

**1- O-glycosides** where the aglycone moiety is 1,8 dihydroxyanthraquinone derivatives, e.g.,



**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 der.)



**Barbaloin**

**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**



**The most widely used drugs that contain anthracene compounds are:**

Consists of the dried leaflet of **Alexandrian or Khartoum** senna, **Cassia senna** (***C.acutifolia***), **Tinnevelly senna** (***C.angustifolia***).

**Constituents:**

**Dimeric anthracene** glycosides derived from two anthrones moieties which may be:



1. Similar anthrone moiety (**Homo-dianthrones**) i.e., 2 rhein anthrone moieties condensate through two C-10 atomes. Thus it can be exist in two optical forms, Sennoside A (L- form) & Sennoside B (meso form).

**Sennosides A &B**

1. Or different (**Hetero-dianthrones**) i.e., one rhein-anthrone & one emodin anthrone, Sennoside C (L- form) and Sennoside D (meso form).



**Sennoside C&D**

The dried bark of ***Rhamnus* *purshiana*** Family **Rhamnaceae. B. P.** specified that the collection must be made at least one year before the bark is used (fresh bark contains an emetic principle).

**Constituents:**

**A- Four primary glycosides:**

1- cascarosides A&B (glycosides of barbaloin)

2- cascarosides C&D (glycosides of chrysaloin)

**B-Two 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.



**E- Free anthraquinones:**

Aloe emodin, chysophanol and emodin.

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



1. hydrolysis of glucofrangulin yields frangulin and glucose.
2. Hydrolysis of frangulin gives frangula emodin and rhamnose.
3. Consist of glycoside of rhein, rhein anthrone, chrysophanol and aloe emodin.
4. Dianthrones of heteroanthrone types are palmidin A, B, C, Rheidins, sennosides A&B and their oxalate esters (sennosides E&F).
5. The presence of **tannins** in rhubarb makes the drug constipating. So **in small doses**, rhubarb exerts no purgative action but acts only as intestinal astringent, but **large doses** cause purgation.

Cascara is a purgative, mainly in the form of liquid extract, elixir or as tablets prepared from a dry extract.

**The laxative action of the crude drugs is always higher than from their content of anthracene der. The different anthracene der. contained by the crude drug are said to exert a synergistic action.**

**Thus, the naturally occurring anthracene glycosides were found superior to the synthesis of numerous hydroxyl anthracene der.**

**Some of these synthetic compounds act too drastically and also caused kidney damage.**

**The only compound which is used to some extent in current medicine is danthrone. It is also used as a standared in colorimetric assays of anthraquinone glycosides.**



**Danthrone**

Note:

1. The 1ry glycosides are **more active** than the aloins while the free **anthraquinon** have little purgative activity.
2. C-C glycosides, aloins are very resistance to hydrolysis and are not easily hydrolysed (like other anthrones and anthranols) to corresponding anthraquinones.
3. **Aloin** type glycosides are present in aloes and other anthracene bearing drugs of the family liliaceae.
4. **Glycosilation:**

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).

1. **Hydroxylation:**

Hydroxylation of C-1, C-8 is essential for activity. Increase hydroxylation leading to increase solubility.

1. **Oxidation level:**

The degree of oxidation at positions C-9 & C-10 plays an important role in the pharmacological activity. Higher oxidation level at C-9 & C-10 caused lowering of activity. i.e., anthrones and anthranols are more potent than their corresponding oxanthrones, which in turn more active than their corresponding anthraquinones. Complete reduction of C-10 &C-9 lead to complete loss of activity.

1. **The nature of substances at C-3:**

Derivative with CH2OH (as in aloe emodin) are more active than those with CH3 substitution. The latter more active than derivative with COOH substitution at C-3.

Anthraquinone glycosides containing adimer more active than a monomer.

1. **Effect of storage on the active of anthracene glycosides:**
2. 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.
3. Drugs as senna, Aloe and cascara preparations **retain their activity** for a long time.
4. Cascara and frangula must be aged for **one year** before it is used for medicinal preparation.**WHY?**

**Stability is achieved as follows:**

1. **In senna,** there is dimeric glycoside in which a C-C bridge between two anthrone units is formed (the C-10 position of one anthrone is involved in a C-C-covalent bonding with C-10 of the other anthrone). Thus, the C-10 position cannot be easily oxidized and the anthrone structure is stabilized.
2. **In the aloe,** the aloins (barbaloin & chrysaloin) contain C-C glycosidic linkage (anhydroglycosides) stabilise the anthrone structure.
3. **In cascara,** cascarosides have an additional O-glycosidic linkage (beside the C-10-C glycosidic linkage. The solubility of cascarosides is increased and thus, produce higher pharmacological activity.

The glycosides are extracted and hydrolyzed by boiling the drug with acids.

The **aglycones** are extracted from the acidic solution with ether or benzene. Upon shaking the ether or benzene layer with aqueous alkali or ammonia solution, the aqueous layer assumes a deep red color, because of the formation of anthraquinone salts.

**Borntrager’s reaction** can distinguish anthraquinones from anthrones and anthranols which **do not** give the test unless they are converted to anthraquinone by oxidation with mild oxidants such as hydrogen peroxide or ferric chloride.

**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