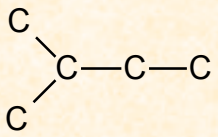
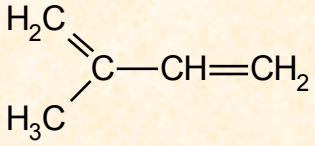
General characteristic of **isoprenoids**.
General characteristic of **iridoids**.
Medicinal plant and plant material containing iridoids and other bitters

- The **isoprenoids**, sometimes called **terpenoids**, are a large and diverse class of naturally-occurring organic chemicals similar to terpenes, derived from five-carbon isoprene units assembled and modified in thousands of ways.
- Most are multicyclic structures that differ from one another not only in functional groups but also in their basic carbon skeletons.
- These lipids are the largest group of natural products.
- Terpenes may be classified by the number of terpene units in the molecule; a prefix in the name indicates the number of terpene units needed to assemble the molecule.



C_5-unit



isoprene

CLASSIFICATION

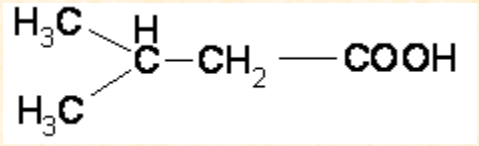
Group of terpenes	Formula	Occurrence in nature
Hemiterpenes	**C_5H_8**	consist of *a single isoprene* unit. Isoprene itself is considered the only hemiterpene, but oxygen-containing derivatives such as prenol and isovaleric acid are hemiterpenoids.
Monoterpenes	**$(C_5H_8)_2$ $C_{10}H_{16}$**	consist of *two isoprene* units. Examples of monoterpenes are: geraniol, limonene and terpineol; iridoids.
Sesquiterpenes	**$(C_5H_8)_3$ $C_{15}H_{24}$**	consist of *three isoprene* units. Examples of sesquiterpenes are: farnesenes, farnesol. The *sesqui-* prefix means one and a half.
Diterpenes	**$(C_5H_8)_4$ $C_{20}H_{32}$**	composed for *four isoprene* units. They derive from geranyl pyrophosphate. Examples of diterpenes are cafestrol, taxadiene (precursor of taxol). Diterpenes also form the basis for biologically important compounds such as retinol, retinal, and phytol. They are known to be antimicrobial and antiinflammatory.

CLASSIFICATION

Group of terpenes	Formula	Occurrence in nature
Triterpenes	**$(C_5H_8)_6$ $C_{30}H_{48}$**	consist of *six isoprene* units. The linear triterpene squalene the major constituent of shark liver oil, is derived from the reductive coupling of two molecules of farnesyl pyrophosphate. Squalene is then processed biosynthetically to generate either lanosterol or cycloartenol, the structural precursors to all the steroids.
Tetraterpenes	**$(C_5H_8)_8$ $C_{40}H_{64}$**	contain *eight isoprene* units. Biologically important tetraterpenes include the acyclic lycopene, the monocyclic γ-carotene, and the bicyclic α- and β- carotenes.
Polyterpenes	**$(C_5H_8)n$**	consist of long chains of *many isoprene* units. Natural rubber consists of polyisoprene in which the double bonds are cis. Some plants produce a polyisoprene with trans double bonds, known as gutta-percha.

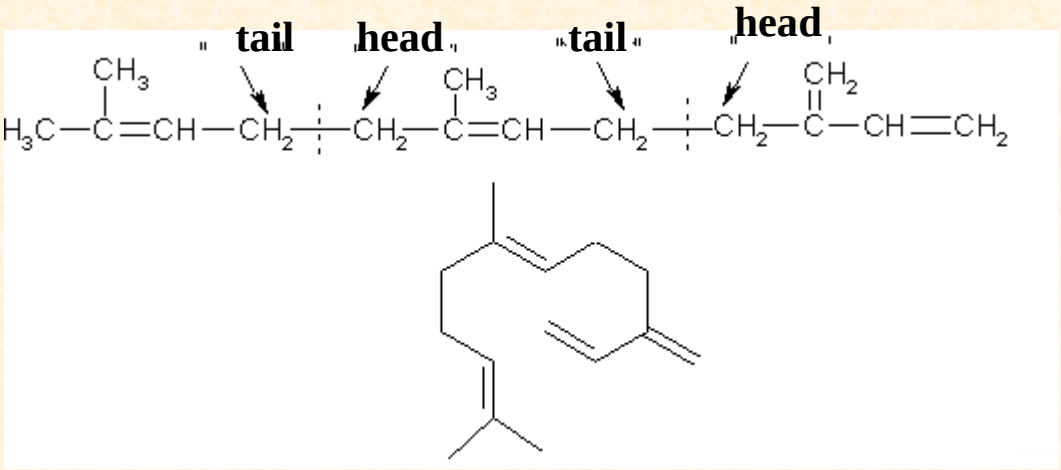
Some examples of isoprenoids

C_5H_8



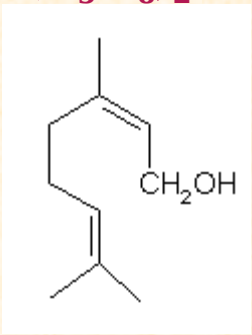
Isovaleric acid

$(C_5H_8)_3$



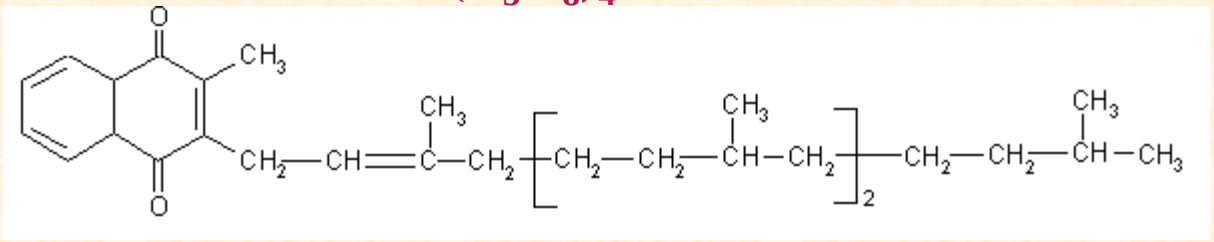
Farnesen

$(C_5H_8)_2$



Geraniol

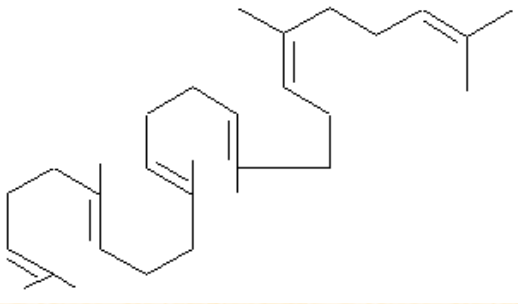
$(C_5H_8)_4$



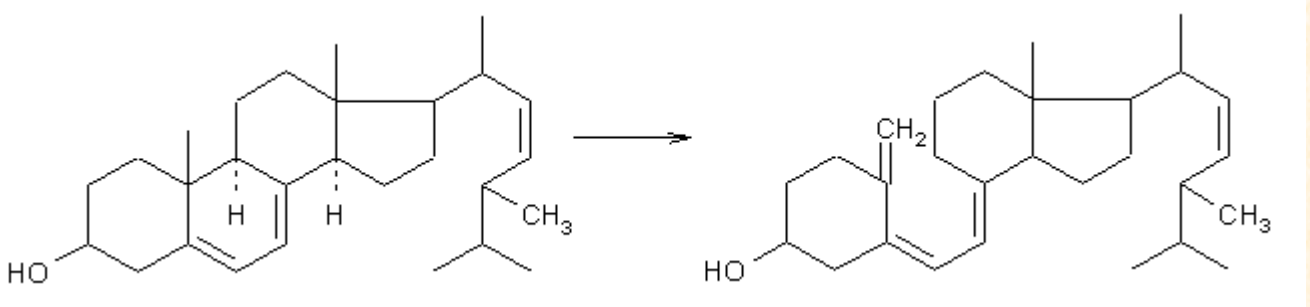
Vitamin K

Some examples of isoprenoids

$(C_5H_8)_6$

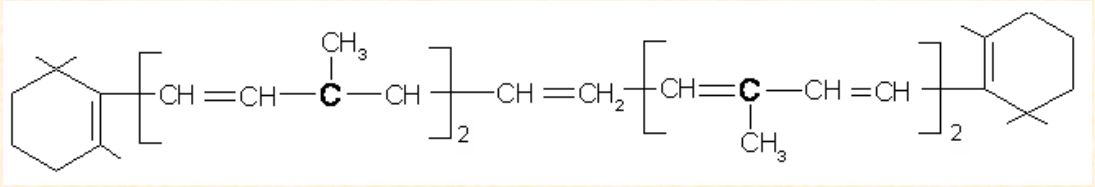


Squalene



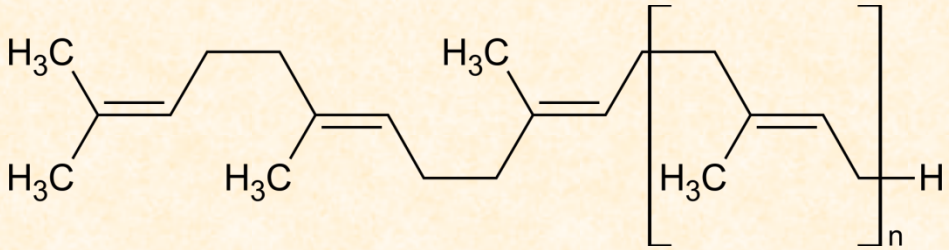
Ergosterine **Ergocalciferol**

$(C_5H_8)_8$



β-Carotene

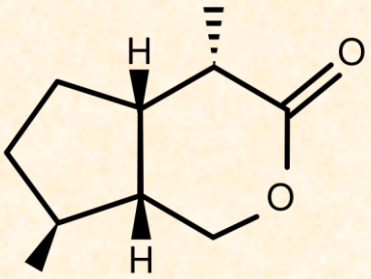
$(C_5H_8)_n$



Gutta-percha

IRIDOIDS $(C_5H_8)_2$ are a class of secondary metabolites found in a wide variety of plants and in some animals. They are monoterpenes biosynthesized from isoprene and they are often intermediates in the biosynthesis of alkaloids.

- Chemically, the iridoids usually consist of a cyclopentane ring fused to a six-membered oxygen heterocycle. The chemical structure is exemplified by iridomyrmecin, a defensive chemical produced by the *Iridomyrmex* genus, for which iridoids are named.



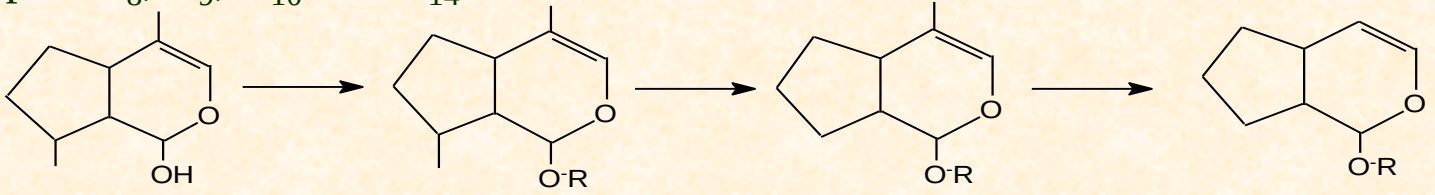
iridomyrmecin

- Iridoids are found in many medicinal plants and may be responsible for some of their pharmaceutical activities. Isolated and purified, iridoids exhibit a wide range of bioactivities including cardiovascular, cholerectic, hypoglycemic, analgesic, anti-inflammatory, antimutagenic, antispasmodic, antitumor, antiviral, immunomodulatory, and purgative activities.
- Iridoids are produced by plants primarily as a defense against herbivores or against infection by microorganisms. To humans and other mammals, iridoids are often characterized by a deterrent bitter taste.

Classification

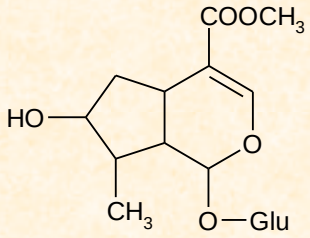
1. Cyclopentane types

According to number of C atoms in the skeleton of aglycone they could be divided into 4 types: C_8, C_9, C_{10} and C_{14}.

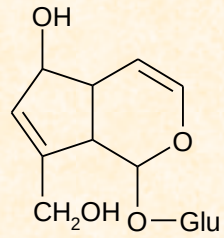


Iridodial C_{10}-Iridoid C_9- Iridoid C_8- Iridoid

Iridoids are typically found in plants as glycosides, most often bound to glucose.

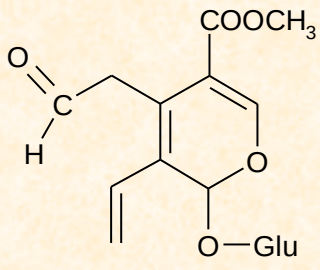


Loganin

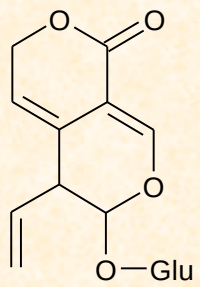


Aucubin

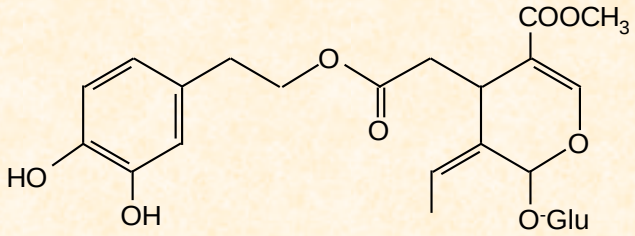
2. Seco-iridoids. Cleavage of a bond in the cyclopentane ring gives rise to seco-iridoids.



Secologanin



Gentiopicrozide

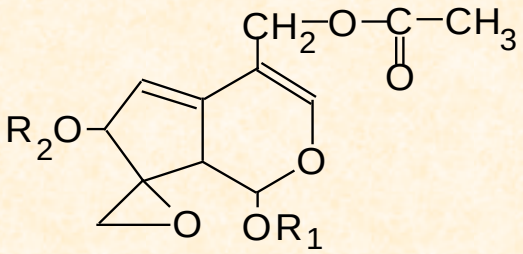


Oleuropeine

Classification

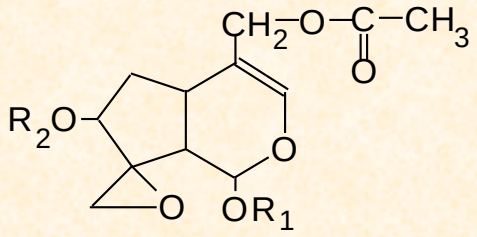
3. Iridoids of plants from family *Valerianaceae*

Bicyclic monoterpenes or valepotriates (“***Val****eriana* - ***Epo****xy* - ***tri****ester*”).



Valtrate

R_1=R_2 – Isovalerianic acid



Dihydrovaltrate

R_1 – Isovalerianic acid;

R_2 – Acetoxyisovalerianic acid

4. Iridoids-alkaloids – complex of indole alkaloids, containing as non-amine part iridoid (determine in plants from family *Rubiaceae*, *Apocynaceae*)

Physical and chemical properties of iridoids

- Colorless crystals,
- Bitter compounds,
- They are soluble in water, ethanol, acetone, methanol
- They occur as glycosides or complex epoxides in plants
- Aglycones of iridoids are non-stable: they are sensitive to enzymes and acids, while acetylated iridoids - to alkali.
- When treated by acids or under the influence of enzymes in presence of oxygen, iridoids form colored (dark blue or violet-blue) non-soluble in water products.

Biological activity

- Stimulates secretions in the gastrointestinal tract, especially of gastric juice,
- purgative,
- antimicrobial, antiviral,
- anti-inflammatory and analgesic,
- immunomodulatory,
- sedative (***valepotriates***),
- Diuretic (*catalpol* and catalposide),
- antimutagenic,
- antitumor (*valtrate*)
- Cardiovascular,
- hypoglycemic,
- antispasmodic.

Bitter principles (*Amara*) are heterogenous compounds of bitter taste.

The chemistry of bitter principles has been in many cases incompletely studied . This group comprises natural vegetable products belonging to different chemical groupings.

MPM	BAC	Index of bitterness	Compound
Pure bitter – *Amara tonica*			
Radices Gentianae	Iridoids	**10000-30000**	Gentiopicrin and its isomers
Herba Centaurii	- " -	**10000**	Erythrocentaurin
Folia Menyanthydis	- " -	**4000-10000**	Foliamenthin, Loganin, Sweroside
Radices Taraxaci	Sesquiterpene lactone		Eudesmanolides and germacranolides as aglycones and glycosides
Radices Cichorii intybi	- " -		Lactucin, Lactucopicrin
Folia Cynarae	Sesquiterpene lactone and cinnamic acids	30	Cynaropicrin, Cinarin, chlorogenic acid
Aromatic bitter – *Amara aromatica*			
Herba Absinthii	Sesquiterpenes	**10000-25000**	Absinthin, anabsinthin, artabsin
Herba Millefolii	- " -		Eudesmanolides (tauremisin), guaianolide (achifolid), germacranolides
Rhizomata Calami	- " -		Acorone, acorenone, acoric acid
Folia Lauri	Sesquiterpene lactone		Costunolide (guaiane type)
Fructus Cubebae	Sesquiterpenes and lignans		Cubebin, piperin
Spices - *Amara acria*			
Lignum Quassiae	Triterpenes	**40000-50000**	Quassine
Rhizomata Zingiberis	Sesquiterpenes and phenilalcans		Zingeberin, gingerol
Fructus Piperis nigri	Mono- and sesquiterpenes		Phellandrene, caryophyllene, dipentene
Fructus Capsici	Amides (protoalkaloids)		Capsaicinoids
Different MRM			
Cortex Chinae	Alkaloids		Quinine
Strobili Lupuli	Phenolic compounds		Bitter acids – humulone, lupulone
Folia Salviae	Diterpenes		Carnosol (picrosalvin)
Herba Leonuri	Iridoids, diterpenes		Leonuride, marrubin
Pericarpium Aurantii amari	Flavanones; triterpenes	**600-1500**	Neohesperidin, naringin; limonine

Bitter substances can be determined chemically. However, since they are mostly composed of two or more constituents with various degrees of bitterness, it is first necessary to measure total bitterness by taste.

The bitter properties of plant material are determined by comparing the threshold bitter concentration of an extract of the materials with that of a dilute solution of quinine hydrochloride R. The bitterness value is expressed in units equivalent to the bitterness of a solution containing 1g of quinine hydrochloride R in 2000 ml.

Sensitivity to bitterness varies from person to person, and even for the same person it may be different at different times (because of fatigue, smoking, or after eating strongly flavoured food). Therefore, the same person should taste both the material to be tested and the quinine hydrochloride solution within a short space of time. The bitter sensation is not felt by the whole surface of the tongue, but is limited to the middle section of the upper surface of the tongue. A certain amount of training is required to perform this test.

A person who does not feel bitter taste when tasting a solution of 0.058 mg of quinine hydrochloride R in 10 ml of water is not suitable to undertake this determination.

The preparation of the stock solution of each individual plant material (S*T)* should be specified in the test procedure. In each test series, unless otherwise indicated, the determination should start with the lowest concentration in order to retain sufficient sensitivity of the taste buds.

Calculate the bitterness value in units per g using the following formula:

$$\frac{2000 \times c}{a \times b}$$

- where a = the concentration of the stock solution (ST) (mg/ml),
- b = the volume of ST (in ml) in the tube with the threshold bitter concentration,
- c = the quantity of quinine hydrochloride R (in mg) in the tube with the
- threshold bitter concentration.

Gentian root – Radix Gentianae
Gentian - Gentiana lutea L.
Family - Gentianaceae

Yellow gentian grows in the mountains and would remain from the times of glaciation. It grows in fields and pastures over an altitude of 800 metres, evoking big candlesticks someone would have placed here and there.

The drug consists of the brownish, reddish brown or deep brown roots, which are up to several centimeters thick and often fragments of the rhizome, which is transversely wrinkled on the surface: the roots are longitudinally grooved. In the transverse section of the broken drug there is relatively narrow bark (with a coarsely wrinkled cork) and a distinct ring of cambium delimiting the xylem. Odour: Weak and peculiarly sweetish, reminiscent of dried gigs. Taste: At first sweetish, then persistently and intensely bitter

Act. Const.

- The root contains: secoiridoids bitter principles: the main component is gentiopicroside (1 to 3.5 %). **Root has a very high bitter value 58000000.**
- triterpenes: steroids (phytosterol)
- enzymes (invertin, emulsin, oxidase, peroxidase),
- phenolic acids: gentisic acid, shikimates:
- xanthones (gentisin, isogentisin, gentioside),
- tannins,
- alkaloids: gentianine, gentialutine,
- traces of essential oil.

Uses

Gentian has antiasthenic, anti-inflammatory and antipyretic properties. By stimulating the taste buds and influencing especially the encephalic phase of secretion, the drug brings about reflex promotion of gastric juice and saliva production; it is also has cholagogic effect. Used externally, the plant heals sores.

Food Gentian is extensively used to make liqueurs. Cosmetic: Gentian is used for its softening and purifying virtues. It is moreover a good tonifying agent. Gentian is also recommended for its astringent properties. the plant is a good ingredient in: - shampoos and lotions for greasy, damaged and delicate, dull and limp hair, - body milks, - soothing hand creams.

Pharmacopoeial and Other Monographs: DAB, Ph Helv., BHP, Ph. Eur.

CENTAURY HERB – *Herba Centaurii*

Centaury - *Centaurium erythraea Rafn. (C. minus, C. umbellatum)*

Fam. *Gentianaceae*

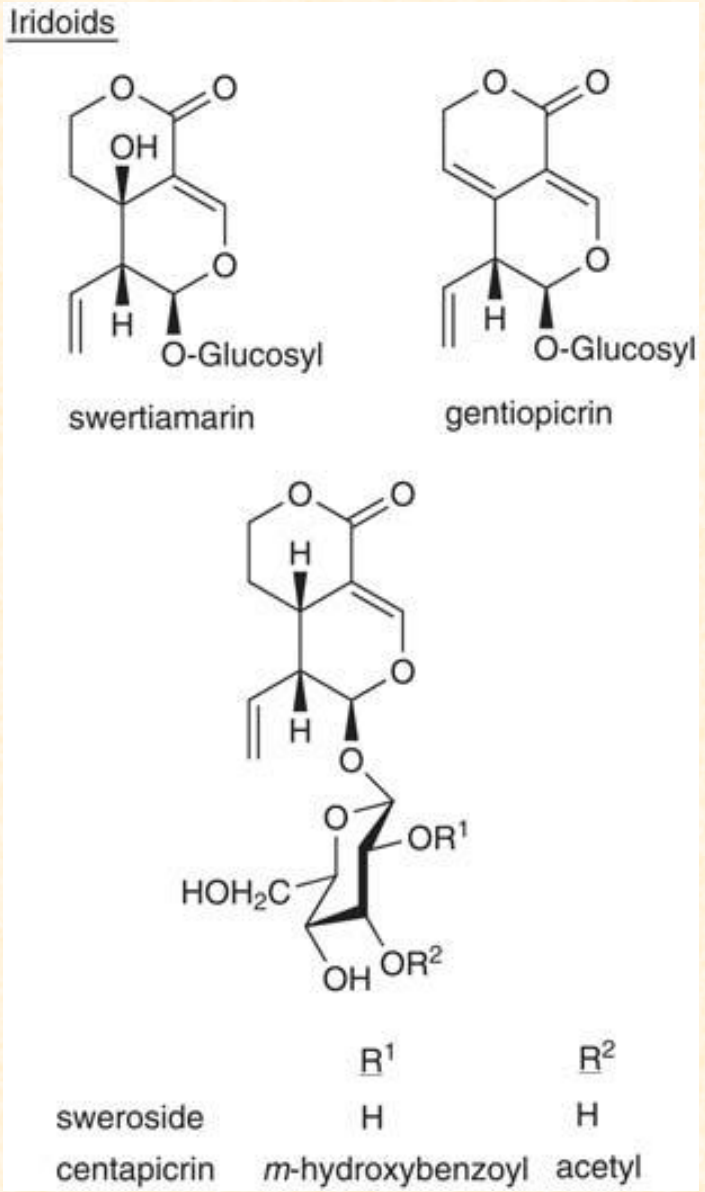
Scattered to widespread in Europe, North America, North Africa, and western Asia.

Prominent features of the drug, which consists of aerial parts of the flowering plant, are the mostly yellowish, 4-angled, hollow pieces of stem and the up to 8 mm long reddish flowers. Fragments of the small, entire, and glabrous opposite leaves, on the other hand, are less conspicuous. Occasionally waved dehiscent fruits are present, together with the loose, very small seeds discharged from them. Another characteristic feature is the anthers which become spirally twisted after releasing their pollen. ,

Act. Const.

Small amounts of intensely bitter-tasting secoiridoid glycosides, gentiopicroside (about 2%) as major, others include centapicrin, sweroside and swertiamarin; intensely bitter m-hydroxybenzoylesters of sweroside and catapicrin.

- Among triterpenoids it includes α- and β-amyrin, erythrodiol, crataegolic acid, oleanolic acid and sitosterol.
- Herb contains highly methylated xanthones, including eustomin and 8-demethyleustomin; phenolic acids - vanillic, syringic, p-coumaric, ferulic, sinapic and caffeic; pyridine-type alkaloids; traces of gentianine, gentianidine, gentioflavine and flavonoids, fatty acids, alkanes and waxes.



CENTAURY HERB

Uses

- Centaury is reputed to act as a bitter, aromatic and stomachic. Traditionally, it has been used for anorexia and dyspepsia.

Contraindications:

- Centaury is contra-indicated for individuals with peptic ulcers.

Drug:

- Canephron N, Herbion Drops for the Stomach, Original Grosser Bittner Balsam.

Pharmacopoeial and Other Monographs:

- BHP 1996, BP 2007, Complete German Commission E, ESCOP 2003, Martindale 35th edition, Ph Eur 2007.

BOGBEAN LEAF - MENYANTHIDIS FOLIUM

Bogbean - Menyanthes trifoliata L.,

Fam. Menyanthaceae

Synonyms: Buckbean or Marsh trefoil

The leaves are ternate ("trefoil"), with 10 cm long petiole, and the individual leaflets are 5-10 cm long, elliptic, glabrous. and with an entire margin. The leaf fragments in the cut drug are greyish green, partly with the shrivelled, brownish nerves: because on drying the aerenchymu shrivels more, the fragments of the thicker petiole an- wrinkled and longitudinally grooved.

Very occasionally, petiole fragments with the three points where the leaflets were attached are recognizable.

Taste: Very bitter.

BOGBEAN LEAF

Act. Const.

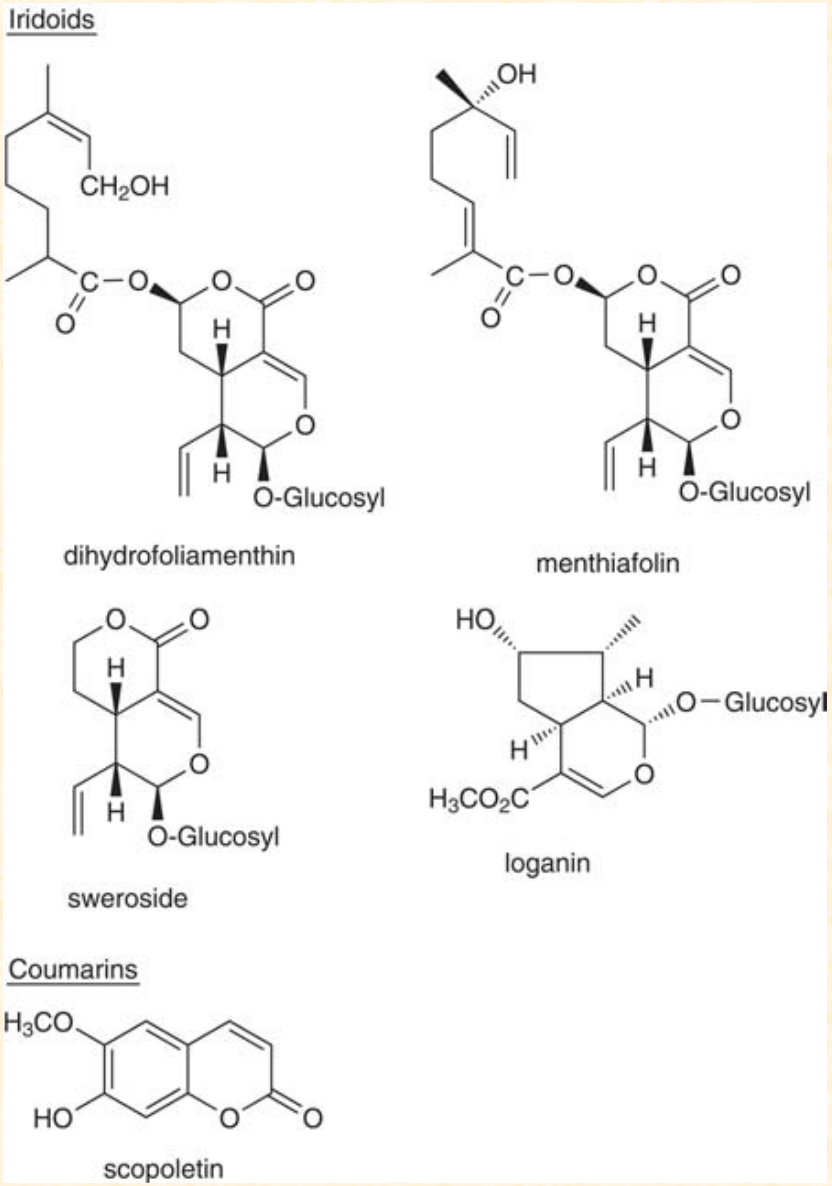
The bitter substances are the secoiridoid glycosides di- hydrofoliamenthin. menthiafolin and loganin, however, foliamenthin is absent from the leaves, though present in the rhizomes.

The monoterpenoid alkaloids gentianine and geritianidine are possibly artefacts arising during the isolation procedure.

Also present are: small amounts of Flavonoids - Hyperin, kaempferol, quercetin, rutin and trifolioside;

Coumarins - Scopoletin;

Caffeic acid, chlorogenic acid, ferulic acid, p-hydroxybenzoicacid, protocatechuic acid, salicylic acid, vanillic acid;folic acid and palmitic acid



Bogbean

Uses.

- Bogbean is stated to possess bitter and diuretic properties. It has been used for rheumatism, rheumatoid arthritis, and specifically for muscular rheumatism associated with general asthenia.

Contraindications:

- Excessive doses may be irritant to the gastrointestinal tract, causing diarrhoea, griping pains, nausea and vomiting.

Drug:

- Original Grosser Bittner Balsam

Pharmacopoeial and Other Monographs:

BHP 1996, BP 2007, Complete German Commission E, Martindale 35th edition, Ph Eur 2007

High-bush cranberry bark – Cortex Viburni
High-bush cranberry - Viburnum opulus L.
Fam. – Caprifoliaceae

Act.const:

- Vit. C, K_1 group B, carotenoids;
- iridoids;
- triterpenoids;
- tannins;
- resins;
- Organic acids

Usage

Infuse and liquid extract have hemostipic, astringent, uterotonic, antiinflammatory action.

Rhizoma cum radicibus Valerianae - *Rhizomata cum radicibus Valerianae*

Valerian, Cat's Valerian - *Valeriana officinalis*

Family - *Valerianaceae*

A tall perennial herb whose underground portion consists of a vertical rhizome bearing numerous rootlets and one or more stolons.

The rhizome is obconical to cylindrical, up to 50 mm long and up to 30 mm in diameter; the base is elongated or compressed, usually entirely covered by numerous roots. The apex usually exhibits a cup-shaped scar from the aerial parts; stem bases are rarely present. In longitudinal section, the pith exhibits a central cavity transversed by septa. The roots are numerous, almost cylindrical, of the same colour as the rhizome, 1 mm to 3 mm in diameter and sometimes more than 100 mm long. A few filiform fragile secondary roots are present. The fracture is short. The stolons show prominent nodes separated by longitudinally striated internodes, each 20 mm to 50 mm long, with a fibrous fracture. The odor is characteristically valeric acid like, becoming stronger on ageing. The taste sweetish, camphoraceous and somewhat bitter.

Chemical composition

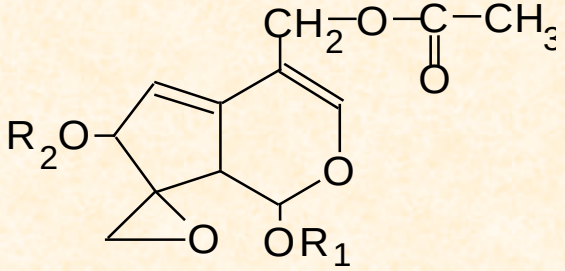
• **Volatile oil (up to 2%):** bornylisovalerianate, bornyl formiate, bornyl acetate and bornyl butyrate, camphene, borneol and pinene;

• **alkoloids:** chalinine and valerianine,

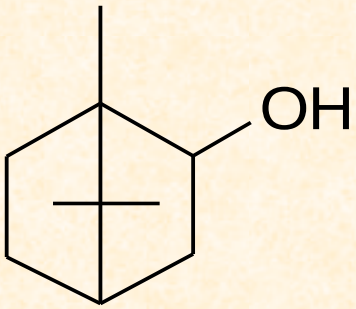
• **iridoids-valepotriates:** valtrate, isovaltrate, acevaltrate,

• **phenolic acids:** caffeic acid, chlorogenic acid,

• **flavonoids**



valepotriate



borneol

Use in medicine

Infusion, liquid extract, extract in tablets, tincture, Cardiophit, Valocormid, Cardiovalen, drops **- sedative, spasmolytic, analgesic, stomachic medicine.**

DANDELION ROOT – RADIX TARAXACI

Dandelion - Taraxacum officinale Weber, Fam. Asteraceae

Native throughout the northern hemisphere, with many varieties and microspecies; introduced into South America. The drug is collected from both wild and cultivated plants.

The drug consists of dark brown to blackish pieces of root have coarse longitudinal wrinkles on the outside. In transverse section there are several concentric zones with tangentiallv connected brown laticifers in the broad greyish white to brownish cortex.

The darker cambial one surrounds a lemon-yellow porous, not radiate xylem. which in some fragments may also be fissured. The fracture is cartilaginous and short, not fibrous. Odour: Faint and characteristic, taste: Somewhat bitter.

DANDELION ROOT

Sesquiterpene lactones taraxinic acid (germacranolide) esterified with glucose, and eudesmanolides. Inulin,

Triterpenes (b-amyrin, taraxol, taraxerol).

Carotenoids, choline, pectin, phytosterols (sitosterol, stigmasterol, taraxasterol, homotaraxasterol),

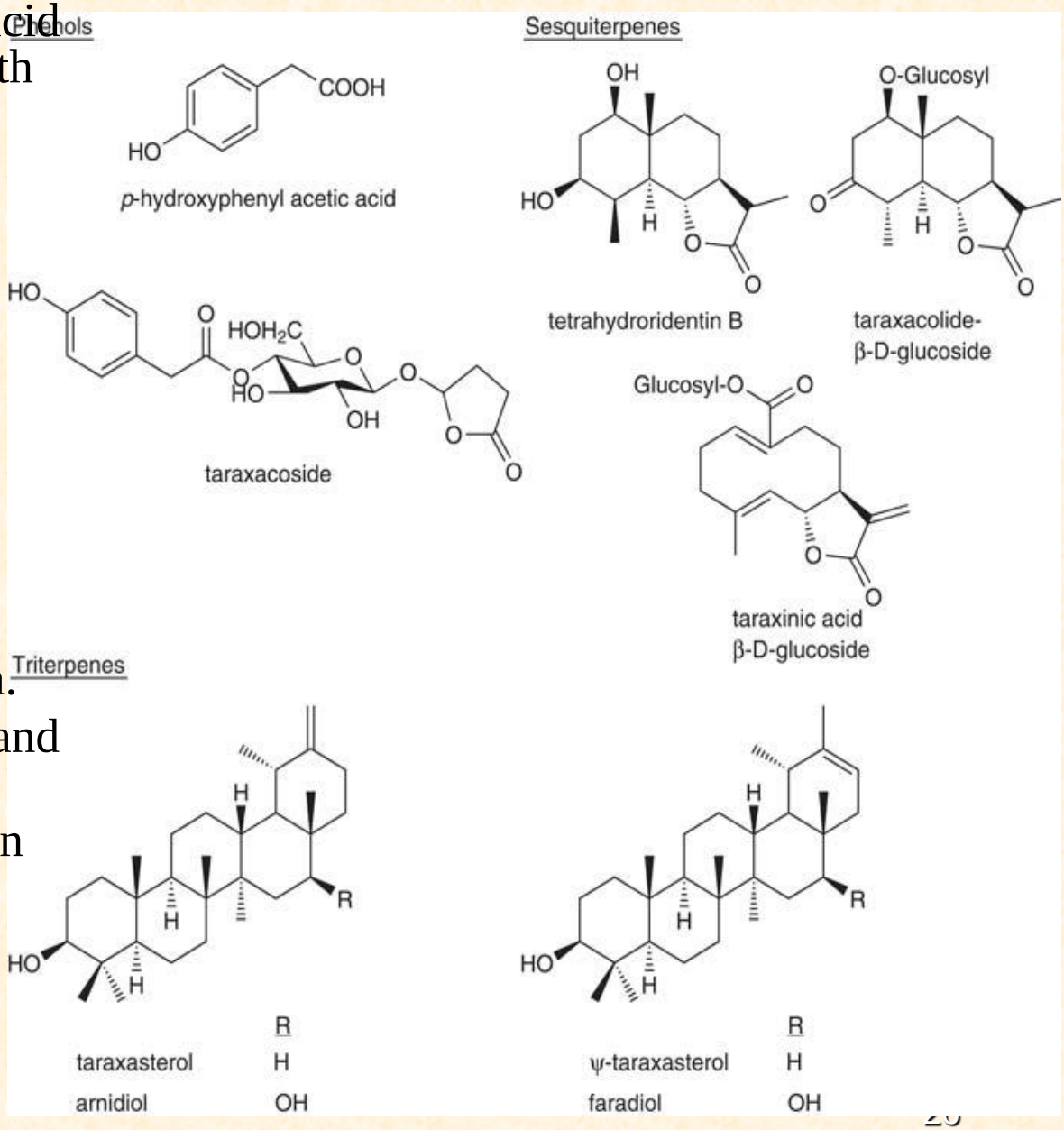
chlorogenic acid, cichoric acid, taraxacoside.

Coumarins Cichoriin and aesculin.

Flavonoids Luteolin-7-glucoside and luteolin-7-diglucosides.

Minerals: K 4.5% in leaf, 2.45% in root.

Resin Undefined bitter complex (taraxacin).



Uses.

Dandelion is a well-known traditional herbal remedy, although limited scientific information, particularly clinical research, is available to justify the reputed uses. Several investigations have failed to demonstrate significant diuretic effects in laboratory animals and have proposed that any diuretic activity is due to the high potassium content of the leaf and root. Dandelion is stated to possess ***diuretic, laxative, cholagogue*** and ***antirheumatic properties***. It has been used for cholecystitis, gallstones, jaundice, atonic dyspepsia with constipation, muscular rheumatism, oliguria, and specifically for cholecystitis and dyspepsia.

Side Effects:

Animal studies indicate dandelion to be of low toxicity. Contact allergic reactions to dandelion have been documented and animal studies have reported dandelion to have a weak sensitising capacity. Sesquiterpene lactones are thought to be the allergenic principles in dandelion. These compounds contain an exocyclic a-methylene b-lactone moiety, which is thought to be a prerequisite for allergenic activity of sesquiterpene lactones. The acute toxicity of dandelion appears to be low, with LD50 values (mice, intraperitoneal injection) estimated at 36.8 g/kg and 28.8 g/kg for the root and herb, respectively.

Pharmacopoeial and Other Monographs:

BHC 1992, BHP 1996, Complete German Commission E, ESCOP 2003, Martindale 35th edition.

HOPS FRUIT – *STROBILI LUPULI*
Hops - *Humulus lupulus L.*
Fam. Cannabaceae

Hops consist of the 2 cm long, yellowish green female inflorescence (strobile), which is built up from imbricated ovale bracts, in the axils of each are two female flowers, each one surrounded by a small oblique ovate bract. The leaf fragments of the drug clearly show the golden-yellow shining glandular trichomes (hop grains) Odour: intensely spicy. Taste: Somewhat bitter and harsh.

Hop grains are the glandular trichomes obtained from the hops by sieving. They form a greenish yellow to orange-yelbw sticky powder. Odour: Characteristic, Taste: strongly spicy.

Uses

- Health disorders such as restlessness, anxiety states, and insomnia.

Drug: Novo-Passit; Doppelherz Vitalotonik; Sanason, **«Urolesan», «Valocardin»,**