GLYCOSIDES AND GLYCOSIDE CONTAINING DRUGS

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SUB
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; e.g. cascara, rhubarb, aloe and senna.

These anthracene glycosides are sometimes referred to as the anthraquinone glycosides or the anthraglycosides.
These anthraquinone derivatives are glycosides, often glucosides or rhamnosides.

The presence of the sugar residue is a prerequisite for the pharmacological effects.

Anthraquinones are colored substances and many of them are used technically as dyes e.g. alizarin.

Reduced forms of anthraquinones, which exhibit keto-enol tautomerism, are often encountered.

The anthracene derivatives occur in vegetable drugs in different forms at different oxidation levels; like anthraquinones, anthrones, anthranols, or oxanthrones.
Interrelationship of anthraquinone derivatives

Anthraquinone → Anthranol (enol form) → Anthrone (keto form) → Dianthrone

Anthraquinone

O

A B C

6 5 4 3

O

2 H

Oxanthrone

Dianthrone

OH

− 2 H

Taut.

4 H

Anthrone (keto form)

OH

Anthranol (enol form)
A. Anthraquinones

- Although anthraquinone is not used extensively in medical practice, it is the starting material for the preparation of several synthetic laxatives and represent the basic structure of a number of important laxatives and dyestuffs.

- *Borntrager’s test* is often used for their detection.

- The derivatives of anthraquinone present in purgative drugs may be dihydroxy phenols such as chrysophanol, trihydroxy phenols such as emodin or tetrahydroxy phenols such as carminic acid.
Chrysarobin

(1,8-dihydroxy-3-methyl-9-anthrone; 3-methyl-1,8,9-anthracenetriol)
These are intermediate products between anthraquinones and anthranols.

They give anthraquinones on oxidation with 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 are important aglycones in species of *Cassia*, *Rheum* and *Rhamnus*.
- One of the best known is sennoside derived from two molecules of glucose and two molecules of rhein-anthrone.
- On hydrolysis, sennoside yields the aglycone sennidin.
Aloin-type or C-glycosides

- Aloin (Barbaloin) was obtained from species of Aloe.
- It is strongly resistant to normal acid hydrolysis.
- In aloin, the sugar is joined to aglycone with a direct C-C linkage (a C-glycoside).
- Two aloins (A and B) are known and arise from the chiral centre at C-10.
Biological Name:

- Cassia senna (Alexandrian senna)
- Cassia angustifolia (Tinnevelly senna)

Part used:
- Dried leaflets
- Dried pods
- Dried ripe fruits
- Indigenous to Africa (tropical regions)
- Used since 9th – 10th century
- Introduced into medicine by Arab physicians (used both the leaves and pods)
- Exported by Alexandria – name of the Sudanese drug.
Senna – Constituents

- 2 active glycosides:
  - Sennoside A
  - Sennoside B
- Both hydrolyse:
  - 2 molecules glucose + aglycones: Sennidin A and Sennidin B.
- Sennoside C & Sennoside D
- Rhein
- Aloe-emodin
- Palmidin A (Rhubarb)
SENNOSIDE A

SENNOSIDE B
- Kaempferol (yellow flavanol) + glucoside (kaempferin)
- Mucilage
- Calcium oxalates
- Resin

- Active constituents – found in the pericarp
- Similar to those actives of the leaves
  - Sennoside A
  - Sennidin
Comparison of Alexandrian and Tinnevelly Senna

- **Macroscopical**
  - Seldom larger than 4 cm in length
  - Grey-green
  - Asymmetric at base
  - Broken and curled at edges
  - Few press markings

- **Macroscopical**
  - Seldom exceeds 5 cm in length
  - Yellow-green
  - Less asymmetric at base
  - Seldom broken and normally flat
  - Often shows impressions (mid vein)
Microscopical

- Hairs – numerous (approximately 3 epidermal cells apart)
- Most stomata have 2 subsidiary cells

Microscopical

- Hairs less numerous (approximately 6 epidermal cells apart)
- Stomata have 2-3 subsidiary cells with the respective ratio 7:3
Chemical Tests

- Ether extract of hydrolysed acid solution of herb with methanolic magnesioum acetate solution gives
  Pink colour in daylight
  Pale green-orange colour in filtered UV light

Chemical Tests

- Same Test
  - Orange colour in daylight
  - Yellow-green colour in filtered UV light
TLC
- Hydroxymusizin glycoside present

TLC
- Tinnevellin glycoside present
Bombay, Mecca and Arabian Sennas (found in *Cassia angustifolia* from Arabia).

- **Dog senna** – *Cassia obovata*
- *Cassia auriculata* – Indian Senna
- *Cassia podocarpa*

**Substitutes or Adulterants**
- Argel leaves – *Solenostemma argel*
- *Coriario myrtifolia*
Senna - Uses

- Laxatives (habitual constipation or occasional use).
- Astringent
- Vermifuge - A medication capable of causing the evacuation of parasitic intestinal worms
- Diuretic
- Febrifuge - Any medicine that lowers body temperature to prevent or alleviate fever
- Also used to treat –
  - Flatulence - A state of excessive gas in the alimentary canal
[Boxed list]

- **Gout** - A painful inflammation of the big toe and foot caused by defects in uric acid metabolism resulting in deposits of the acid and its salts in the blood and joints

- **Fever** - A rise in the temperature of the body; frequently a symptom of infection

- Poultice prepared with vinegar to treat pimples (**A small inflamed elevation of the skin; a pustule or papule; common symptom in acne**)

- Senna may cause urine to become reddish – no clinical significance.
Contra-indications
- Colitis - Inflammation of the colon
- GI inflammation.

Should not be used with cardiac glycosides.

Seeds/pods give gentler action than leaves: more appropriate for the young, elderly and those prone to stomach cramps.

Over-use causes dependency.

Overdose –
- Nausea - The state that precedes vomiting
- Bloody diarrhoea
- Vomiting
- Nephritis - An inflammation of the kidney
- Long-term use: dehydration & electrolyte depletion, worsening constipation and weakening intestinal muscles.
Cascara Bark

- **Botanical Name:** *Rhamnus purshianus.*
- **Part used:** Dried bark
- **Bark is collected from wild trees**

- **Common Names**
  - Bearwood
  - Bitterbark
  - Buckthorn
  - Coffeeberry
  - Mountain cranberry
Constituents

- 4 main glycosides – Called Cascarosides
  - Cascaroside A, Cascaroside B, Cascaroside C
  - Cascaroside D

- 2 aloins:
  - C – Glycosides
  - Breakdown products of Cascarosides A-D
    - Barbaloin (derived from aloe-emodin)
    - Chrysaloin (derived from chrysopanol anthrone)
- O-glycosides
  - Derived from
    - Emodin
    - Emodin oxanthrone
    - Aloe emodin
    - Chrysophanol

- Dianthrones
  - Those from
    - Emodin
    - Aloe-emodin
    - Chrysophanol
    - Hetrodianthrones
      - Palmidin A, B and C (Rhubarb)

- Emodin
- Aloe-emodin
- Chrysophanol (in the free state)
Substitutes

- *Rhamnus alnifolia* (too rare)
- *Rhamnus crocea* (bark is very different from official drug)
- *Rhamnus californica* (so closely related to *Rhamnus purshianus* some botanists do not consider them to be separate species).
- *Rhamnus fallax*
Uses

- Purgative - stimulates evacuation of the bowels
- Similar to Senna
- Normally as a tablet
- Also used on animals
Physiological Action

- **Astringent (bark – tannins)** - A drug that causes contraction of body tissues and canals
- **Bitter tonic**
- **Chologogue – increase bile secretion**
- **Emetic – Induce vomiting**

**Medicinal Uses**

Move Relating to or involving the stomach, clear heat.

The most widely used laxative world-wide.

**Topically:** Used as a wash for herpes lesions (An injury to living tissue (especially an injury involving a cut or break in the skin))
- **Excessive use:** nausea, vomiting, heamatorrhoea.

- **Long term use:** Weakens intestinal muscles.

- **Contra-indications:** children younger than 14, during pregnancy, lactation, intestinal obstruction, and idiopathic abdominal pain.
**Rhubarb**

- **Botanical Name:** *Rheum palmatum*
- **Family:** Polygonaceae
- **Other species and hybrids of Rheum, except R. Rhaponticum**
- **Part used - Rhizome**
Constituents

1. Anthraquinones without a carboxyl group - chrysophanol, emodin, aloe-emodin & physcion.
   Also the glycosides of these substances.

3. Anthrones and dianthrones of chrysophanol, emodin, aloe-emodin or physcoid.

4. Dianthrone glucosides of rhein (Sennosides A and B).

5. Hetrodianthrones derived from 2 different anthrone molecules: Palmidin A and Palmidin B.
Free anthraquinones: chrysophanol, emodin, aloe-emodin and rhein.

Some of the above constituents may also occur as glycosides.
Uses

- Bitter stomachic
- Diarrhoea (low doses) – contains tannins
- **Purgative** (high doses) – followed by an astringent effect.
- Suitable only for occasional use, not for chronic constipation.
Medicinal Actions
- Anti-helminthnic, anti-bacterial, anti-inflammatory, antiseptic, astringent (low doses)

Topical Uses:
- Poultice to treat boils, burns, wounds. Used to stop bleeding (tannins – stypic and astringent). Used as a mouthwash for oral ulcers.

Other uses: Acid content: fresh root can be used to polish brass.

Caution
- Leaves should be avoided – high calcium oxalate - toxic
Aloe

- Aloes are the solid residue obtained by evaporating the liquid which drains from the transversely cut leaves of various *Aloe* species. The juice is usually concentrated by boiling and solidifies on cooling.

- Botanical name:
  - Cape Aloes - South Africa and Kenya - *Aloe ferox*
  - Curacao Aloes - West Indies - *Aloe barbadensis*
  - *Family* - Liliaceae
Cape Aloes - Characteristics

- Dark brown or Green-brown
- Glassy masses
- Thin fragments have a deep olive colour
- Semi-transparent.
- Powder: green-yellow
- Rub 2 pieces of drug together – powder is found on the surfaces.
- Characteristic sour odour
- Taste: nauseous and bitter.
- Microscopy: powder in lactophenol – amorphous.
Characteristics of Curacao Aloe

- Colour: yellow-brown – chocolate brown.
- Poor qualities (overheated) black colour.
- Opaque
- Breaks with a waxy facture
- Semi-transparent
- More opaque on keeping.
- Nauseous and bitter taste.
- Characteristic iodoform odour.
- Microscopy: lactophenol – acicular crystals
Aloes – Constituents

- C-glycosides
- Resins
- Glycosides
  - Aloin
    - Barbaloin
    - Isobarbaloin
- Aloe-emodin

Cape Aloes: Also Contain

Aloinoside A & Aloinoside B (O-glycosides of barbaloin)
Figure 3. Structural formulas of compounds isolated from *Aloe barbadensis.*
Unlike C-glycosides, O-glycosides of *Aloe* are not hydrolysed by heating with dilute acids or alkali.

- Can be decomposed with ferric chloride & dilute HLC –

- **NB:** Modified Borntrager’s Test – oxidative hydrolysis. Anthraquinones give a **red** colour when shaken with dilute ammonia.

- **NB:** All Aloes give a strong **green fluorescence** with borax (characteristic of anthranols) - General test for aloes.
Aloe - Uses

- **Purgative**

- *Seldom prescribed alone - activity is increased when administered with small quantities of soap or alkaline salts; Carminatives* *(Relieving gas in the alimentary tract colic or flatulence or griping)* moderate **griping** *(Acute abdominal pain)* tendency.
Medicinal Uses:

- Anti-bacterial, anti-fungal
- Emmenogogue - Any agent that promotes menstrual discharge
- anti-inflammatory
- Demulcent
- immune-stimulating (gel).
- Radiation burns (internal and external use)

Contra-indications - Pregnancy & lactation (internal uses)
Aloe vera Products

- These are derived from the mucilage gel - parenchyma cells
- Should not be confused with aloes (juice of pericycle - juice used for laxative effect).
- Cosmetic industry (usefulness often exaggerated) - Used as suntan (increase pigmentation by sun light) lotions, tonics and food additives.
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