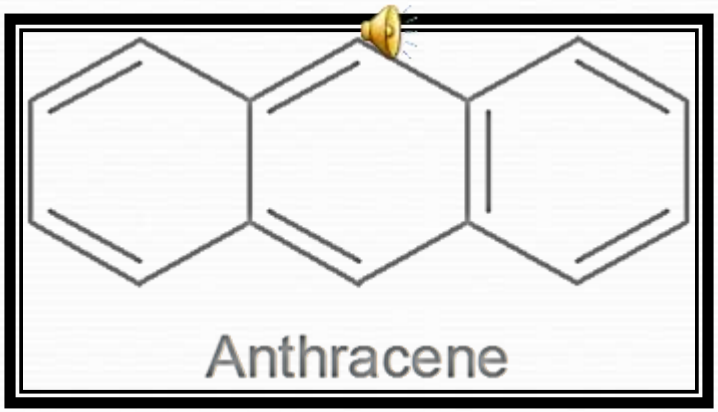
Anthraquinone glycosides

A number of glycosides with aglycones related to anthracene occur as a pharmacologically active constituents of several cathartics of plant origin; e.g. cascara, rhubarb, aloe and senna.

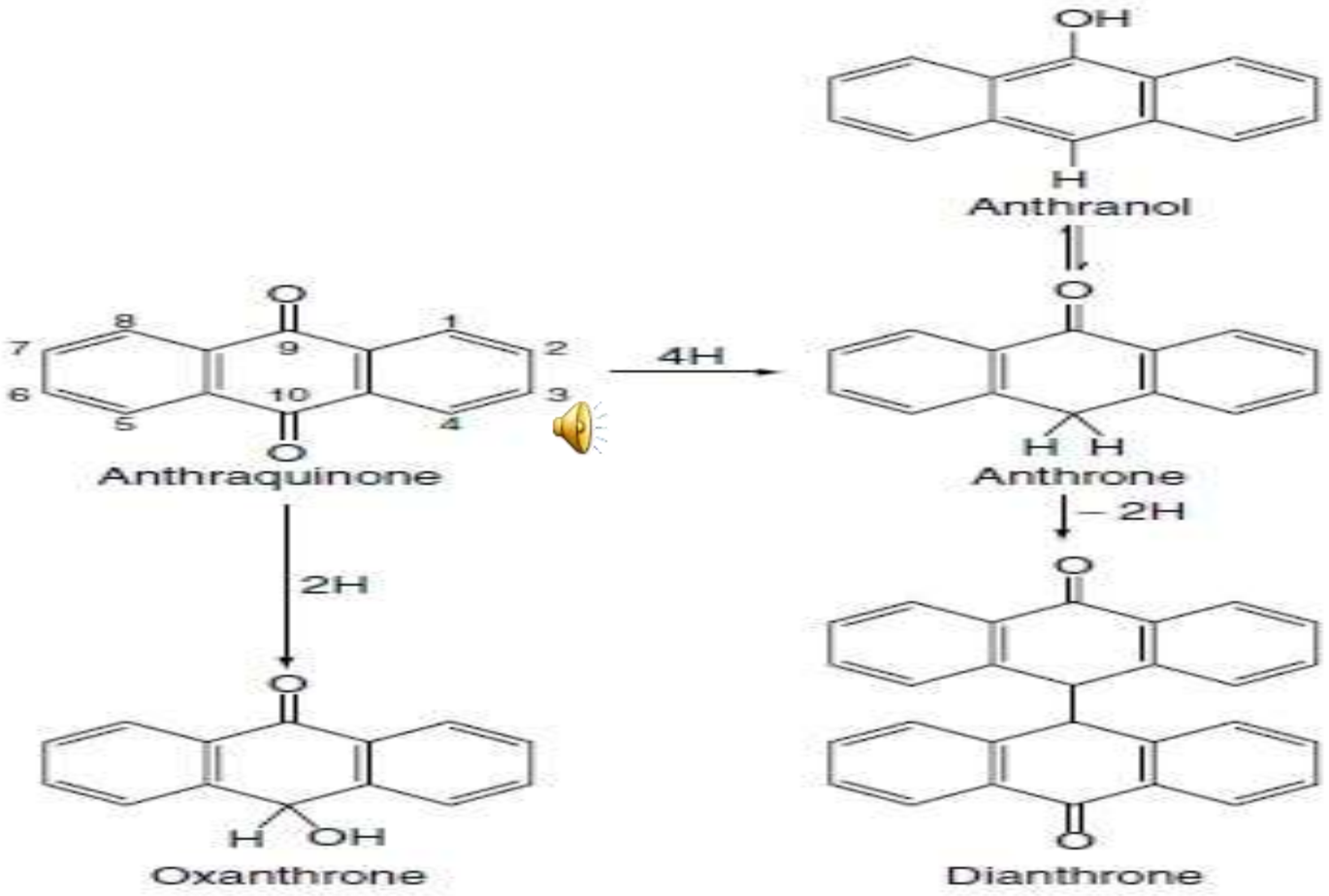


Long before anything was known about their chemistry, **rhubarb**, **aloes**, **senna** and **cascara** were recognized as forming a natural group of **purgative drugs**.

Substances of the anthraquinone type were first recognized both in the free state and as glycosides. Further work showed that natural products also contain reduced derivatives of the anthraquinones (**oxanthrones**, **anthranols** and **anthrones**) and compounds formed by the union of **two anthrone** molecules (i.e. the **dianthrones**). Because glycosides are often easily hydrolysed, the earlier workers tended to isolate products of hydrolysis rather than the primary glycosides. The following aglycones have long been established: **chrysophanol** or **chrysophanic acid** from rhubarb and cascara; **aloe-emodin** from rhubarb and senna; **rhein** from rhubarb and senna; **emodin** or **frangulaemodin** from rhubarb and cascara.

Improved extraction methods, led to the isolation of the main senna glycosides, **sennosides A and B**, and many new glycosides including ***C*-glycosides** and various stereoisomers have been isolated and their structures were determined.

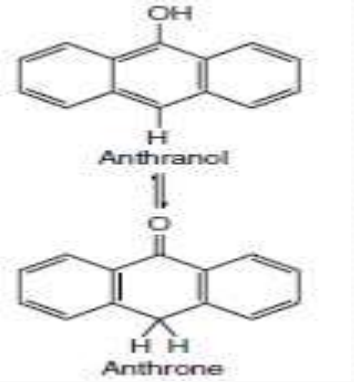
Natural anthraquinones are synthesized either via the **acetate–malonate** pathway or they are derived from **shikimate** and **mevalonate**.



Interrelationship of anthraquinone derivatives.

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. Borntrager's test is often used for their detection.

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.



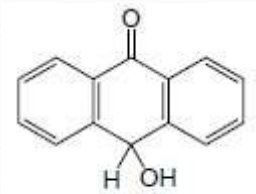
Anthranols and anthrones

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.

Oxanthrones

These are intermediate products between anthraquinones and anthranols, they give anthraquinones on oxidation .

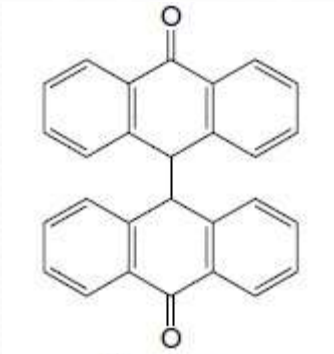


Oxanthrone

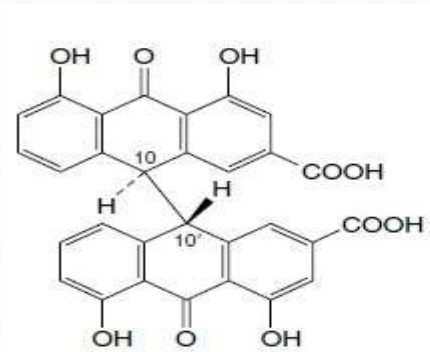
Dianthrones

These are compounds derived from two anthrone molecules, which may be identical or different; they are formed as a result of mild oxidation of the anthrone or mixed anthrones (e.g. a solution in acetone and presence of atmospheric oxygen).

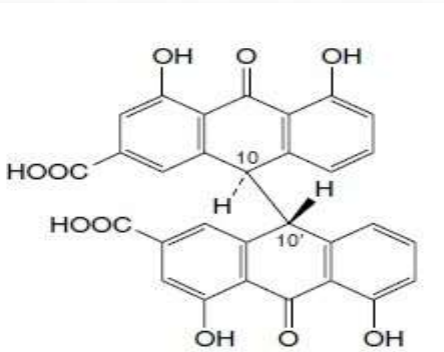
They are important aglycones in species of ***Cassia***, ***Rheum*** and ***Rhamnus***; in this group the **sennidins** (aglycones of the **sennosides**) are among the best known examples.



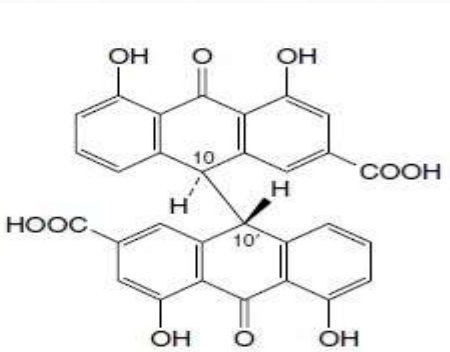
Dianthrone



Sennidin A (10*S*, 10′*S*)



Sennidin A (10*R*, 10′*R*)



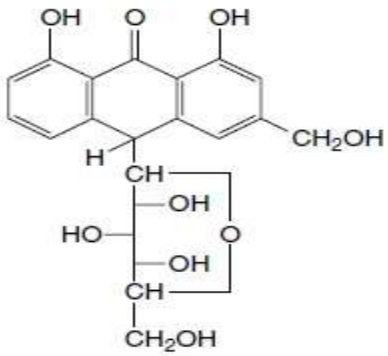
Sennidin B (*meso*)

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**.
The two chiral centers (at **C-10** and **C-10′**) are present in the dianthrones, and for a compound having two identical anthrone moieties, e.g. **sennidin A**, two forms (the 10S, 10′S and 10R, 10′R) are possible together with the meso form (**sennidin B**). These compounds also occur in the plant as their 1,1′-diglucosides.

Aloin-type or C-glycosides

The aloin obtained from species of ***Aloe***, although one of the first glycosides to be isolated, was a problem for investigators for a long time. It is strongly resistant to normal acid hydrolysis but may be oxidized with ferric chloride. A sugar is joined to the aglycone with a direct **C–C** linkage (a **C-glycoside**). Two **aloins** (**A** and **B**) are known and arise from the chiral center at **C-10**.

C-Glycosides unlike O-Glycosides in that they are not hydrolyzed by heating with dilute acids but can be decomposed by oxidative hydrolysis with reagents such as ferric chloride



Aloin

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. It has been suggested that the common anthraquinone and anthranol derivatives influence the ion transport across colon cells by inhibition of Cl^- channels.

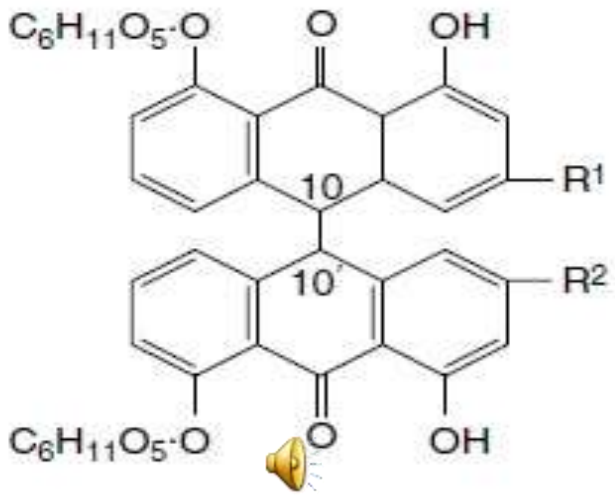
Senna Leaf

Senna (*Sennae Folium*) consists of the dried leaflets of ***Cassia senna (Cassia acutifolia)***, which are known in commerce as **Alexandrian** or **Khartoum senna**, and of ***Cassia angustifolia***, which are known in commerce as **Tinnevelly senna**. The senna plants are small shrubs of the family **Leguminosae**, about 1 m high, with compound leaves. ***C. senna*** is indigenous to tropical Africa and is cultivated in the Sudan. ***C. angustifolia*** is indigenous to Somaliland and Arabia and is cultivated in South India (Tinnevelly).

Senna is considered as stimulant laxative. Senna derivatives act on the large intestine, or colon, to stimulate fluid secretion and contractions of the colonic wall known as peristalsis. Senna is used for the short term treatment of symptomatic constipation. It may also be used to aid in the evacuation of the bowel prior to surgery or invasive rectal or colonic examinations. The breakdown products of senna act directly as irritants on the colonic wall to induce fluid secretion and colonic contraction

Constituents:

Sennoside A and **sennoside B** which both hydrolyse to give two molecules of glucose and the aglycones **sennidin A** and **B**.
Sennidin A is dextrorotatory and **B** is its mesoform formed by intramolecular compensation, other constituents include: **sennosides C** and **D** (which are the glycosides of heterodianthrones involving **rhein** and **aloe-emodin**); palmidin A; aloe-emodin dianthrone-diglycoside, rhein-anthrone-8-glycoside, rhein-8-diglucoside, aloe-emodin-8-glucoside, aloe-emodin-anthrone-diglucoside, possibly rhein-1-glucose, and a primary glycoside having greater potency than sennosides A and B and distinguished from them by the addition of two glucose molecules.



	R^1	R^2	10–10′
Sennoside A	COOH	COOH	*trans*
Sennoside B	COOH	COOH	*meso*
Sennoside C	CH_2OH	COOH	*trans*
Sennoside D	CH_2OH	COOH	*meso*
Aloe-emodin-dianthrone-diglucoside	CH_2OH	CH_2OH	*trans*
Aloe-emodin-dianthrone-diglucoside	CH_2OH	CH_2OH	*meso*