

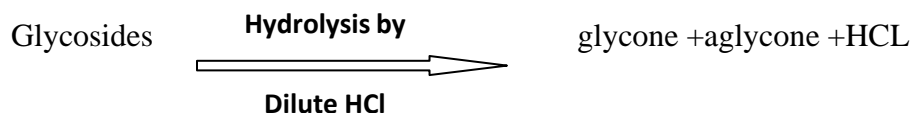
## Glycosides

Organic natural compounds present in a lot of plants and some animals, these compounds upon hydrolysis give one or more sugars (glycone) and non-sugar (aglycone) or called genin.

### Solubility:

glycosides are water soluble compounds and insoluble in the organic solvents. Glycone part: water soluble, insoluble in the organic solvents. Aglycone part: water insoluble, soluble in the organic solvents. Some glycosides soluble in alcohol.

### Separation between glycosides parts:



Then we can separate glycon and a glycon part by using separatory funnel

### Physico-chemical properties of glycosides (general) :

- Colorless, solid, amorphous, nonvolatile (flavonoid- yellow, anthraquinone-red or orange).
- Give positive reaction with Molisch's .
- They are water soluble compounds, insoluble in organic solvents
- Most of them have bitter taste (except: populin, glycyrrhizin, stevioside).
- Odorless except saponin (glycyrrhizin).
- when a glycosides has a lot of sugars its solubility in water decrease.
- Glycosides hydrolyzed by using mineral acids and temperature or by using enzymes such as:

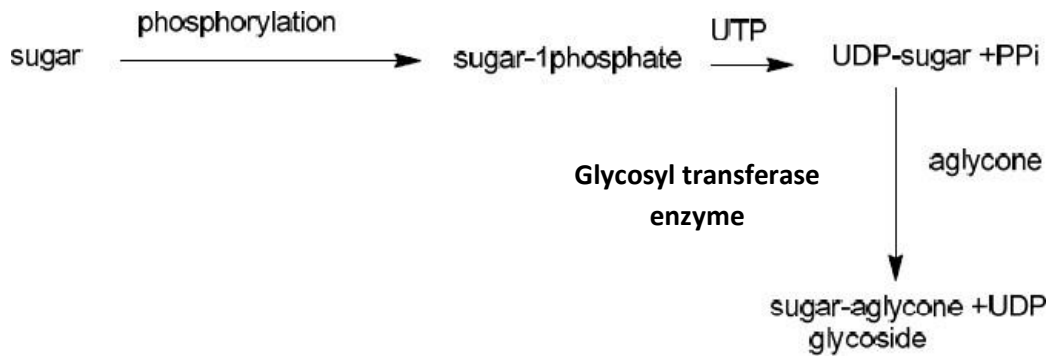
**a- Emolsin**      Bitter almond seeds.

**b- Myrosin or Myrosinase**      black mustard seeds.

**c- Rhamnase**      glycosides containing rhamnose as sugar part.

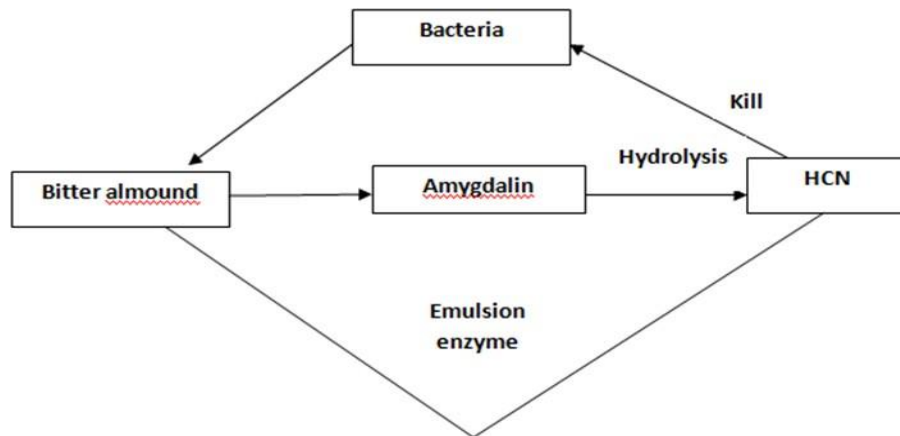
**d- Invertase**      can hydrolyze  $\alpha$ - glycosides

### Biosynthesis of glycosides (O-glycosides) :



### The function or the role of glycosides in the plant organism

- Converting toxic materials to non or less toxic.
- Transfer water insoluble substances by using monosaccharide.
- Source of energy (sugar reservoir).
- Storing harmful products such as phenol.
- Regulation for certain functions(growth).
- Some glycosides have antibacterial activity, so they protect the plants from bacteria and diseases.



## Stability of Glycosides:

### 1- Effect of acid hydrolysis:

- Acids split sugars from the aglycones.
- C-glycosides are resistant to acid hydrolysis.

### 2- Effect of alkaline hydrolysis:

#### A- Strong alkalis:

- Hydrolysis of ester groups.
- Opening of lactone rings e.g. Cardiac glycosides.

#### B- Mild alkalis:

- Hydrolysis of ester groups
- Opening of lactone rings e.g. Cardiac glycosides.

### 3- Enzymatic hydrolysis:

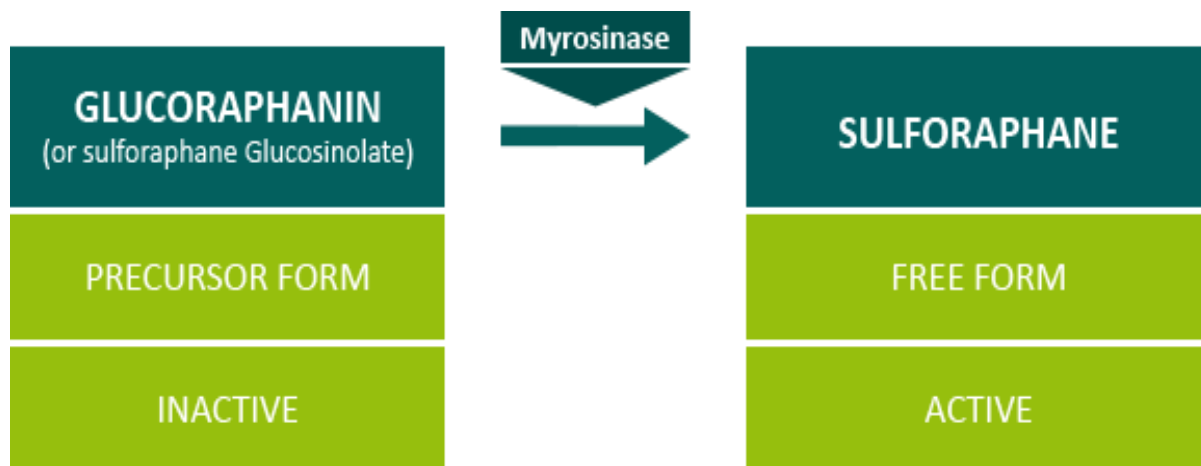
- Split the sugars stepwise starting from the terminal sugars.
- All plants producing glycosides have enzyme that can hydrolyze these glycosides.
- **Hydrolysis of glycosides**
- All natural glycosides are hydrolyzed into a sugar and another organic compound by boiling with mineral acids; but differ in the ease with which this hydrolysis is performed. Enzymatic hydrolysis is more specific.

### Examples :

**1-Amygdalin** which is also called laetrile is the aromatic cyanogenic glycoside. It is also known as vitamin B17 easily isolated from apricot stones, almonds, cherries, peaches and plums. Its chemical formula is  $C_{20}H_{10}NO_{11}$ . Amygdalin itself is nontoxic but it produces poisonous substance HCN which is decomposed by **Emolsin** enzyme.

**2-Glucoraphanin** in broccoli is enzymatically hydrolyzed by **myrosinase**, an enzyme compartmentally separated from glucoraphanin in plant cells. Myrosinase is released when the plant is chewed or processed. Heating broccoli partially denatures and inactivates myrosinase, leaving the glucoraphanin at least partially intact. In the gut of healthy individuals any intact glucoraphanin is then metabolized by myrosinase-producing bacteria. Because broccoli sprout or seed extracts taken orally contain no myrosinase to hydrolyze the glucoraphanin, transformation to sulforaphane must be carried out by the gut microflora. In individuals with compromised

intestinal flora and low myrosinase activity, it is unclear if glucoraphanin exerts the same systemic effects as observed in individuals with normal intestinal flora. Once glucoraphanin is converted to sulforaphane, it becomes a potent antioxidant in the body and helps to boost the body's natural detoxification pathways. By eliminating harmful toxins and pollutants alcohol , cigarette smoke , ultraviolet light , high fructose corn syrup and other toxins that creep into our daily lives .



### Do you know how antioxidants work?

The main purpose of antioxidants is to protect the cells in the body from damage caused by oxidative stress, namely free radicals, which are unstable compounds missing an electron (a negative charge) on their outside layer. Free radicals are both created as a byproduct of normal cellular respiration as well as environmental byproducts of pollution, sunlight, etc. Because of their instability they steal electrons from any source they can find in the body to help stabilize them. The most readily available source of electrons in the body is the phospholipid bilayer that surrounds each cell. Over time, the chronic exposure of the cell walls to free radicals will break down the walls, which can have a variety of negative effects, both acute and chronic. In some cases it is a major cause of a disease, such as seen in Alzheimer's . In others, it simply makes an already existing condition worse, as in asthma or Rheumatoid Arthritis.

By definition, antioxidants are electron donors; they act as sacrificial lambs by offering free radicals another source of electrons besides the cell wall. They can give their electrons to free radicals, neutralizing them and thereby preventing them from stealing any more electrons and doing further damage.



## Classification of glycosides :

### 1- Classifications of glycosides according to their therapeutic effects :

- CHF and cardiac muscles stimulators such as: Digitalis glycosides: digoxin, digitoxin, gitoxin (Fox glove leaves).
- Laxative group of glycosides: Sennoside A,B,C,D (Senna leaves and fruits).

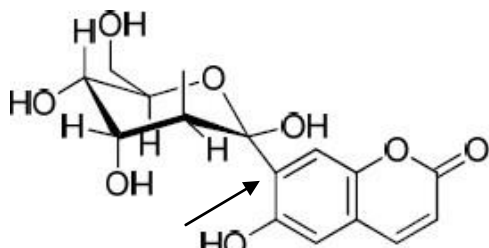
### 2- Classification of glycosides according to glycone part :

- Glucose \_ glucoside group like in Sennoside.
- Rhamnose \_ Rhamnoside like in frangullin.
- Digitoxose \_ Digitoxoside like in digoxin

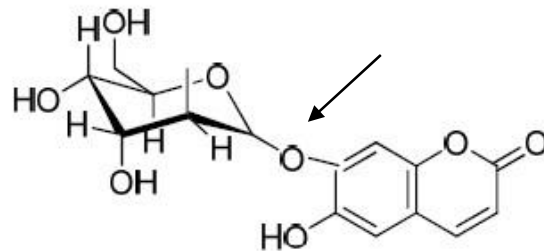
### 3- Classification of glycosides on the basis of the linkage between glycone and aglycone part :

- O-glycosides (if the glycosidic bond is via oxygen); the most abundant form in plants
- C-glycosides (linkage via a carbon); this type of linkage is resistant to hydrolysis
- S-glycosides (linkage via a sulfur; aglycone must have —SH group) present in glucosinolates (thioglycosides)
- N-glycosides (linkage via a nitrogen; aglycone must have —NH group) present in nucleosides.

**Note : C-glycosides are not hydrolyzed by acids or alkalis or by enzymes mainly**

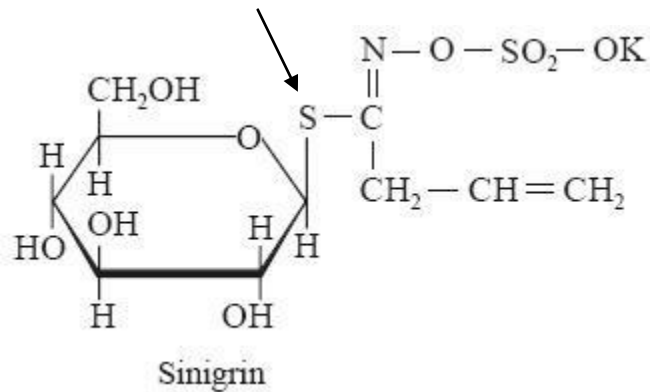


C-glycoside



O-glycoside

Example of S-glycoside : **Sinigrin**, obtained from black mustard seeds



### Classification of glycosides according to a glycone part :

- 1- if a glycone part alcohol -this group called alcoholic group like Salicin
- 2- if a glycone part aldehyde- this group called aldehydic gr. like glucovanillin.
- 3- if phenol called phenolic group like arbutin .
- 4-if cyanone called cyanogenic or cyanophoric or cyanoside like amygdalin.

**Most of glycoside may be classified according to the plant from which they isolated for example:**

- 1-salicin –salix
- 2-aloin- Aloe vera
- 3- sennoside – senna

### Classification depending number of sugars :

- |                |           |               |
|----------------|-----------|---------------|
| ■ One sugar    | monosides | e.g. Salicin. |
| ■ Two sugar    | Biosides  | e.g. Diosmin. |
| ■ Three sugars | Triosides | e.g. Digoxin  |

### Glycoside biological activity:

- Glycosides are biologically active because : aglycon part
- Sugar (Glycon) part will participate in absorption, transportation to the site of action (i.e. they help to increase the bioavailability ) .

## **Glycosylation:**

glycosylation refers to the process wherein a carbohydrate (referred to as glycan) and other organic molecules are combined through the aid of certain enzymes. Specific plant glycosyltransferases (GTs) using nucleotide-sugars as donors can attach specific sugar moieties to an acceptor molecule. Glycosylation of metabolites in plants serves multiple purposes. Upon glycosylation, hydrophobic metabolites become more water-soluble which improves their bio-distribution and metabolism, increased solubility and amphiphilicity of glycosylated metabolites may assist their transport across cell membranes, The attachment of sugars to small metabolites raises their molecular weight and melting point. This allows synthesis and storage of precursors of volatile compounds that can be released on demand after hydrolysis, The stability of glycosylated metabolites may depend on the position where the sugar moiety is attached, for example the 6-O-glucosides of ascorbic acid are chemically less stable than the 2-O-glucoside form or non-glycosylated ascorbic acid. Furthermore, detoxification of harmful molecules can take place through glycosylation. Glycosylation may generate a non-toxic agent that later can be re-activated and used as aglycone in defense against parasites and plant-eating organisms such as herbivores. Examples are cyanogenic glycosides produced by plants.

## **Examples on importance of Glycosides in medicine:**

Many biologically active compounds are glycosides. Glycosides comprise several important classes of compounds such as hormones, sweeteners, alkaloids, flavonoids, antibiotics. it is nearly impossible to define general pattern of biological activities of the glycosides compared to the respective aglycons. It is generally accepted that glycosides are more watersoluble than the respective aglycons. Attaching of the glycosidic moiety into the molecule increases its hydrophilicity. This effect influences pharmacokinetic properties of the respective compounds, e.g., circulation, elimination and the concentrations in the body fluids. Some glycosides with specific individual biological activity that cannot be simply derived from the activity of the respective aglycone. The final activity is then given by the overall molecular structure.

### **1- GLYCOSIDES OF VITAMINS:**

Glycosides of vitamins, both hydrophilic and lipophylic, often occur in nature. Some of them were, however, prepared by chemical and biochemical methods. Glycosylated vitamins have an advantage over the respective aglycones in their better solubility in water (especially the lipophylic ones), stability against UV-light, heat and oxidation, reduction of the bitter taste and odour (e.g., thiamine), and resistance to an enzymatic action. Some of the vitamin glycoconjugates have altered or improved pharmacokinetic properties.

\* **Thiamine:** Thiamine (vitamin B1) occurs in the nature in a free and a phosphorylated form. Its glycosides have not been identified in the natural material. Thiamine artificial glycosylation was motivated mostly by the needs to remove unpleasant taste and odor of the compound and to increase its stability, particularly against UV light.

## 2- Glycosides as sweetener :

Stevia is the generic term used to refer to different forms of the sweetener, including the whole plant *Stevia (Srebaudiana Bertoni)* and the leaves where the sweet compounds are found. Stevia extract is a generic name for a preparation made by steeping the leaves of the Stevia plant to extract the sweet compounds from the leaf material. On the other hand, high-purity stevia leaf extract contains 95% or greater steviol glycosides (**Table below ↓**)

Steviol glycosides	Sweetening power relative to sucrose
Stevioside	150–300
Rebaudioside A	200-400
Rebaudioside B	300-350
Rebaudioside C	50-120
Rebaudioside D	200–300
Rebaudioside E	250–300
Rebaudioside F	Not available
Rubusoside	110
Steviolmonoside	Not available
Steviolbioside	100-125
Dulcoside A	50–120



**Stevia Metabolism:** The backbone of all steviol glycosides is steviol, to which various glycoside (glucose) groups attach to form the variety of sweet compounds in stevia . Steviol glycosides pass through the upper gastrointestinal tract fully intact. Gut bacteria in the colon hydrolyze steviol glycosides into steviol by snipping off their glucose units. Steviol is then absorbed via the portal vein and primarily metabolized by the liver, forming steviol glucuronide, which is primarily excreted in the urine. Research shows that there is no accumulation of stevia (or any component or byproduct of stevia) in the body and that it passes through the body during metabolism. Energy from fermentation of glucose units (usually assessed as 2 kcal/g) is so low that it is minimal, and so, effectively, stevia can be said to provide zero calories.

**3-Glycosides represent a large group of drugs, supplements and precursor for many drugs:  
for example**

\*Flavonoids glycosides

\*Saponins glycosides

\*Cardiac glycosides

\*Cynogenic glycosides