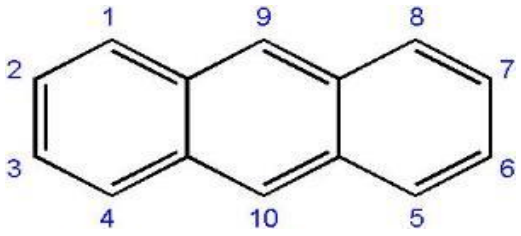
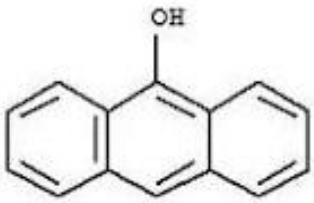
Anthraquinone glycosides

A number of glycosides in which the aglycones are anthracene derivatives occur as the pharmacologically active constituents of several cathartics of plant origin.

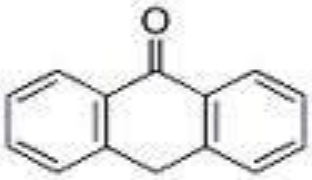


Anthracene

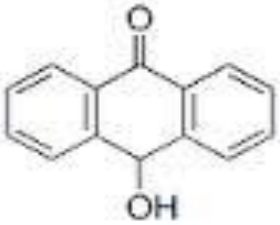
The anthracene occurs in these medicinal plants in various forms of different oxidation-levels as derivatives of anthraquinone, of anthrone, or oxanthrone or anthranol, as well as in a dimeric forms (dianthrone) in some cases.



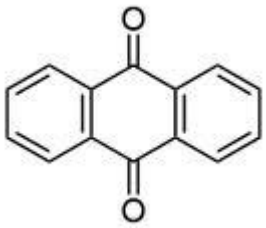
Anthranol



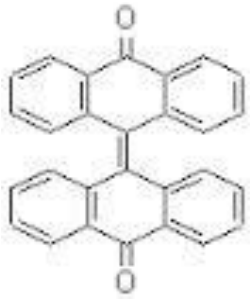
anthrone



oxanthrone

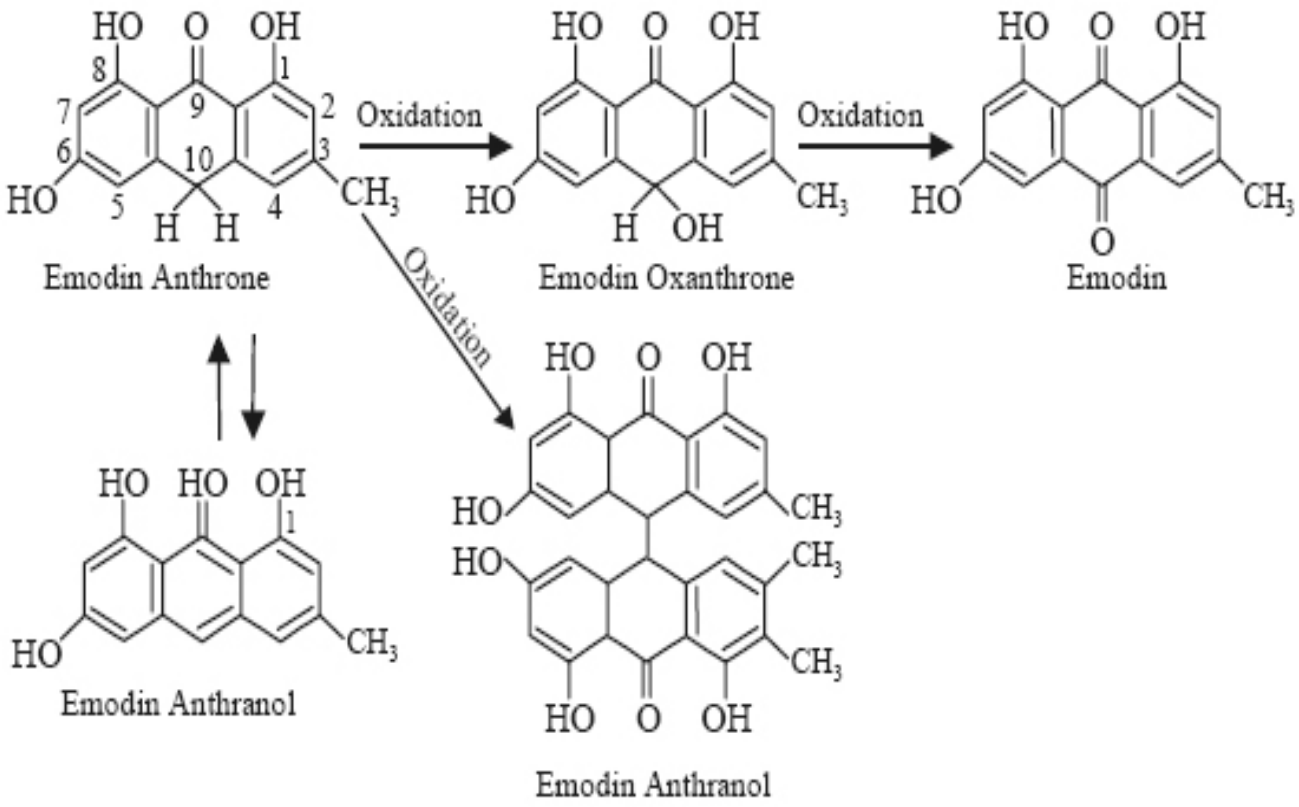


Anthraquinone



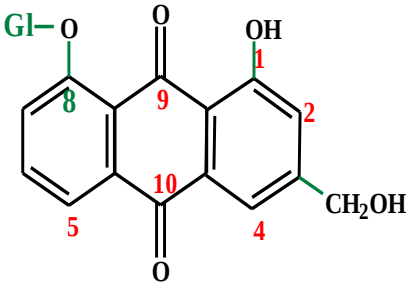
dianthrone

With the exception of chrysarobin (which is too irritant) & cochineal (which is a coloring agent) these are cathartic. The glycosides on hydrolysis, yield aglycones which are di, tri, or tetra hydroxyl anthraquinones or modifications of these compounds. Without the sugar moieties, free anthraquinone exhibit little therapeutic activity. The sugar is essential because it serves to transport the aglycone to the site of action in the large intestine. Anthraquinone group are inter changeable to each other either by oxidation or reduction as shown below: -

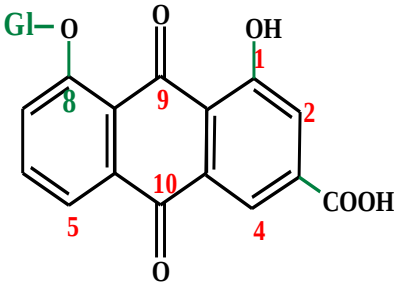


Types of anthraquinone glycosides

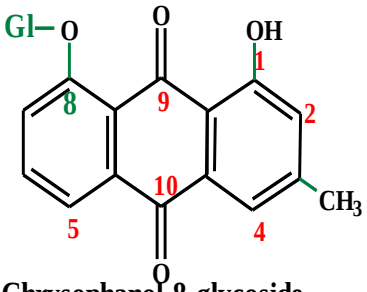
1- O-glycosides where the aglycone moiety is 1,8 dihydroxy anthraquinone derivatives, e.g.: -



Aloe-emodin-8-glycoside

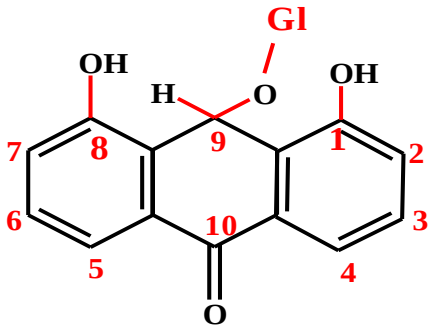


Rhein-8-glycoside



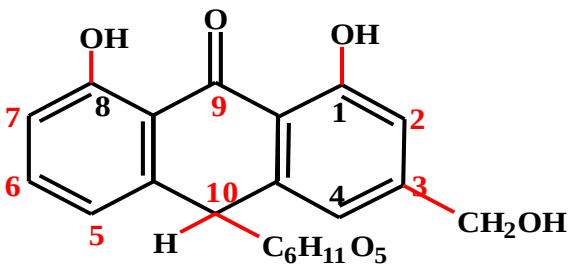
Chrysophanol-8-glycoside

2- O-glycoside where the aglycone moiety partially reduced 1,8 dihydroxy anthraquinone, e.g., Oxanthrone-type.



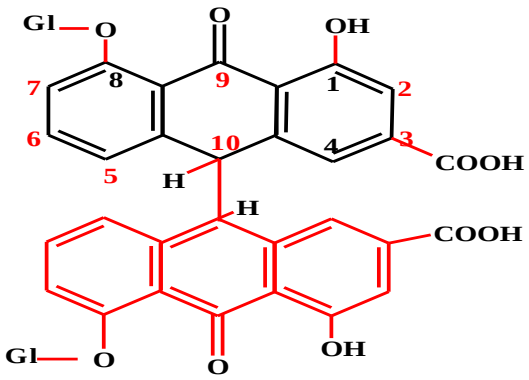
Emodin-oxanthrone-9-glucoside

3- C-glycoside where the aglycone structure (anthrone derivative).



Barbalion

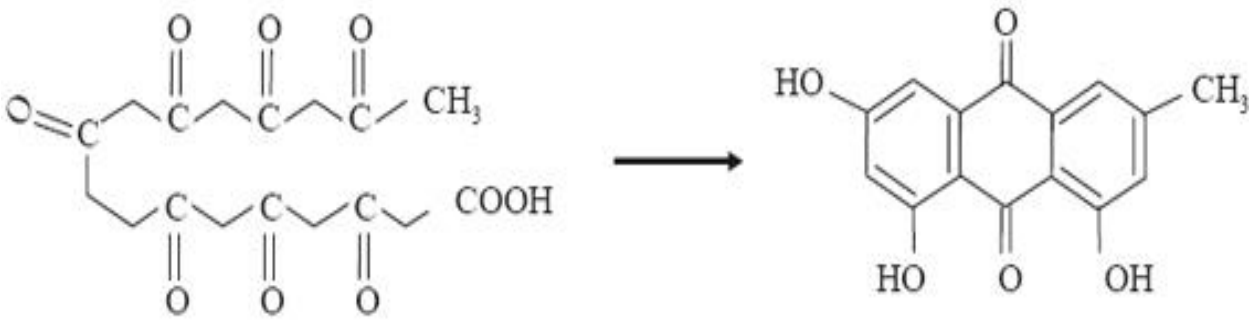
4- O-glycosides where the aglycone moiety is di-anthrone der. (i.e., **dimmer)** e.g., Sennosides where there is **C-C** bridge between the anthranol units.



Sennoside A&B

Biosynthesis of anthraquinone glycosides

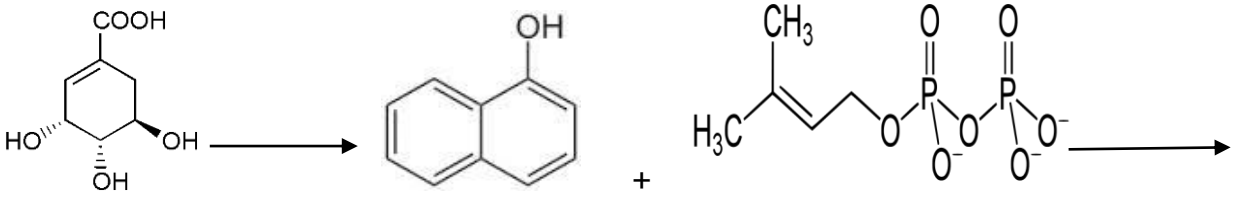
Feeding of labeled acetate to ***Pencillium islandicum***, a species which produces several anthraquinone derivatives have revealed that the distribution of radioactivity in these compounds is consistent with the formation of poly-β-ketomethylene acid intermediate via a head-to-tail condensation of eight acetate units, followed by intra molecular condensation.



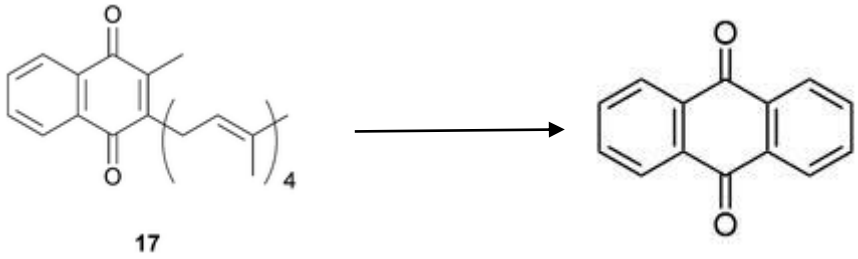
Poly—β-Ketomethylene Acid
[An intemediate with
8-Acetate Units]

Emodin & other Related
Derivatives

Presumably the emodin-type anthraquinones are formed in higher plants by a similar pathway. However, it is known that a second pathway starting with **shikimc acid** is operative in the Rubiaceae family. This will be carried on via formation of **1,4-naphthoquinone**, condensation of **isopentenyl pyrophosphate** with the naphthalenic moiety & cyclization yield the anthraquinone nucleus.



Shikimic acid 1-naphthol dimethyl allyl PP



Intermediate anthraquinone

Notes: -

1. The primary glycosides are **more active** than the aloins while the free **anthraquinon** have little purgative activity.

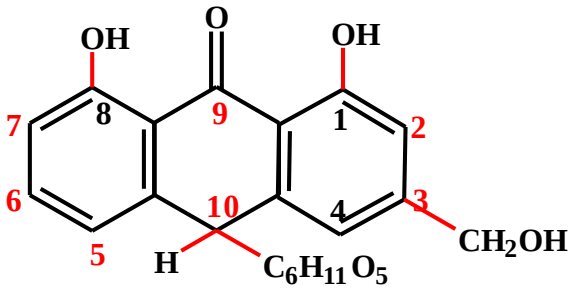
2. C-C glycosides, aloins are very **resistant** to hydrolysis and are not easily hydrolysed (like other anthrones and anthranols) to corresponding anthraquinones. It is not hydrolyzed by heating with dilute acids or alkalies. It can, however, be decomposed by oxidative hydrolysis with reagents such as ferric chloride.

3. Drugs containing **reduced** forms of anthraquinone glycosides should be stored for at least **1 year** before use in order to change the reduced form which has drastic griping action into the corresponding oxidized form which has less griping action i.e. Prolonged storage of anthracene bearing drugs may bring oxidation of anthranols and anthrones to give the **less active** anthraquinones. Thus, the activity of drugs decreases by time. However, **anthraquinone** glycosides do not cause any **griping action (like anthranol and anthone)**, thus no antispasmodic such as **belladonna** is prescribed with them.

4. The purgative action of anthracene bearing drugs is owed to their anthracene glycosidal content rather than their content of free anthracene aglycones (i.e., glycosylation is the main requirement for activity, as the sugar moiety serve to transport the aglycone to the site of action in the large intestine).

Numbering system & nomenclature

Starting from any corner provided that you give the substituents the smallest number

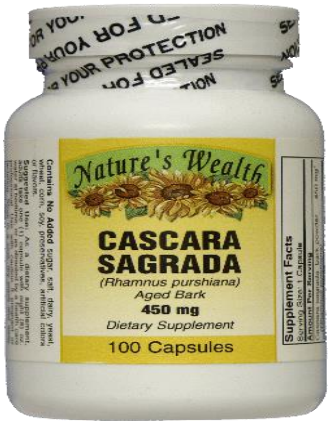


1, 8-Dihydroxy- 3-hydroxymethyl-9-anthrone-10-glucoside

Drugs containing anthraquinone glycosides:

1)) Cascara sagrada: -

Is the dried bark of ***Rhamnus purshiana*** F: Rhamnaceae. It should be aged for at least one year prior to use in medicinal preparations (to lose its gripping properties). **B. P.** specified that the collection must be made at least one year before the bark is used (fresh bark contains an emetic principle).

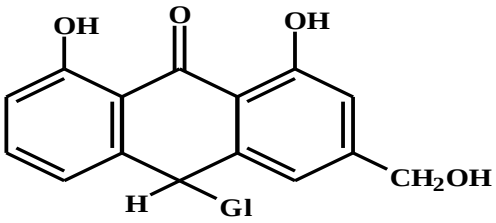
Images of Cascara & its preparations

Constituents: -

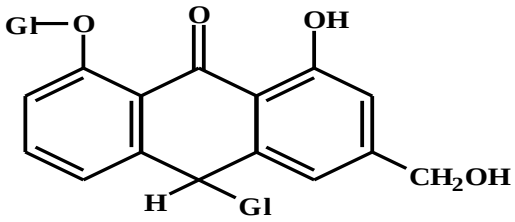
A- primary glycosides:

1- cascarosides A&B (glycosides of **barbaloin**)

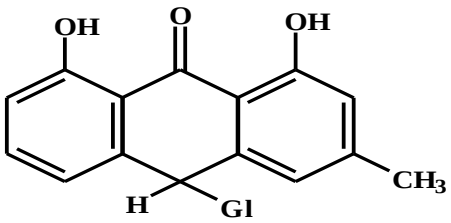
2- cascarosides C&D (glycosides of **chrysaloin** which is deoxy barbaloin)



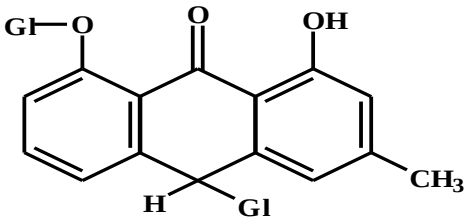
Barbaloin



Cascaroside A& B



Chrysaloin

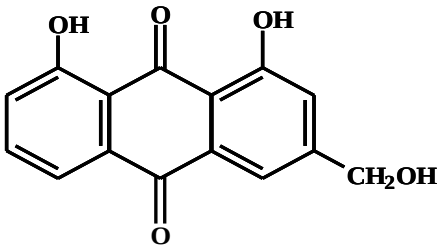


Cascaroside C & D

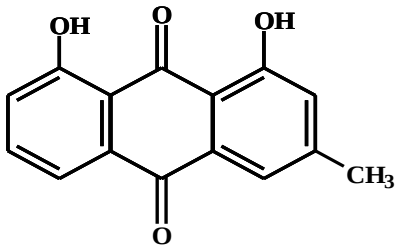
B- aloins (secondary glycosides): -

Barbaloin derived from (C-10-C-glycoside) of aloe-emodin anthrone and **chrysaloin** derived from (C-10-C-glycoside) of chrysophanol anthrone.

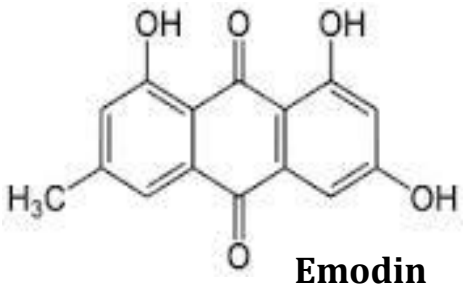
C- A number of O- glycosides: - e.g., derived from emodin, emodine oxanthrone, aloe emodin and chrysophanol.



Aloe emodin



Chrysophanol



Emodin

Uses & dose:-

Cascara is used as a cathartic. Its principle use is in the habitual constipation where it not only acts as a laxative but restore natural tone of the colon. Usual dose of Cascara sagrada fluid extract is **1ml**; of aromatic fluid extract is **5ml**; of Cascara sagrada extract is **300mg**.

2)) Frangula (Buckthorn): -

Is the dried bark of ***Rhamnus frangula*** F: Rhamnaceae. The name frangula means "brittle" in reference to the brittle stem of this species. Like Cascara, the bark should be aged a year or more before use in medicinal preparations. The commercial supply is from Russia.

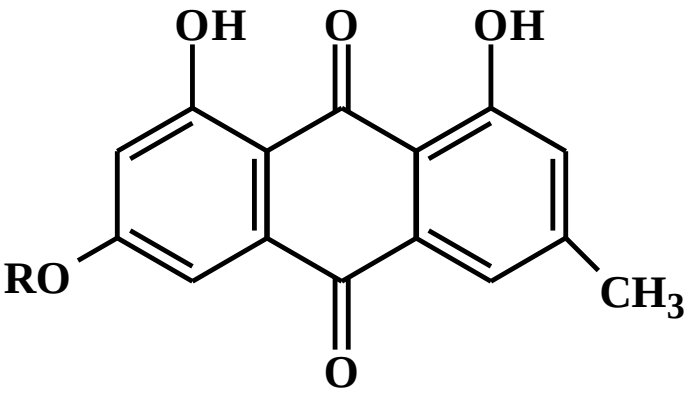
Images of Frangula & its preparation

Constituents:

1. **Frangulin** (frangula emodin rhamnoside).
2. **Glucofrangulin** (frangula emodin glucorhamnoside).

Hydrolysis of glucofrangulin yields frangulin and glucose while hydrolysis of frangulin gives frangula emodin and rhamnose.

Uses: - as a mild cathartic.



Frangulin R= Rhamnose

Glucofrangulin R= Rhamnose-glucose

3.Aloe: -

Aloe or Aloes is the dried juice of the leaves of ***Aloe perri*** or ***Aloe barbadensis*** F: liliaceae. Aloe is from the Arabic word alloeh or the Hebrew halal, meaning shining bitter substance. Barbadensis refers to the Barbados island (of the west indies federation). There are about 50 species of Aloe known, most of which are indigenous to Africa.







Images of different species of *Aloe* & its gel

Constituents: -

An important anthracene-glycoside in Aloe is **barbaloin** (aloe-emodin anthrone C-10-glucoside). O-glycoside of barbaloin with an additional sugar have been isolated from Aloe & been designated as aloinoside. Free (non glycosidal) **aloe-emodin** is also present as free & combined. The active constituents of aloe vary qualitatively & quantitatively according to the species from which the drug is obtained. In addition, aloe contains a considerable amount of resinous material & volatile oils.

Uses: -

As a cathartic by acting on the large intestine. The fresh **juice** has been used in the treatment of burns & other skin irritations by the natives. The extracted **gel** could be blended with a special lanolin base to form an ointment recommended for the treatment of sunburn, deep thermal burns & radiation burns. If affords relief from pain & itching & tends to minimize kurtosis & ulceration, thus retarding & possibly prevent any changes toward malignancy.

Products: -

Alophen pills; Aloin pills

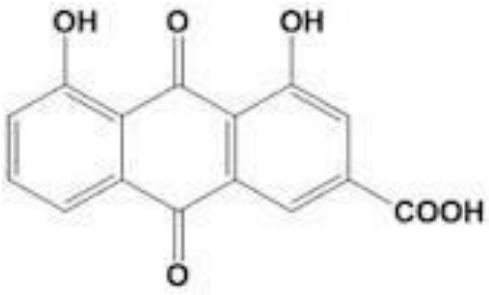
4. Rhubarb (Rheum or Chinese rhubarb):

Is the dried rhizomes & root deprived from epidermis tissue of ***Rheum Officinal*** F: polygonaceae.

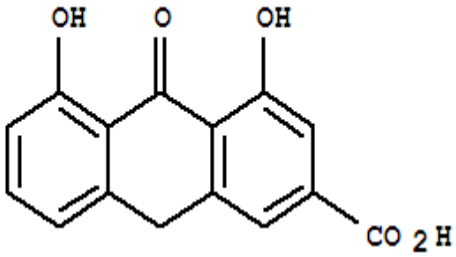
Images of Rhubarb & its different products

Constituents: -

The principle constituents are glycosides of rhein anthrones. Several other anthracene compounds in their free forms or as glycosides, have also been shown to be present, & they include rhein, emodin, chrysophanol & aloe-emodin. It also contains gallic acid & cathechin.



Rhein



Rhein anthrone

Uses: -

As cathartic & possesses astringent properties. Rhapontic rhubarb contain no rhein & emodin or aloe-emodin, so it has no cathartic properties.

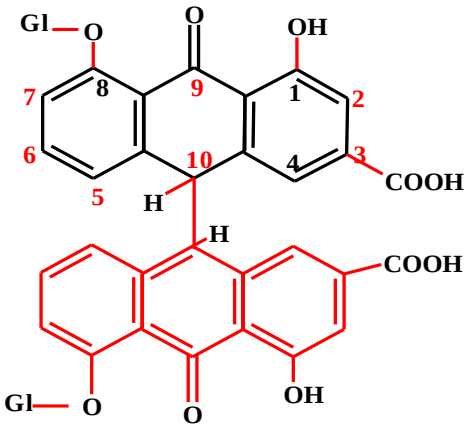
5. Senna: -

Senna or senna leaves consists of the dried leaflet of *Cassia acutifolia* known in commerce as Alexandria senna or *Cassia angustifolia* F: Leguminoseae (Fabaceae).

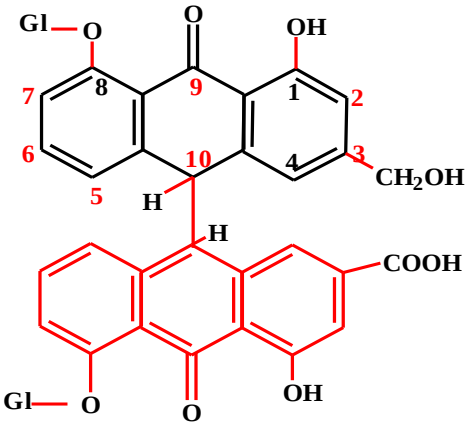
Images of Senna tree

Constituents: -

Dimeric glycosides, the aglycone of which are composed of aloe-emodin & rhein. Those are sennoside A & sennoside B (major content) & sennoside C & sennoside D (minor content).



Sennoside A&B



Sennoside C&D

So sennoside A&B are a pair of optical isomers in which the aglycones are rhein dianthrone; sennoside C&D compaired of one molecule of rhein & one of aloe-emodin

Uses: Cathartic

Preparations: senokot, persunnide

Images of Senna preparations

Official anthraquinone drugs in B.P and U.S.P.:

1- Senna leaf & senna fruit (pod).

2- Aloes.

3- Cascara tablets, elixir, dry exract, liquid extract.

4- Rhubarb powdered, tincture.

5- Danthrone.

6- Frangula bark.