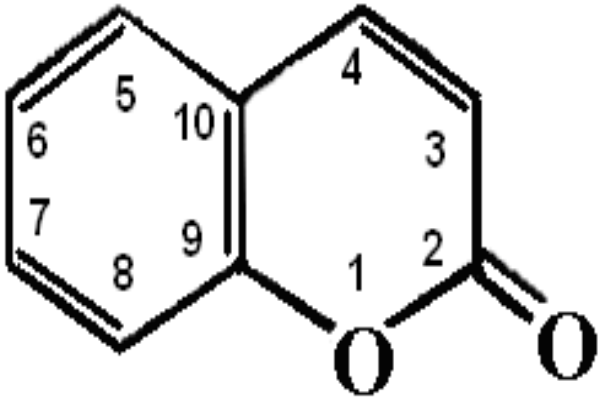
Coumarins. Medicinal plants and raw materials containing coumarins

1. Coumarins. Concept and classification
2. Physico-chemical properties
3. Methods of isolation
4. Qualitative and quantitative analysis
5. Medicinal plant raw materials containing coumarins

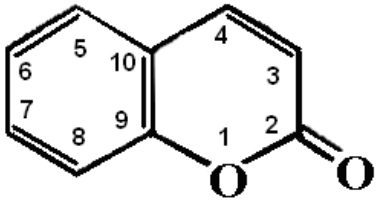
Coumarins are natural compounds based on 9,10-benzo-alpha-pyrone (a lactone of cis-ortho-hydroxycinnamic acid).



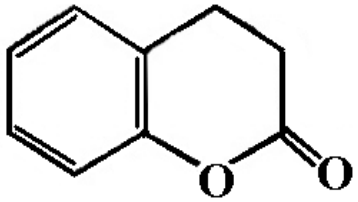
CLASSIFICATION

(Speth, depending on the chemical structure)

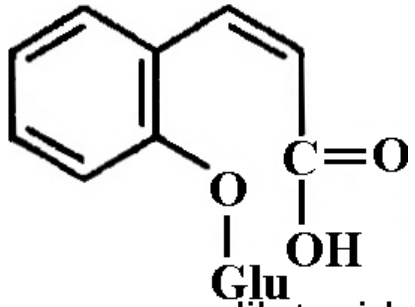
1. Simple coumarins and their glycosides :



coumarin

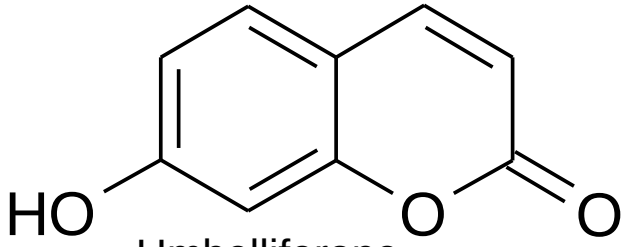


dihydrocoumarin



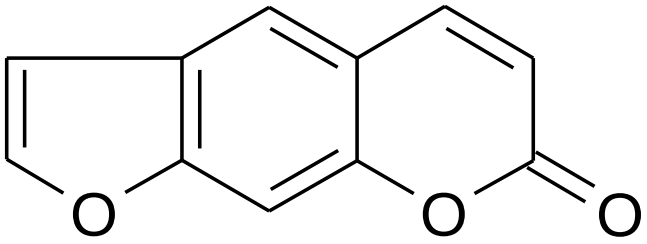
melilotoside

2. Hydroxy-, methoxy- (alkoxy-) and methylenedihydroxycoumarins and their glycosides.

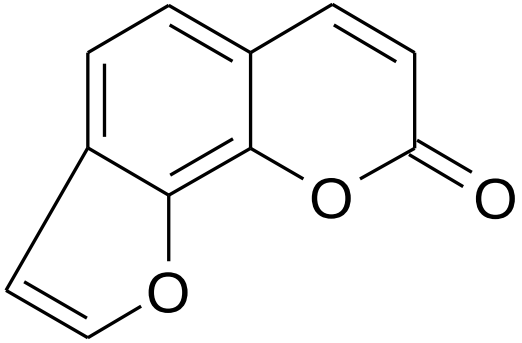


Umbelliferone
7-hydroxycoumarin

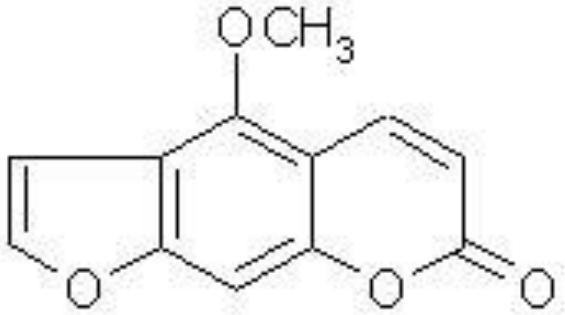
3. *Furocoumarins*



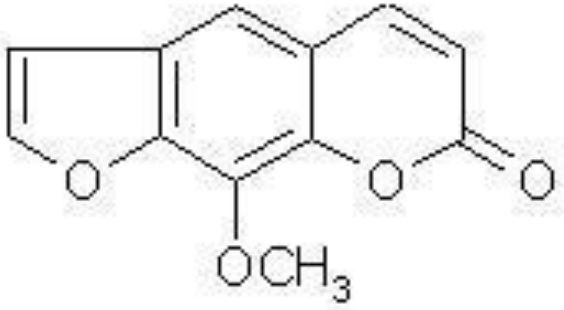
Psoralen
(6,7-furocoumarin)
(found in fig leaves, psoralea fruit)



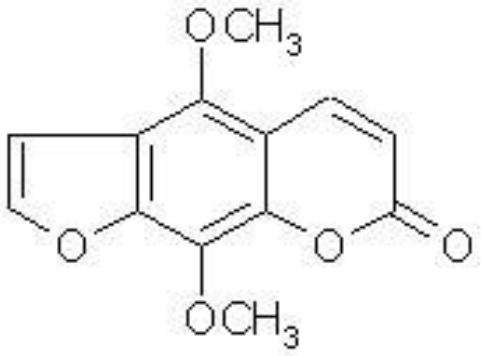
Angelicin
(7,8-furocoumarin)
(is found in the fruit of the Pastinaca sativa)



Bergapten



Xanthotoxin

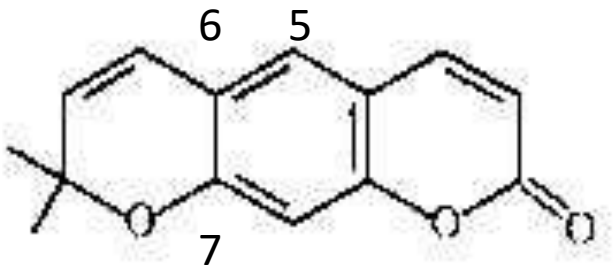


Isopimpinelline

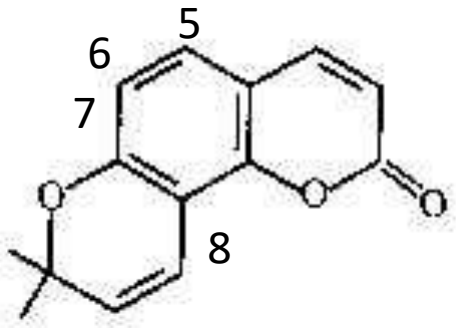
4. Pyranocoumarins.

Depending on the site of condensation,
they are subdivided into 3 groups:

a) derivatives of 5,6-pyranocoumarin;
b) derivatives of 6,7-pyranocoumarin;
c) derivatives of 7,8-pyranocoumarin.

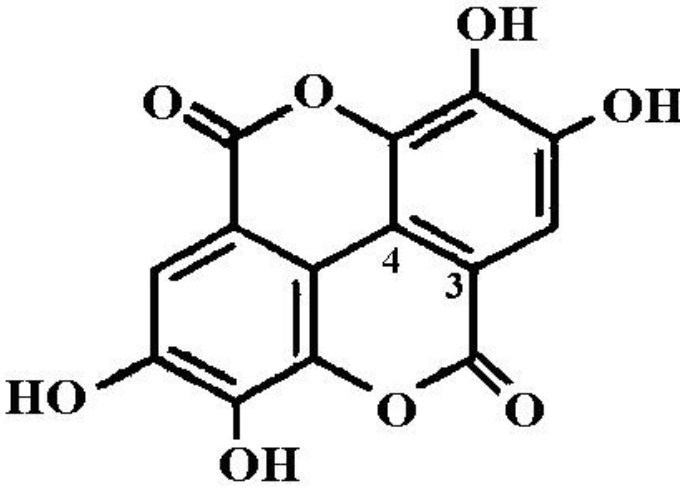


6-7- pyranocoumarins



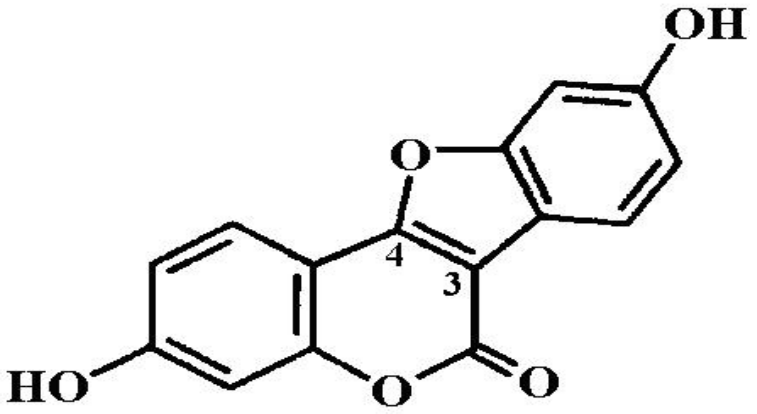
7-8- pyranocoumarins

5. Benzocoumarins.



Ellagic acid

6. Kumestans.



7. More complex compounds, which include the coumarin system.

Physical and chemical properties

PHYSICAL PROPERTIES

Coumarins are crystalline substances, colorless or slightly yellowish. They have a pleasant odor resembling the smell of fresh hay. Coumarins are well soluble in organic solvents, as well as fats and fatty oils. Coumarins are mostly insoluble in water; their glycosides are generally soluble in water and insoluble in organic solvents.

When heated to 100 ºC, coumarins ignite to form needle-shaped crystals.

Many coumarins show very characteristic fluorescence (blue, violet, green or yellow) in UV light.

CHEMICAL PROPERTIES

1. **Lactone ring rupture reaction (lactone test).**

Based on lactone ring breakage under the action of alkali with the formation of salts of ortho-hydroxycinnamic acid (ortho-coumaric acid).

2**. Reaction of azo combination with diazonium salts.**

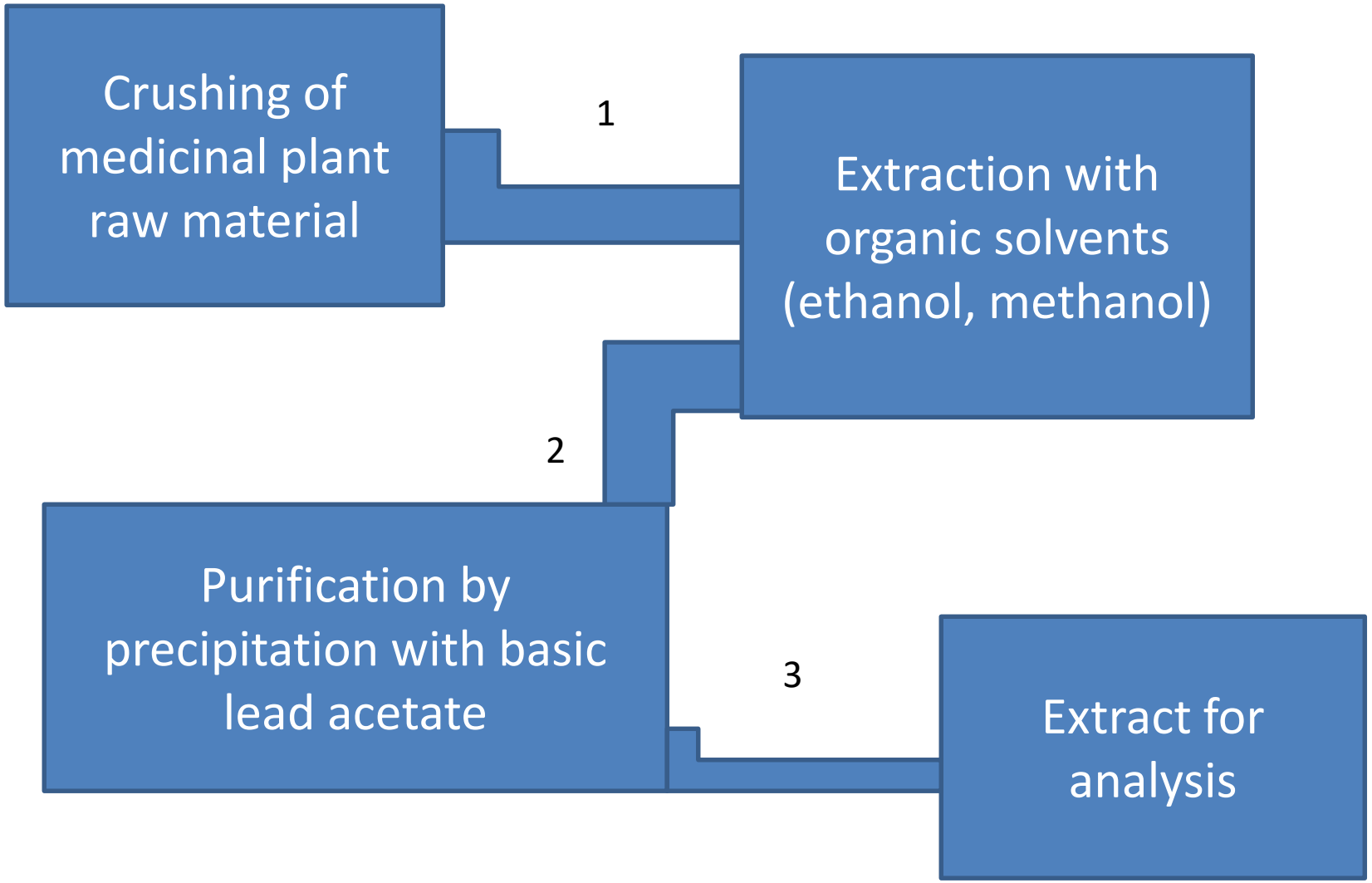
The products of alkaline hydrolysis form in weakly alkaline medium salts of cis-ortho-hydroxycinnamic acid (coumarinates), the phenolic hydroxyl of which orients the azo group to ortho- or para-position 6 or 8 to form an azo dye.

3. Alloying reaction with alkali. When fused with crystalline sodium hydroxide, the lactone ring is broken to form simple phenols (e.g. resorcinol).

4. Hydrogenation.

At elevated pressure and in the presence of a catalyst, hydrogen addition at position 3,4 and hydrogenation of double bonds in the aromatic ring is possible.

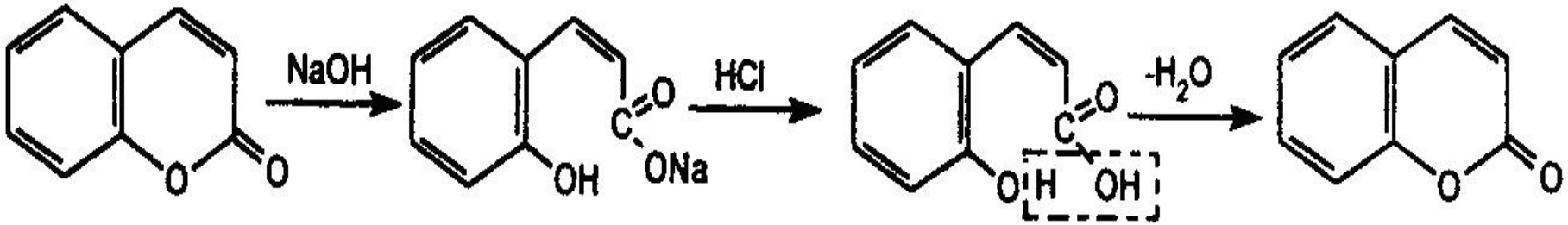
EXTRACTION


Crushing of medicinal plant raw material
1
Extraction with organic solvents (ethanol, methanol)
2
Purification by precipitation with basic lead acetate
3
Extract for analysis

QUALITATIVE ANALYSIS

Coumarins are able to:
-engage in lactone ring breaking reactions (lactone test);
-give coloured solutions with diazo compounds;
-fluoresce in UV light.

1. Lactone test (proposed by G.A. Kuznetsova)



2. Reaction for the formation of azo dye.

3. Microsublimation reaction

QUANTITATIVE DETERMINATION

1. ***Polarographic method.*** Used to determine the content of furocoumarins in parsnip fruits**.**
2. ***Spectrophotometric method.*** It is used to determine the content of simple coumarins in the herb yellow sweet-clover.
3. ***Chromatographic-spectrophotometric method.*** Used to determine the content of furocoumarins in fruits of Ammi visnaga and fig leaves.
4. ***Gravimetric method***.
5. ***Neutralisation method***
6. ***Colorimetric method***
7. ***7. Fluorimetric method***

PHARMACOLOGICAL ACTIVITY AND MEDICAL USE

EMOLLIENT EFFECT (melilot herb in the form of cautery)

PHOTOSENSITIZING EFFECT"Beroxan", "Psoralen", "Ammifurin", "Psoberan"

ANTICOAGULANT EFFECT"Esflazid", "Escuzan liquidum", "Escuzan".

CORONARY DILATING AND ANTISPASMODIC ACTION"Floverine," "Safinor."

VENOTONIZING AND CAPILLARY-STRENGTHENING EFFECT (horse chestnut coumarins)

ANTITUMOR EFFECT(coumarins of mountain bitterroot)

Melilot herb – Meliloti herba

Yellow sweet-clover – Melilotus officinalis (L.) Pall.

Tall melilot - Melilotus altissimus Thuill.

Family Fabaceae

Melilotus officinalis, known as **sweet yellow clover**, **yellow melilot**, **ribbed melilot** and **common melilot**.

Melilotus officinalis can be an annual or biennial plant, and is 120–180 centimetres high at maturity.

Leaves alternate on the stem and possess three leaflets.

Yellow flowers bloom in spring and summer and produce fruit in pods typically containing one seed.

Plants have large taproots and tend to grow in groups. Plants have a characteristic sweet odor.

M. officinalis is native to Europe and Asia and has been introduced to North America as a forage crop. Common places where it can be found include open disturbed land, prairies, and savannahs, and it grows in full or partial sunlight. It is an invasive species in areas where it has been introduced, especially in open grasslands and woodlands where it shades and outcompetes native plant species.

Medium to tall hairless plant to 1.5 metres, stems erect and branched. Leaves oblong, sharply toothed, stipules slender, untoothed. Flowers yellow, 5 to 7 mm long, in many-flowered racemes, the wings equalling the keel. Pod oval, 5 to 6 mm, hairy and net veined, black when ripe with a persistent style.

Habitat

Damp habitats, woodland margins, roadsides.

Impurity

Melilotus albus is an annual or biennial legume that can reach 2.5 m in height. Flowers are small, white, tubular at the base and become broader toward the outer edges and wing and keel petals are about equal in length.

Melilotus dentatus is a species of shrub. They have a self-supporting growth form. They have compound, broad leaves. Individuals can grow to 0.38 m.

Melilotus suaveolens is a annual/biennial growing to 1 m. The species is hermaphrodite (has both male and female organs) and is pollinated by Bees.
It can fix Nitrogen.
Suitable for: light (sandy), medium (loamy) and heavy (clay) soils and prefers well-drained soil.

The flowering tops of plants (up to 30 cm long) are used as medicinal raw materials.flowering tops of plants (up to 30 cm long), in which the bulk is made up of leaves and flowers.leaves and flowers. The plants are usually cut or mown whole when harvesting. whole, and after drying, the raw material is threshed. Drying. air-shade drying at a temperature not exceeding 40 ºC.

Chemical composition

Medicinal herb raw material contains coumarins (0.4-0.9 %): coumarin, dihydrocoumarin (melilotin), dicoumarol and ortho-coumaric acid glucoside melilotoside. It also contains essential oil, polysaccharides (mucilage), saponins, and amino acids.

Standardisation (FS.2.5.0011.15 GF XIV ed.): content of coumarins not less than 0.3 %

Pharmacotherapeutic group.

Softening (topical) agent.

Uses.

Sweet-clover herb is included in the softening collections forcauterisations, with which accelerates the resorption and opening of abscesses.

In folk medicine used expectorant, softening,vetrogonic, analgesic, sedative properties of melon. Most oftenDonnica used in inflammatory diseases of the respiratory system, andas well as with hyperexcitability and insomnia.

parsnip frucrus ***- Pastinacae sativae fructus***
(Fructus pastinacae sativae)

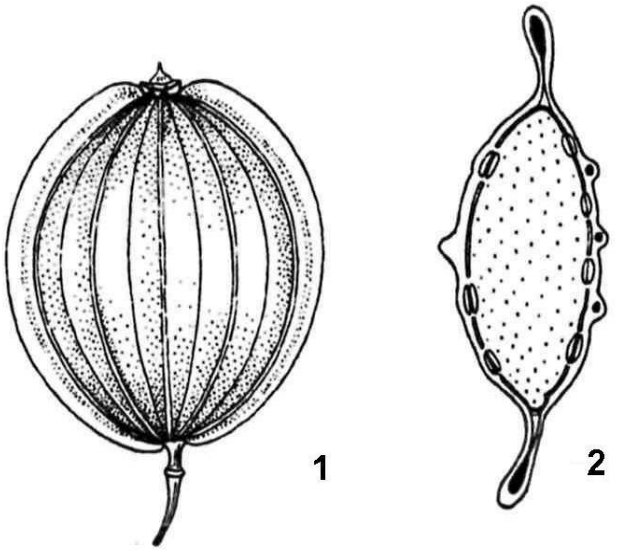
Parsnip –
Pastinaca sativa L.

Family *Apiaceae*

The parsnip is a biennial plant with a rosette of roughly hairy leaves that have a pungent odor when crushed. Parsnips are grown for their fleshy, edible, cream-colored taproots. The roots are generally smooth, although lateral roots sometimes form. Most are narrowly conical, but some cultivars have a more bulbous shape, which generally tends to be favored by foo processors as it is more resistant to breakage. The plant's apical meristem produces a rosette of pinnate leaves, each with several pairs of leaflets with toothed margins. The lower leaves have short stems, the upper ones are stemless, and the terminal leaves have three lobes. The leaves are once- or twice-pinnate with broad, ovate, sometimes lobed leaflets with toothed margins; they grow up to 40 cm long. The petioles are grooved and have sheathed bases. The floral stem develops in the second year and can grow to more than 150 cm tall. It is hairy, grooved, hollow (except at the nodes), and sparsely branched. It has a few stalkless, single-lobed leaves measuring 5 to 10 cm long that are arranged in opposite pairs.

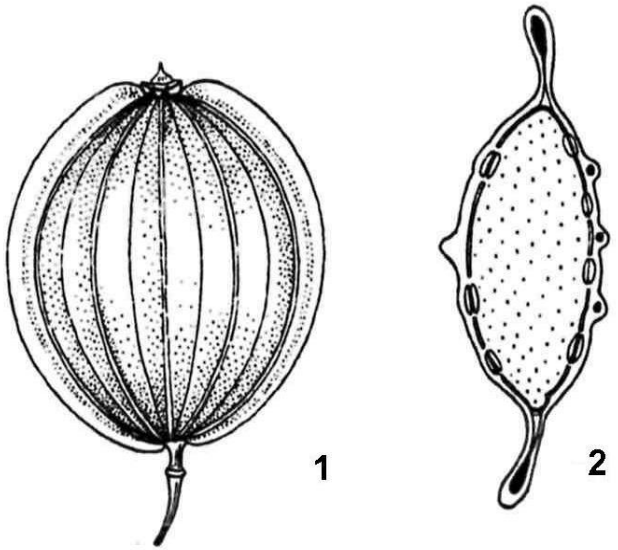
The yellow flowers are in a loose, compound umbel measuring 10 to 20 cm in diameter. Six to 25 straight pedicels are present, each measuring 2 to 5 cm that support the umbellets (secondary umbels). The umbels and umbellets usually have no upper or lower bracts. The flowers have tiny sepals or lack them entirely, and measure about 3.5 mm. They consist of five yellow petals that are curled inward, five stamens, and one pistil. The fruits, or schizocarps, are oval and flat, with narrow wings and short, spreading styles. They are colored straw to light brown, and measure 4 to 8 mm long.

Pastinacae sativae fructus



Fruits are harvested by separate or direct harvestingharvesting, when yellow colour of 50% of umbrellas turns to brown.brown. After threshing of peduncles and sorting, fruits are cleaned of impurities and dried in the shade in ventilated rooms.impurities and dried in the shade in ventilated rooms, placing a layer of 4-5 cm.cm.

Pastinacae sativae fructus



External features. Rounded-elliptical, flattened fruits.visoplodniki, usually splitting in the raw material into two semi-fruits -mericarpy. The mericarps on the dorsal side are slightly convex with threefiliform and two marginal wing-like ribs. In the troughsbetween the ribs there are 4 dark brown secretory ducts, on theon the ventral side there are 2 such ducts. Fruit length is 4-8 mm, width 3-6 mm.Colour from greenish straw to dark brown. The odour is pleasant,peculiar. The flavour is spicy, slightly burning.

Chemical composition.

Parsnip fruits contain furocoumarins - bergapten, xanthotoxin, sfondin, as well as polyins, flavonoids - rutin, parsnoside, hyperin, essential oil - up to 3.6 %. Heptyl, hexyl and octyl-butyl esters of butyric acid give a spicy odour to the plant. The fruits contain K, Ca, Mg, Fe, Mn, Zn, Cg, Al, Cu. The plant accumulates Se.

Standardisation (FS 42-2548- 88): Content of the sum of furocoumarins in terms of xanthotoxin not less than 1 % (polarographic method)

Pharmacotherapeutic group.

Photosensitising agent. The raw material is used to produce drugswith photosensitising properties.

Fig leaves - Fici caricae folia
(Folia Fici caricae)

Common fig - Ficus carica L.
Family Moraceae

Ficus carica is a gynodioecious, deciduous tree or large shrub that grows up to 7–10 m tall, with smooth white bark. Its fragrant leaves are 12–25 cm long and 10–18 cm wide, and are deeply lobed (three or five lobes).

The fig fruit develops as a hollow, fleshy structure called the syconium that is lined internally with numerous unisexual flowers. The tiny flowers bloom inside this cup-like structure. Although commonly called a fruit, the syconium is botanically an infructescence, a type of multiple fruit. The small fig flowers and later small single-seeded (true) fruits line its interior surface. A small opening or ostiole, visible on the middle of the fruit, is a narrow passage that allows the specialized fig wasp, Blastophaga psenes, to enter the inflorescence and pollinate the flowers, after which each fertilized ovule (one per flower, in its ovary) develops into a seed. At maturity, these 'seeds' (actually single-seeded fruits) line the inside of each fig.

The edible mature syconium develops into a fleshy false fruit bearing the numerous one-seeded fruits, which are technically drupelets. The whole fig fruit is 3–5 cm (1–2 in) long, with a green skin that sometimes ripens toward purple or brown. Ficus carica has milky sap, produced by laticifer cells. The sap of the green parts is an irritant to human skin.

Destribition. Fig tree is one of the oldest cultivated plants.plants. In Asia its culture has been known for 5000 years, in Europe - 2000 years. On the territory of the CISCIS territory it is cultivated in Transcaucasia and Central Asia. The mainfig plantations are located in Uzbekistan in the Fergana Valley. In the wildThe fig tree can be found in Transcaucasia, in some parts of Central Asia (Uzbekistan, Tajikistan, Turkmenistan), and in some parts of Central Asia (Uzbekistan, Tajikistan, Turkmenistan).Asia (Uzbekistan, Tajikistan, Turkmenistan) at an altitude of 600 to 1000 metres above sea level on the slopes of mountains and in some parts of Central Asia.

Chemical composition

Fig leaves contain furocoumarins (psoralen, bergapten), triterpenoids, steroidal compounds (sitosterol, stigmasterol, ficusogenin), organic acids, tannins, flavonoids, essential oil. The fruits contain pectin substances (5-6%); sugars (up to 75%); tannins (2%); organic acids; triterpene saponins; vitamins C, B1, B2, A, E, PP; trace elements. In addition, they contain an enzyme - ficin, which has fibrinolytic properties.

Standardisation (VFS 42-878-79): content of the sum of furocoumarins not less than 0.7 %; content of psoralen not less than 0.42 % (chromatospectrophotometric method)

Pharmacotherapeutic group.

Photosensitising agent.

Uses. The leaves are used to prepare the preparation "Psoberan", containing aa mixture of furocoumarins, mainly psoralen and bergapten.It is used as a photosensitising agent in vitiligo(leucoderma), alopecia areata (baldness), ulcers and furuncles. Fruitsfigs have a mild emollient and mild loosening effect.

Благодарю

КУМАРИНЫ

ЗА ВНИМАНИЕ!