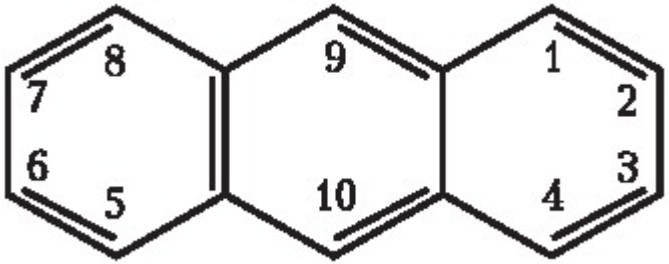
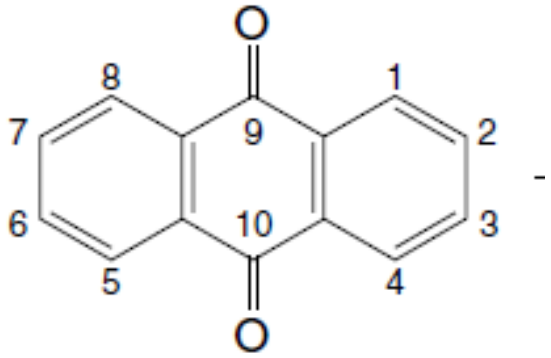
Anthraquinones and glycosides. Classification, methods of analysis. Medicinal plants and raw materials containing anthracene derivatives.

Anthracene glycosides are aromatic organic compounds and derivatives of anthracene.



Anthraquinones derivatives are organic compounds containing the 9,10-anthracenedione nucleus of different oxidation levels, types of connection and condensation of monomer structures. The general formula is C 6 -C 2 -C 6.

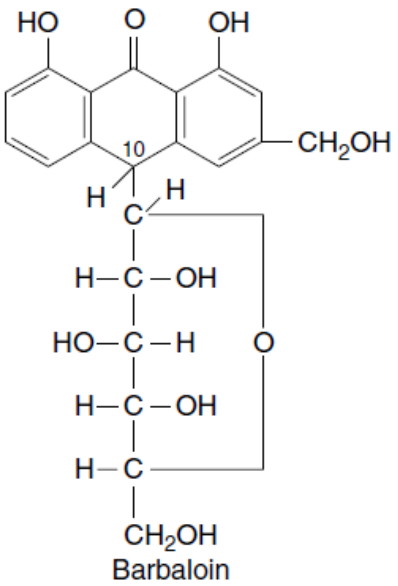


Anthraquinone

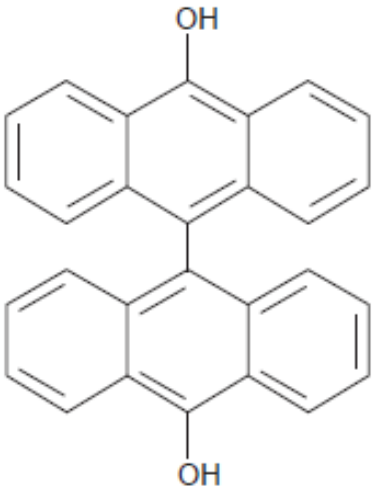
Anthracene glycosides are chiefly found in dicot plants but to some extent it is also found in monocot and lower plants. It consists of glycosides formed from aglycone moieties like anthraquinones, anthranols, anthrones or dimers of anthrones or their derivatives. Anthrones are insoluble in alkali and do not show strong fluorescence with them, while anthronols which are soluble in alkali show strong fluorescence. The reduced anthraquinones are biologically more active. Anthroquinones that are present in fresh drugs are in reduced form, which on long storage get oxidized and hydrolysed, Glycosides of reduced derivatives are more active than oxidized aglycones. This is due to the fact that sugars take the glycosides to the site of action and thus are more active.

Classification

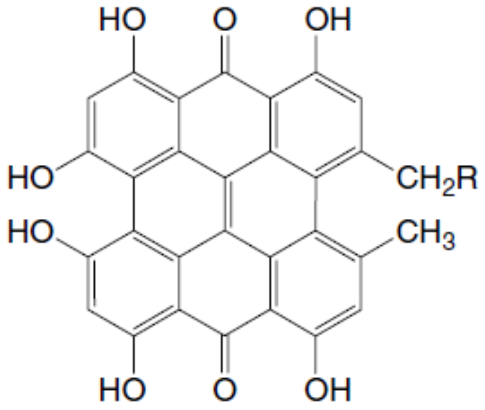
I. Monomers – anthracene derivatives with one anthracene molecule.
II. Dimers – compounds with two molecules of anthracene.
III. Condensed – anthracene derivatives, in which two monomers linked between each other with 2 – mono and 1 – double bounds.



Barbaloin



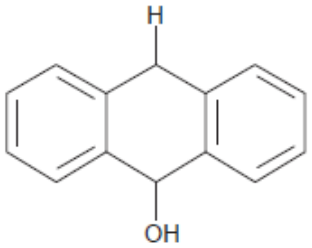
Dianthranol



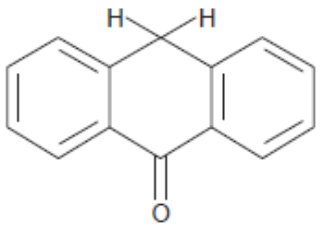
Hypericin, R = H
Pseudohypericin, R = OH

Monomer compounds

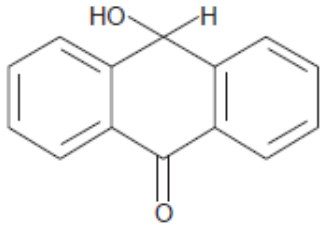
of the ***reduced form***



Anthranol

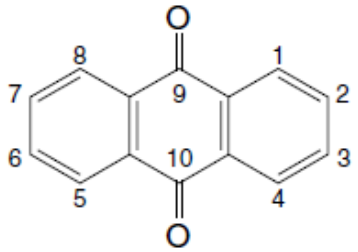


Anthrone



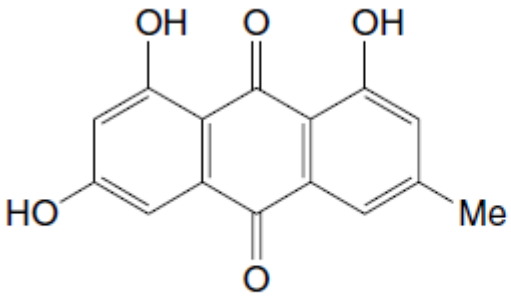
Oxanthrone

of the **oxidizing form**

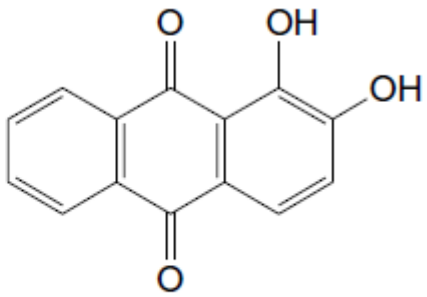


Anthraquinone

According to the location of OH-group, monomer compounds divided on the emodin (chrysacin) and alizarin classes 1,8-dihydroxiantrachinine 1,2-dihydroxiantrachinine



Emodin



Alizarin

Physical and chemical properties

Anthraquinone derivatives are often orange-red compounds, which may sometimes be observed *in situ (e.g. in the medullary rays of* rhubarb and cascara). They are usually soluble in hot water or dilute alcohol. Borntrдger's test is often used for their detection. The powdered drug is macerated with an immiscible organic solvent, ether is recommended, and after filtration aqueous ammonia or caustic soda is added, when a pink, red or violet colour in the aqueous layer after shaking indicates the presence of free anthraquinone derivatives.

If glycosides only are present, the test should be modified by first hydrolysing with alcoholic potassium hydroxide solution or 2 m acid. When alkali is added to powdered drugs or to sections, the red colour produced serves to locate the anthraquinone derivatives in the tissues (e.g. in the medullary rays of cascara bark). If the drug being tested contains either very stable anthraquinone glycosides or reduced derivatives of the anthranol type, Borntrger's test will be negative.

Anthraquinones containing a free carboxylic acid group (e.g. rhein) can be separated from other anthraquinones by extraction from an organic solution with sodium bicarbonate solution.

Anthranols and anthrones

These reduced anthraquinone derivatives occur either free or combined as glycosides. They are isomeric and one may be partially converted to the other in solution. The parent substance, anthrone, is a pale yellow, non-fluorescent substance which is insoluble in alkali; its isomer, anthranol, is brownish-yellow and forms a strongly fluorescent solution in alkali. Anthranol derivatives, such as are found in aloes, have similar properties, and the strong green fluorescence which aloes give in borax or other alkaline solution has long been used as a test for its identification. Anthranols and anthrones are the main constituents of chrysarobin, a mixture of substances prepared by benzene extraction from the material (araroba) found in the trunk cavities of the tree *Andira araroba. If a little chrysarobin is treated on a white tile with a* drop of fuming nitric acid, the anthranols are converted into anthraquinones.

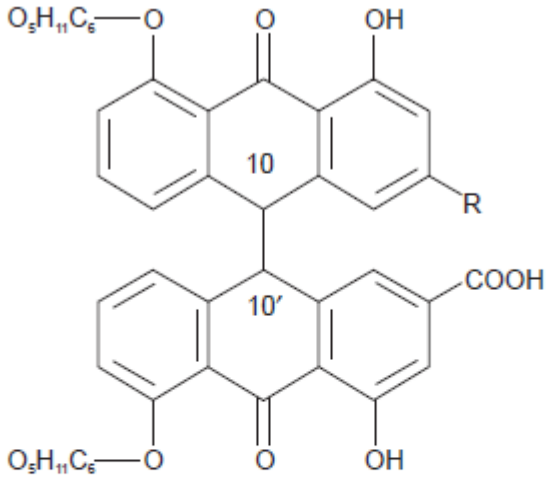
A drop of ammonia allowed to mix gradually with the acid liquid produces a violet colour. This modification of Borntrger's test had been used as a test for identity before the underlying chemistry was known.

Oxanthrones

The formula given shows that these are intermediate products between anthraquinones and anthranols. They give anthraquinones on oxidation and Fairbairn's modification of the Borntrger test accomplishes this by means of hydrogen peroxide. An oxanthrone has been reported as a constituent of cascara bark.

Dianthrones

These are compounds derived from two anthrone molecules, which may be identical or different; they readily form as a result of mild oxidation of the anthrone or mixed anthrones (e.g. a solution in acetone and presence of atmospheric oxygen). They are important aglycones in species of *Cassia, Rheum and Rhamnus; in this group the sennidins,* aglycones of the sennosides (see formula), are among the bestknown examples. Reidin A, B and C which occur in senna and rhubarb are heterodianthrones, i.e. composed of unlike anthrones, and involve aloe-emodin, rhein, chryophanol or physcion.



Glycoside	10 - 10′	R
Sennoside A	trans	COOH
Sennoside B	meso	COOH
Sennoside C	trans	CH_2OH
Sennoside D	meso	CH_2OH

Chemical Test

1. *Borntrager test for anthraquinones: The medicinal raw materials are boiled* with dilute sulphuric acid and filtered. To the filtrate organic solvent like benzene, ether or chloroform is
added and shaken. The organic layer is separated, and to it add ammonia solution. The ammoniacal layer produces pink to red colour indicating the presence
of anthraquinone glycoside.

2. Anthracene glucosides give red colour with 5% potassium hydroxide solution.

3. Sublimation reaction or microdistillation.

4. Reaction with an alcohol solution of magnesium acetate.

5. The identification of anthracene derivatives is accomplished by the use of paperand thin layer chromatography.

Pharmacological action

The action of the anthraquinone laxatives is restricted to the large bowel; hence their effect is delayed for up to 6 h or longer. The nature of the peristaltic initiation is not known for certain but it has been suggested that the common anthraquinone and anthranol derivatives influence the ion transport across colon cells by inhibition of Cl^- channels

Medicinal raw materials containing anthraquinones and glycosides.

Senna Leaf - Sennae folia

Senna (*Sennae Folium) consists of the dried leaflets of Cassia senna L.* (*C. acutifolia Delile), which are known in commerce as Alexandrian* or Khartoum senna, and of *Cassia angustifolia Vahl, which are known* in commerce as Tinnevelly senna.

Family Fabaceae

History. Senna appears to have been used since the ninth or tenth century, its introduction into medicine being due to the Arabian physicians, who used both the leaves and the pods. It was formerly exported through Alexandria, from where the name of the Sudanese drug is derived.

Cassia acutifolia is a small undershrub, two or three feet high, with a straight, woody, branching, whitish stem; but, according to Landerer, the senna plant attains the height of eight or ten feet in the African deserts. The leaves are alternate and pinnate, with glandless petioles, and two small narrow pointed stipules at the base. The leaflets, of which from four to six pairs belong to each leaf, are almost sessile, oval-lanceolate, acute, oblique at their base, nerved, from half an inch to an inch long, and of a yellowish-green color. The flowers are yellow, and in axillary spikes. The fruit is a flat, elliptical, obtuse, membranous, smooth, grayish-brown, bivalvular legume, about an inch long and half an inch broad, scarcely if at all curved, and divided into six or seven cells, each containing a hard, heart-shaped, ash-colored seed.

Cassia angustifolia, as usually grown is annual, but with care it may be made to live through the year, and then assumes the character of an undershrub. It has an erect, smooth stem, and pinnate leaves, with from four to eight pairs of leaflets. These are nearly sessile, lanceolate, obscurely mucronate, oblique at the base, smooth above and somewhat downy beneath, with the veins turned inward so as to form a wavy line immediately within the edge of the leaflet. The most striking character of the leaflet is its length, which varies from 2 to 5 cm. The petioles are without glands; the stipules minute, spreading and semi-hastate. The flowers are bright yellow, and arranged in axillary and terminal racemes rather longer than the leaves. The legume is oblong, membranous, tapering abruptly at the base, rounded at the summit, and 4 to 5 cm. long by about 1.5 cm. broad.

Destribution

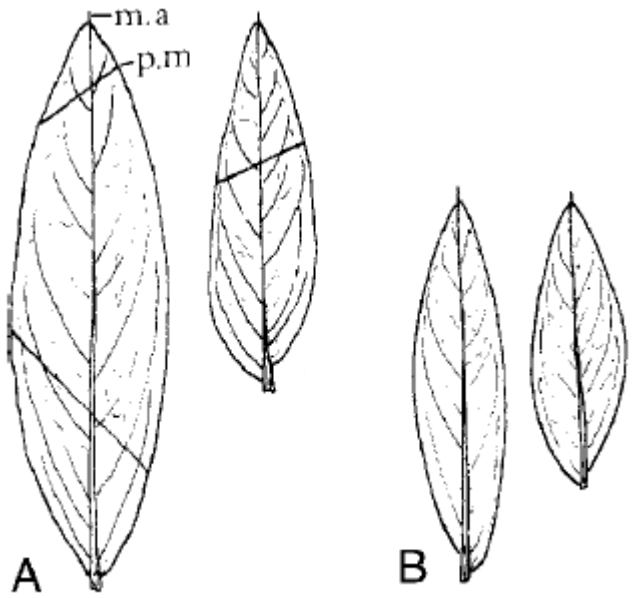
C. senna is indigenous to tropical Africa and is cultivated in the Sudan (Kordofan, Sennar). *C. angustifolia is indigenous* to Somaliland, Arabia, Sind and the Punjab, and is cultivated in South India.

Characteristics

Senna leaflets are 3–5 cm long, 2 cm wide and about 0.5 mm thick. It shows acute apex, entire margin and asymmetric base. Outline is lanceolate to ovate lanceolate. Pubescent lamina is found on both the surfaces. Leaves show greyish green colour for Alexandrian senna and yellowish green for Tinnevelly senna. Leaves of Tinnevelly senna are somewhat larger, less broken and firmer in texture than that of Alexandrian senna. Odour of leaves is slight but characteristic and the taste is bitter, mucilagenous. Both the types of leaflets show impression or transverse markings due to the pressing of midrib.

Distinguishing characters of Alexandrian and Indian senna

Character	Indian Senna	Alexandrian senna
Appearance	Generally entire and less broken in good condition	Broken and brittle in nature
Size	2.5–5.0 cm long and 7–9 mm wide	2.4 cm long and 6–12 mm wide.
Shape	Lanceolate	Ovate lanceolate
Apex	Less acute with a sharp spine	Acute with a sharp spine
Margin	Entire, flat	Entire curled
Base	Less asymmetrical	Conspicuously asymmetrical
Veins	Pinnate, distinct towards the under surface and anastomosing towards margin	Pinnate, distinct towards the under surface and anastomosing towards margin
Surface	Transverse and oblique impressions, less pubescent (hairy)	Without transverse and oblique impressions and more pubescent
Texture	Flexible and less brittle	Thin more brittle
Odour	Faint	Faint
Colour	Light green	Light greyish green
Test	Bitter mucilaginous	Bitter mucilaginous
Vein Islet Number	19–22.5	25–29.5
Stomatal index	14–20	10–15
Palisade ratio	4–12	4.5–18

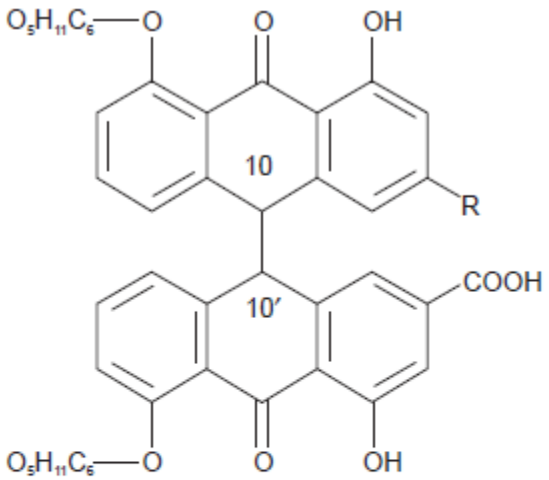


Senna leaflets.
A, Indian senna; B, Alexandrian senna

Chemical Constituents

Senna contains sennosides A and B (2.5%) based on the aglycones sennidin A and B, sennosides C and D which are glycosides of heterodianthrones of aloe-emodin and rhein are present. Others include palmidin A, rhein anthrone and aloe-emodin glycosides. Senna also contains free chrysophanol, emodin and their glycosides and free aloe-emodin, rhein, their monoanthrones, dianthrones and their glycosides.

Mucilage is present in the epidermis of the leaf and gives red colour with ruthenium red.



Glycoside	10 - 10′	R
Sennoside A	trans	COOH
Sennoside B	meso	COOH
Sennoside C	trans	CH_2OH
Sennoside D	meso	CH_2OH

Uses

Senna leaves are used as laxative. It causes irritation of large intestine and have some griping effect. Thus they are prescribed along with carminatives. Senna is stimulant cathartic and exerts its action by increasing the tone of the smooth muscles in large intestine.

Frangula Bark – Frangulae alni cortex

Frangula bark, alder buckthorn, is obtained from *Rhamnus frangula* L. (*Frangula alnus* Mill)

Family Rhamnaceae

It is shrub 3–5 m high and found in Britain and Europe. Commerical supplies are available from Balkan countries and a little from Russia. The plant differs from the common buckthorn, *R. cathartica*, in that it does not possess thorns; it bears dark-purple berries whose medicinal properties have long been accepted.

The leaves are arranged alternately on 8–15-millimetre petioles. They are ovate, 3–7 cm in long by 2.5–4 cm in wide. They have 6–10 pairs of prominently grooved and slightly downy veins and an entire margin.

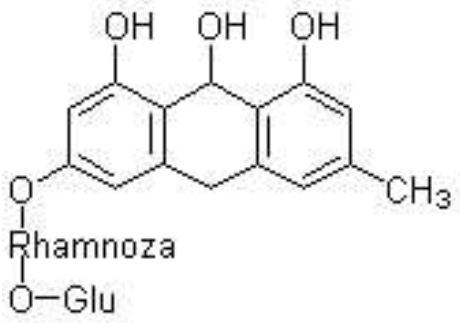
The flowers are small, 3–5 mm in diameter, star-shaped with five greenish-white acute triangular petals, hermaphroditic, and insect-pollinated, flowering in May to June in clusters of two to ten in the leaf axils.

The fruit is a small black berry 6–10 mm in diameter, ripening from green through red in late summer to dark purple or black in early autumn, containing two or three pale brown 5-millimetre seeds. The seeds are primarily dispersed by frugivorous birds, which readily eat the fruit.

Chemical Constituents

Frangula contains anthraquinone derivatives present mainly in the form of glycosides. The rhamnoside franguloside, or frangulin, was isolated in 1857. This is now known to consist of two isomers, frangulosides A and B, formed by partical hydrolysis of the corresponding rhamnoglucosides, glucofrangulins A and B. The fresh bark also contains anthranols and anthrones, which are unstable and readily oxidize to the corresponding anthraquinones; Lemli (1965, 1966) detected emodin-dianthrone, palmidin C, palmidin C monorhamnoside and emodin-dianthrone monorhamnoside.

Wagner *et al.* characterized frangulin B as 6-*O*-(d-apiofuranosyl)-1,6,8-trihydroxy-3-methylanthraquinone and more recently reported the new glycoside emodin-8-*O*-β-gentiobioside.



Characteristics

These are tubular or grooved pieces of bark of varying lengths, 0.5 - 2 mm thick. The outer surface is dark brown,grayish-brown, dark gray or grayish, often with whitish, laterally elongated lenticels or gray spots. A light scraping of the outer part of the cork reveals a red (franguline) layer. The inside surface is smooth, yellowish-orange or reddish-brown colour. The fracture is uniformly fine-bristled, light yellow. The smell is faint, and the taste is bitter.

Uses. Buckthorn bark is used as a laxative for atonic constipation, spastic colitis and to soften stools for rectal fissures, haemorrhoids, etc.

Common buckthorn fruits – Rhamni catharticae fructus

Common buckthorn fruits, is obtained from *Rhamnus cathartica* L.

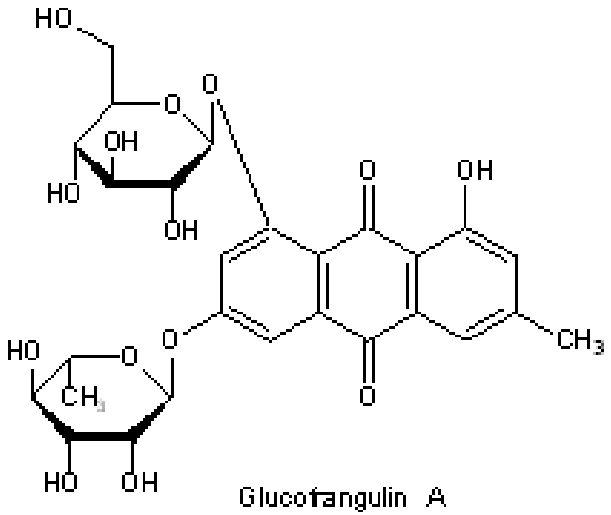
Family Rhamnaceae

Rhamnus cathartica is a dioecious shrub or small tree growing up to 10 metres tall, with grey-brown bark and often thorny branches. The leaves are elliptic to oval, 25–90 mm in long and 12–35 mm in broad; they are green, turning yellow in autumn, and are arranged somewhat variably in opposite to subopposite pairs or alternately. The flowers are yellowish-green, with four petals; they are dioecious and insect pollinated. The fruit is a globose black drupe, 6–10 mm in across, and contains two to four seeds.

It is native to Europe, northwest Africa and western Asia, from the central British Isles south to Morocco, and east to Kyrgyzstan. It was introduced to North America as an ornamental shrub.

Chemical Constituents

The composition of the anthraglycosides of common buckthorn is similar to that of alder buckthorn. Unlike the alder buckthorn, common buckthorn has also joosterol, that is a glycoside of a frangulaemodin. The glucofranguline in common buckthorn is called rhamnocathartin.



Glucofrangulin A

External features.

Spherical stone fruits with glossy, wrinkled surface, 5-8 mm in diameter, with a retained peduncle or a depressioncavity at the place of detachment. Flesh is brown, with 3-4 (less frequently 2) dark brownish, triangular or ovoid spicules.trihedral or ovoid pips. The colour of the fruit is almost black. The smell is faint and unpleasant. The taste is sweetish-bitter.

Raw material should not be an impurity in the fruits of alder buckthorn. It is black, globular, stone with 2 (3) lenticels with a cartilaginous club-shaped protuberance. The taste of the flesh is sweet.

Used as a laxative for chronic constipation in the form of decoction. The fruits of common buckthorn are included in the laxative collection and in the collection Zdrenko.
If unripe fruits are eaten (mostly by children), severe poisoning may occur (fatal cases have been reported).

RHUBARB ROOTS – RHEI PALMATUM RADICES

Rhubarb consists of the peeled dried rhizomes and roots of *Rheum palmatum* Linn., belonging to family Polygonaceae.

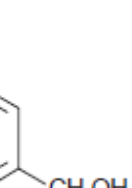
Rheum palmatum is a herbaceous perennial related to the edible rhubarb. The stem is erect, round, hollow, jointed, branched towards the top, from 2 to 3 m high. Rhizomes are large and roots are thick branched. Its lobed leaves are large, jagged and hand-shaped, growing in width to two feet. Mature specimens give rise to a towering inflorescence, either dark red or occasionally creamy-yellow and the tiny flowers are followed by small oblong-ellipsoid fruits with characteristic longitudinal wings turning reddish-purple as the seed develops.

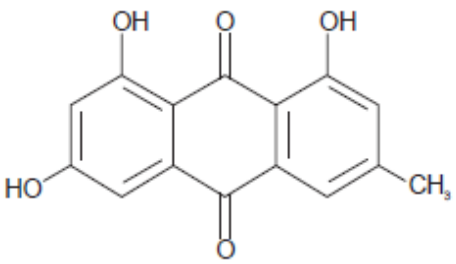
Drug is collected in autumn in September or October from 6 to 15 years old plants. Rhizomes are dug out, crown and lateral roots are removed and the outer bark is separated by peeling. The rhizomes that are small in size are kept as such or cut into transverse slices and so they are round.

These slices are dried by boring holes in the flat pieces and passing thread through the holes and hanging between shades of trees. In absence of the required climatic conditions the drugs are dried artificially heated stones, which are previously heated by woodfire. Drug dried in this way is called high dried. The drugs that are dried in above said manner exerts an unpleasant odour and darker in colour and is considered inferior. The remaining bark is peeled off and graded according to size, shape and quality.

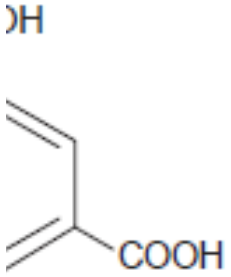
Chemical Constituents

Rhubarb contains free anthraquinones, their glycosides, reduced derivatives, anthrones, or dianthrone and heterodianthrones. The anthraquinones of rhubarb are chrysophanol, aloe-emodin, emodin, physcion and rhein. Anthrones or dianthrones are of chrysophanol, emodin and aloe-emodin. Heterodianthrones contain two different molecules of anthrones and they are from above anthrones. It also contains tannoid constituents, starch and calcium oxalate. There are also several resinous matters, one of which, Phaoretin, is purgative, and mineral compounds are also present. The astringency of Rhubarb is due to a peculiar tannic acid (Rheotannic), which is soluble in water and alcohol.

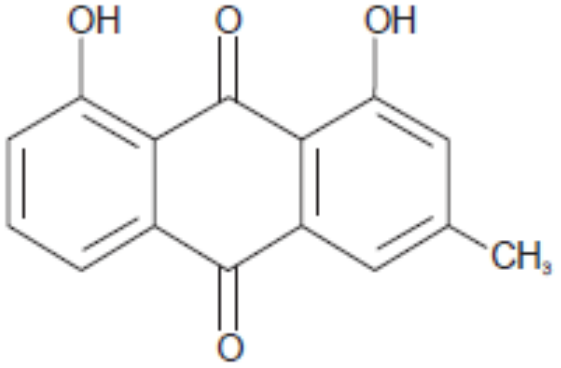




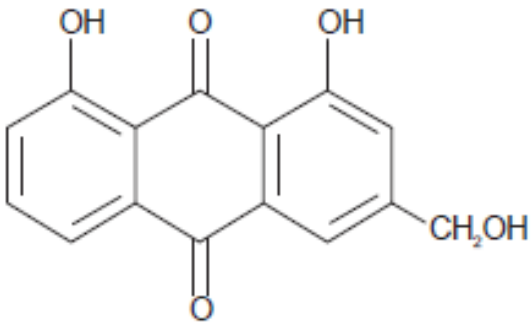
Emodin



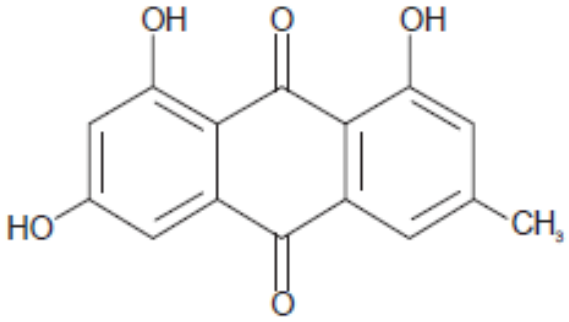
Rhein



Chrysophanol



Aloe-emodin



Emodin

Uses

The root is anticholesterolemic, antiseptic, antispasmodic, antitumor, aperient, astringent, cholagogue, demulcent, diuretic, laxative, purgative, stomachic and tonic. The roots contain anthraquinones, which have a purgative effect, and also tannins and bitters, which have an opposite astringent effect. When taken in small doses, it acts as an astringent tonic to the digestive system, whilst larger doses act as a mild laxative. The root is taken internally in the treatment of chronic constipation, diarrhoea, liver and gall bladder complaints, haemorrhoids, menstrual problems and skin eruptions due to an accumulation of toxins. This remedy is not prescribed for pregnant or lactating women, or for patients with intestinal obstruction. Externally, the root is used in the treatment of burns.


Thank you
For your
Attention