

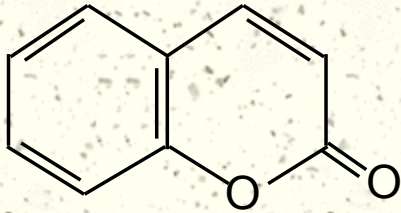


Coumarins & Chromones

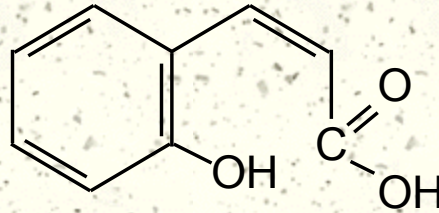
Plan

1. The general characteristic of coumarins
2. Physico-chemical properties of coumarins
3. Qualitative and quantitative determination of coumarins
4. Medicinal plants and crude drugs containing coumarins

Coumarins - are natural biologically active substances with the general formula C_6-C_3 , benzo- α -pyrone derivatives, possessing antispasmodic, anticoagulant, coronary vasodilatory and other effects.



benzo- α -pyrone
(coumarin)



cis-ortho-
hydroxycinnamic acid
(*O*-coumaric acid)

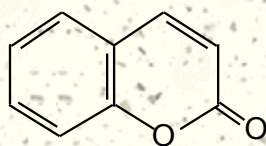
Coumarin was found in about 150 species belonging to over 30 different families. It has the characteristic odor and occurs in many members of the *Fabaceae* family, such as tonco beans which contain about 1-3% coumarins (*Dipteryx odorata*, *Fabaceae*); «coumarouna».



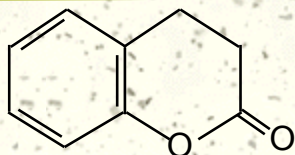
Classification

1. Simple coumarin and its glycosides
2. Hydroxy-, methoxy- (alkoxy-) and methylenedioxy coumarins
3. Furanocoumarins
4. Pyranocoumarins
5. Benzocoumarins
6. Furanobenzocoumarins
7. Complex coumarins

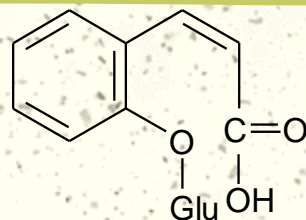
1. Simple coumarin and its glycosides



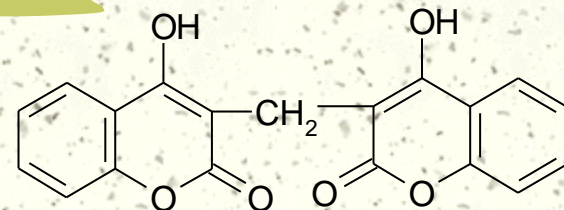
Coumarin



Dihydrocoumarin

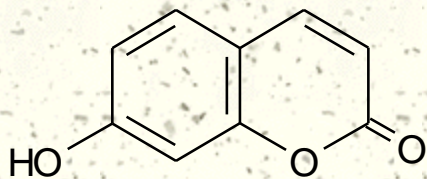


Melilotoside



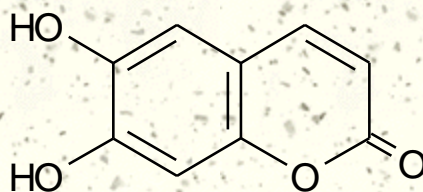
Dicoumarol

2. Coumarin readily forms a large number of hydroxy derivatives in the plant tissues. **Hydroxy-, methoxy- (alkoxy-) and methylenedioxy**coumarins mainly occur in *Apiaceae* and *Rutaceae* plants .



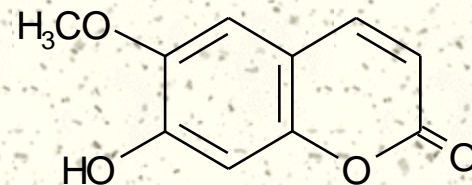
Umbelliferon

(7-hydroxycoumarin)



Aesculetin

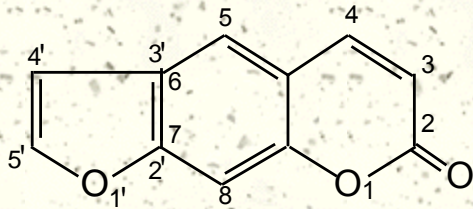
(6,7- dihydroxycoumarin)



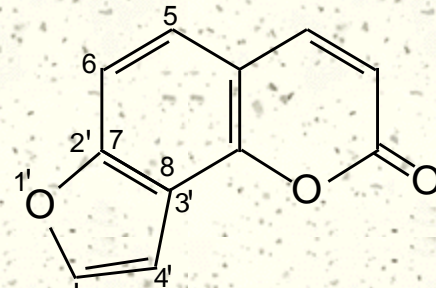
Scopoletin

(6-methoxy-7-hydroxy coumarin)

3. Furanocoumarins are formed by furan ring and coumarin nucleus condensation at 6,7-carbon atoms (psoralen derivatives) or at 7,8-carbon atoms (angelicin derivatives)

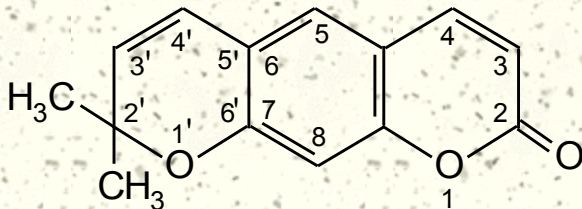


Psoralen
(furo-2',3':7,6-coumarin)

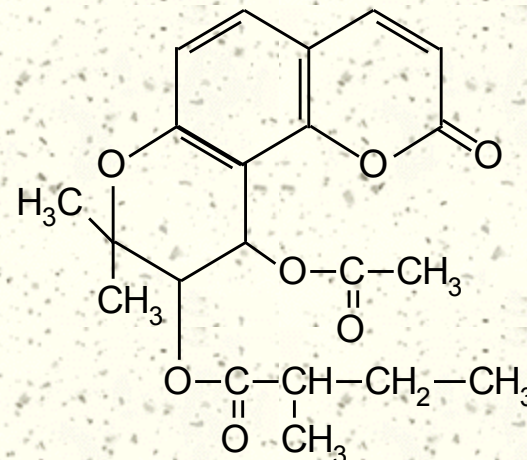


Angelicin (isopsoralen)
(furo-2',3':7,8-coumarin)

4. Pyranocoumarins are formed by 2,2-dimethyl-pyran ring and coumarin nucleus condensation at 5',6'; 6,7 or 7,8 carbon atoms.

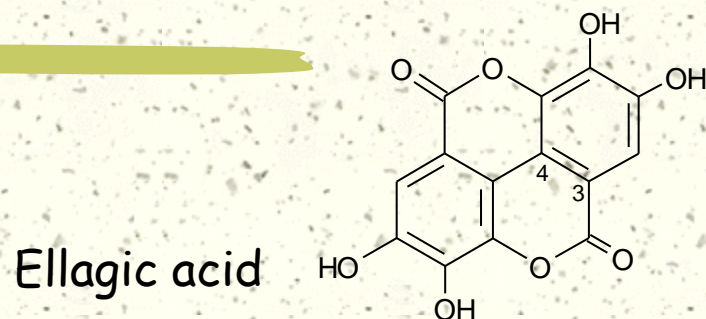


2',2'-dimethylxanthyletin
(2',2'-dimethylpyran-5',6':6,7-coumarin)

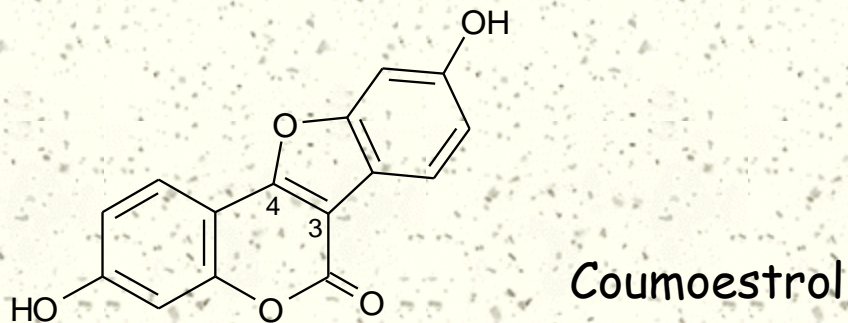


Visnadin

5. **Benzocoumarins** contain benzene ring, connected to coumarin at 3,4-carbon atoms



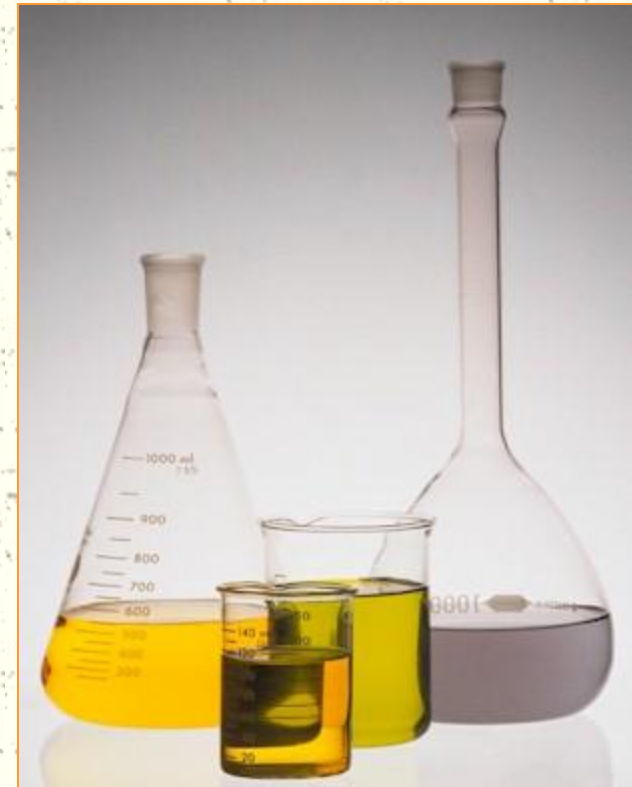
6. **Furanobenzocoumarins** contain benzofuran, connected to coumarin at 3,4-carbon atoms (Coumoestrol)



7. **Complex coumarins** include more complex compounds, containing the coumarin system .

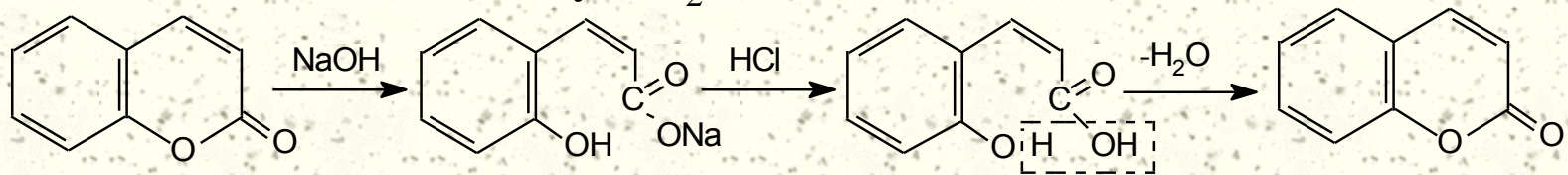
Physical and chemical properties of coumarins

- colorless crystals;
- the distinctive sweet smell to newly-mown hay
- when heating sublimable
- They are soluble in ethanol, methanol, chloroform, fatty oil, alkaline water solution;
- They are not soluble in water;
- give blue, green, violet and yellow fluorescence under the UV-light.

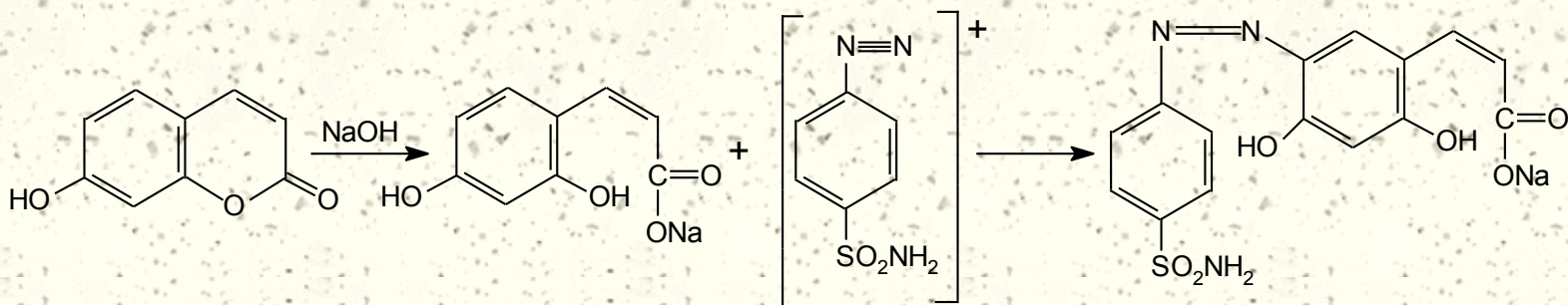


Identification

1. **Lactone test.** Coumarins are slowly hydrolyzed by dilute alkali and form yellow solution of *O*-coumaric acid salts. Coumarins regenerate after acidification or saturation by CO₂.



2. **Azocoupling test.** Diazotized radical connects to C₆ atom of coumarin in alkaline media. The solution gains red color.



Quantitative determination

- **Spectrophotometric**
- **High performance liquid chromatography**
- **Gravimetric**
- **Titration**
- **Fluorometric**
- **Polarographic**

Activity

- **Photosensitizing action** – (Furanocoumarins)
- **Spasmolytic** - (Hydroxy-, methoxycoumarins, Pyranocoumarins)
- **P-vitamin,**
- **anticoagulant action.** Coumarin is an anticoagulant that represses the synthesis of prothrombin, a plasma protein produced in the liver in the presence of vitamin K. Prothrombin is the precursor of the enzyme thrombin which catalyzes the conversion of fibrinogen to fibrin in the clotting process.

Melilot herb- Herba Meliloti
Melilot (sweet clover hay) - *Melilotus officinalis*
Fam. - Fabaceae

Widely distributed in Europe and Asia along roadsides.

The drug consist of leaf fragments with a blunt to sharply serrate dentate margin and which are glabrous or pubescent only on the lower surface along the nervative. The stem fragments are hollow with longitudinal grooves. Characteristic are the pale yellow papilionaceous flowers, which are arranged in one –sided racemes. The small straw yellow pods are mostly glabrous. Odor sweetish, of coumarin. Taste bitter, somewhat pungent and salty.



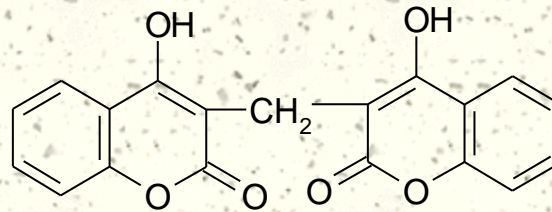
Act. Const.

∞ Coumarin 0,1%: dicoumarol, coumarin and 3,4-dihydrocoumarin, melilotoside, melilotin,

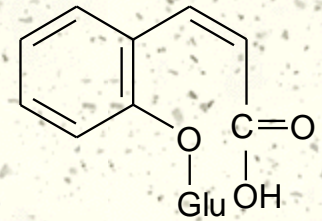
∞ Flavonoids: kaempferol and quercetin derivatives,

∞ Phenolic carboxylic acids,

∞ Saponins



dicoumarol



melilotoside

Uses

Disorders arising from chronic venous insufficiency such as pain, heaviness in the legs, night cramps in the legs and swellings. For the supportive treatment of the thrombophlebitis, post thrombic syndromes, hemorrhoids, and lymphatic congestion.

Side effect

Headaches occur in rare cases.

«*Cardiophyt*» – cardioprotector

Horse chestnut seed- Semen Hippocastani

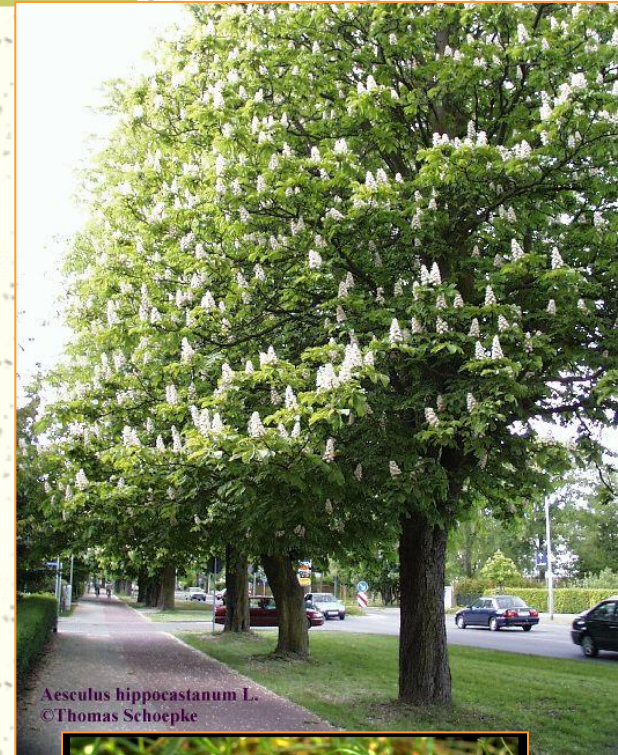
Horse chestnut - Aesculus hippocastanum

Fam.- Hippocastanaceae

The material of commerce is imported predominantly from eastern European countries.

The ripe and spherical , fruit capsule, up to 6 cm in diameter, is yellowish green and releases 1 (rarely 2 or 3) dark brown seeds, which are shiny when fresh; they are 2-4 cm in diameter, ovoid or subspherical and somewhat flattened at the base, with a large yellowish gray-brown and nearly circular hilum. The hard and brittle testa is closely surrounding the large , faintly yellow cotyledons of the embryo; the radicle is situated at the surface , in the form of a ridge.

Odorless. Taste: sweetish at first , then strongly bitter; the testa is astringent.



Act. Const.

- Saponins of complex composition: β -Aescin fraction is poorly soluble in water and consist of more than 30 triterpenoidal glycosides. α -Aescin fraction is water soluble.

- Coumarins: aesculetin, aesculin, fraxetin, fraxin, scopoletin, scopolin;

- Flavonoids: quercetin and kempferol, their 3-*O*-arabinosides, and 3-*O*-rhamnosides.

- Tannins;

- Volatile oil.

- Fatty oil;

- Sterols: stigmasterol, sitosterol, campesterol,

- Proteins, lectins;

- Starch.

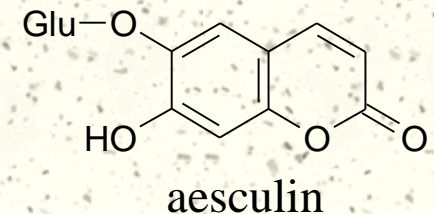
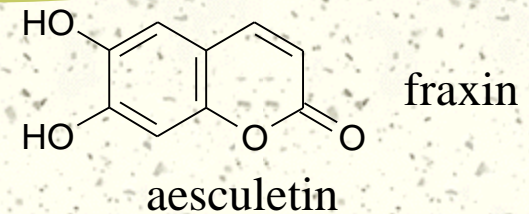
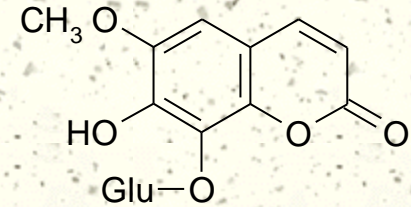
Uses

Treatment of varicose veins, hemorrhoids, phlebitis.

The main active constituent of horse chestnut seed extract, the triterpene glycoside mixture referred to as aescin, has shown anti- exudative and vascular-tightening effects in various animal experimental models. There are indications that horse chestnut seed extract reduces the activity of lysosomal enzymes that is increased in chronic venous disorders, so that the breakdown of glycocalix (mucopolysaccharides) in the region of the capillary walls is prevented.

Side effect

After oral ingestion in individual cases, itch, nausea, and gastric complaints may occur.



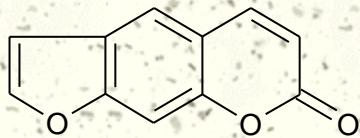
Greater ammi fruits - *Fructus Ammi majoris*

Greater ammi - *Ammi majus*

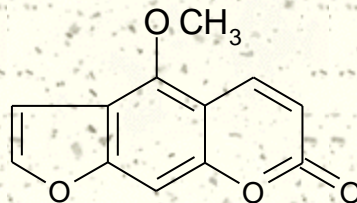
Fam. - Apiaceae

Act const

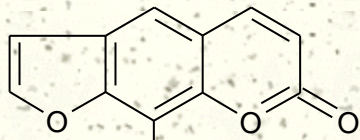
ℳ furanocoumarins: psoralen, bergapten, xanthotoxin, isopimpinellin,



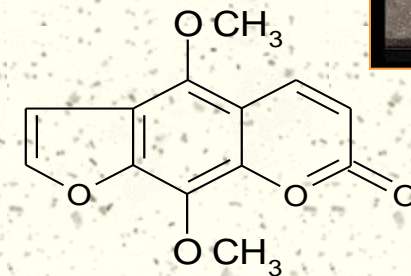
Psoralen



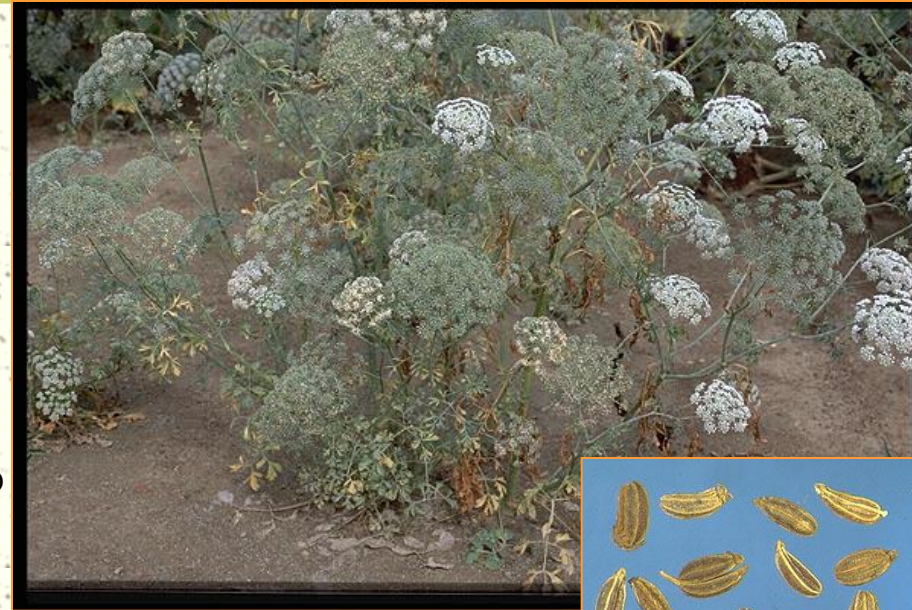
Bergapten



Xanthotoxin



Isopimpinellin



Uses

«*Ammifurin*» - photosensitizing action

Parsnip fruits - *Fructus Pastinacae*

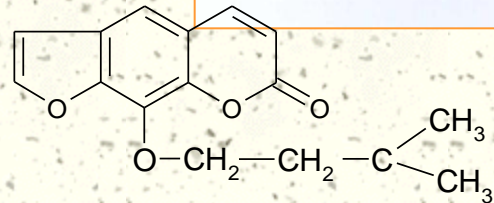
Parsnip - *Pastinaca sativa*

Fam. - *Apiaceae*

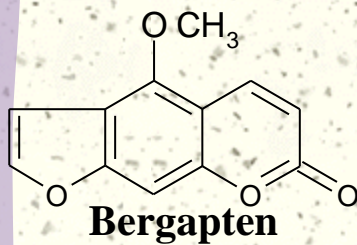
Act. Const.

M furanocoumarins:
 imperatorin,
 bergapten,
 xanthotoxin,
 isopimpinellin

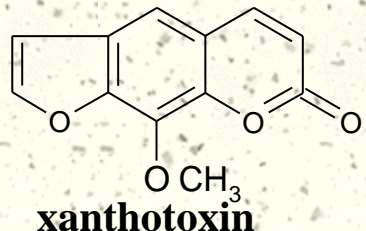
M flavonoids,
 M volatile oil



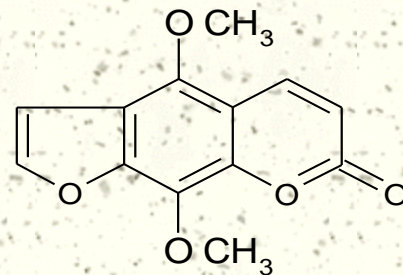
Imperatorin



Bergapten



xanthotoxin



Isopimpinellin

Uses

«*Beroxan*» – photosensitizing action
 «*Pastinacin*» – spasmolytic

Common fig leaves - *Folium Ficus caricae*

Common fig fruit - *Fructus Ficus caricae*

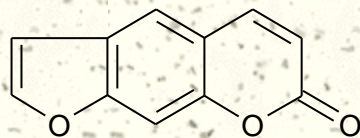
Common fig tree - *Ficus carica*

Fam. - *Moraceae*

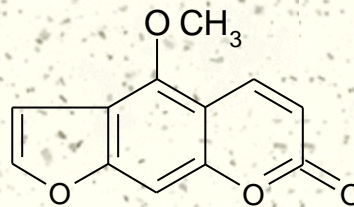
The common fig is a deciduous shrub or tree of up to 9 m in height. All parts exude milky latex. Large leaves on long stalks are borne near the branch ends. They are three to five lobbed, rough in texture above and somewhat hairy below. The figs are solitary green, purplish or brown and pear shaped.

Act. const.

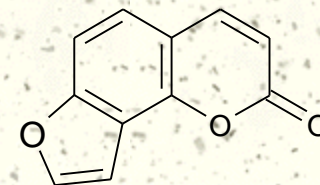
Phototoxic furanocoumarins



Psoralen



Bergapten



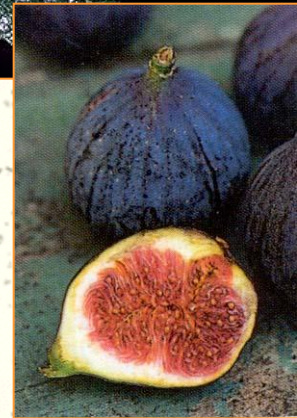
Angelicin

Uses

To treat the signs of vitiligo. In the presence of sunlight, furanocoumarins cause dermatitis. «*Psoberan*»



Ficus carica
Moraceae
©Gerald D. Carr



Angelica root - Rhizomata et radices Angelicae
Angelica - Angelica archangelica
Fam. - Apiaceae

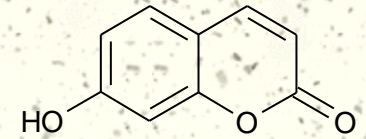
It is native throughout temperate zones of Europe and Asia. The root pieces are gray, reddish or dark brown on the outside with longitudinal furrows, often with thin roots having a radially structured, yellow xylem and secretory canals in the bark. The drug contains fragments of rhizomes, also with secretory canals. Odor strongly aromatic, taste spicy at first, then pungent, bitter, and persistently burning.



© Thomas Schöpke

Act. Const.

- Furanocoumarins;
- Coumarins: osthenol, osthol, umbelliferon;
- Chromones;
- Volatile oil 0,35 – 1,3%;
- Sesquiterpenoids;
- Phenolic compounds:
- Caffeic acid derivatives,
- tannins,
- flavanones,
- Sitosterol,
- Fatty acids.



Umbelliferon

Uses

Coumarins and furanocoumarins are reported to have potent coronary vasodilatory effects and are calcium antagonists.

Due to its bitter principles and volatile oil content it belongs to the group of the aromatic bitters which stimulate gastric and pancreatic secretions. It is used as appetite stimulant, as a stomachic in dyspepsia with insufficient gastric secretion as well as antispasmodic and antimicrobial, carminative.

In folk medicine it is used as an antiseptic, expectorant, as a diuretic and for insomnia.

«**Energotonic Doppelherz**»

Wild Carrot fruits - *Fructus Dauci carotae*
Wild Carrot - *Daucus carota*
Fam. - *Apiaceae*

Wild carrot should not be confused with the common cultivated carrot, *D. carota* L. *subsp. sativus* (Hoffm.), which has the familiar fleshy orange-red edible root. Wild carrot has an inedible tough whitish root.

Wild carrot is listed by the Council of Europe as a natural source of food flavouring



Act. const.

- ℳ Coumarins: 8-Methoxypsoralen and 5-methoxypsoralen (0.01-0.02 µg/g fresh weight) in fresh plant
- ℳ **Flavones** (e.g. apigenin, chrysin, luteolin), flavonols (e.g. kaempferol, quercetin) and various glycosides,
- ℳ daucine (alkaloid),
- ℳ **Volatile oils**: α-pinene, β-pinene, geraniol, geranyl acetate, limonene; β-bisabolene, β-elemene, caryophyllene, carotol, daucol (sesquiterpenes); asarone (phenylpropanoid derivative)
- ℳ Choline,
- ℳ fatty acids (butyric, palmitic).

Uses

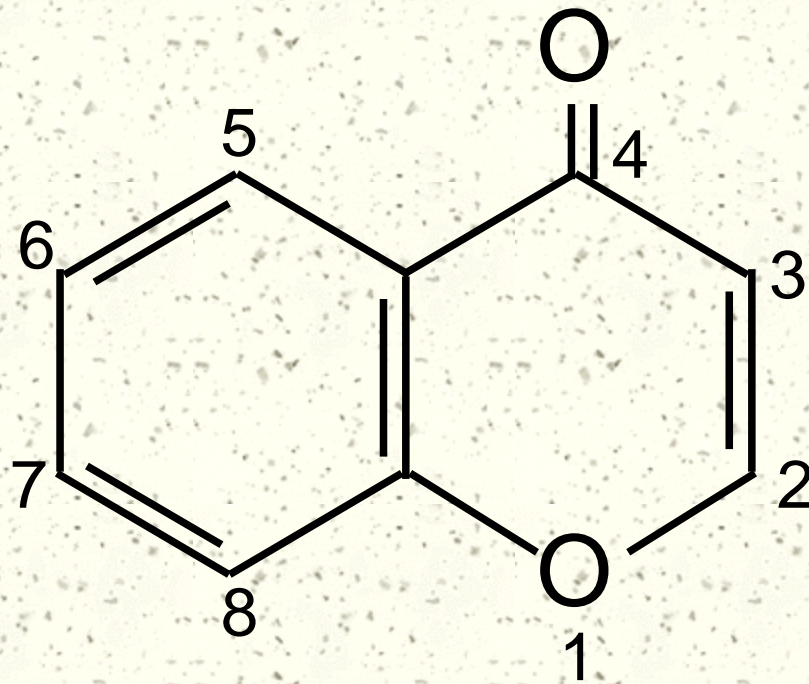
Wild carrot is stated to possess diuretic, litholytic, and carminative properties. Traditionally, it has been used for urinary calculus, lithuria, cystitis, gout, and specifically for urinary gravel or calculus

«*Urolesan*» - Spasmolytic, anti-inflammatory, cholagogue, diuretic, litholytic.

Side-effects

- # Hypersensitivity reactions, occupational dermatitis and positive patch tests have been reported for wild carrot. Wild carrot is reported to have a slight photosensitising effect. Furanocoumarins are known photosensitisers.
- # Toxicity data only refer to the oil and indicate low toxicity. However, in view of the documented mild oestrogenic activity and potential for internal irritation by the oil, excessive ingestion should be avoided.

Chromones - are natural biologically active substances with the general formula C_6-C_3 , 9,10-benzo- γ -pyrone derivatives.

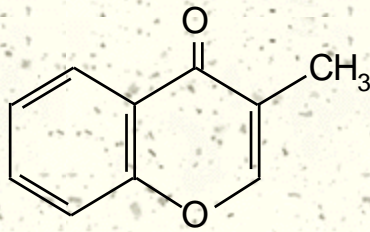


9,10- benzo- γ -pyrone (chromone)

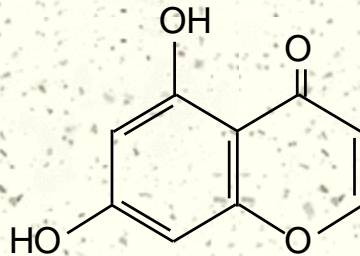
Classification

1. **Simple chromones** contain hydroxy-, alkoxy-groups, linked to 9,10-benzo- γ -pyrone, and their glycosides:

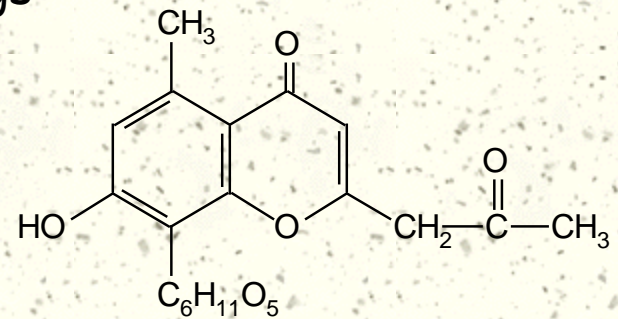
- a) radical linked to γ -pyrone ring
- b) radical linked to benzene ring
- c) radical linked to benzene and γ -pyrone rings



3-Methylchromone



5,7-Dihydroxychromone

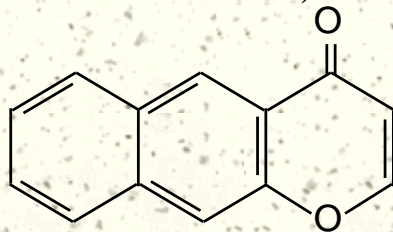


Aloezone

2. Benzochromones

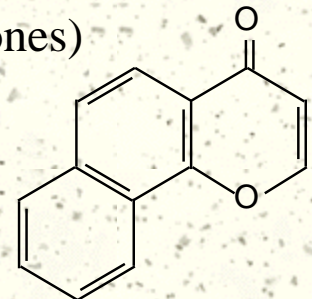
a) **Linear**

(6,7-benzochromones)

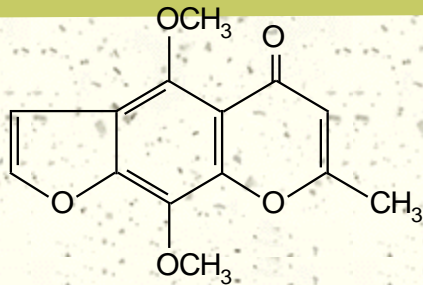


b) **Angular**

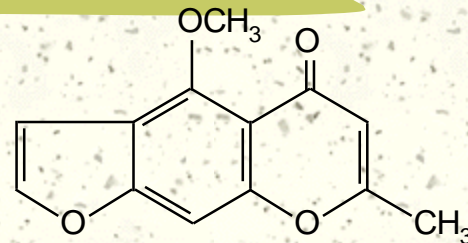
(7,8-benzochromones)



3. Furanochromones and their glycosides



Khellin

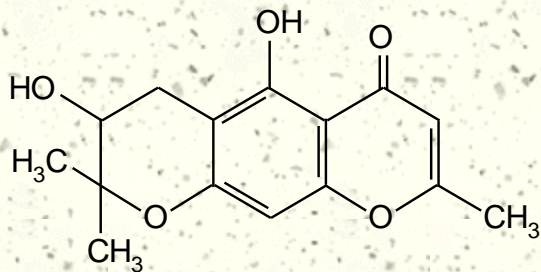


Visnagin

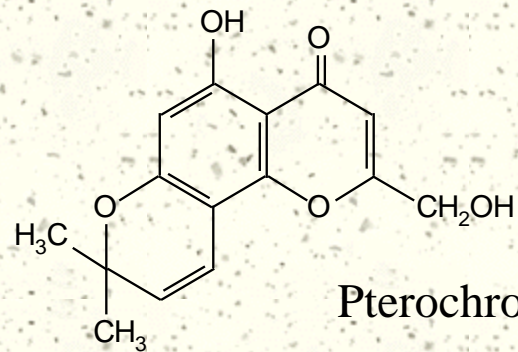
4. Pyranochromones

a) **Linear (6,7-pyranochromone)**

b) **Angular (7,8-pyranochromone)**



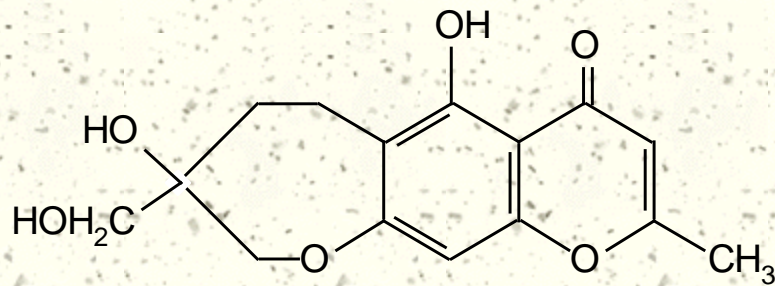
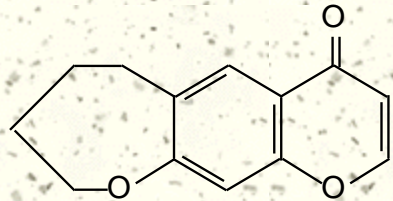
Gammaudol



Pterochromanol

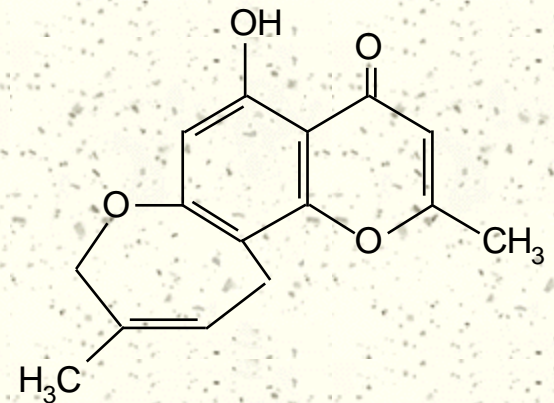
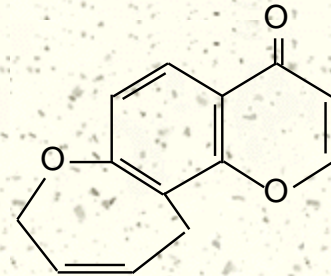
5. Oxepinochromones

a) Linear (6,7-hydroxepinochromones)



Ptaeroglycol

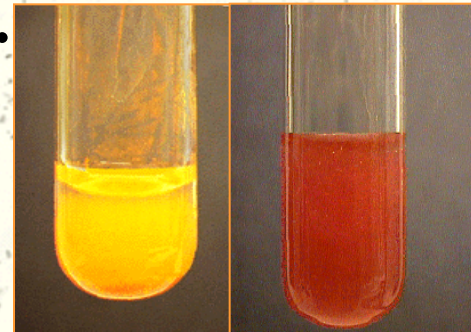
b) Angular (7,8-hydroxepinochromones)



Pteroxilin

Physical and chemical properties:

- ↳ specific odor;
- ↳ form *O*-hydroxy- β -diketones with alkali solution without regeneration of **γ -pyrone ring** (unlike coumarins);
- ↳ give fluorescence under the UV-light (blue, yellow, greenish yellow, yellowish brown or brown);
- ↳ **don't form** colored compounds with diazotized sulphanic acid, 2% solution of aluminum chloride, with magnesium and concentrated hydrochloric acid (unlike flavonoids);
- ↳ **form** colored compounds with concentrated acids (**citric** color), and concentrated alkali (**purple** color).



Activity

- ↳ Spasmolytic,
- ↳ Antibacterial,
- ↳ Anticoagulant,
- ↳ Analgetic,
- ↳ Antiallergic.



Visnaga (Khella) fruit - Fructus Visnagae daucoides (Fructus Ammi visnagae)

Visnaga (Khella) - *Visnaga daucoides*
Fam. - Apiaceae

It is indigenous to the Nile delta, the Mediterranean region and the near East. It is cultivated in Egypt, Sought America.

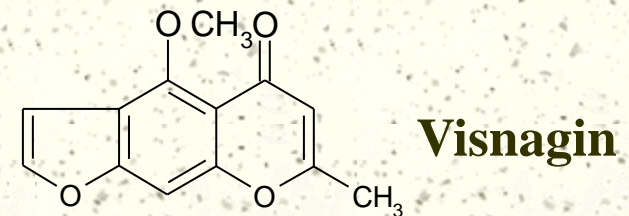
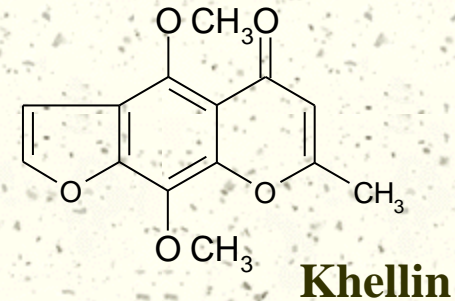
The drug consist of separate mericarps ; each mericarp is about 0,8-1,2 mm wide, 0,8-1mm thick, and 2,0 - 2,5mm long. The mericarp is ovoid lanceolate in outline and mostly split into mesicarps , greenish brown and glabrous, with 5vyellowish primary ridges.

Odor somewhat aromatic. Taste faintly bitter.



Act. Const.

- The main active compound is khellin;
- Visnagin;
- Khellol glucoside;
- Traces of furanocoumarins;
- Flavonoids;
- Volatile oil;
- Fatty oils;
- Proteins.



Uses

The drug relaxes smooth muscles and lowers the tonicity of the urethra. A decoction is used to ease the passage of kidney calculi.

«Khellin»; Khellin, as component of «Avisan», «khellatirin», «khellavirin», «Vicalin», «Phytolit», «Marelin» - **spasmolytic**

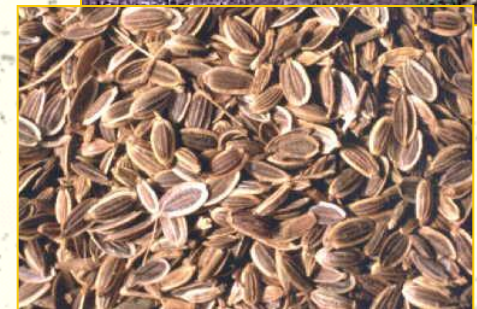
Side effect

Khella has been shown to have weak phototoxic effect.

Dill fruits- Fructus Anethi graveolentis
Dill - Anethum graveolens
Fam. - Apiaceae

It is indigenous to the Mediterranean districts and southern Russia. It is cultivated in England, Germany and Romania. It consists of separated mericarps. Each mericarp is dorsally compressed, broadly oval and about 3 to 4 mm wide and 1 mm thick. The mericarp is brown with white yellowish membranous wings, which are the extended lateral ridges. Odor strong aromatic. Taste faintly bitter, specific.

Photo Henriette Kress
<http://www.ibiblio.org/herbmed>



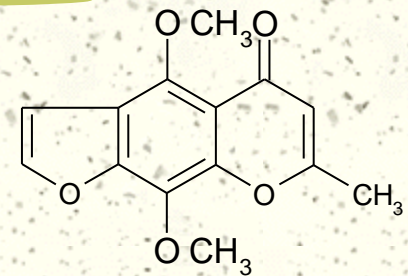
Act. Const.

Chromones: khellin, visnagin

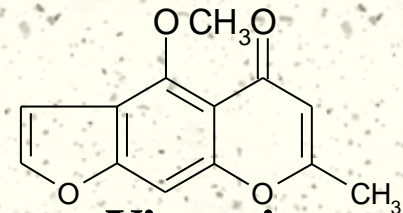
Volatile oil;

Fixed oil;

Protein.



Khellin



Visnagin

Uses

Aromatic stimulant, carminative, being given to infants to relieve flatulence.

Medicine «*Anethin*» - spasmolytic.

Literature

1. Pharmacognosy / ed. by prof. V.S. Kyslychenko Kharkiv/ NUPh, "Zoloti storinky". - 2011. - 600 p.
2. Trease G.E., Evans W.C. Pharmacognosy. - London; Philadelphia; Toronto; Sydney; Tokyo; WB Saunders, 1996. - 832 s.
3. Tyler V.E., Brady L.R., Robbers J.E. Pharmacognosy, 9-th ed. - Leo and Fabiger. Philadelphia, 1988.-856 p.
4. British Herbal Pharmacopoeia / British Herbal Medicine Association.- London, 1996. - 212 p
5. European Pharmacopoeia - Fourth edition. - counsel of Europe, Strasbourg, 2001
6. Практикум по фармакогнозии: учебное пособие для студ. вузов / под ред В.Н.Ковалева. - Х: Изд-во НФАУ, Золотые страницы, 2003. - 512 с.