and/or *Viola tricolor* L. It contains minimum 1.5% of flavonoids, expressed as violanthin and calculated with reference to the dried drug.

Figure 13.40
*Viola* *tricolor* aerial parts

Constituents

The most important constituents of the drug are flavonoids (up to 3%) such as rutin (quercetin-3-O-rutinoside), quercetin (flavonol type), violanthin (flavon-C-glycoside) and luteolin-7-O-glucoside (flavone type). The flowers also contain anthocyanidins
such as violanin [delphinidin-3-(6-p-coumaroyl-rhamnosylglucoside)-5-glucoside]. The
drug contains approx. 0.1-0.3% of phenolic acid derivatives [e.g. salicylic acid, methyl
salicylate, violutin (methyl salicylate arabinosylglucoside)]. Other important
constituents are the carotenoids (e.g. violaxanthin, lutein and 15-cis-violaxanthin).
Other constituents include 10% of mucilage, 2.5% tannins, ascorbic acid and minerals
(mainly potassium salts). Saponins were not detected either in V. tricolor or in V.
arvensis, contrary to an earlier report of about 5% saponins in V. tricolor.

![Chemical structures](image)

Figure 13.41-44

The structure of quercetin, rutin (quercetin-3-O-rutinoside), luteolin-7-O-glucoside and
violanthin.

**Uses**

Therapeutic indications include skin disorders, such as eczema, seborrhoea, impetigo
and acne, as well as cradle cap and nappy rash of infants. Efficacy in these indications is
plausible on the basis of human experience and long-standing use.

**Dosage**

**Internal use**

*Adults*: 1.5-4 g of the drug as an infusion three times daily; fluid extract (1:1, ethanol
25%) 2-4 ml three times daily; dry extract (6:1) 2-4 g daily

*Children*: proportion of adult daily dose according to age or body weight

**External use**

3-4 g of the drug in 150 ml of hot water as a compress or poultice, several times daily

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the product should not
be used during pregnancy or lactation without medical advice.
Drugs containing flavonoids

**Gingko folium**

**Plant**

*Ginkgo biloba* L. – Ginkgo (Ginkgoaceae)

Ginkgo has no close living relatives. This plant is a living fossil and it is native to China, but the tree is widely cultivated.

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**Figure 13.45**

Ginkgo (*Ginkgo biloba* L.)

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**Drug**

*Ginkgo folium* (Gingko leaf, Ph. Eur.).

The drug consists of the whole or fragmented, dried leaf of *Ginkgo biloba* L. It contains not less than 0.5% of flavonoids, expressed as flavone glycosides and calculated with reference to the dried drug. Ginkgo leaf is greyish or yellowish-green or yellowish-brown.

*Standardised Ginkgo dry extract:* It consists of an extract produced from ginkgo leaf. It contains 22.0 to 27.0% of flavonoids, expressed as flavone glycosides, and 5.0 to 7.0% of terpene lactones including 2.8 to 3.4 % of ginkgolides A, B and C, and 2.6 to 3.2% of bilobalide.
Constituents

The active constituents of the drug are flavonoids and terpenes. The main flavonoids are mono-, di- and triglycosides of the flavonols quercetin, kaempferol and isorhamnatin. Diglycosides esterified with p-coumaric acid are also present. Other flavonoids include biflavones (e.g. bilobetin, amentoflavone, ginkgetin), monomeric flavan-3-ols such as (+)-catechin, (-)-epicatechin, (-)-epigallocatechin and (+)-gallocatechin, and oligomeric and polymeric procyanidins. The principal terpenes are diterpene trilactones called ginkgolides (A, B and C), which differ in the number and position of their hydroxyl groups, and the sesquiterpene trilactone bilobalide. The dried leaf of pharmacopoeial quality should contain not less than 0.1% of terpene lactones, calculated as the sum of bilobalide and ginkkolide A, B and C. Long chain alkylphenolic acids (ginkgolic acid), organic acids and phytosterols are also present.
Drugs containing flavonoids

Figure 13.47-49
The structure of biflavones (bilobetin, amentoflavon, ginkgetin), diterpene lactones (ginkgolide A, B, C and D) and sesquiterpene lactone (bilobalide).

Uses
Therapeutic indications include the symptomatic treatment of mild to moderate dementia syndromes including primary degenerative dementia, vascular dementia and mixed forms; cerebral insufficiency; neurosensory disturbances such as dizziness/vertigo and tinnitus; enhancement of cognitive performance; and symptomatic treatment of peripheral arterial occlusive disease (intermittent claudication).

Dosage

*Adult and elderly daily dose:* 120-240 mg of standardized ginkgo dry extract divided into 2-3 doses and equivalent preparations. No data available for children.

In cases of dementia, treatment should be maintained for at least 12 weeks. After this period an evaluation should be carried out to determine whether the patient is a responder or a non-responder. The treatment should be continued only in the case of a responder.

Undesirable effects
In rare cases, mild gastrointestinal disorders, headache or allergic skin reactions have been reported.

Overdose
No significant adverse reactions have been reported in patients ingesting up to 600 mg of dry extract in single doses.

Contra-indications
Hypersensibility or intolerance to ginkgo leaf preparations may develop.
Interaction with other medicaments and other form of interaction

An interaction with substances that inhibit blood coagulation cannot be excluded.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Hyperici herba

Plant

*Hypericum perforatum* L. – St. John’s Wort (Hypericaceae)

The description of this plant can be found in Chapter 12.

Ribis nigri folium

Plant

*Ribes nigrum* L. - Blackcurrant (Grossulariaceae)

This shrub is native to temperate parts of central and northern Europe and northern Asia where it prefers damp fertile soils and is widely cultivated both commercially and domestically.

![Blackcurrant](image)

**Figure 13.50**

Blackcurrant (*Ribes nigrum* L.)

Drug

*Ribis nigri folium* (Blackcurrant leaf). **Other Drug** *Ribis nigri fructus* (Blackcurrant fruit)
The drug consists of the dried leaves of *Ribes nigrum* L. It contains not less than 1.5% of flavonoids, expressed as rutin and calculated with reference to the dried drug. In phytotherapy the fruits can also be used.

**Figure 13.51**

*Ribis nigri folium* (Blackcurrant leaf)

Constituents

The characteristic constituents of the leaf are approx. 0.5% of flavonoids (mono- and diglycosides of quercetin and kaempferol mainly isoquercitrin and rutin, myricetin), proanthocyanidins (e.g. dimeric prodelphinidin) and hydroxycinnamic acid derivatives including caffeic, chlorogenic and *p*-coumaric acids. The leaf contains traces of essential oil. In the fruit the following constituents are present: 10% of sugar, organic acids, flavonol glycosides and anthocyanidins (cyanidin-, delphinidin-glucoside).
Uses

The preparations of the leaves can be used as an adjuvant in the treatment of rheumatic conditions. The preparations of the fruits have a mild antihypertensive, antioxidant and antifungal activities. The fresh products (e.g. fruit juice, wine and jam) play a role in the prevention of atherosclerosis and the treatment of anaemia.

Dosage (of the leaves)

*Adults:* Dried leaf as an infusion (20-50 g/L, infused for 15 minutes), 250-500 ml daily. Fluid extract (1:1), 5 ml twice daily, taken before meals.

Interaction with other medicaments and other form of interaction

The leaf has a diuretic action, therefore it should not be taken simultaneously with diuretics indicated for cardiac or renal insufficiency except on medical advice.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Stoechados flos (= Helichrysi flos)**

**Plant**

*Helichrysum arenarium* (L.) Moench. – Dwarf everlast (Asteraceae)

This perennial plant is found in Eastern France to Denmark as well as in the mountains of Uzbekistan on sandy grasslands, and heathland. It is also widely spread on the Dalmatian Coast in Croatia. The flower heads are arranged in a loose panicle.

**Drug**

*Stoechados flos* (Dwarf everlast flowers, Ph. Helv.)

The drug consists of the dried flowers of *Helichrysum arenarium* (L.) Moench.
Drugs containing flavonoids

Constituents
The main characteristic constituents of the drug are flavonoids (up to 0.4%) mainly the chalcon isosalipurpuroside, helicrysin (naringenin-5-O-glucoside) and the flavon-type apigenin, luteolin and their glucosides. Other constituents include coumarins (e.g. umbelliferone, scopoletin), sesquiterpene lactones and 0.05% essential oil.

Uses
The drug has choleretic and spasmolytic effects. The therapeutic indications include the treatment of chronic gallbladder inflammation and the spasmodic pains of gallbladder. Efficacy in these indications is plausible on the basis of long-standing use.

Dosage
Adults: 3 g of the drug as an infusion, daily.
Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

**Populi gemma**

**Plant**

*Populus nigra* L. – Black poplar (Salicaceae)

This tree is native to Europe, southwest and central Asia, and northwest Africa.

**Drug**

*Populi gemma* (Black poplar buds or balm of Gilead buds)

The drug consists of the dried, unopened leaf buds of *Populus nigra* L.

![Populi gemma](image)

**Figure 13.57**

*Populi gemma* (Black poplar buds or balm of Gilead buds)

**Constituents**

The main characteristic constituents of the drug are different types of flavonoids (e.g. crysin, apigenin, pinocembrin) and phenol glycosides (salicin, populin). Other constituents include 0.5% of essential oil (containing mainly sesquiterpenes) and wax.
Drugs containing flavonoids

**Figure 13.58-60**
The structure of pinocembrin (flavanon type), crysin (flavon type) and apigenin (flavon type).

**Uses**
The drug has anti-inflammatory, antibacterial, diuretic and expectorant activities. Its preparations stimulate wound healing. Therapeutic uses include superficial skin injuries, external hemorrhoids, frostbite and sunburn. Cosmetic industry also uses the drug in different products, e.g. creams, hair tonic.

**Dosage**
Semi-solid preparations equivalent to 20-30% of the drug.

**Contra-indications**
Sensitivity to poplar buds, propolis or salycilate.

**Side effects**
Occasional allergic skin reaction.

**Pregnancy and lactation**
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
**Propolis**

**Source**

*Apis mellifica* L. – Honey bee (Apidae)

**Drug**

*Propolis* (Propolis or bee glue)

Propolis is the special material with which the honey bee seals cracks and crevices, and varnishes surfaces within the hive. Like honey, its composition varies according to botanical and geographical source. In temperate regions of Europe the resinous coating of poplar buds (*Populus nigra* and other *Populus* sp.) forms a major collection source for the bees.

**Constituents**

The main characteristic constituents of the drug are flavonoids (up to 6%), cinnamic acid derivatives (e.g. *p*-coumaric acid, caffeeic acid, ferulic acid, vanillin, eugenol), mono- and sesquiterpenes, lipids, wax and microelements (e.g. Mn, Cu, Zn).

**Uses**

Propolis can be used in apitherapy. It has been shown to exhibit antiseptic, anti-inflammatory, antibacterial, antiviral and local anaesthetic properties. The drug and its preparations can be used in the case of different inflammations: gum, sore throat, ulceration of the leg.

**Dosage**

Tincture (90-96% ethanol), 20 drops, three times daily

**Contra-indications**

Sensitivity to poplar buds, propolis or salycilate. Allergy may occur.

**Side effects**

Occasional allergic skin reaction.

**Pregnancy and lactation**

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

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**13.2 Flavonolignans**

Flavonolignans are natural phenols composed of a flavonoid part and a lignan part. A number of flavonolignans arise from oxidative coupling of the 3-hydroxyflavanone taxifolin with coniferyl alcohol. The most important flavonolignans, e.g. silybin and silymarin, are produced by *Silybum marianum* (L.) Gärtn. These constituents have anti-hepatotoxic properties. Three flavonolignans derived from the flavone tricin have been isolated from the herb *Avena sativa*. Rhodiolin, the product of the oxidative coupling of coniferyl alcohol with the 7,8-dihydroxy grouping of the flavonol herbacetin, can be found in the rhizome of *Rhodiola rosea*. 
Drugs containing flavonoids

Figure 13.61-62
The structure of taxifolin and coniferyl alcohol.

Drugs

Silybi mariani fructus

Plant

*Silybum marianum* (L.) Gärtn. - Milk thistle (Marian thistle) (Asteraceae)

The plant is native to the Mediterranean region, from Southern Europe to Asia, it is now found throughout the world. As a cultivated plant it is grown as an annual or biennial ornamental for its attractive foliage.
Figure 13.63
Marian thistle (*Silybum marianum* (L.) Gärtn.)

**Drug**

*Silybi mariani fructus* (Milk thistle fruit, Ph. Eur.). **Other Drug** *Silybi mariani extractum siccum raffinatum et normatum* (Milk thistle refined and standardized dry extract, Ph. Eur.)

The drug consists of the mature fruit, devoid of the pappus, of *Silybum marianum* L. Gaertner. It contains minimum 1.5% of silymarin expressed as silibinin and calculated with reference to the dried drug.

Milk thistle dry extract consists of a refined and standardized dry extract produced from milk thistle fruit. It contains 90% of the nominal content of silymarin, expressed as silibinin, stated on the label. The nominal content of silymarin is within the range 30-65% m/m, calculated with reference to the dried extract.
Constituents
The active constituents of the drug are flavonolignans, collectively known as silymarin (1.5-3% by HPLC). Silymarin consists of silibinin, isosilibinin, silicristin and silidianin. Other constituents include the flavonoids taxifolin, quercetin, kaempferol, apigenin and eriodictyol; fatty oil (20-30%); phytosterols; the dimer dehydrodiconiferylalcohol, 5,7-dihydroxychromone and essential oil.

![Silibinin A and B (diastereoisomers)](image)

Figure 13.65-67
The structure of silibinin A and B, silicristin and silidianin.
Uses
Therapeutic indications of the drug include toxic liver damage, supportive treatment in patients with chronic inflammatory liver conditions and hepatic cirrhosis.

Dosage
*Adult daily dose:* Solid or liquid extract equivalent to 154-324 mg of silymarin (HPLC method of the European Pharmacopoeia) or 200-420 mg of silymarin (UV spectroscopic method), taken in 2-3 divided doses. Silymarin can be dissolved poorly in water, therefore preparation of an infusion from the drug is not recommended.

Interaction with other medicaments and other form of interaction
It can moderately decrease the plasma level of indinavir (used in AIDS therapy).

Pregnancy and lactation
No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.
14.1 Tannins

Tannins are polyphenolic secondary metabolites of higher plants. They comprise either galloyl esters and their derivatives (gallotannins, ellagitannins and complex tannins) or they are oligomeric and polymeric proanthocyanidins and can possess different interflavanyl coupling and substitution patterns (condensed tannins).

The hydrolysable tannins are gallotannins and ellagitannins (Figure 14.1-6). They are polyesters of glucose and can be hydrolysed by acids or enzymes such as tannase. They release sugar upon hydrolysis. Gallotannins are the simplest hydrolysable tannins, containing a polyphenolic and a polyol residue (mostly derived from D-glucose). Tannic acid is a polymer of about eight monomers of gallic acid and glucose. Ellagitannins are formed from the gallotannins by the oxidative coupling of at least two galloyl units, yielding an axially chiral hexahydroxydiphenoyl (HHDP) unit. Ellagitannins are unstable and hydrolysed over time with formation of free ellagic acid and decrease of their solubility. Condensed tannins (Figure 14.7-11) are not very stable; they can be oxidized into soluble phlobaphens, which have no tanning properties anymore. Condensed and hydrolysable tannins can be distinguished with ferric chloride reaction but this reaction is not specific, every compound containing phenolic OH-groups gives this reaction. The structure of the complex can be seen in Figure 14.12. The color of the complex depends on the number and the position of the phenolic OH-groups. The hydrolysable-type tannins (they contain gallic and ellagic acids) produce blue color with ferric-(III)-chloride and the condensed-type tannins (catechins) green (greenish-blue), respectively. This reaction is accomplished in neutral or mildly acidic medium. The Fe$^{3+}$-ions can produce chelate complexes with phenolic, electron donor OH-groups located in ortho positions.

Tannins can be distinguished from other phenolic compounds based on their chemical reactivities and biological activities. Tannins were traditionally used for “tanning”, converting animal hides to leather. This refers to one of their leading properties, the ability to interact with proteins and precipitate them. Tannin-containing drugs have been used traditionally as styptics. Internally they can be used for the protection of inflamed surfaces of mouth and throat. They have antidiarrhoeal effect, and they have been applied as antidotes in heavy metal and alkaloid poisoning.

The internal absorption of concomitantly administerd medicines may be delayed by tannin containing-drugs. For this reason, the product should be taken 1 hour or more before or after intake of other medicinal products. Allergic reactions and mucous membrane irritation have been reported, patients susceptible to allergic reactions should use tannin-containing drugs carefully or not use them at all. Safety during pregnancy and lactation, as well as in children under the age of 18 has not been established, therefore, the use of these drugs during pregnancy and lactation, as well as in children under the age of 18 is not recommended. Their use is contraindicated in inflammatory bowel diseases and constipation, as well. Long-term use of tannin-containing drugs may be hepatotoxic. If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted in all cases.
Derivatives of gallic acid and ellagic acid.

Figure 14.1-6
Derivatives of gallic acid and ellagic acid.

Figure 14.7-11
Derivatives of catechin.
Drugs containing polyphenols

![Chemical structure of polyphenols](image)

**Figure 14.12**
The complex developed after the reaction of phenolic OH-groups with FeCl₃.

## Drugs

### Quercus cortex

**Plant**

*Quercus robur* L. - Pedunculate oak, *Q. petraea* Liebl. - Sessile oak (Fagaceae)

These plants are native to Europe and the Caucasus. Oak bark is harvested in spring from March to April.

![Oak tree](image)

**Figure 14.13**
Pedunculate oak (*Quercus robur* L.)

**Drug**

*Quercus cortex* (Oak bark, Ph. Eur)

The drug is the cut and dried bark of the fresh young branches of *Quercus robur* L., *Q. petraea* (Matt.) Liebl. and *Q. pubescens* Willd. It contains not less than 3.0% of tannins, expressed as pyrogallol calculated with reference to the dried drug.
Constituents

Oak bark contains 8-20% tannins, hydrolyzable (gallotannins and elagitannins), condensed tannins, flavano-ellagittannins (acutissimins A an B, eugenigrandin A, guajavin B, stenophyllanin), procyanidinoellagitannin (mongolicanin), oligomeric proanthocyanidins, triterpenes (friedelin, friedelinol, 3-friedelanol), insoluble lipid polyesters (suberins) and volatile acids (acetic and formic acid).

Figure 14.14
Quercus cortex (Oak bark)

Figure 14.15-18
The structure of gallic acid, ellagic acid, catechin and gallocatechin.
Uses

It is used internally in diarrhoea, externally against pharyngitis (inflammation of the throat) and stomatitis (inflammation of the mucous membrane of the mouth), or hemorrhoids.

Dosage

*Adult and elderly daily dose:* 2 g of dried, ground drug should be boiled with 100 mL water for 5 minutes and filtered. This extract can be used to paint, gargle, or wash wounds, but it is recommended not to use for more than 1 week. Internally, in the case of severe diarrhoea, the single dose is 1 g, the maximum daily dose is 3 g, but do not use longer than 3 days. The dose of a dry extract is 140 mg, 4 times daily.

*Children:* The use in children and adolescents under 18 years of age is not recommended due to lack of adequate data.

*Overdose:* No case of overdose has been reported.

Interactions

Internal absorption of concomitantly administered medicine may be delayed. For this reason, the product should be taken 1 hour or more before or after intake of other medicinal products.

Contra-indications

Allergic reactions have been reported, but their frequency is unknown.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Gall

Plant

*Quercus infectoria* Oliv. – Aleppo oak (Fagaceae)

Drug

*Galla (Gall)*

It is an apple-like gall commonly found on many species of oak developing from the leaf buds due to chemicals injected by the larva of certain kinds of gall wasps.
Constituents
The characteristic constituents are tannins (derivatives of gallic acid, 40-60%), gallic acid and ellagic acid. The drug also contains starch.

![Chemical structures of gallic acid and ellagic acid](image)

**Figure 14.19**
*Galla* (Gall)

**Figure 14.20-21**
The structure of gallic acid and ellagic acid.

Uses
Externally the extract is traditionally used as adstringent, hemostatic, and for the treatment of thrush and gingivitis. However, the scientific documentation of these effects is sparse.

Dosage
*Adult and elderly daily dose:* Prepare a 1% decoction or tincture for a daily rinse.
**Ratanhiae radix**

**Plant**

*Krameria triandra* Ruiz et Pavon (syn: *Krameria lappacea* Burdet et Simpson) – Peruvian rhatany (Krameriaceae)

The plant is native to the mountain slopes of Peru and Bolivia.

**Drug**

*Ratanhiae radix* (Rhatany root, Ph. Eur.). **Other Drug** *Ratanhiae tinctura* (Rhatany tincture, Ph. Eur.)

The drug is the dried root of Peruvian rhatany, a perennial shrub. Rhatany root, known as Peruvian rhatany, consists of the dried, usually fragmented, underground organs of *Krameria triandra* Ruiz and Pavon. It contains not less than 5% of tannins, expressed as pyrogallol calculated with reference to the dried drug.

The tincture produced from Rhatany root contains not less than 1% m/m of tannins, expressed as pyrogallol.

![Figure 14.22](image)

*Ratanhiae radix* (Rhatany root)

**Constituents**

It contains 5-15% of catechin tannins, phlobaphenes („rhatania-red”) and neolignans.
Uses

It is traditionally used as adstringent, against stomatitis, bleeding of the gums, gingivitis (inflammation of the gums), and pharyngitis (especially as a tincture). However, the scientific documentation of these effects is sparse.

Dosage

*Adult and elderly daily dose:* If rhatany root is used internally, the single dose is 0.5-1.5 g, and the maximum daily dose is 1.5-4.5 g, but it should be used internally only for a short period of time. For external use, a 2% extract should be prepared with 5 minutes of boiling.

**Hamamelidis folium**

Plant

*Hamamelis virginiana* L. - Virginian witch hazel (Hamamelidaceae)

The plant is a deciduous large shrub native to eastern North America.

Drug

*Hamamelidis folium* (Hamamelis leaf, Ph. Eur.).

Hamamelis leaf consists of the whole or cut, dried leaf of *Hamamelis virginiana* L. It contains not less than 3% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.
Drugs containing polyphenols

Constituents
The characteristic constituents are tannins (5-10%), including condensed tannins, e.g. proanthocyanidin oligomers with catechin and/or gallocatechin units, hydrolysable tannins such as hamamelitannin, (+)-catechin, (+)-gallocatechin, (-)-epicatechin-gallate and (-)-epigallocatechin gallate. Other constituents are flavonoids, phenolic acids and essential oil.

Figure 14.26
Hamamelidis folium (Hamamelis leaf)

Figure 14.27-30
The structure of catechin, gallocatechin, epicatechin gallate and epigallocatechin gallate.
Uses

It is traditionally used for relief of minor skin inflammation and dryness of the skin, for the temporary relief of the symptoms associated with hemorrhoids, such as itching, burning sensation or pain, and used as a mouthwash for relief of minor inflammatory conditions of the oral mucosa.

Dosage

Adult and elderly daily dose: For cutaneous use, the tincture should be used several times daily in a strength corresponding to 5-10% in semisolid preparations. The dry extract in a strength corresponding to 1.3% as an ointment should be used several times daily. The average duration of use is 1 week. For anorectal use, the tincture in a strength corresponding to 5-10% in semisolid and liquid preparations should be used several times daily. Comminuted herbal substances should be used as decoction: 5-10g/250 ml, up to 3 times a day as impregnated dressings. For rectal use, one suppository containing 66 mg of dry extract (5-7.7:1; ethanol 30% m/m) should be used two or three times a day. The recommended duration of use is 4 days. For gargles, 2-4 ml tincture (1:10; ethanol 45% (diluted (1:3) with water) should be used three times daily, or comminuted herbal substance as herbal tea: 2-3 g up to 3 times a day.

Children: Due to the lack of adequate data the use is not recommended in children and adolescents under 18 years of age.

Overdose: No case of overdose has been reported.

Contraindications

Hypersensitivity to the active substance(s). Allergic contact dermatitis has been reported. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a qualified health care practitioner should be consulted. Available tests on carcinogenicity and genotoxicity did not give any reason for concern.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Tormentillae rhizoma

Plant

*Potentilla erecta* (L.) Rauschel (syn.: *Tormentilla erecta* L.) – Common tormentil (Rosaceae)

The plant is native to North and Middle Europe, as well as North Asia. It occurs frequently in the Hungarian Mountains and rarely in the Great Hungarian Plain. The plant can be cultivated.

Drug

*Tormentillae rhizoma* (Tormentil, Ph. Eur.). **Other Drug** *Tormentillae tinctura* (Tormentil tincture, Ph. Eur.)

The drug is the whole or cut, dried rhizome of *Potentilla erecta* (L.) Rausch. (*P. tormentilla* Stokes). It contains not less than 7% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.
The drug has a bitter taste.

The tincture produced from *Tormentil* contains minimum 1.5% **m/m** of tannins, expressed as pyrogallol. The tincture is produced from 1 part of comminuted drug and 5 parts of ethanol (70 per cent **V/V**) by a suitable procedure. It is a red or reddish-brown liquid.

**Constituents**

It contains 15-22% of total tannins (15-20% condensed tannins, about 3.5% hydrolysable tannins, plus 7% red, soluble phlobaphene), hydrolyzable ellagitannins, flavonoids, phenolcarboxylic acids, proanthocyanidins, triterpene saponins (e.g. tormentosid) and fatty acids.

![Ellagic acid](image1.png) ![Gallic acid](image2.png)

**Figure 14.31-34**
The structure of ellagic acid, gallic acid, catechin and epicatechin.

**Uses**

It is traditionally used as an adstringent, antibacterial, antiviral, anti-inflammatory drug; internally as antidiarrhoeal, in the case of enterocolitis and dysentery; externally as gargle and mouth rinse. However, the scientific documentation of these effects is sparse.

**Dosage**

*Adult and elderly daily dose*: The daily internal dose of tormentil is 4-6 g in 2-3 portions, in the form of an infusion (made with 200 mL water, boiled for 10 minutes).

*Children*: There are no data from clinical trials or observational trials for the above mentioned herbal preparations available. Therefore the use should be restricted to adults. The use of the dry extract was allowed in Germany for adolescents in case of unspecific acute diarrhoea.

**Contra-indications**

The only reported side effects were mild gastrointestinal symptoms. The medicinal use of *Tormentillae rhizoma* can be regarded as safe.
Pregnancy and lactation

No data are available on the safe use during pregnancy and lactation. Therefore the use of tormentil is not recommended during pregnancy and lactation.

**Anserinae herba**

**Plant**

*Potentilla anserina* L. - Common silverweed (Rosaceae)

The plant is native throughout the temperate Northern Hemisphere.

![Common silverweed](image)

**Figure 14.35**

Common silverweed (*Potentilla anserina* L.)

**Drug**

*Anserinae herba* (Silverweed flowering shoot, DAC). **Other Drug** *Anserinae radix* (Silverweed root)

Silverweed flowering shoot consists of the dried aerial parts of *Potentilla anserina* L. collected during flowering.
Constituents

The drug contains 6-10% of tannins (mainly ellagitannins), flavonoids, leucoanthocyanidins, coumarins (umbelliferon, scopoletin) and triterpenes.

**Figure 14.36**
*Anserinae herba* (Silverweed flowering shoot)

**Figure 14.37-41**
The structure of ellagic acid, kaempferol, quercetin, umbelliferone and scopoletin.
Pharmacognosy 2

Uses
It is traditionally used as antibacterial, adstringent, anti-inflammatory in gastritis and enteritis (also in children). However, the scientific documentation of these effects is sparse.

Dosage
*Adult and elderly daily dose:* The maximal daily dose is 4 g prepared in 200 mL water in the form of infusion or decoction, in 2-3 portions.

**Gei rhizoma et radix**

**Plant**
*Geum urbanum* L. – Colewort (Rosaceae)
The plant is native to Europe, and the temperate regions of Asia and North Africa. It is a perennial herbaceous plant living in forests (especially in oak forests) and brushwoods.

**Drug**
*Gei urbani rhizoma et radix* (Colewort rhizome and root)
The drug consists of the dried underground parts of *Geum urbanum* L.
Drugs containing polyphenols

Constituents
It contains 12-28% of tannins (mainly gallotannins and ellagitannins), catechin, caffeic acid, 0.02-0.3% of essential oil (eugenol in 50-89%, gein), triterpenes, phenolcarbonic acids, ascorbic acid, malic acid and sugars.

![Chemical structures of eugenol, gein, gallic acid, and 6-galloyl-glucose.](image)

**Figure 14.44-47**
The structure of eugenol, gein, gallic acid, and 6-galloyl-glucose.

Uses
The rhizome and the root is adstringent, antidiarrhoeal, antibacterial, anti-inflammatory, anti-haemorrhoidal. However, the scientific documentation of these effects is sparse. It is also processed by the liqueur industry.
Dosage

Adult and elderly daily dose: For internal use, an infusion (10 minutes) should be made from 0.5-1 g drug and 150-200 mL water. For external use, pour 200 mL lukewarm water to 0.5-1 g drug, and boil it for 5-10 minutes.

Agrimoniae herba

Plant

*Agrimonia eupatoria* L. - Common agrimony (Rosaceae)

The plant occurs both in grassy and shrubby habitats.

![Figure 14.48](image)

Common agrimony (*Agrimonia eupatoria* L.)

Drug

*Agrimoniae herba* (Agrimony, Ph. Eur.).

The drug is the dried flowering tops of *Agrimonia eupatoria* L. It contains not less than 2% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.
Drugs containing polyphenols

Constituents
It contains 4-10% of catechin tannins, 5-6% of ellagitannins and gallotannins, triterpenes (mainly ursolic acid) and flavonoids.

![Gallic acid, ellagic acid, catechin](image)

Uses
It is traditionally used as mild adstringent and antibacterial, therefore internally can be used in cases of gastroenteritis, cholecystitis (inflammation of the gallbladder) and cholangitis (inflammation of the bile ducts). It can also be used as a gargle. Its tea is particularly good for summer diarrhoea, enteritis and colitis. However, the scientific documentation of these effects is sparse.
Dosage

*Adult and elderly daily dose*: For treatment of skin disorders, it is used in the form of bath. The infusion (100 g of dried drug and 2 L water) should be added to the bath. For internal use, the daily dose is 1.5 g prepared with 150-200 mL water, as infusion or decoction. Long-term use is not recommended.

**Fragariae folium**

Plant

*Fragaria vesca* L. - Wild strawberry (Rosaceae)

The plant is native to Europe and Asia.

![Wild strawberry](image)

*Figure 14.53*

Wild strawberry (*Fragaria vesca* L.)

Drug

*Fragariae folium* (Wild strawberry leaf, DAC).

Strawberry leaf consists of the dried leaves of *Fragaria vesca* L.
Constituents
The drug contains 5-10% of ellagitannins, oligomeric proanthocyanidins, flavonoids, caffeic acid derivatives and traces of essential oil.

![Ellagic Acid](image)

ellagic acid

Uses
It is traditionally used as adstringent in the case of diarrhoea, and as mild anti-inflammatory in inflammations of the mucous membrane of the mouth. However, the scientific documentation of these effects is sparse. Wild strawberry fruit is processed by the food industry (syrups, jams).

Dosage
*Adult and elderly daily dose:* 250 mL boiling water should be poured on 2 g drug, and filtered after 15 minutes.
Alchemillae herba

Plant

*Alchemilla vulgaris* L. - Lady’s mantle/Alchemilla (Rosaceae)

The plant is native to meadows and sparse forests.

![Lady’s mantle/Alchemilla](image)

**Figure 14.56**
Lady’s mantle/Alchemilla (*Alchemilla vulgaris* L.)

Drug

*Alchemillae herba* (Alchemilla, Ph. Eur.).

Alchemilla consists of the whole or cut, dried, flowering aerial parts of *Alchemilla vulgaris* L. s. l. It contains not less than 6% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.
Constituents

It contains 5-8% of gallic acid derivatives (the main component is agrimoniin), ellagic acid, pedunculagin, flavonoids and salicylic acid in traces.

Figure 14.58-59
The structure of agrimoniin and pedunculagin.
Uses

It is traditionally used as adstringent, antidiarrhoeal, antiviral, antioxidant, and antimutagenic; internally in cases of diarrhoea, and as a gargle; externally as local hemostyptic, against eczema, rashes, or dermatitis. However, the scientific documentation of these effects is sparse.

Dosage

*Adult and elderly daily dose*: The daily dose is 5-10 g. The single dose is 2-4 g, which should be prepared with 200-250 mL boiling water as infusion, and filtered after 10 minutes.

**Polygoni avicularis herba**

Plant

*Polygonum aviculare* L. – Knotgrass (Polygonaceae)

The plant is native to Europe and Temperate Asia.

![Figure 14.60](image)

**Figure 14.60**

Knotgrass (*Polygonum aviculare* L.)

Drug

*Polygoni avicularis herba* (Knotgrass, Ph. Eur.).

The drug is the whole or cut dried flowering aerial parts of *Polygonum aviculare* L. s.l. It contains not less than 0.30% of flavonoids, expressed as hyperoside, calculated with reference to the dried drug.
Drugs containing polyphenols

Figure 14.61
Polygoni avicularis herba (Knotgrass)

Constituents
The drug contains 3.6% of tannins (gallic acid and catechin derivatives), flavonoids (e.g. avicularin), mucilage and coumarins.

![Structure of avicularin, catechin, and gallic acid](image)

Figure 14.62-64
The structure of avicularin, catechin and gallic acid.

Uses
It is traditionally used as expectorant, diuretic, and against mild inflammation of the respiratory tracts. However, the scientific documentation of these effects is sparse.

Dosage
Adult and elderly daily dose: Infusion should be made from 2 g drug with 200 mL water, which can be administered 2-3 times daily.
**Rubi fruticosi folium**

**Plant**

*Rubus fruticosus* L. - Blackberry (Rosaceae)

The plant is native to the northern hemisphere.

![Figure 14.65](image)

**Figure 14.65**
Blackberry (*Rubus fruticosus* L.)

**Drug**

*Rubi fruticosi folium* (Blackberry leaf, DAC). **Other drugs:** *Rubi fruticosi fructus*, (Blackberry fruit), *Rubi fruticosi radix* (Blackberry root)

Blackberry leaf consists of the dried leaves of *Rubus fruticosus* L.
Constituents

*In the leaf:* 8-10% of hydrolyzable gallo-tannins, dimeric ellagitannins, organic acids, flavonoids, cyanidine glycosides, pentacyclic triterpene acids. *In the fruit:* special cyanidine glycosides, organic acids, alcohols and esters, sugars, pectin.

![Gallic acid and ellagic acid](image)

**Figure 14.67-68**
The structure of gallic acid and ellagic acid.

Uses

It is traditionally used as adstringent, antidiarrhoeal, diaphoretic, for gargle, and against menstrual cramps. However, the scientific documentation of these effects is sparse. It is the best alternative to caffeine containing types of tea. The raw fruits or the fruit juice and jam are rich in vitamins, trace elements and antioxidants.

Dosage

*Adult and elderly daily dose:* The daily dose is 200 mL decoction prepared from 1.5 g drug.
**Rubi idaei folium**

**Plant**

*Rubus idaeus* L. – Raspberry (Rosaceae)

The plant is native to the northern hemisphere. It can be cultivated.

**Figure 14.69**

Raspberry (*Rubus idaeus* L.)

**Drug**

*Rubi idaei folium* (Raspberry leaf, DAC). **Other drugs**: *Rubi idaei fructus* (Raspberry fruit).

Raspberry leaf consists of the dried leaves of *Rubus idaeus* L.
Figure 14.70
*Rubi idaei folium* (Raspberry leaf)

**Constituents**

Similar to those in blackberry. In the fruit there are special cyanidine glycosides, organic acids, alcohols and esters, sugars and pectin.

**Uses**

It is traditionally used for the symptomatic relief of minor spasms associated with menstrual periods, for the symptomatic treatment of mild inflammation in the mouth or throat, for the symptomatic treatment of mild diarrhoea. However, the scientific documentation of these effects is sparse and of questionable quality.

**Dosage**

*Adult and elderly daily dose:* For relief of minor spasms associated with menstrual periods, the single dose of dry extract is 113-226 mg up to 3 to 4 times daily. For the symptomatic treatment of mild inflammation in the mouth or throat, the single dose for an infusion for oromucosal use is 1.5-8 g of the comminuted herbal substance in 150 mL of boiling water 3 times daily. For the symptomatic treatment of mild diarrhoea, the single dose is 1.5-8 g of the comminuted herbal substance in 150 mL of boiling water as an infusion 3 times daily.

*Children:* The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.

*Overdose:* No case of overdose has been reported.

**Contraindications**

Hypersensitivity to the active substance(s).
Pregnancy and lactation
Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Coryli folium
Plant
*Corylus avellana* L. – (Common) hazel (Betulaceae)
The plant is native to Europe and Asia Minor. It is cultivated.

![Figure 14.71](image)

**Figure 14.71**
*Fig. 14.71 Common hazel (Corylus avellana L.)*

Drug
Coryli (avellanae) folium (Hazel leaf).
Hazel leaf consists of the dried leaves of *Corylus avellana* L.
Drugs containing polyphenols

Constituents
It contains 3-5% of tannins, flavonoids, chlorogenic acid, taraxasterol, β-sitosterol and essential oil.

Uses
It is traditionally used as anti-hemorrhoidal, anti-inflammatory (e.g. gingivitis), tissue regeneration inducing (wound healing) drug. However, the scientific documentation of these effects is sparse.

Dosage
*Adult and elderly daily dose:* The daily dose is 3-5 g, from which an infusion should be made, and it should be macerated for hours.

**Myrtilli fructus**

Plant
*Vaccinium myrtillus* L. – Bilberry / European blueberry (Ericaceae)
The plant is native to Europe, and Northwest Asia.
Figure 14.73
Bilberry / European blueberry (*Vaccinium myrtillus* L.)

**Drug**

*Myrtilli fructus siccus* (Bilberry fruit, dried, Ph. Eur.), *Myrtilli fructus recens* (Bilberry fruit, fresh, Ph. Eur.). **Other drugs:** *Myrtilli folium et fructus* (Bilberry leaves and berries)

The drug is the dried ripe fruit of *Vaccinium myrtillus* L. It contains not less than 1% of tannins, expressed as pyrogallol, and calculated with reference to the dried drug.

The drug is the fresh or frozen ripe fruit of *Vaccinium myrtillus* L. It contains not less than 0.30% of anthocyanins, expressed as cyanidin-3-glucoside chloride (chrysanthenin), and calculated with reference to the dried drug.
Drugs containing polyphenols

Constituents

*In the leaf:* 0.8-6.7% catechin tannins, catechin, epicatechin, gallocatechin, proanthocyanidin, flavonoids, iridoids, phenoliccarboxylic acids (chlorogenic acid) quinolizidine alkaloids (myrtine, epi-myrtine), hydroquinone and arbutin, about 1 mg% chrome. *In the fruit:* about 1% of catechin tannins, anthocyanidins, flavonoid glycosides (e.g. astragalin), phenolic carboxylic acids, iridoids, inverted sugar, pectin, resveratrol.
Uses
For internal purposes the drug can be used for the symptomatic treatment of problems related to varicose veins such as painful and heavy legs. Dried bilberry fruit is used in the treatment of acute, non-specific diarrhoea. The drug is also applied in the topical treatment of mild inflammation of the mucous membranes of the mouth and throat.

Dosage
Adult and elderly daily dose: For internal use, the daily dose of the leaf is 1 g (infusion prepared with 200 mL water). Standardized extracts of bilberry fruit containing 36% of anthocyanidins: 320-480 mg/day; dried bilberry fruit: 20-60 g/day. For external use (washing or poultice), prepare an infusion from 1-2 g leaf with 250 mL water, and filter it after 15 minutes.

2.5-5.0 g fruit should be boiled with 150-200 mL water for 10 minutes, or macerated for 2-3 hours.

Pregnancy and lactation
Anthocyanins are well tolerated in pregnancy, they do not induce side-effects, but consultation with a doctor is always recommended.

Pelargonii radix

Plant

*Pelargonium sidoides* DC. – South African geranium, *Pelargonium reniforme* Curt. –, (Geraniaceae)

The plants are native to South Africa.
Drugs containing polyphenols

Drug

Pelargonii radix (Pelargonium root, Ph. Eur.).

Pelargonium root consists of the dried, usually fragmented, underground organs of Pelargonium sidoides DC. and/or Pelargonium reniforme Curt. It contains not less than 2% of tannins, expressed as pyrogallol, and calculated with reference to the dried drug.

Constituents

The drug contains gallic acid, catechin, procyanidin polymer composed of catechin monomers and procyanidin polymer composed of gallocatechin monomers. Other constituents include coumarins (e.g. scopoletin, 5,6,7-trimethoxycoumarin, 6,8-dihydroxy-7-methoxycoumarin, 6,8-dihydroxy-5,7-dimethoxycoumarine, umckalin-7-β-glucoside, 5,6-dimethoxycoumarin-7-sulfate), flavonoids and sterols.

![Structures](image)

**Figure 14.82-85**

The structure of gallic acid, catechin, procyanidin polymer composed of catechin monomers and procyanidin polymer composed of gallocatechin monomers.

Uses

It is traditionally used for the symptomatic treatment of common cold. Based on the available clinical data, the efficacy of Pelargonii radix in the symptomatic treatment of acute respiratory diseases, e.g. acute bronchitis, sinusitis, tonsillopharyngitis and common cold is not proven properly.

Dosage

*Adult and elderly daily dose:* Single dose: 1.14 g, 3 times daily.

*Children:* Single dose: 0.76 g, 3 times daily. The use in children under 6 years of age is not recommended due to lack of adequate data.
Overdose: No case of overdose has been reported.

Contra-indications

Hypersensitivity to the active substance(s). Although there is limited knowledge about pharmacokinetic parameters and toxicological data of Pelargonium extract, the current non-clinical results (including data regarding the constituents) suggest that the application of Pelargonium preparations is probably safe.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Cotini folium

Plant

*Cotinus coggygria* Scop. – Eurasian smoketree (Anacardiaceae)

The plant is native to Europe, Asia and China. In Hungary it can be found in karst scrub forests.

![Figure 14.86](image)

Eurasian smoketree (*Cotinus coggygria* Scop.)

Drug

*Cotini folium* (Smoke tree leaf)

The drug consists of the green summer leaves of the bush or small tree *Cotinus coggygria* (Scop.).
Constituents
The characteristic constituents of the drug are tannins (18-20%) including gallotannins, ellagic acid and catechin-derivatives. Other constituents include flavonoids and essential oil.

Uses
The drug has adstringent, hemostyptic and antibacterial activities. It is traditionally used for rinsing the mouth e.g. after tooth extraction and in gingivitis.
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Literature

Recommended homepages and databases

1. Cochrane Library: http://www.thecochranelibrary.com
4. National Institute for Food and Nutrition Science: www.oeti.hu
## Appendices

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<td>Cola nitida</td>
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<td>Violet willow</td>
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<td>Crack willow</td>
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<td>Salix purpurea</td>
<td>Purple willow</td>
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<td>Japanese mint essential oil partially deprived of menthol</td>
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<td>Feverfew</td>
<td>Tanaceti parthenii herba</td>
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<td>Ipecacuanha, Prepared ipecacuanha, Standardized ipecacuanha liquid extract, Standardized ipecacuanha tincture</td>
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<td>Eucalyptus smithii</td>
<td>Gully gum</td>
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<td>Foeniculi dulcis fructus</td>
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<td>Glycyrrhiza glabra</td>
<td>Liquiriae radix, Liquiriae extractum fluidum ethanolicum normatum, Liquiriae extractum siccum ad saporandum</td>
<td>Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring</td>
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<td>Hedera helix</td>
<td>Hederae folium</td>
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## Indications

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<td><em>Illicium verum</em></td>
<td>Star anise</td>
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<td>Star anise, Star anise oil</td>
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<td><em>Mentha canadensis</em></td>
<td>Japanese mint</td>
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<td>Japanese mint essential oil partially deprived of menthol</td>
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<td>Anisi fructus, Anisi aetheroleum</td>
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<td>Mugo pine</td>
<td>Pini pumilionis aetheroleum</td>
<td>Dwarf pine needle oil</td>
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<td><em>Pinus pinaster</em></td>
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<td>Terebinthae aetheroleum ab Pinum pinastrum</td>
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<td>Pini sylvestris aetheroleum</td>
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<td>Plantaginis lanceolatae folium</td>
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<td>Seneca snakeroot</td>
<td>Polygalae radix</td>
<td>Senega root</td>
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<td><em>Polygonum aviculare</em></td>
<td>Common knotgrass</td>
<td>Polygoni avicularis herba</td>
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<td>Oxlip</td>
<td>Primulae radix</td>
<td>Primula root</td>
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<td><em>Primula veris</em></td>
<td>Cowslip</td>
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<td>Verbasci flos</td>
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<td><em>Verbascum phlomoides</em></td>
<td>Orange mullein</td>
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<td><em>Verbascum thapsus</em></td>
<td>Great/common mullein</td>
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### Excessive sweating (hyperhydrosis)

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<td>Sage</td>
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### Tinnitus

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<td>Melaleuca linariifolia</td>
<td>Snow-in-Summer, Cajeput tree, Flax-leaved paperbark</td>
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<td>Gastritis and peptic ulcers</td>
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<td>Marshmallow</td>
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<td>Flax</td>
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## Indications

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<td>Thymus zygis</td>
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<td>Rheum palmatum</td>
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<td>Virgin Castor oil, Hydrogenated castor oil, Refined castor oil</td>
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Heart failure (cardiac insufficiency)

| Crataegus azarolus      | Azarole                  | Crataegi folium cum flore, Crataegi folii cum flore extractum siccum, Crataegi fructus | Hawthorn leaf and flower, Hawthorn leaf and flower dry extract, Hawthorn berries |
| Crataegus laevigata     | Woodland hawthorn        |                                        |                           |
| Crataegus monogyna      | Common hawthorn          |                                        |                           |
| Crataegus nigra         | Hungarian hawthorn       |                                        |                           |
| Crataegus pentagyna     | Small-flowered black hawthorn |                                        |                           |
| Digitalis purpurea      | Common foxglove, Purple foxglove | Digitalis purpureae folium | Digitalis leaf |

Anxiety, sleep disorders

| Humulus lupulus         | Common hop               | Lupuli flos                        | Hop stro bile              |
| Lavandula angustifolia  | True (narrow-leaved) lavander | Lavandulae flos, Lavandulae aetheroleum | Lavender flower, Lavender oil |
| Melissa officinalis     | Melissa, Lemon balm      | Melissae folium, Melissae folii extractum siccum | Melissa leaf, Melissa leaves dried extract |
| Passiflora incarnata    | Purple passion flower    | Passiflorae herba, Passiflorae herbae extractum siccum | Passion flower, Passion flower dry extract |
### Indications

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<tr>
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<td>Motherwort</td>
<td>Leonuri cardicae herba</td>
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<td>Quercus robur</td>
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## Contraindications

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<td>Desert indianwheat</td>
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<td>Rheum palmatum</td>
<td>Chinese rhubarb</td>
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## Contraindications

<table>
<thead>
<tr>
<th>Latin name of species</th>
<th>English name of species</th>
<th>Latin name of drug/drugs</th>
<th>English name of drug/drugs</th>
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<tr>
<td><strong>Skin injuries</strong></td>
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<td>Capsicum, Refined and quantified capsicum oleoresin, Capsicum tincture</td>
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<td>Capsicum frutescens</td>
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<td>Cape aloes, Barbados aloes, Standardized aloes dry extract</td>
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<td>Cape aloe, Bitter aloe, Red aloe, Tap aloe</td>
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<td>Tinnevelly senna</td>
<td>Sennae fructus angustifoliae</td>
<td>Tinnevelly senna pods</td>
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<td>Sennae fructus acutifoliae</td>
<td>Alexandrian senna pods</td>
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<td>Senna leaf, Senna leaf dry extract</td>
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<td>Alexandrian senna</td>
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<td>Alder buckthorn</td>
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<td>Zhong Ma Huang</td>
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<td>Muzei Ma Huang</td>
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<td>French psyllium, Sand plantain</td>
<td>Psylli semen</td>
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<td>Plantago ovata</td>
<td>Desert indianwheat</td>
<td>Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum</td>
<td>Ispaghula seed, Ispaghula husk</td>
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## Contraindications

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<tr>
<th>Latin name of species</th>
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<tr>
<td><strong>Inflammation of the gallbladder (cholecystitis), gallstone (cholelithiasis)</strong></td>
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<td>Curcuma xanthorrhiza</td>
<td>Javanese turmeric</td>
<td>Curcumae xanthorrhizae rhizoma</td>
<td>Javanese turmeric</td>
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<td>Cynara scolymus</td>
<td>Artichoke</td>
<td>Cynarae folium, Cynarae folii extractus siccum</td>
<td>Artichoke leaf, Artichoke leaf dry extract</td>
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<td>Harpagophytum procumbens</td>
<td>Devil’s claw</td>
<td>Harpagophyti radix, Harpagophyti extractum siccum</td>
<td>Devil's claw root, Devil's claw root dried extract</td>
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<tr>
<td>Harpagophytum zeyheri</td>
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<tr>
<td>Mentha canadensis</td>
<td>Japanese mint</td>
<td>Menthae arvensis aetheroleum partim mentholi depletum</td>
<td>Japanese mint essential oil partially deprived of menthol</td>
</tr>
<tr>
<td>Mentha x piperita</td>
<td>Peppermint</td>
<td>Menthae piperitae folium, Menthae piperitae aetheroleum</td>
<td>Peppermint leaf, Peppermint oil</td>
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<td>Peumus boldus</td>
<td>Boldo tree</td>
<td>Boldi folium</td>
<td>Boldo leaf</td>
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<td>Zingiber officinale</td>
<td>Ginger</td>
<td>Zingiberis rhizoma</td>
<td>Ginger</td>
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<td><strong>Cholestatic liver disease</strong></td>
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<td>Glycyrrhiza glabra</td>
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<td>Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring</td>
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<td><strong>Inflammation and blockage of the bile ducts (cholangitis and biliary obstruction)</strong></td>
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<td>Curcuma xanthorrhiza</td>
<td>Javanese turmeric</td>
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<td>Cynara scolymus</td>
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<td>Blue mallee</td>
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<td>Eucalyptus smithii</td>
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<td>Japanese mint essential oil partially deprived of menthol</td>
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<tr>
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<td>Olive</td>
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<td>Taraxaci officinalis radix cum herba, Taraxaci officinalis radix</td>
<td>Dandelion root, Dandelion root with herb</td>
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## Contraindications

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<th>Latin name of species</th>
<th>English name of species</th>
<th>Latin name of drug/drugs</th>
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<td>Aloë ferox</td>
<td>Cape aloe, Bitter aloe, Red aloe, Tap aloe</td>
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<td>Cassia angustifolia</td>
<td>Tinnevelly senna</td>
<td>Sennae fructus angustifoilae</td>
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<td>Alexandrian senna pods</td>
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<td>Rhei radix</td>
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<td><strong>Gastric and duodenal ulcers</strong></td>
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<td>Harpagophytum zeypheri</td>
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<td>Aloë ferox</td>
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<td>Tinnevelly senna</td>
<td>Sennae fructus angustifolae</td>
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<td>Cassia senna</td>
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<td>Cassia senna</td>
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<td>Rheum palmatum</td>
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<td>Datura stramonium</td>
<td>Thorn apple</td>
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<td>Pale purple coneflower</td>
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<td>Echinacea purpurea</td>
<td>Purple coneflower</td>
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<td>Siberian ginseng</td>
<td>Eleuterococci radix</td>
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<td>Ephedrae herba</td>
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<td>Ephedra intermedia</td>
<td>Zhong Ma Huang</td>
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<td>Ephedra equisetina</td>
<td>Muzei Ma Huang</td>
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<td>Glycyrrhiza glabra</td>
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<td>Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum</td>
<td>Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring</td>
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<td>French psyllium, Sand plantain</td>
<td>Psylli semen</td>
<td>Psyllium seed</td>
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<td>Plantago ovata</td>
<td>Desert indianwheat</td>
<td>Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum</td>
<td>Ispaghula seed, Ispaghula husk</td>
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<td>Enlarged prostate</td>
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<td>Mugo pine</td>
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<td>Dwarf pine needle oil</td>
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<td>Downy/white birch</td>
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**Pregnancy**

<p>| Aloë barbadensis       | True/medicinal aloe    | Aloë barbadensis, Aloë capensis, Aloès extractum siccum normatum | Cape aoes, Barbados aoes, Standardized aoes dry extract |
| Aloë ferox             | Cape aloe, Bitter aloe, Red aloe, Tapi aloe |                          |                          |
| Arctostaphylos uva-ursi | Bearberry             | Uvae ursi folium         | Bearberry leaf           |
| Artemisia absinthium   | Absinthe wormwood     | Absinthii herba          | Wormwood                 |
| Astragalus membranaceus | Huang qi              | Astragali mongholici radix | Membranous milk-vetch root ? |
| Cassia angustifolia    | Tinnevelly senna      | Sennae fructus angustifoliae | Tinnevelly senna pods    |
| Cassia senna           | Alexandrian senna     | Sennae fructus acutifoliae | Alexandrian senna pods   |
| Cassia angustifolia    | Tinnevelly senna      | Sennae folium, Sennae folii extractum siccum normatum | Senna leaf, Senna leaf dry extract |
| Cassia senna           | Alexandrian senna     |                          |                          |
| Cinchona calisaya      | Cinchona               | Cinchonae cortex, Cinchonae extractum fluidum normatum | Cinchona bark, Standardised cinchona liquid extract |
| Cinchona ledgeriana    |                         |                          |                          |
| Cinchona pubescens     | Quinine tree           |                          |                          |</p>
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<td>Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring</td>
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## Side effects

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## Side effects

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### Side effects

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### Allergic reactions of the respiratory system

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<td>Menthae piperitae folium, Menthae piperitae aetheroleum</td>
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### High blood pressure (hypertension)

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### Sodium retention

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