

GLYCOSIDES

Some of the more interesting, if not important, derivatives synthesized by plants are glycosides. Most glycosides are thought to function as deterrents to herbivores. The term **glycoside** (Gr. *glykys*, sweet) refers to the bond formed (called a glycosidic bond) when a sugar molecule condenses with another molecule containing a hydroxyl group.

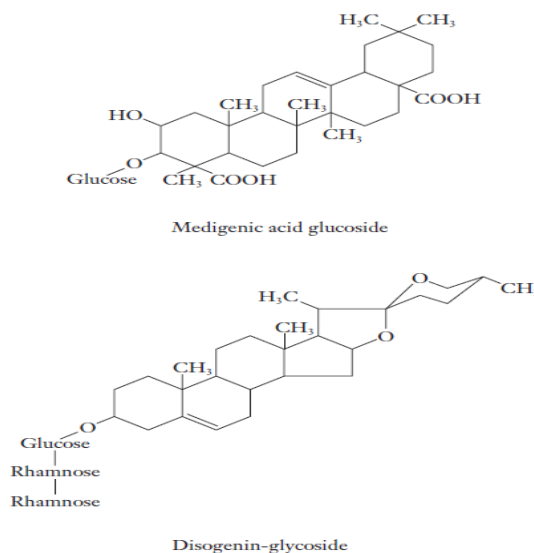
Sugars may form together to form polysaccharides, or with hydroxyl groups on non-carbohydrate molecules, such as steroids or amino acids. The sugar most commonly found in glycosides is glucose, although specific glycosides often contain rare sugars.

Three particularly interesting glycosides are the saponins, the cardiac glycosides (cardenolides), and the cyanogenic glycosides.

A. Saponins are terpene glycosides with detergent properties

Saponins may take the form of (1) steroid glycosides, (2) steroid-alkaloid glycosides, or (3) triterpene glycosides.

FIGURE 27.8 Saponins are triterpenoids or steroids containing one or more sugar units. Medigenic acid glucoside is a triterpenoid saponin from alfalfa (*Medicago sativa*). Disogenin glycoside is a steroidal saponin isolated from clover (*Medicago spp.*). The addition of a hydrophilic sugar group to a normally hydrophobic terpene gives saponins surfactant properties similar to soap.



Saponins may also occur as aglycones (e.g., the terpene without the sugar), which are known as **sapogenins**. In much the same way as soap, which is the sodium salt of a fatty acid, the combination of a relatively hydrophobic triterpene with a hydrophilic sugar gives saponins the properties of a detergent. When agitated in water, saponins form a stable soapy foam.

The principal role of saponins appears to be as a preformed defense against attack by fungi. Evidence indicates that saponins form complexes with sterols containing an unsubstituted 3- β -hydroxyl group. When the saponins react with sterols in the membranes of invading fungal hyphae, the result is a loss of membrane integrity.

In a classic example of one-upmanship, however, many pathogenic fungi have developed strategies, such as the development of detoxifying enzymes, for circumventing this defense mechanism. Oat (*Avena*), for example, produces a triterpenoid saponin, avenacin A-1, which is localized in the root epidermal cells and effectively protects against an invasion by a fungal pathogen (*Gaeumannomyces graminis* var. *tritici*) that infects the roots of both wheat (*Triticum*) and barley (*Hordeum*). However, another strain of *G. graminis* (var. *avenae*) produces an enzyme, avenacinase, that detoxifies avenacin A-1 and allows the pathogen to invade oats as well as wheat and rye.

The effect of saponins on eukaryotic membranes is highly nonspecific and it is not clear how plants protect their own membranes against the deleterious effects of their own saponins.

One possibility is that the saponins are stored in the form of a biologically inactive molecule, called a **bidesmosidic saponin**, which has two sugar chains rather than one. When under attack, the inactive form may be converted to the active **monodesmosidic** form by hydrolytic removal of the second sugar chain.

Alternatively, biologically active, monodesmosidic saponins may be sequestered in vacuoles or organelles whose membranes contain a high proportion of sterols with a protected 3- β -hydroxyl position.

The effect of saponins on animals is somewhat variable. While not significantly toxic to mammals, saponins do have a bitter, acrid taste and will cause severe gastric irritation if ingested. Saponins will hemolyze red blood cells, however, if injected into the bloodstream.

On the other hand, saponins are highly toxic to fish and have been used as fish poisons. Saponins have also been implicated in reports of livestock poisoning.

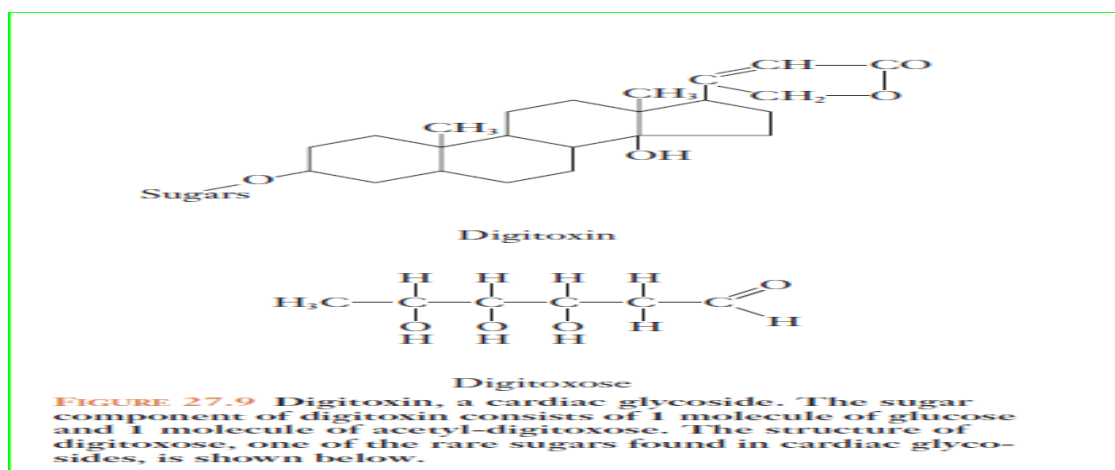
Alfalfa saponins, for example, can cause digestive problems and bloating in cattle. At the same time, there are reports that saponins contained in alfalfa

sprouts will lower serum cholesterol levels. Commercially, saponins from the bark of *Quillaja saponaria* have been used in shampoos, liquid detergents, toothpastes, and beverages.

The saponin **glycyrrhizin** from licorice (*Glycyrrhiza glabra*) has been used in medicines and as a sweetener and flavor-enhancer in foods and cigarettes.

B. Cardiac glycosides are highly toxic steroid glycosides

The **cardiac glycosides or (cardenolides)** are structurally similar to the steroid saponins and have similar detergent properties. They are distinguished from other steroid glycosides by the presence of a lactone ring (attached at C17) and the rare sugars (found almost exclusively in this group of steroids) that form the glycoside.



Like the saponins, cardenolides occur naturally as either the glycoside or the aglycone.

The cardenolides have a wide distribution; they have been recorded in more than 200 species representing 55 genera and 12 families and are a principal agent in accidental poisonings of humans. Perhaps the best known is **digitalis**, a mixture of cardenolides extracted from the seeds, leaves, and roots of purple foxglove, *Digitalis purpurea* or Grecian foxglove, *D. lanata*. The two principal cardenolides in digitalis are **digitoxin** and its close analog **digoxin**. *Digitalis* is also the source of a saponin, **digitonin**.

Since the late eighteenth century, digitalis has been used for its therapeutic value in treating heart conditions such as atherosclerosis. Because

they disrupt the heart muscle Na^+/K^+ -ATPase pumps (hence the appellation *cardiac*), cardenolides are highly toxic to vertebrates.

The extreme toxicity of cardenolides has long been exploited by African hunters, who coated their arrows and spears with cardenolide-rich extract from plants. In therapeutic use, however, carefully regulated doses can both slow and strengthen the heartbeat. Unfortunately, the lethal and therapeutic doses are very close, so the therapy must be carefully monitored.

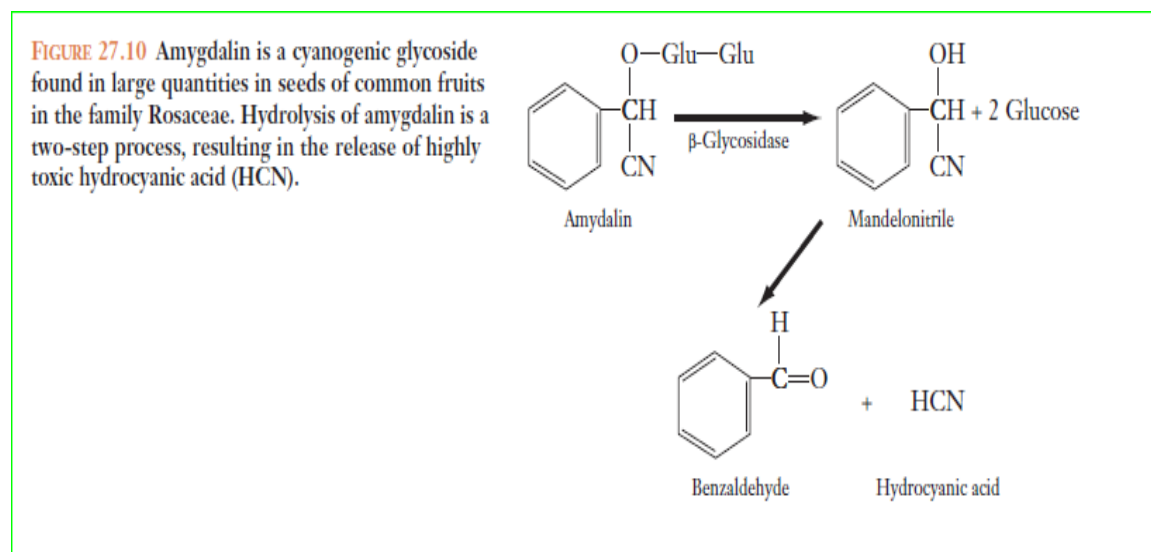
C. Cyanogenic glycosides are a natural source of hydrogen cyanide

It might seem odd that plants synthesize chemicals capable of releasing deadly hydrogen cyanide or prussic acid (HCN), but more than 60 different cyanogenic compounds of plant origin have been described from more than a 12 plant families. Predominant among these are the **cyanogenic glycosides**.

A common cyanogenic glycoside is **amygdalin** which occurs in many representatives of the family **Rosaceae**. It is found in the seeds of apples and pears and in the bark, leaves, and seed of the stone fruits (apricot, peaches, and cherries). Most cyanogenic glycosides appear to be derived from one of four amino acids (phenylalanine, tyrosine, valine, and isoleucine).

Intact cyanogenic glycosides are not themselves toxic, but when the plant is damaged by a herbivore, the glycoside undergoes an enzymatic breakdown and cyanide is released. Cyanide, a noncompetitive inhibitor of cytochrome oxidase, is acutely toxic.

The enzymatic breakdown of cyanogenic glycosides is a two-step process.



First, the sugars are released by the enzyme β -**glycosidase**. The resulting hydroxynitrile is moderately unstable and will slowly decompose, liberating HCN in the process. Normally, however, decomposition is accelerated by a second enzyme, **hydroxynitrile lyase**. Enzymatic release of cyanide does not normally occur in intact plants because the enzymes and the substrate are spatially separated.

There is some evidence that the presence of cyanogenic glycosides deters feeding by insects and other herbivores, although most animals have the ability to detoxify small quantities of cyanide. Clearly the effectiveness of cyanogenic glycosides as a deterrent depends on many factors, such as the amount present, the rate of release of cyanide, and the ability of the animal to detoxify.

The level of cyanogenic glycosides in plants is highly variable, influenced by both genetic control and environmental stress. The latter is a concern when using *Sorghum* for livestock forage. Dhurrin accumulates rapidly and can cause livestock poisoning when *Sorghum* plants are stressed by drought or frost.

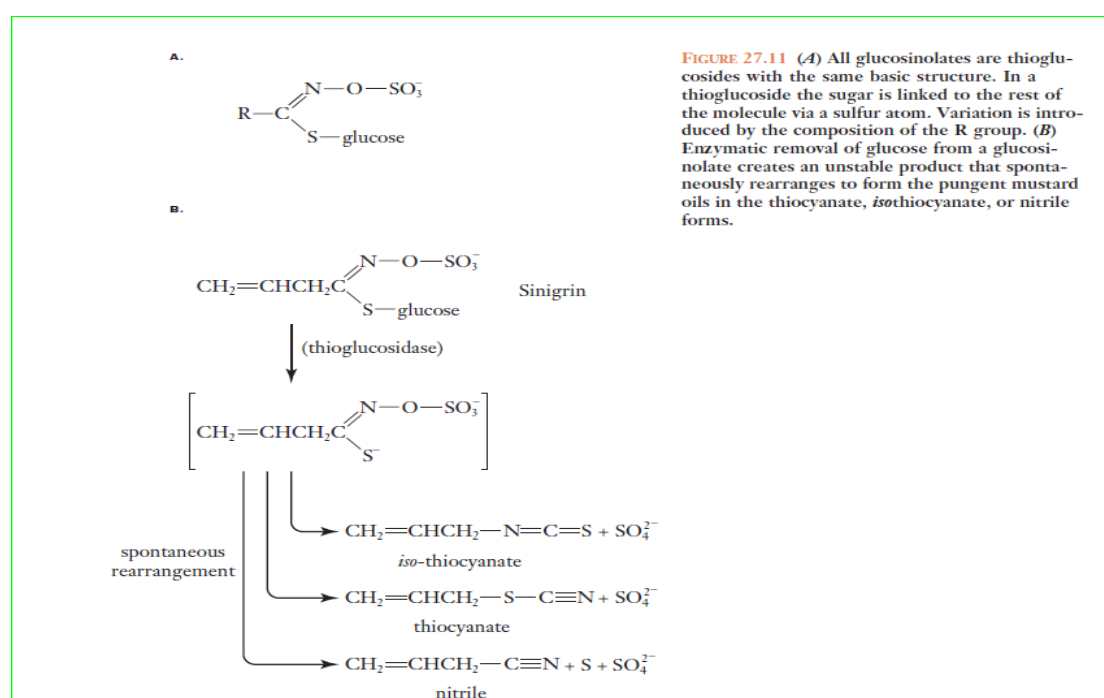
Many common food plants naturally contain cyanogenic glycosides in concentration sufficiently low that they are not normally a health hazard. These include soy and other beans (Fabaceae); apples, apricots, peaches and other fruits in the family Rosaceae; and flax seed (*Linum*), which is a popular health food.

However, poisoning is avoided by careful preparation of the plant. This includes grinding the root and expressing the fluids, or boiling the root in several changes of water.

Glucosinolates are sulphur containing precursors to mustard oils

Glucosinolates are found primarily in the mustard family (Brassicaceae) and related families in the order Capparales. They are precursors to the mustard oils; an economically important class of flavour constituents that gives the pungent taste to condiments such as mustards as well as the distinctive flavour of cabbages and broccoli.

All glucosinolates are **thioglucosides** (*thio*, sulphur) with the general structure shown in Figure.



The sugar is always glucose. The diversity encountered in structure and properties is due to the R group, which may range from a simple methyl group to large linear or branched chains containing aromatic or heterocyclic structures. The biological activity of glucosinolates depends primarily on their hydrolysis to **mustard oils**.

Hydrolysis of glucosinolates is catalyzed by an enzyme called myrosinase (a thioglucosidase). The hydrolysis product is unstable and immediately undergoes a rearrangement to form a thiocyanate or *isothiocyanate*.

Like the cyanogenic glycosides, glucosinolates are spatially separated from the hydrolytic enzymes so that the mustard oils are normally formed only when the cells are disrupted, allowing the enzyme and substrate to come

together. As with other defense compounds, some herbivores are deterred or repelled by the presence of glucosinolates in a plant, while others have adapted to use the glucosinolates or mustard oils as attractants to stimulate feeding and ovipositing.

Glucosinolates, or rather their absence, have had a significant impact on the oilseed industry. Rape seed (principally *Brassica napus*) is a good source of vegetable oil, but its high content of glucosinolate together with high erucic acid (a 22-carbon fatty acid) gives the oil undesirable taste and poor storage properties. New strains have been bred with low glucosinolates and erucic acid. These strains, called **canola** in order to distinguish them from normal rape, are now an economically important oil source.