PharmacognosyII

Lec. 3 **3rd stage 1st semester** **Year 23-24**

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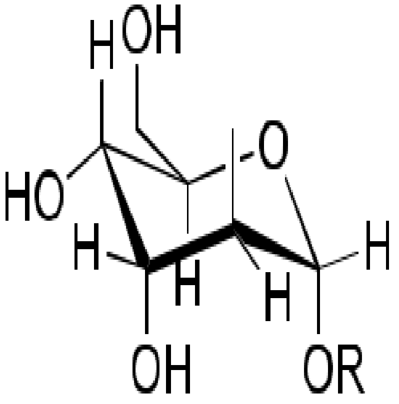
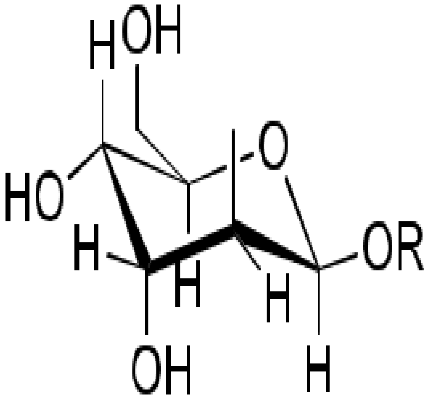
Glycosides

Glycosides are compounds that yield one or more sugars upon hydrolysis. The term glycoside is a generic term for natural product that is chemically bound to a sugar. Thus, the glycoside composes of two parts: the sugar and the aglycone. The aglycon may be a terpene, a flavonoid, a coumarine or any other natural product. Glycoside showed extra chemical diversity. Among the sugars found in natural glycosides, D-glucose is the most abundant one, L rhamnose and L-fructose also occur quite frequently. Of the pentoses: L-arabinose is more common than D-xylose. The sugar part can be disaccharide.

Because of the cyclic structure of the sugar, two diastereoisomers of the glycoside exist depending on the configuration of the anomeric carbon. These diastereoisomers are called anomers and are designated as α and β. This classification depends on the glycosidic linkage (above the linkage is β), below the linkage is α.



Alpha anomer



Beta anomer

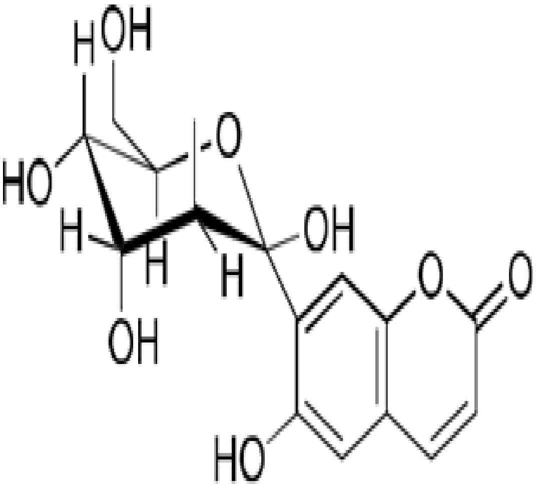
Chemically, glycosides are usually mixed acetals in which the hydroxyl group on the anomeric carbon is replaced by a moiety possessing a nucleophilic joined to the aglycone via: atom. Thus, the sugar moiety of a glycoside can be:

Oxygen atom (O-glycosides)

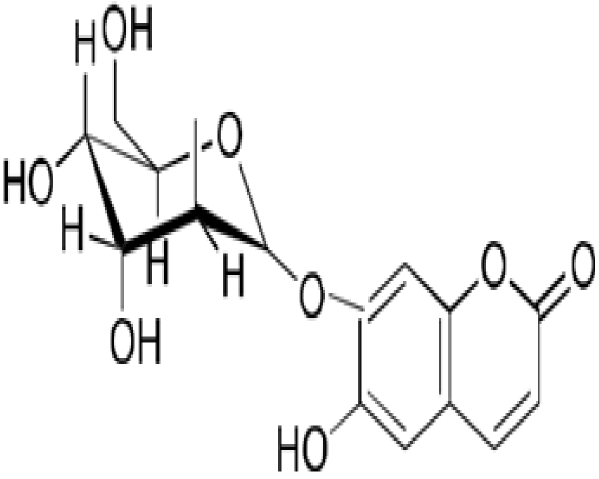
Carbon atom (C-glycosides)

Nitrogen atom (N-glycosides)

Sulfur atom (S-glycosides)



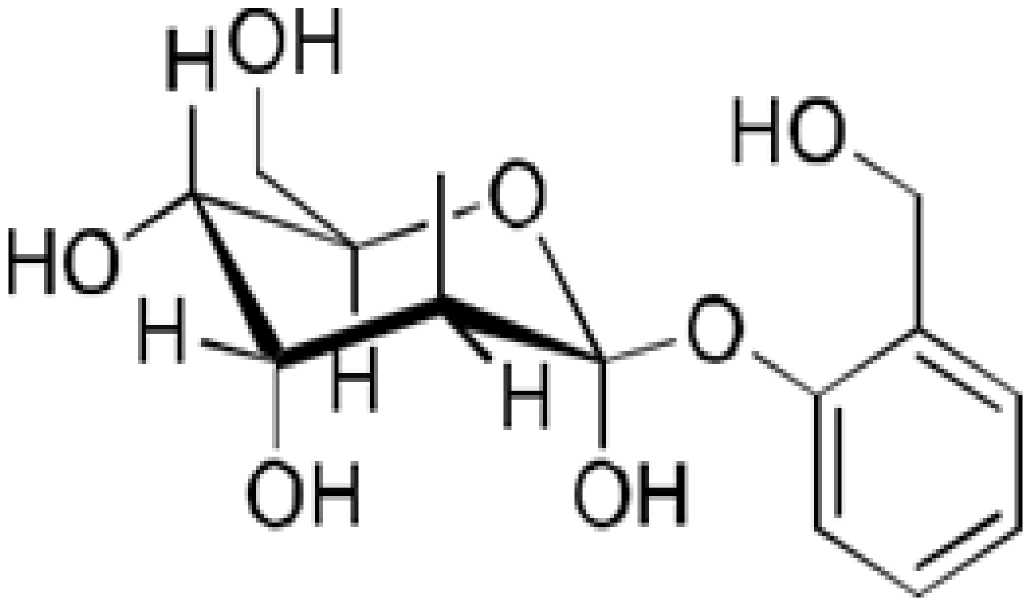
C-glycoside



O-glycoside

Nomenclature of glycosides

In the nomenclature of glycosides the trivial names have an “in” ending, and the names indicate the source of glycoside, for example, digitoxin from Digitalis, salicin from Salix, and prunasin from Prunus. The systematic names are usually formed by replacing the “ose” suffix of the parent sugar with “oside”. The anomeric prefix (α- or β-) and the configurationally prefix (D or L) immediately precede the sugar stem name, and the chemical name of the aglycone precedes the name of the sugar. For example the name of salicin is o-hydroxy-methylphenyl β-D-glycopyranoside.



salicin

o-hydroxy-methylphenyl β-D-glycopyranoside

Classification of glycosides

The classification of glycosides is a difficult matter.

If the classification is based on the sugar group, a number of rare sugars are involved; for example, glucosides and rhamnosides,

If the aglycone group is used as a basis of classification, all classes of natural products will be involved, **e.g**., lignan glycosides, alkaloidal glycosides, etc.

A therapeutic classification, although excellent from a pharmaceutical viewpoint.

Based on properties or function.

Glycosides that have soap like properties are called saponin. Similarly, glycosides that liberate hydrocyanic acid (HCN) on hydrolysis are known as cyanogenic glycosides.

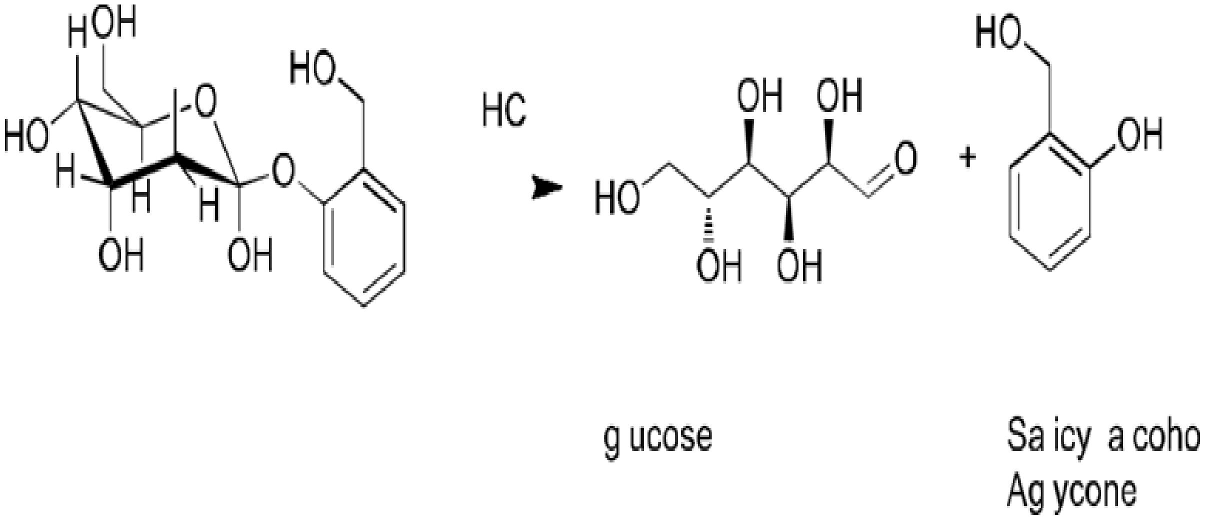
Accordingly, the types of glycosides are:

Cardiac glycosides
Cyanogenic glycosides
Phenolic glycosides (flavonoids, lignans and other phenolic compounds)
Aldehyde glycosides
Anthraquinone glycosides
Saponine glycosides [terpene (triterpenoid) and sterol unit]
Cyanogenic glycosides

Hydrolysis of glycosides

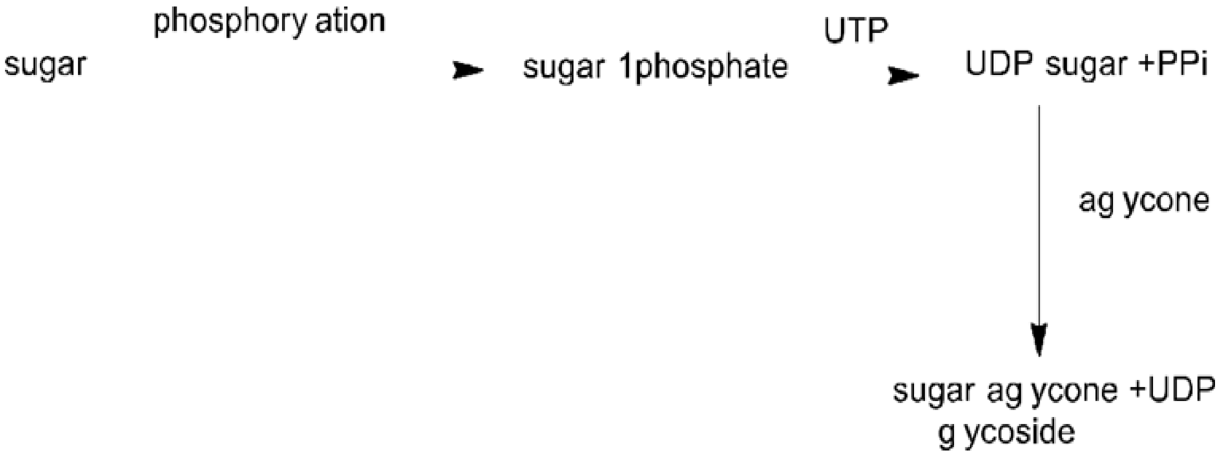
All natural glycosides are hydrolyzed into a sugar and another organic compound by boiling with mineral acids; but differ in the in the ease with which this hydrolysis is performed.

Enzymatic hydrolysis is more specific. Many of the enzymes hydrolyzed only a single glycoside; however, two enzymes, namely **emulsin** of almond and **myrosinase** of black mustard seeds, each hydrolyze a considerable number of glycosides. **Rhamnase** is the enzymes that hydrolyze rhamnoside glycosides.



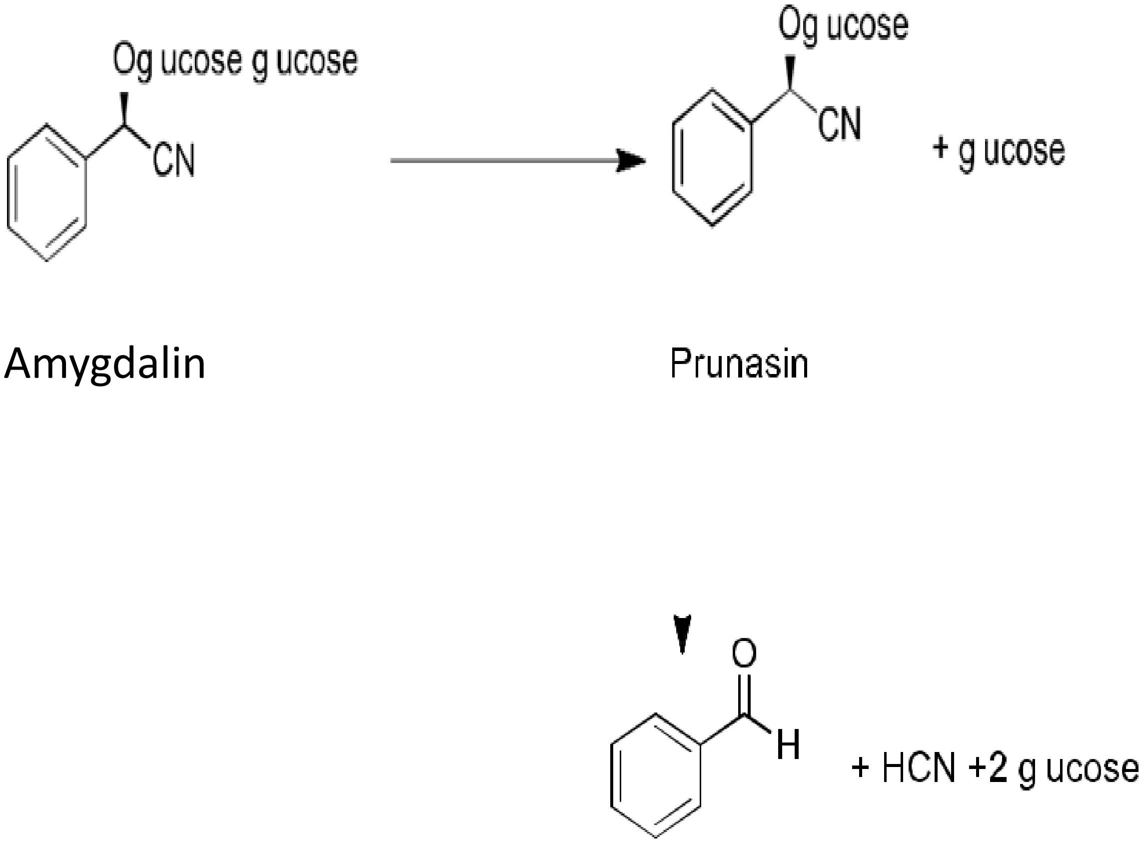
Biosynthesis of glycosides

The biosynthetic pathways are widely variable depending on the type of aglycone as well as the glycone units. The aglycone and the sugar parts are biosynthesized separately, and then coupled to form a glycoside. The coupling of the two parts occurs via phosphorylation of a sugar to yields a sugar 1-phosphate which reacts with a uridine (uracil nucleo base and ribose) triphosphate to form a uridine diphosphate sugar (UDP-sugar) and inorganic phosphate. This UDP sugar reacts with the aglycone to form the glycoside and a free UDP.



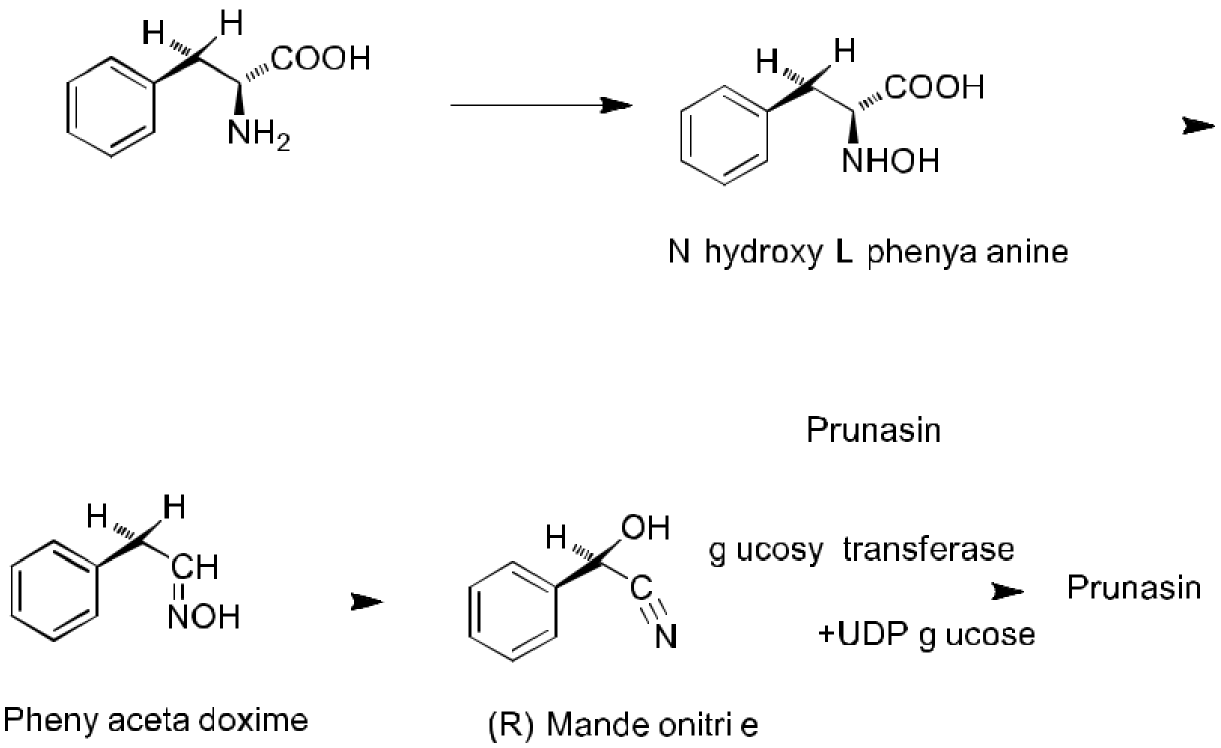
Cyanogenic glycosides

Cyanogenic glycosides names come from (yield HCN on hydrolysis)



Cyanogenic glycoside yeild HCN on hydrolysis

Biosynthesis of these glycosides begin with L-phenylalanine



Amygdalin found in almond (prunus amygdalus) Fam: Rosaceae.

Linseed (linum sativum) Fam: Linaceae contain the glycoside linamarin.

HCN liberated on hydrolysis can be determined by a simple color test using sodium picrate (yellow) which turns red in contact with HCN.

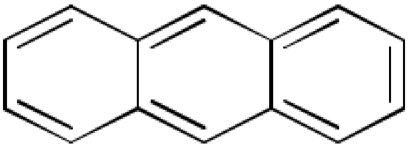
Uses and side effects

The extracts of plants that contain the cyanogenic glycoside are used as flavoring agents in many pharmaceutical preparations. Amygdalin has been used for treatment for cancer and as cough suppressant.

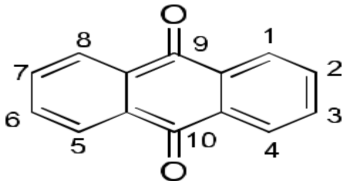
Excessive ingestion of this glycoside can be fatal. Some foodstuffs containing cyanogenic glycosides can cause severe gastric irritation and damage if not properly handled.

Anthraquinone glycosides

These glycosides are anthracene derivatives most of them contain anthraquinone skeleton such as cascara sagrada, frangula, aloe, rhubarb and senna.

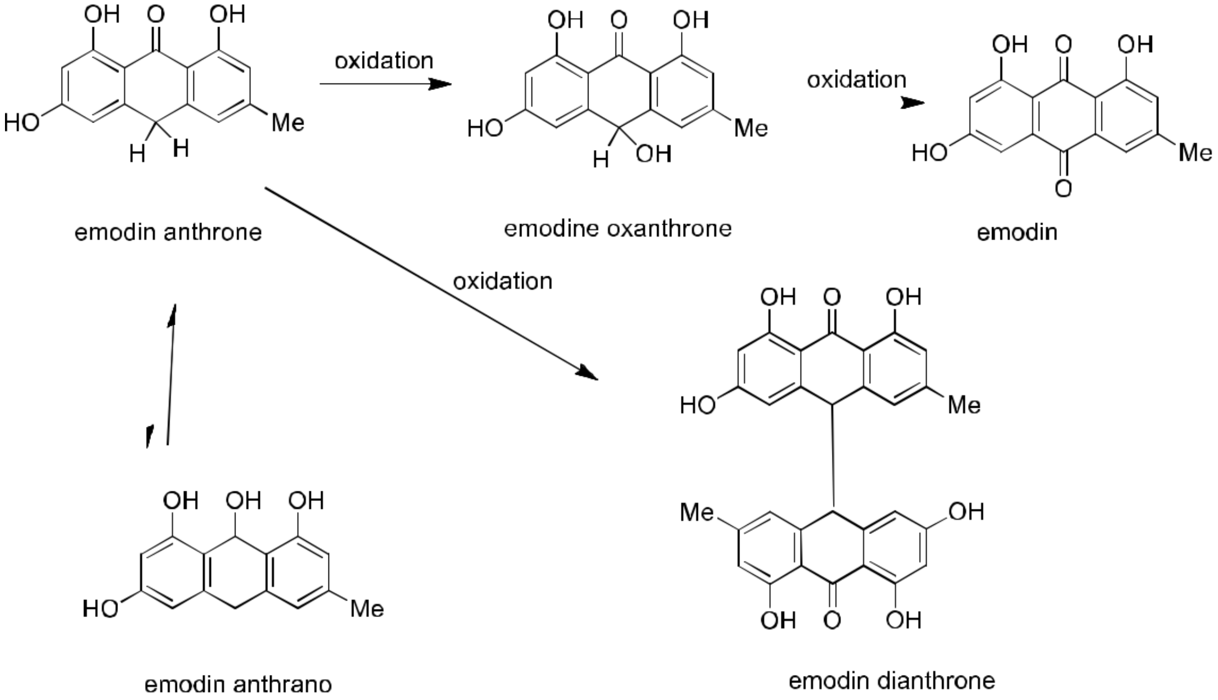


anthracene

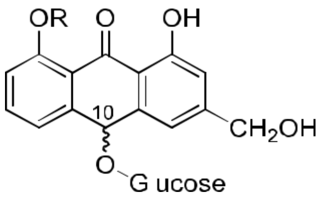


9,10 anthraquinone

These drugs are used as cathartics. The glycosides, upon hydrolysis, yield aglycones that are di-, tri-, or tetrahydroxyanthraquinones or modifications of these compounds. A typical example is frangulin A, which hydrolyses to form emodin (1,6,8-trihydroxy-3-methylanthraquinone) and rhamnose. The structural relationships of emodin are shown in the following figure.

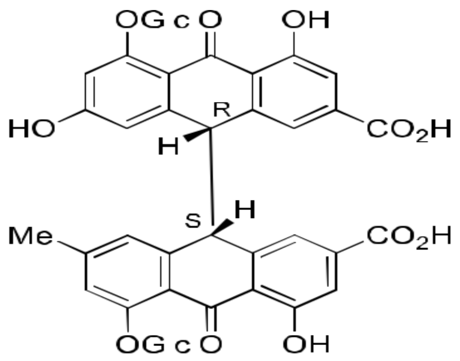


Glycosides of anthranols, dianthrones, and oxanthrones have significant therapeutic action. They employed as cathartic which exert their action by increasing the tone of the smooth muscle in the wall of the colon and stimulate the secretion of water and electrolytes into the large intestine (bulk laxatives). Glycosides of anthranols and anthrone (Aloe and Rhubarb) elicit a more drastic action than other anthraquinone leading to discomforting gripping action. The drug of choice is cascara and senna. Aloe is used for treatment of minor burns. The action is due to presences of aloin A and Aloin B. Action of senna due to presence of the glycosides (sinnoside A and B).



10 R aloin A

10 S aloin B



Sennoside B, R,S configuration

Sennoside A, R,R configuration

Biosynthesis of anthraquinone glycosides

Feeding of labeled acetate to organisms produce anthraquinone glycosides have revealed that the distribution of radioactivity in these compounds is consistent with formation via a head to tail condensation of acetate units.

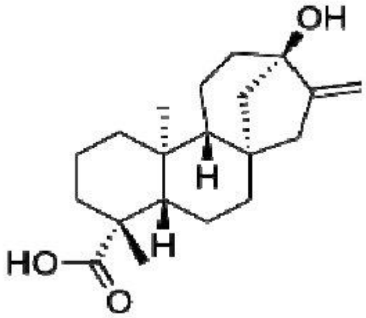
Test for anthraquinone glycosides

Powdered plant material is mixed with organic solvent and filtered. Aqueous base (NaOH or NH4OH) is added to it. A pink or violet color in the base layer indicates the presence of anthraquinone nucleus. This test is specific for aglycone, therefore hydrolysis with HCl in case of O-glycosides and ferric chloride/HCl for C-glycosides must be performed.

Isoprenoids glycosides

The aglycone of this type of glycosides is biosynthetically derived from isoprene units. There are three types of isoprenoid glycosides: diterpene, saponins and cardiac glycosides.

Steviol glycosides

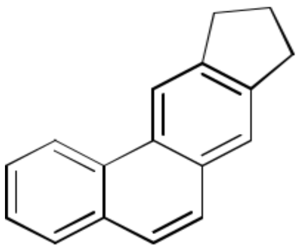


Steviol is a diterpene first isolated from *Stevia rebaudiana* in 1931. Its chemical structure was not fully elucidated until 1960
Steviol is found in the form of glycosides including the sweet chemical compound stevioside.

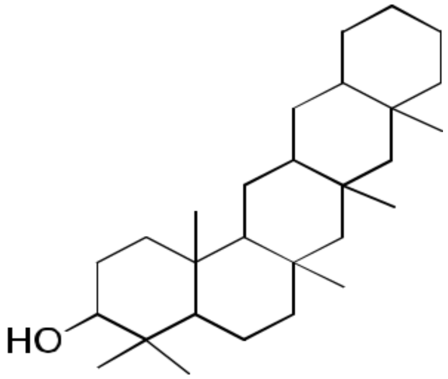
Steviol glycosides are high intensity sweeteners, 250-300 times sweeter than sucrose.
They are isolated and purified from the leaves of the stevia plant (*Stevia rebaudiana* Bertoni), where it is present at levels up to 13%.

Saponine glycosides

Saponins form colloidal solutions in water that foam upon shaking. They have a bitter acrid taste and have irritation action to mucous membrane. They destroyed red blood corpuscles by hemolysis and are toxic. Upon hydrolysis they yield an aglycone known as a sapogenin which can be one of two possible chemical classes either steroid (cyclopentaphenanthrene) or triterpenoid (pentacyclic structures).



cyclopentaphenanthrene



pentacyclic triterpenoid