

# Amino Acids Derivatives

## Glucosinolates

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Glucosinolates, formerly called thioglucosides, are anionic glycosides responsible for the potent and characteristic flavors of numerous Brassicaceae (mustard, radish, rutabaga, cabbage), and of various species pertaining to other botanically close families (Capparidaceae, Tropaeolaceae, Resedaceae). The glucosinolate content varies with the species, the plant part, and the cultivation and climatic conditions. It often ranges, before cooking, from 0.5 to 1 g/kg and can reach 3.9 g/kg in some Brussel sprouts.

### 1. STRUCTURE AND NOMENCLATURE

Although some authors persist in using a nomenclature system combining the prefix "gluco" with a term reminiscent of the name of the plant (e.g., clove glucocheiroline, cabbage glucobrassicin), it is by far preferable to use a prefix that



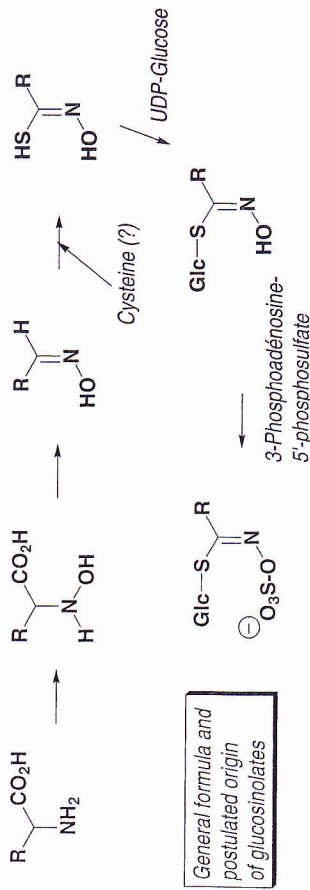
PRUNUS LAUROCERASUS L.

these compounds have been known for a long time, and therefore tend to conserve their common denomination: thus 2*R*-hydroxy-2-butenylglucosinolate is commonly referred to as sinalbin.

The basic structure of glucosinolates comprises a glucose residue, a sulfate group, and a variable aglycone, with the molecule occurring as a potassium salt. The structural diversity of glucosinolates reflects that of their precursor amino acids:

- tyrosine → *p*-hydroxybenzylglucosinolate → sinalbin (white mustard);
- phenylalanine → benzylglucosinolate glucotropæolin → (nasturtium, garden cress);
- tryptophan → 3-indolylmethylglucosinolate → glucobrassicin (cabbage);
- homomethionine → allylglucosinolate → sinigrin (black mustard);
- homophenylalanine → phenethylglucosinolate → gluconasturtiin (watercress).

Biogenetically, glucosinolates are probably formed by decarboxylation of amino acids to aldoximes, which then incorporate a sulfur atom (from cysteine?) before becoming glycosylated (by UDP-glucose) and finally, sulfated (by phosphoadenosine-phosphosulfate).

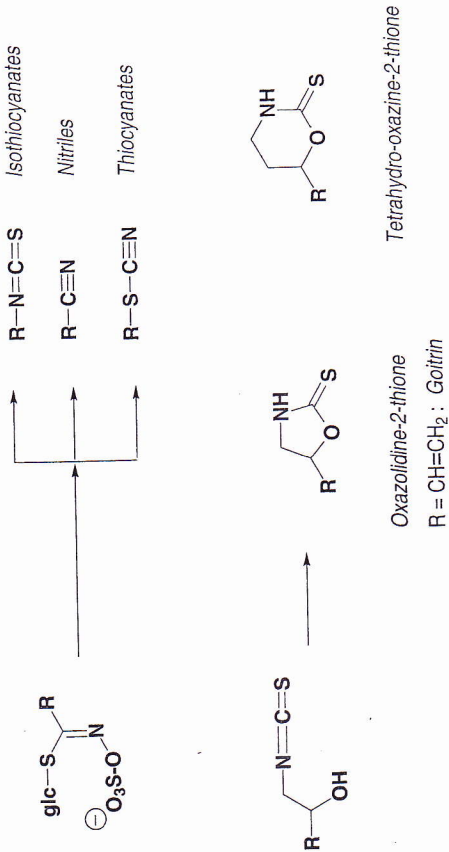


## 2. GLUCOSINOLATE HYDROLYSIS

When the tissues of glucosinolate-containing plants are bruised, the compounds are hydrolyzed by a thioglucosidase (= thioglucoside glucohydrolase = "myrosinase") always found in this type of plant. In all cases, the freed aglycone is unstable and rearranges.

If the pH is neutral, a Lössen rearrangement takes place and yields a very reactive, volatile, and strong-smelling isothiocyanate. In a slightly acidic medium, and in the presence of ferrous ions, sulfur and a nitrile are formed. The formation of thiocyanates is also possible, especially when the glucosinolate aglycone is derived from tryptophan.

Isothiocyanates react with alcohols to form thiocarbamates. A reaction of this type may take place in the case of hydroxylated aglycones: if there is a hydroxyl on



## 3. GLUCOSINOLATE EXTRACTION AND QUANTITATION

These compounds may be isolated only after destroying the enzymes (with boiling alcohol). Due to their ionic nature, glucosinolates can be separated on ion-exchange resins.

The sulfate ions or glucose can be quantitated following the action of thioglucosidases. Other methods have been developed, for example the spectrophotometric quantitation of the 1,3-benzodithiol-2-thiones formed by the condensation of the isothiocyanates with 1,2-benzene-dithiol. Estimating only the resulting isothiocyanates may be insufficient, because of the diversity of the products that can actually be formed. Quantitative and qualitative glucosinolate analysis is also possible by HPLC (see, for example, the glucosinolate quantitation in rapeseed [NF ISO 9167 standard]).

## 4. GLUCOSINOLATE TOXICITY

Several Brassicaceae species, especially cabbages, when ingested in massive amounts by animals (sheep, rabbits, cows), cause hypothyroidism which results in goiters, abortions, and fetal death *in utero*. Mineral thiocyanates capture iodide, and prevent its uptake by the thyroid. In other species, it is goitrin that is the oxazolidine-thione resulting from the hydrolysis of progoitrin (= 2-hydroxy-3-butenylglucosinolate), that inhibits iodine incorporation and the formation of thyroxine. In contrast to the previous one, this antithyroid effect is not canceled by iodine administration.

In man, although an abnormal goiter frequency is observed in populations with a diet poor in iodine and rich in Brassicaceae, there is no proof of a causal relationship between cabbage consumption and goiter growth. There are only a few cases of

still has its adepts (commercial preparations are to be soaked with lukewarm water). Instead of having a therapeutic effect that remains to be demonstrated, this type of treatment, if applied too long, can induce skin lesions.

- **BLACK RADISH,**  
*Raphanus sativus* L. var. *niger* (Mill.) Kerner

This species is a herbaceous plant commonly biennial with tough leaves, white flowers in racemes, and siliques uncontracted between the seeds. The voluminous root (up to 50 cm long) has a black, wrinkled, and rough surface.

The drug composition is only partially known. It contains glucobrassicine (3-indolyl-methylglucosinolate). Pharmacological data are virtually nonexistent: some authors note the concept of "hepatic drain". In the absence of pharmacological or clinical data, black radish-based phytopharmaceutical drugs (roots and fresh plant juice) may be marketed with the following three indications: traditionally used (orally) 1. as a choleric and chologogue 2. during acute benign bronchial disease, and 3. (locally) for sunburns, superficial and limited burns, and diaper rashes [French Expl. Note, 1998]. Phytotherapy grants it the potential for improving "hepatic migraines" and cosmetology that for limiting alopecia.

- **HEDGE MUSTARD,**  
*Sisymbrium officinale* (L.) Scop. = *Erysimum officinale* L.

This herb, very common in western Europe, is a folk remedy for hoarseness, and is considered to be an expectorant and mucolytic. The flower and fresh or dried flowering tops may be used to prepare plant-based medications traditionally used for the symptomatic treatment of cough, during acute benign bronchial disease, and locally (collutorium or lozenges) as an antalgic in buccal or pharynx conditions [French Expl. Note, 1998]. Although scientific data on this species are scarce, several species of the genus *Erysimum*—sometimes considered identical to genus *Sisymbrium*—are known to contain isothiocyanates and glucosinolates, as well as sulfur-containing lactones (e.g., *E. inconspicuum* [S. Watson] Mac Mill. erylsulfone and erylsulfoxide).

#### Other Brassicaceae

The French Explanatory Note of 1998 on plant-based medicines mentions two other Brassicaceae that may be used orally during acute benign bronchial disease, and locally (collutoria, lozenges), as an antalgic in buccal or pharynx conditions: the wild horseradish, *Cochlearia armoracia* L. (root) and scurvy grass, *Cochlearia officinalis* L. (leaf). Almost nothing is known of the composition and activity of

Identical remarks can be made regarding the consumption of milk from animals fed a diet rich in Brassicaceae.

#### 5. GLUCOSINOLATE POTENTIAL

These compounds may be beneficial to human health: according to several authors, the dietary intake of glucosinolates (from broccoli, cabbage, cauliflower, and especially brussel sprouts) might have a protective effect against colon cancer. This hypothesis is based on animal carcinogenesis data obtained by using different inducers and different animal species to test isothiocyanates as well as the indole-3-carbinol arising from the degradation of glucobrassicin. At high doses, the isothiocyanates and indoles interfere with the metabolism of carcinogens: they inhibit procarcinogen activation and induce "phase II" enzymes such as NAD(P)H quinone reductase or glutathione *S*-transferase, which detoxify the electrophilic metabolites capable of altering the structure of nucleic acids. In humans, the regular consumption of Brussel sprouts (300 g/day) causes a rapid (3 weeks) increase in glutathione-*S*-transferase and a decrease in the urinary concentration of a purine metabolite which is a marker of DNA degradation.

#### 6. GLUCOSINOLATE-CONTAINING DRUGS

Brassicaceae and nasturtium (Tropaeolaceae) are now of little importance to pharmacy.

- **MUSTARD: INDIAN MUSTARD, *B. juncea* (L.) Czerniak,**  
**BLACK MUSTARD, *Brassica nigra* (L.) Koch**

Indian mustard is an annual, herbaceous plant, with either pinnate or entire and lanceolate leaves depending on whether they are at the base or at the apex of the stem. The yellow tetramerous flowers are clustered in tight racemes. The fruits, elongated siliques with a beak, contain 12 to 14 seeds. The seeds are spherical and umbilicate and their color varies; their surface is finely reticulate. When coarsely ground in water, they release a pungent odor.

Mustard seeds are rich in mucilage (20%) and in unsaturated fatty acid-containing lipids (erucic, oleic, linoleic acids). The glucosinolate is sinigrin or allylglucosinolate (1-2%), the hydrolysis of which gives allyl isothiocyanate.

Mustard seeds are revulsives due to their "(volatile) mustard oil": the isothiocyanate when applied onto the skin causes tingling, rubefaction, and upon prolonged contact, vesication. The ancient \* use of mustard "plaster" cataplasms

\* We are reminded by P. Delaveau that "they [sinapisms] "make the humor leave the body" -

known of a third species, the shepherd's purse (*Capsella bursa-pastoris* Moench.), whose flowering aerial parts are traditionally used to relieve the subjective symptoms of venous insufficiency such as fullness in the legs, and the symptoms of hemorrhoids (orally and topically, [French Expl. Note, 1998]).

● **NASTURTIUM,**  
*Tropaeolum majus* L., Tropaeolaceae

In temperate climates nasturtium is cultivated for its ornamental flowers. Round peltate leaves, and helmet-shaped (or hood-shaped), vividly colored flowers are characteristic of this herbaceous plant whose "dried blade and petiole" are the subject of a monograph in the 10th edition of the French Pharmacopoeia.

The drug contains flavonoids and a glucosinolate, glucotropaeoline. Hydrolysis of this glucoside releases benzyl isothiocyanate, which has known antibacterial and antifungal properties. Identified by its morphological and microscopic characteristics, and by a positive cyanidin reaction, the drug is controlled by TLC (characterization of isouercitrin in the methanol used for maceration). Classically, nasturtium-based preparations are used in dermatology and cosmetology, to treat skin, nail, and hair (dandruff) ailments. It is used in preparations traditionally used: 1. for dandruff with itching and peeling, and 2. for sunburns, superficial and limited burns, and diaper rashes. Nasturtium is (traditionally) used by the oral route for acute benign bronchial disease [French Expl. Note, 1998].

Nasturtium seed contains 6-10% of an oil that is the highest (currently known) in erucic acid (60-80%, mainly as trierucin).

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