LIPID RELATED COMPOUNDS

Prof. Dr. Ali Hikmet Meriçli

Alkanes, Alcanols and Esters

WAXES (CERA)

Waxes commonly occur on the surface of leaves and fruits, where they form, with cutin, the very hydrophobic cuticle which limits water losses, controls gaseous exchanges, and participates in the protection against pathogenic agents.
Chemically, waxes are mixtures comprising hydrocarbons, free and hydroxylated aliphatic acids, aliphatic alcohols, aliphatic aldehydes, and aliphatic ketones, β-diketones, and esters.
Except for phytochemical or physiological considerations, waxes and their constituents are of very limited interest.

Carnaubae cera **Brazilian wax palm** **Karnauba mumu**

***Copernicia prunifera* (*C. cerifera*)** **Palmae**

The wax is obtained from the leaves of this palm tree from the Brazilian northeast. Chemically, it is a mixture of esters of long-chain aliphatic alcohols and aliphatic acids.

Carnauba wax occurs as a powder, or flakes, or solid lumps. The wax is used as a pharmaceutical aid to polish coated tablets and in food technology.

Jojobae oleum (cera) **Jojoba oil** **Jojoba yağı**

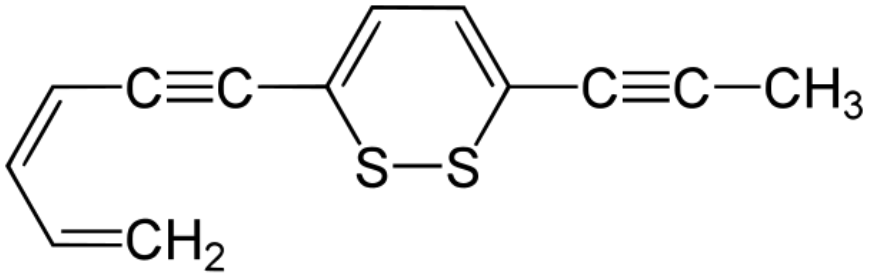
Simmondsia sinensis **Buxaceae**

The jojoba seed contains up to 60% of an «oil» that is in fact a mixture of wax esters. Constituents of this «oil» are esters involving eicosenoic (C_{20}) and decosenoic (C_{22}) acids on the hand, and eicosenol and decosenol on the other hand. In addition to this waxy fraction, these are glycosides with a cyanomethylene-cyclohexyl-substituted aglicone (simmondsin and analogs). A liquid below 10^{o} C, jojoba oil is barely oxidizable, and its behavior permits its use in place of preparations traditionally obtained from cetaceans (spermaceti).

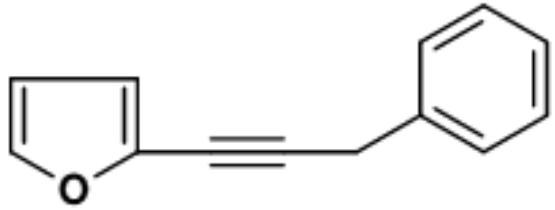
At the present time, cosmetology uses jojoba oil after hydrogenation (it is then a solid up to 65 ^{o}C) in the formulation of creams, lotions, soaps, lipsticks, and other preparations designed to be spread onto the skin or the hair; it is a good, non-greasy lubricant.

Alkine Derivatives

This alkin s or polyalkines can be found especially in Asteraceae species and are often linear, but they can also be partially cyclized. They may contain one or several double bonds and heteroatoms (oxygen, sulfur, chlorine) frequently included in a heterocycle. Biosynthetically, all of these compounds are related to fatty acids : most arise from linoleic acid through a series of desaturation reactions. In most cases, polyalkynes and biogenetically related sulfur containing derivatives are phototoxic.



Thiarubrine

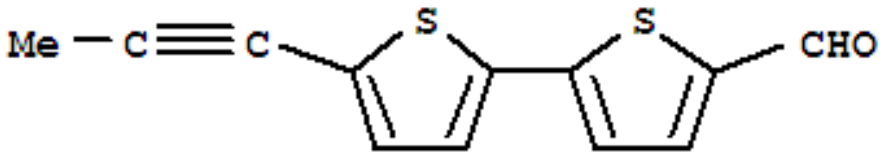


Carlina Oxide

Arctii radix **Burdock** **Pıtırak kökü**

Arctium lappa **Asteraceae**

The drug may contain over 50% inulin and 2-3% phenolic acids; it is rich in polyunsaturated compounds, polyalkenes, and polyalkines.



Arctinal

The reputation of the drug, traditionally used for the treatment of dermatosis and furunculosis, is in part justified by the presence of polyunsaturated compounds whose antimicrobial and antifungal properties have been demonstrated in vitro.

Echinaceae radix, herba **Echinacea, Coneflower**

Ekinasea, Ekinezya

Echinacea purpurea, E. angustifolia, E. pallida

Asteraceae

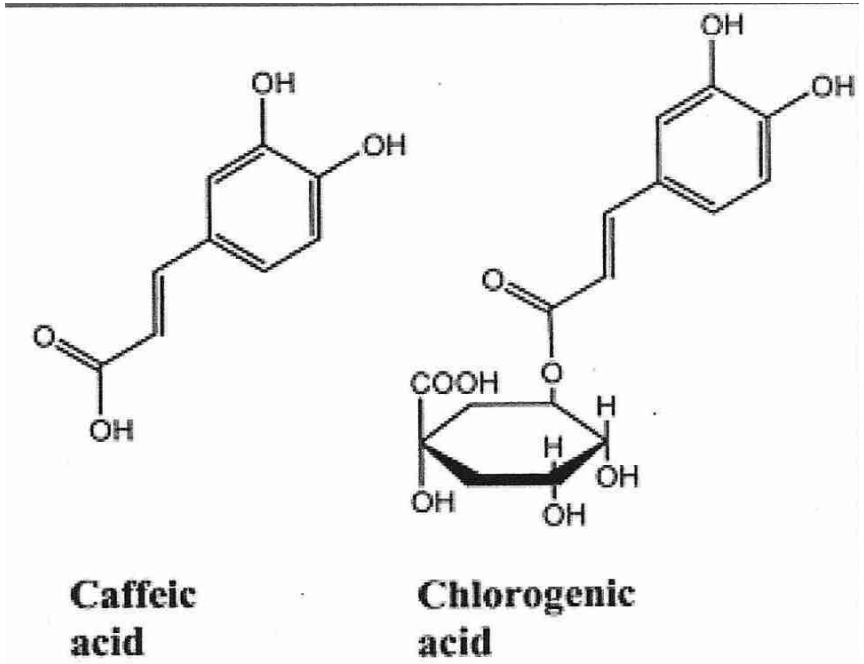
Echinacea purpurea, ***E. angustifolia,*** ***E. pallida***

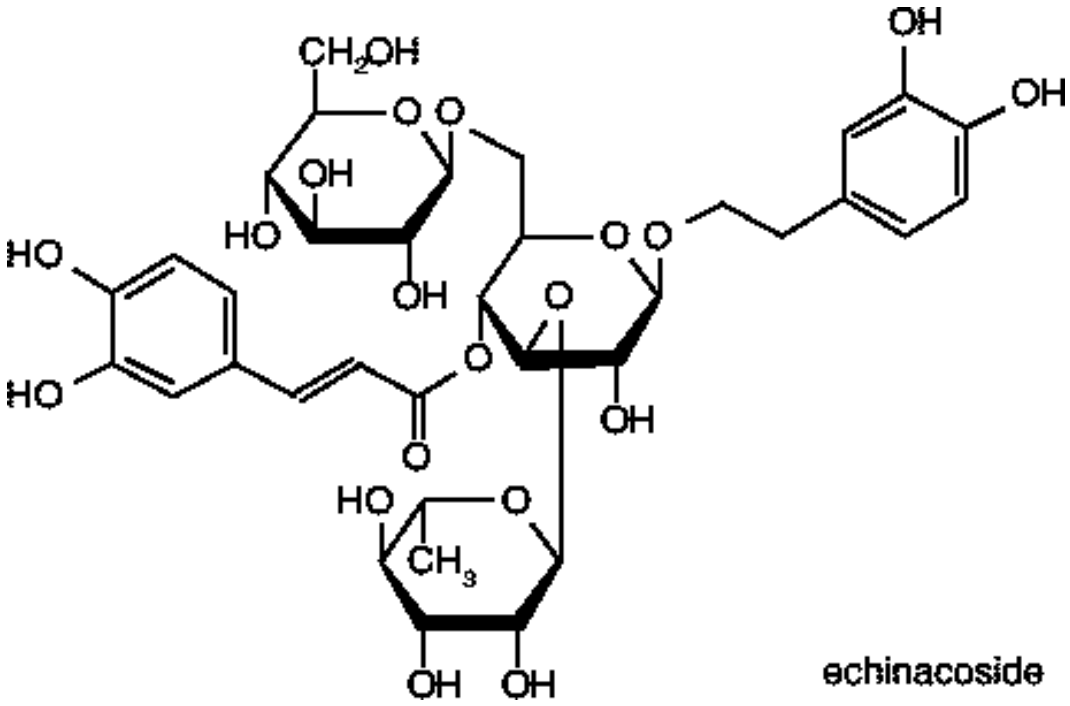
Note : This drug could just as well appear in the chapter of polysaccharides, given the activity attributed to those present by several authors. However, since the lipophilic fractions are also the basis of an activity, *Echinacea* may also be covered here, for its alkenes, alkynes with or without amide functions.

Different species of this genus of North American origin are used in phytotherapy and homeopathy, according to which subterranean or aerial parts possess immunostimulatory properties. Three species have undergone chemical and pharmacological studies : *Echinacea purpurea* (aerial parts), *Echinacea angustifolia* (aerial parts and roots), and *Echinacea pallida* (roots).

Chemical Composition : A substantial number of compounds have been isolated from *Echinacea*, including an essential oil, pyrrolizidine alkaloids, and the compounds in the following list :

- Phenolic compounds derived from caffeic acid : caffeic acid, chlorogenic acid, dicaffeoylquinic acids, sugar esters of caffeic acid (echinacoside)

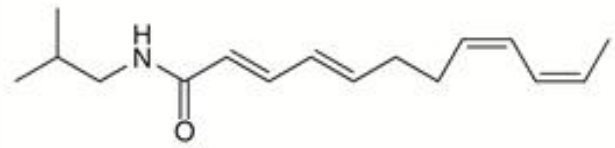




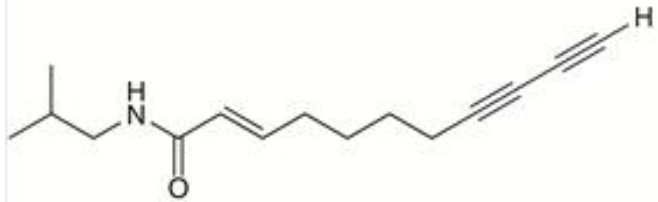
- A large number of unsaturated aliphatic compounds. This include aliphatic amides, isobutylamides of polyenyne acids.

- **Polysaccharides : Fucogalactoxyloglucans, arabinogalactans, glucuronoarabinoxylans.**

Alkamides

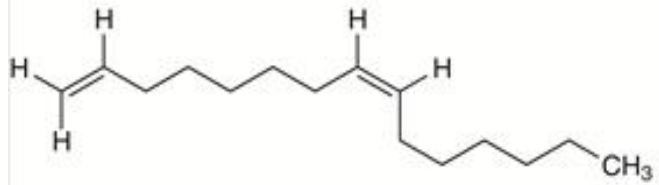


dodeca-2*E*,4*E*,8*Z*,10*Z*-tetraenoic acid isobutylamide

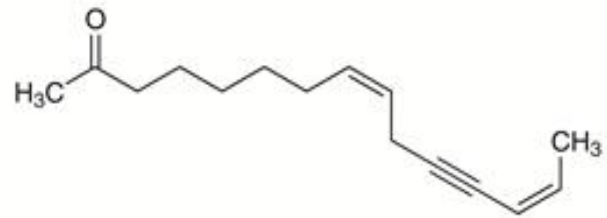


undeca-2*E*-enoic-8,10-diyne acid isobutylamide

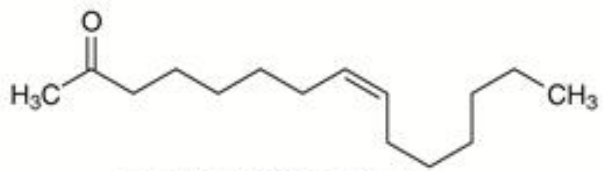
Polyenes



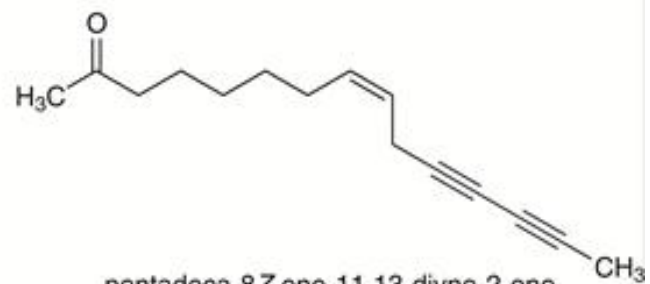
pentadeca-1,8*Z*-diene



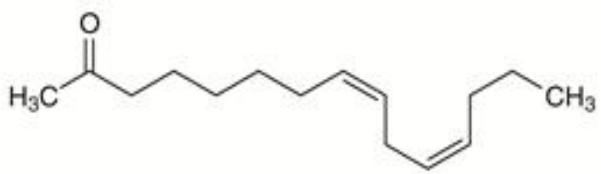
pentadeca-8*Z*,13*Z*-diene-11-yne-2-one



pentadeca-8*Z*-ene-2-one



pentadeca-8*Z*-ene-11,13-diyne-2-one



pentadeca-8*Z*,11*Z*-diene-2-one

Pharmacological activity : Known to Native American Indians echinaceas were used externally as wound healing agents, as well as internally for headaches, stomachaches, or as antitussives. **Today, it presents echinacea-based preperations as immunomodulatory. By this properties, the polysaccharides are active, but in many tests, the lipophilic fraction is also active, and sometimes more so.**

Uses : The German Commission E monograph states that *Echinacea pallida* root (Echinaceae pallidae radix) is used as a supportive treatment for flu-type infections and not be used in case of tuberculosis, multiple sclerosis, and AIDS. Many German practioners, on the basis of possible immunostimulating effects of *Echinacea*, recommend its use as a tincture, mother tincture, or extract, alone or in combination (e.g., *Baptisia, Thuja*) to stimulate defense mechanism : for the prevention and treatment of colds, of the flu, and of various respiratory disorders, as adjunctive therapy to chemotherapy for common ailments, or as prophylactic treatment against oppurtinistic infections in high-risk patients. **The drug and its prepations seem devoid of toxicity.**

TOXIC OR ALLERGENIC POLYALKINE-CONTAINING PLANTS

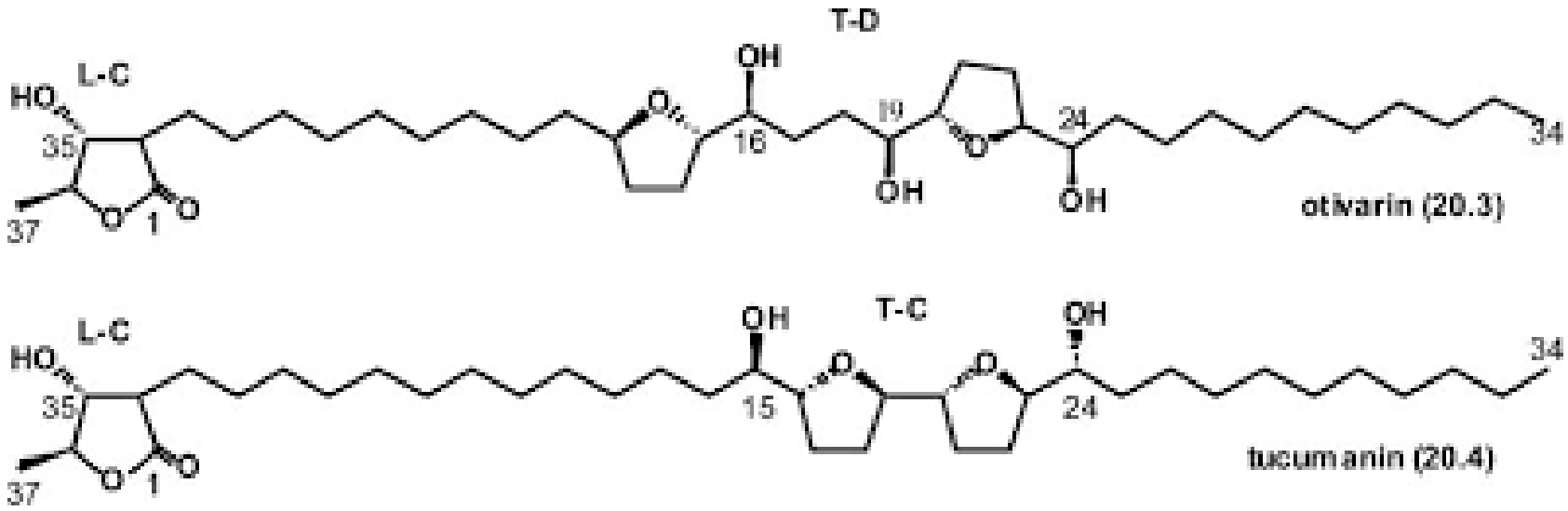
Cicuta virosa European water hemlock su baldıranı Apiaceae
Hedera helix Ivy duvar sarmaşığı Araliaceae

Hedera helix

Cicuta virosa

ACETOGENINS

The name designates long-chain aliphatic compounds with 35 or 37 carbon atoms, ending with aϒ-lactone most often unsaturated and cyclized into one (type A), or two tetrafuran rings that may (type B) or not (type C) be adjacent.



«Gluco-resins» of Convolvulaceae

Convolvulaceae containing **cathartic** gluco-resins have been known since ancient times and have long been prized for their cathartic properties. They include the following :

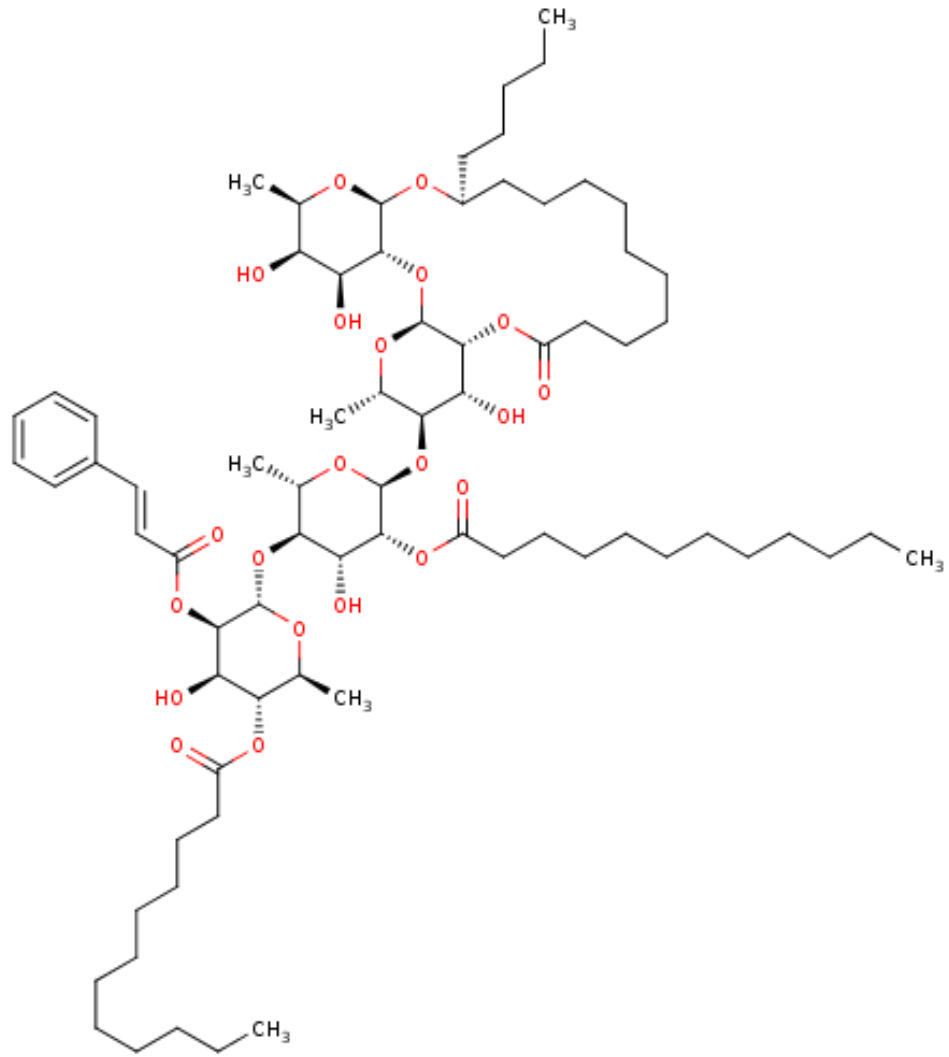
Ipomeae tubera	***Ipomea orizabensis***	**Ipomea**	**mahmude kökü**
Jalapeae tubera	***Ipomea purga***	**Jalap**	**mahmude kökü**
Scammoniae radix	***Convolvulus scammonia***	**Scammony**	**sarmaşık**

Ipomea orizabensis

Ipomea purga

Convolvulus scammonia

All of these species are mostly native to the intertropical nations. The drogs consist of the subterranean parts rich (10-18%) in gluco-resin. It consists of complex glycosides characterized by the presence of an oligosaccharide chiefly composed of 6-deoxy-hexoses (rhamnose, fucose and more). This oligosaccharide constitutes the sugar moiety of a glycoside whose aglycone is a hydroxylated fatty acid (e.g., 11S-hydroxy-decanoic acid or «jalapinolic acid»).
Gluco-resins are contact cathartics which cause an increase in water elimination and in peristalsis.



Jalapinolic acid

AMINO ACIDS AND PEPTIDES
PROTEINS AND ENZYMES

Amino acids are required metabolites as constituents of structural and enzymatic proteins, and they are also precursors of a large veriety secondary metabolites.

The structure and chemical properties of amino acids and peptides, their biosynthetic origin, are detailed in biochemistry textbooks.

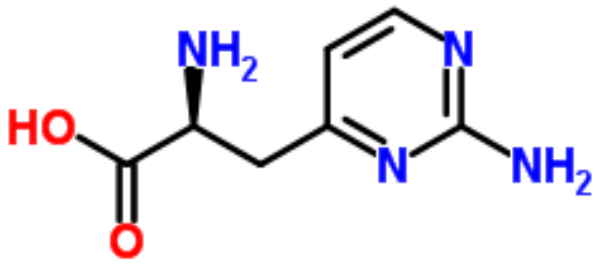
Therefore we shall limit this chapter to only atypical amino acids, and to simple compounds directly derived from them, namely glucosinolates and cyanogenic glycosides.

In the same manner, we shall restrict our brief coverage for vegetable proteins to a few specific cases : sweetener proteins and the lectins (proteins and glycoproteins).

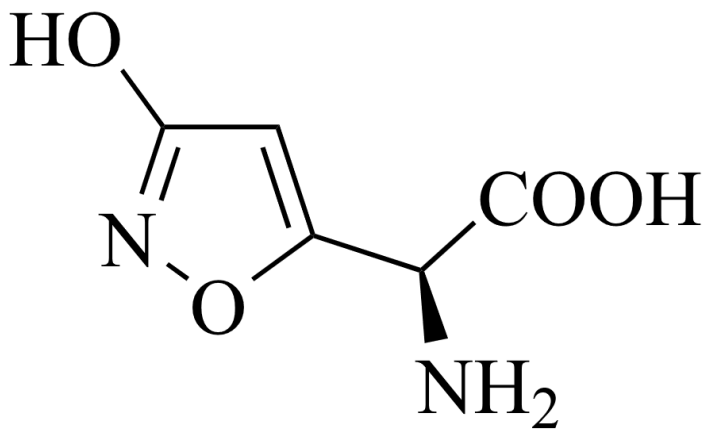
Enzymes are widely used in pharmacy, medicine or industry, but the enzymes used rarely come from higher plants: only papain, bromelain, and ficin will be covered.

AMINO ACIDS WHICH ARE NOT CONSTITUENTS OF PROTEINS

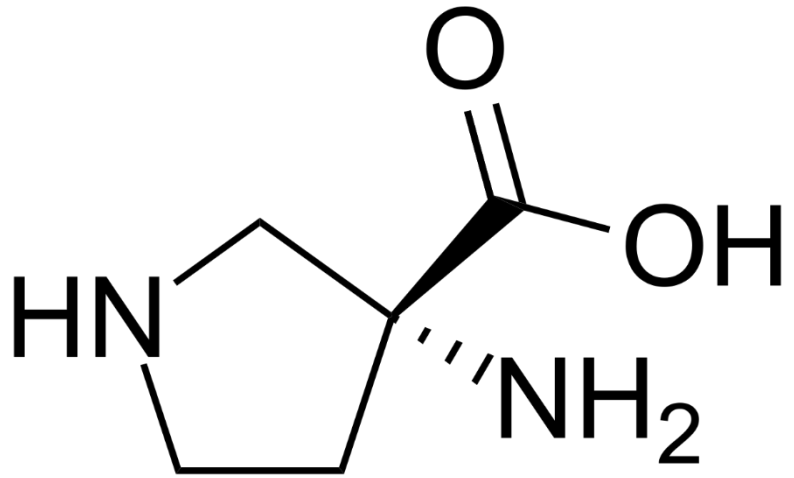
EXAMPLES OF ATYPICAL STRUCTURES



Lathyrine



Ibotenic acid



Cucurbitine

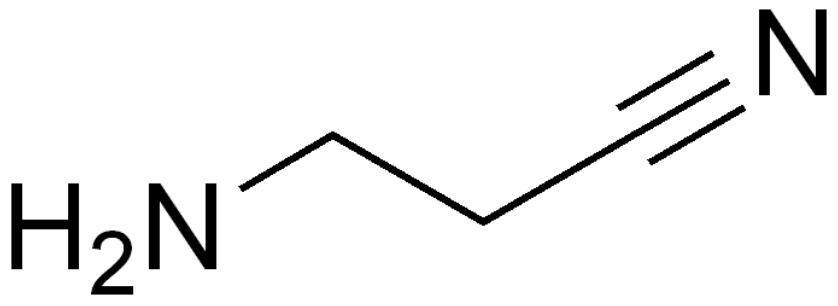
TOXIC AMINO ACID-CONTAINING PLANTS

Pea vine (*Lathyrus*) and Lathyrism

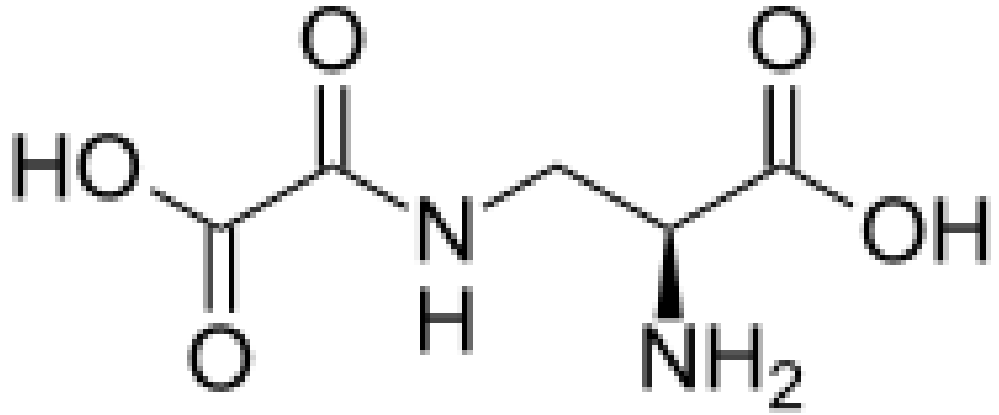
Lathyrism is a toxication characteristic with spastic paraplegia, breathing difficulty, tremors, and paresthesia, in the Mediterranean basin, Asia Minor, and in India where it may still be documented at times. Subsequent to prolonged (3-6 months) ingestion of seeds of various species of pea vine (*Lathyrus sativus*, *L.cicera*) Fabaceae (mürdümük), this intoxication manifests itself in humans by a rigidity and decrease in muscle strength of the legs, followed by their progressive paralysis. This syndrome is linked to a spinal attack and constitutes neurolathyrism.

In animals, an osteolathyrism is observed: joint deformities, ligament separation, skletal deformities, and more.

The agents responsible for the toxicity are amino acid derivatives β-aminopropionitrile (=BAPN), which occurs in the plant as β-(ϒ-L-glutamyl)-aminopropionitrile, and ϒ-N-oxalyl-L-α,β-diaminopropionic acid (=ODAP), the principal agents responsible for osteolathyrism and neurolathyrism, respectively.



β-aminopropionitrile



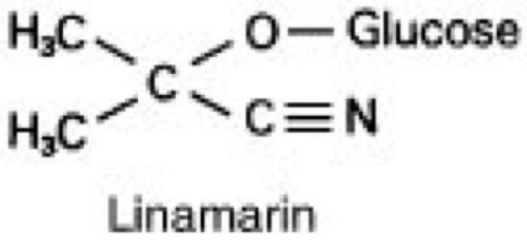
Oxalyldiaminopropionic acid

Lathyrus sativus *Lathyrus cicera*

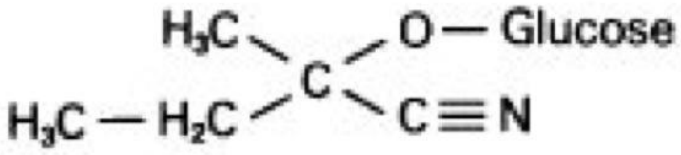
Both species are growing in Cyprus

Cyanogenic Glycosides

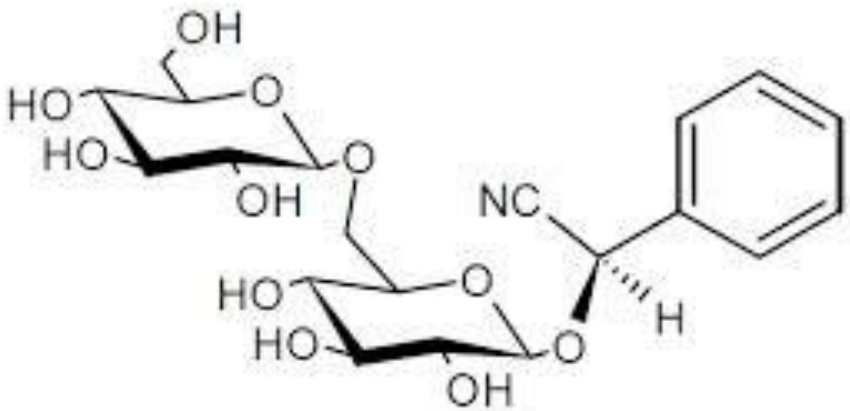
Cyanogenesis is the ability of certain living organisms, plants in particular, to produce hydrocyanic acid. Cyanogenic substances are always glycosides of 2-hydroxynitriles commonly known as cyanogenic (or cyanogenetic) glycosides.



Linamarin

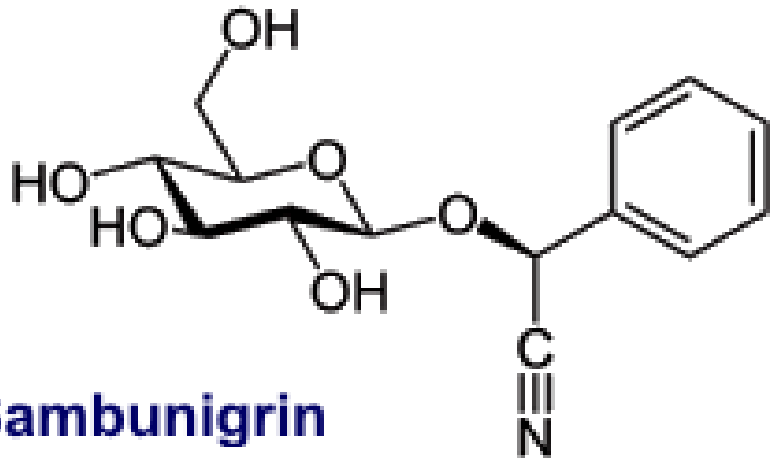


Lotaustralin



Amygdalin

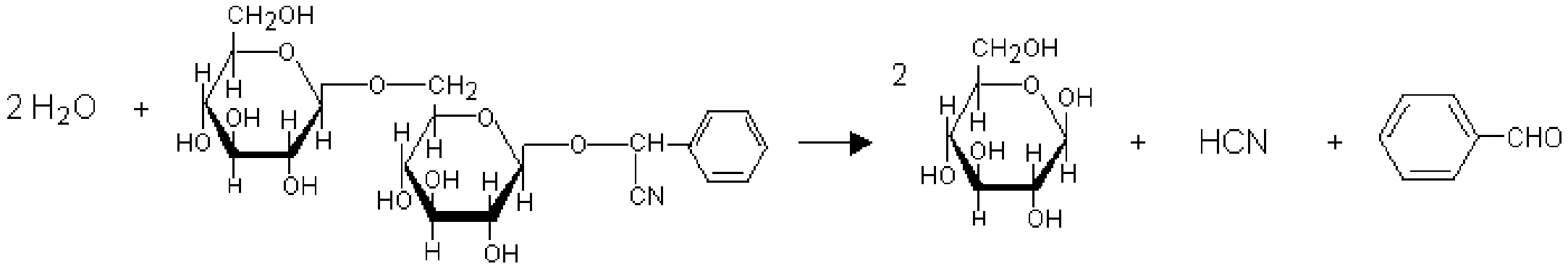
D(-)-Mandelonitril-ß-D-gentiobiosid

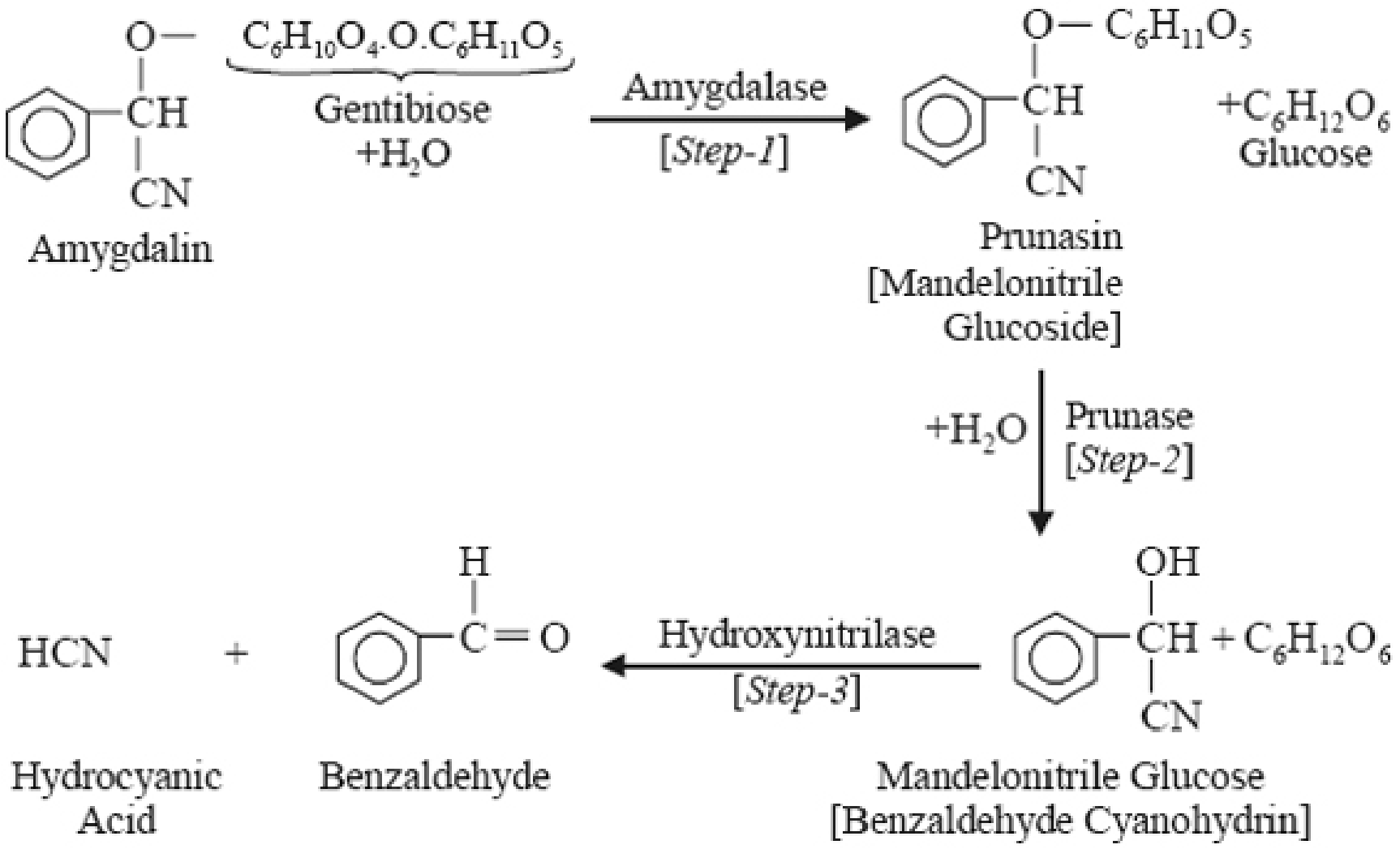


Sambunigrin

PROPERTIES, DETECTION, AND EXTRACTION

Glycosides of 2-hydroxynitriles are readily hydrolyzed, at near neutral pH's by more or less specific β-glucosidases which release a monosaccharide and a cyanohydrin. The latter is unstable and dissociates to hydrocyanic acid and a carbonyl compound, either an aldehyde or a ketone; this second reaction is catalyzed by a hydroxynitrile lyase.



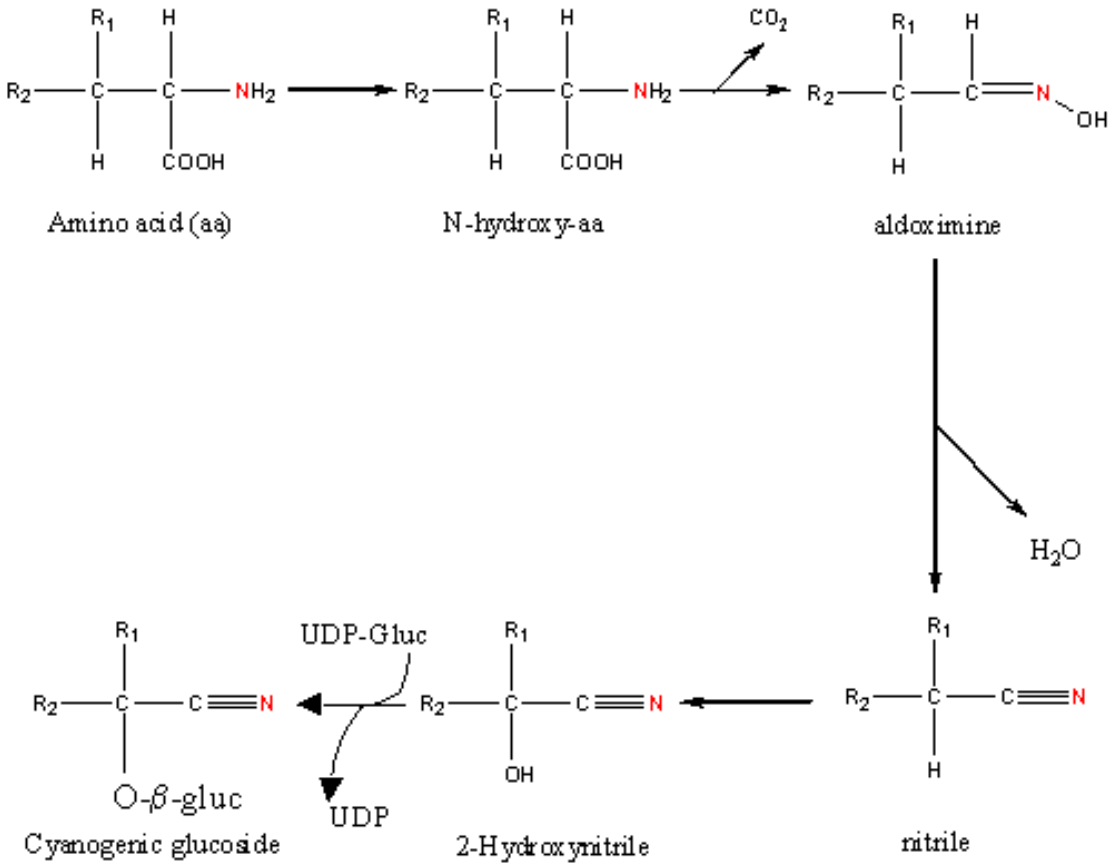

O—
CH
CN
Amygdalin
$C_6H_{10}O_4.O.C_6H_{11}O_5$
Gentibiose
$+H_2O$
Amygdalase
[Step-1]
O— $C_6H_{11}O_5$
CH
CN
Prunasin
[Mandelonitrile Glucoside]
$+C_6H_{12}O_6$
Glucose
$+H_2O$
Prunase
[Step-2]
OH
CH
CN
$+C_6H_{12}O_6$
Mandelonitrile Glucose
[Benzaldehyde Cyanohydrin]
Hydroxynitrilase
[Step-3]
H
C=O
Benzaldehyde
HCN
+
Hydrocyanic Acid

The great fragility of cyanogenic glycosides makes their extraction and purification delicate. The require preliminary inhibition of the enzymes (by soaking in liquid nitrogen) and the use of alcohols and of chromatographic techniques.

Cyanogenic glycosides are easy to detect with a strip of filter paper impregnated with reagents able to give a color reaction with the hydrocyanic acid released upon crushing the plant material (e.g., picric acid/sodium carbonate or benzidine/cupric acetate). The impregnated strip of filter paper is placed at the opening of a test tube containing a small amount of the bruised drug.

BIOSYNTHETIC ORIGIN AND METABOLISM

These compounds arise from amino acids via the corresponding aldoximes, as shown by labeling experiments.



TOXICITY OF HYDROCYANIC ACID AND OF CYANOGENIC PLANTS

Although hydrocyanic acid is a violent poison, it is important to remember that oral intake of cyanogenic drugs does not necessarily cause severe intoxication. This is because the range of dangerous concentrations (0.5-3.5 mg/kg) can only be achieved by rapid and massive ingestion of plant parts rich in cyanogenic glycosides: in the case of fruits, the pulp does not contain glycosides; in the case of leaves, the glycoside content is often high, but in general the leaves are not especially appetizing (e.g., cherry laurel leaves). In addition, the glycosides must be hydrolized in the digestive tract. Moreover, the human organism is known to have the ability to fairly rapidly detoxify cyanides to thiocyanates using a thiosulfate sulfurtransferase; the resulting thiocyanates are eliminated in urine (30-60 mh/h).

Massive intoxication manifests itself by multiple symptoms that result from the cytotoxic anoxia caused by the combination of cyanide ions with chytochrome C oxidase. A chance in respiratory rhythm is frequently observed, as well as headaches, dizziness, and inebriation. Next are consciousness, disturbances, followed by a deep coma and respiratory depression. If the dose is small enough to not cause rapid death, an appropriate treatment must be applied expeditiously: stomach pumping, oxygen therapy, amyl nitrite, chelation of cyanide ions by hydroxycobalamin infusion, and stimulation of detoxification mechanisms (with sodium thiosulfate).

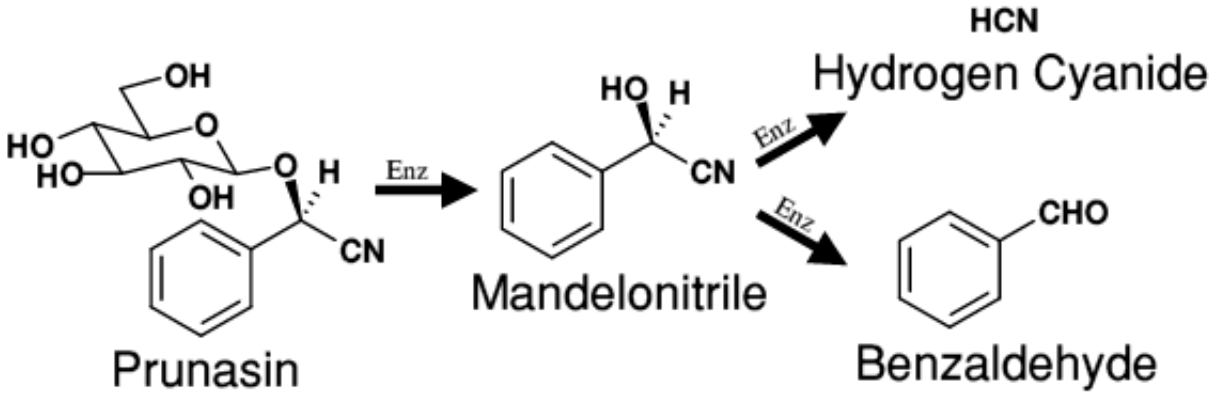
Laurocerasi folium Cherry laurel Taflan yaprağı(yabani kiraz, idris)

Prunus laurocerasus = Laurocerasus officinalis **Rosaceae**

Fresh laurel cherry leaves (Laurocerasi folium) are used to prepare cherry-laurel water (Laurocerasi aqua). Titrated to contain 100 mg/100 g in total HCN, this water is used as an aromatizing agent, antispazmodic, and respiratory stimulant.

When crushed the leaves release a characteristic bitter almond odor.

The prunasin (= (-)-(R)-mandelonitrile-β-D-glucoside) level ranges from 1.2 to 1.8 g per 100 g of fresh leaves.

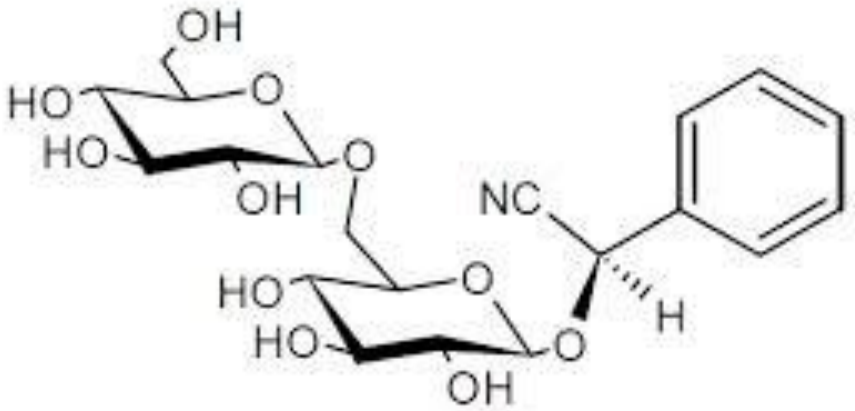


Uses : The sole use of the drug is to obtain cherry-laurel water. Standardized to contain 100 (± 5) milligrams of total hydrocyanic acid per 100 grams, it must not contain more than 25 miligrams per 100 grams of the same acid in the free state; the minimum level of benzaldehyde is 300 milligrams per 100 grams.

Traditionally, cherry-laurel water is used in the formulation of syrups for the treatment of broncho-pulmonary conditions, as a flavor and as a respiratory stimulant, in opiate-containing syrups.

PLANTS WITH TOXIC POTENTIAL FOR HUMANS OR ANIMALS

A number of ornamental Rosaceae elaborate cyanogenic glycosides, prunasin, which predominates in vegetative organs and amygdalin (= (-)-(R)- mandelo-nitrile-β-D-gentiobioside) which accumulates in the seeds. Thus these plants can release hydrocyanic acid.



Amygdalin

D(-)-Mandelonitril-ß-D-gentiobiosid

Prunus amygdalus var. *amara* semen (seeds) bitter almond acı badem

Sorbus aucuparia semen (seeds) mountain ash üvez

Prunus armeniaca semen (seeds) apricot zerdali, kayısı

Glucosinolates

Glucosinolates, formerly called thioglucosides, are anionic glycosides responsible for the potent and characteristic flavors of numerous Brassicaceae (mustard, raddish etc.), and of various species pertaining to other botanically close families (Capparidaceae, 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.

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

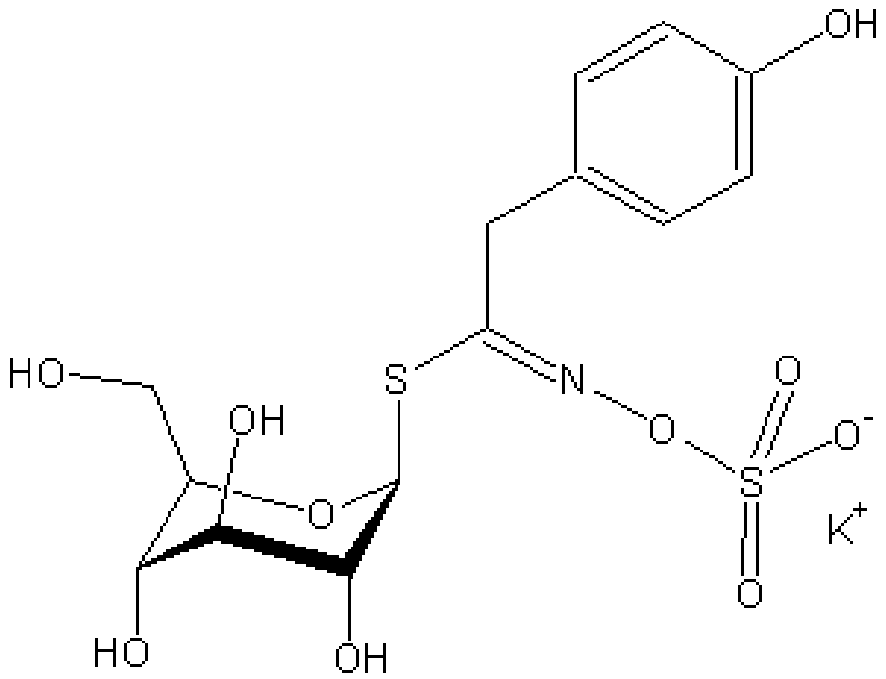
Tyrosine → p-hydroxybenzylglucosinolate → **sinalbin** (white mustard, beyaz hardal)

Homomethionine → allylglucosinolate → **sinigrin** (black mustard, siyah hardal)

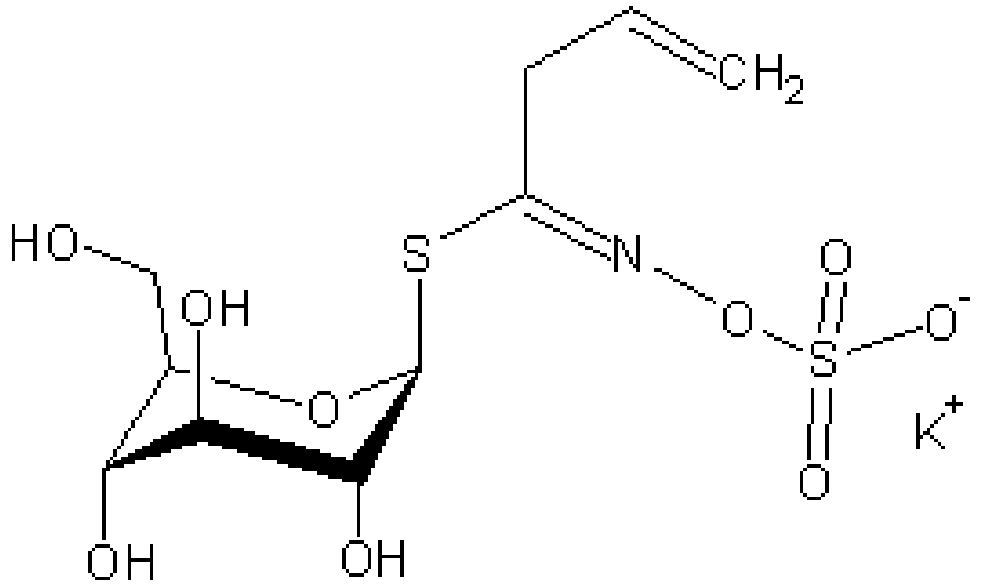
Phenylalanine → benzylglucosinolate → **glucotrapeolin** (garden cress, tere)

Tryptophan → 3-indolylmethylglucosinolate → **glucobrassicin** (cabbage, lahana)

Homophenylalanine → phenethylglucosinolate → **gluconasturtiin** (watercress, su teresi)

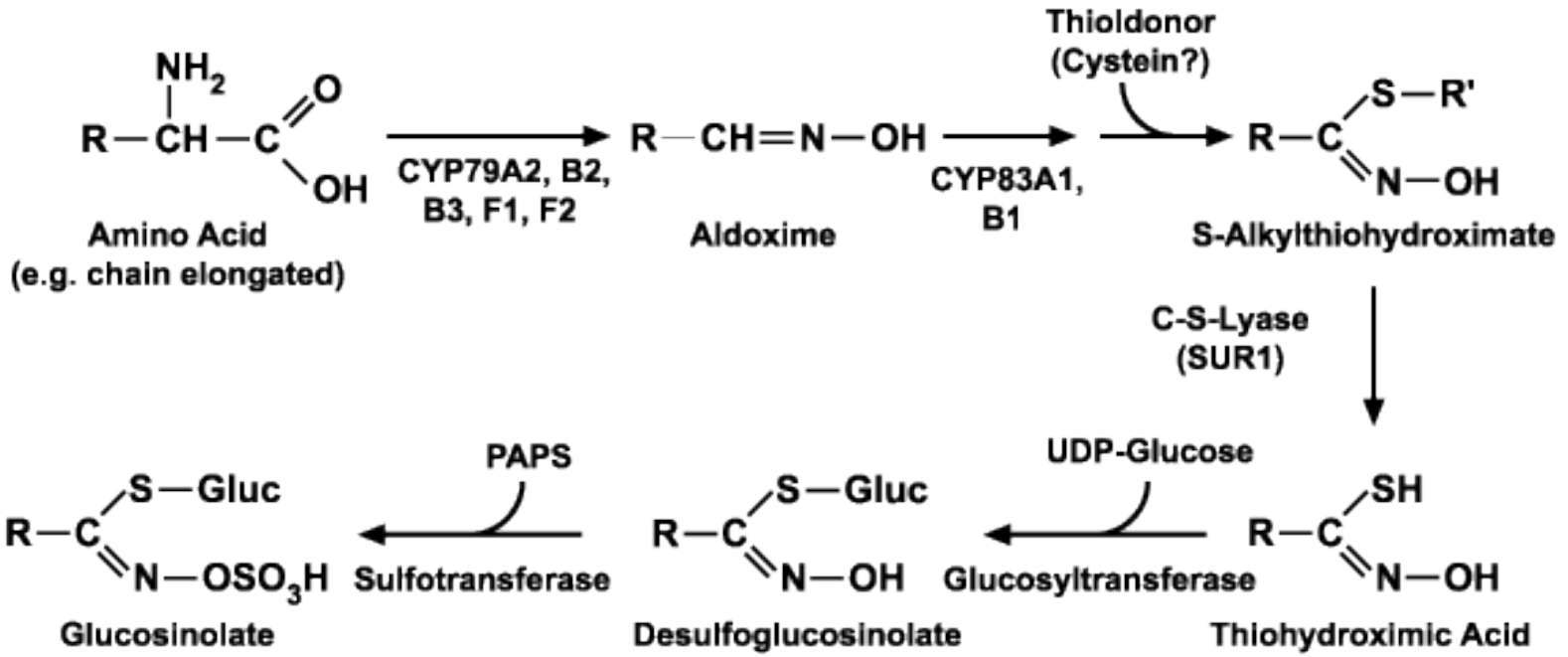


Sinalbin



Sinigrin

Biogenetically, glucosinolates are probably formed by decarboxylation of amino acids to aldoximes.



GLUCOSINOLATE HYDROLYSIS

When the tissues of glucoresinolate-containing plants are bruished, the compounds are hydrolized 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 Lossen 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 nitrile are formed.

Isothiocyanates react with alcohols to form thiocarbamates.

GLUCOSINOLATE EXTRACTION

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.

GLUCOSINOLATE TOXICITY

Sevaral 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. In man, although goiter frequency is observed populations with a diet poor in iodine and rich in Brassicaceae, there is no proof of a casual relationship between cabbage consumption and goiter growth.

GLUCOSINOLATE POTENTIAL

These compounds may be beneficial to human health : according to several authors, the dietary intake of glucosinolates (from broccoli, cabbage, 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.

Brassicae nigrae semen, Brassicae junceae semen

black mustard, mustard **siyah hardal, hardal**

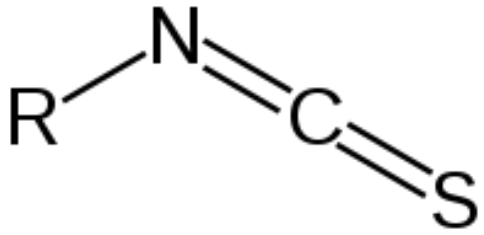
Brassica nigra, Brassica juncea **Brassicaceae**

Brassica nigra

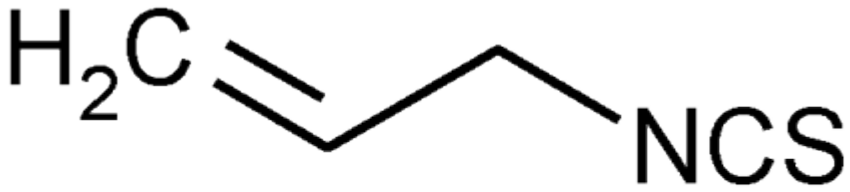
Brassica juncea

Mustard seeds are rich in musilage (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 revulsive due to their (volatile) mustard oil : the isothiocyanate when applied onto the skin causes tingling, rubefaction, and upon prolonged contact, vesication.



Isothiocyanate



Allyl isothiocyanate

OTHER PLANTS

The drug is always : semen The family is always : Brassicae

Sinapis alba white mustard beyaz hardal

Raphanus sativus black raddish turp

Sisymbrium officinale hedge mustard ergelen hardalı

Tropaeolum majus nasturtium latin teresi

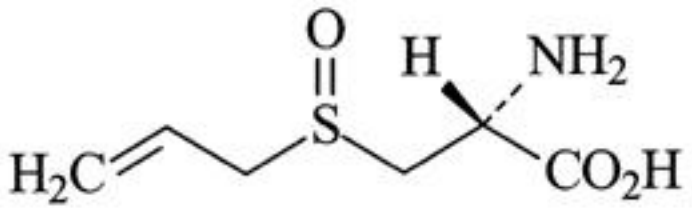
Sinapis alba *Raphanus sativus* *Sisymbrium officinale* *Trapaeolum majus*

Other Sulfur-Containing Compounds

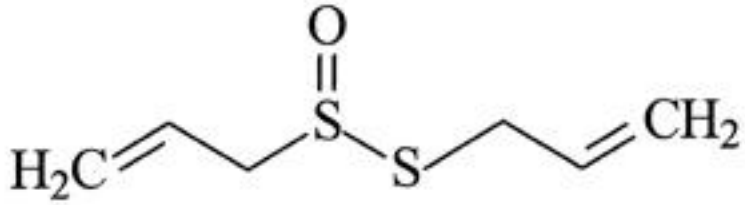
Allii sativi bulbus garlic sarımsak (sarmısak)

Allium sativum **Liliaceae**

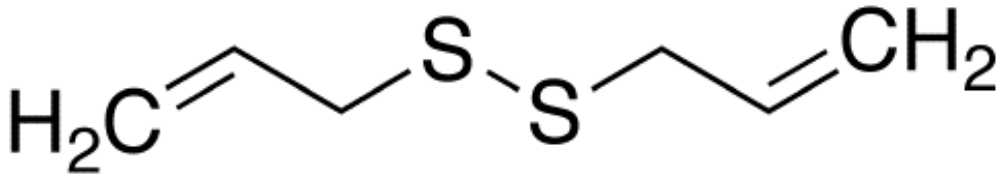
The drug contains carbohydrates (fructans), saponins (furostanol glycosides : sativin, prot-erubin B, and more), **and is mostly known for its sulfur-containing compounds**. **The chief constituent of fresh undamaged garlic is alliin** or S-allyl-L-(+)-cysteine sulfoxide. **Upon cutting or brushing the tissues, alliin is degraded by an enzyme, alliinase** (S-alkyl-L-cysteine lyase), to pyruvic acid and 2-prophensulfenic acid, with the latter being immediately transformed into **allicin** (0.3% of the fresh weight). Air oxidation of allicin leads 1,7-dithiaocta-4,5-diene, known as diallyldisulfide : this is the chief constituent of garlic volatile oil. Through analysis of alcoholic garlic extracts also shows the presence of allicin condensation products 6Z- and 6E-ajoenes, and cycloadducts of propenthial (vinylthiines).



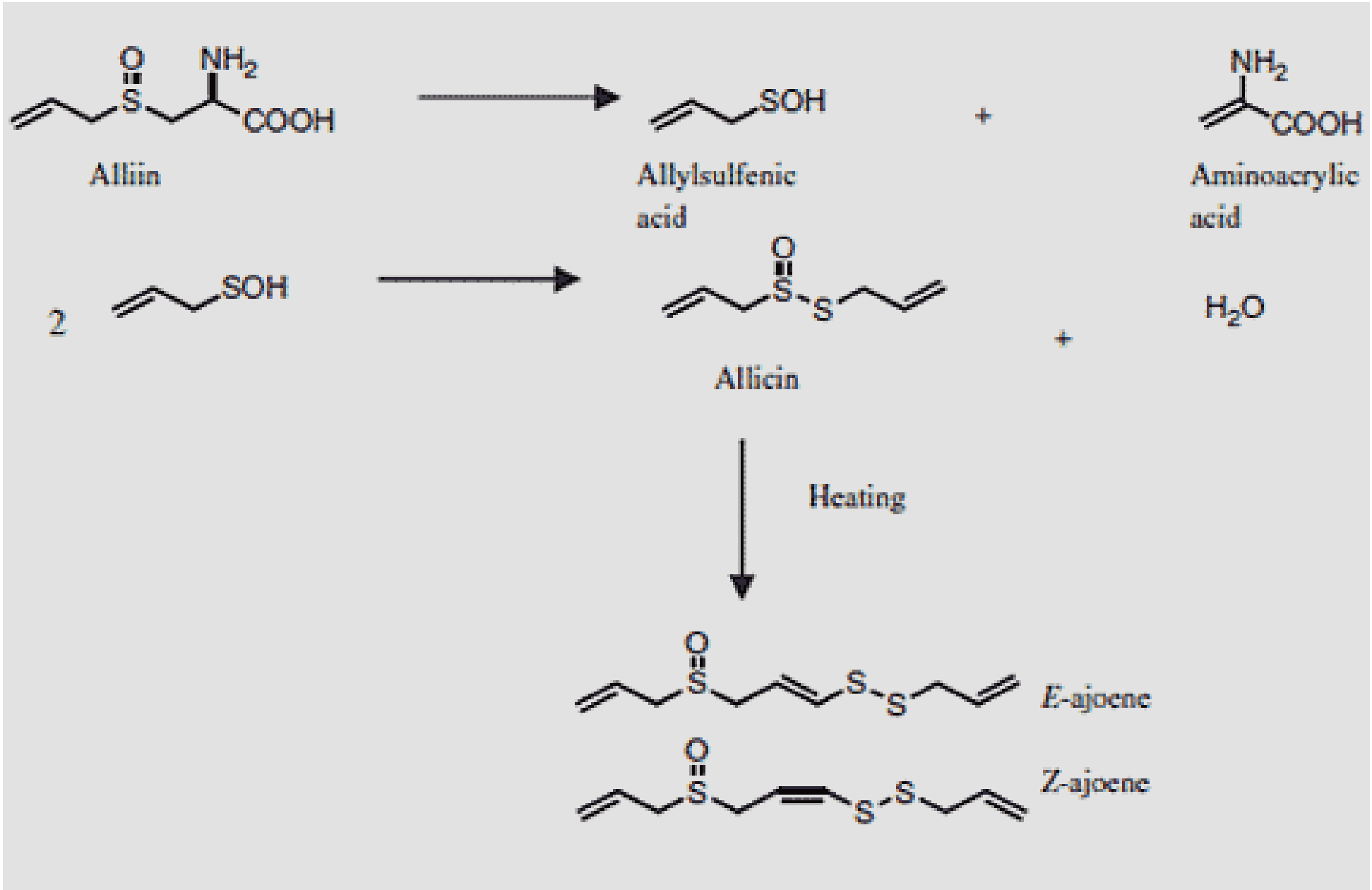
Alliin



Allicin



Diallyldisulfide


Alliin
Allylsulfenic acid
Aminoacrylic acid
2
Allicin
H_2O
Heating
E-ajoene
Z-ajoene

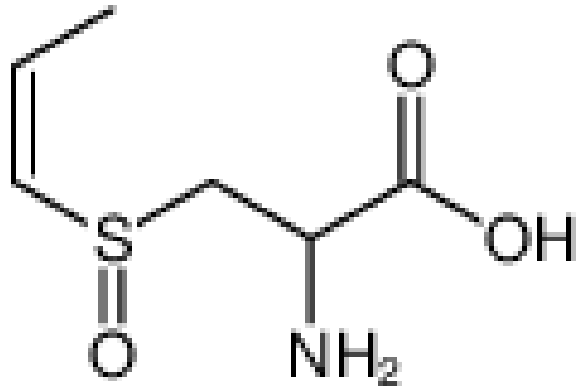
Pharmacological Activity : Tradition attributes to garlic several properties which have been verified experimentally, including the antibacterial and antifungal activities which have been shown in vitro. During the last ten years, animal experiments have demonstrated that garlic extracts are able to decrease blood cholesterol and triglycerides, and have antihypertensive effects. The responsible compound for these activities is always especially allicin. The activity against platelet aggregation, shown in vitro, is linked to ajoenes which inhibit lipoxygenase.

The German Commission E monograph states that garlic bulb is used as a complement in the diet of hyperlipemic patients and for the prophylaxis of the vascular changes induced by aging. The monograph contains a warning that garlic can (rarely) cause gastointestinal distress and that it alters breath and skin odor.

Allii cepae bulbus **onion** **soğan**

Allium cepa **Liliaceae**

A fresh onion bulb contains fructans with a low degree of polymerization, heterogeneous polysaccharides, flavonoids, saponins, sterols, and sulfur-containing compounds : cystein derivatives. Upon bruishing the bulb, the sulfoxides degraded by alliinase and rapidly turn into disulfides. Next, this leads, by addition on the alkyl- and alkenylsulfenic acids, to a series of 1-(methylsulfinyl)- propyl alkyl- or alkenyl-) disulfides.



S-(1-Propenyl)-L-cysteine sulfoxide

Pharmacological activity : Onion is a vegetable and a condiment, nevertheless it is considered by some to have «medicinal properties». Onion juice, known for its diuretic properties is an antimicrobial agent in vitro, and experiments in animals demeonstrate its hypoglycemic activity. Like garlic it has an activity against platelet aggregation and a fibrinolytic activity linked to some of the sulfur-containing compounds; the extracts also have an antiasthma activity and an anti-allergic activity on the skin and the lungs. Unfortunately, the extracts in use are unstable, therefore a valid comparison of the results is not possible.

Protein Sweeteners

THAUMATIN

Thaumatin was initially marketed in the United States and in Japan (Talin®), and is now on the European Unionlist of approved additives. It is a mixture of proteins isolated from the fruit of an African Marantaceae, *Thaumatococcus danielli*.

Thaumatococci fructus ***Thaumatococcus danielli***

Maranthaceae

The frozen fruits undergo an aquaeous extraction and the protein fraction is resolved by physical techniques (ultrafiltration). The extract contains two chief proteins (thaumatin I and II) which are each composed of 207 amino acids and differ from one another only in five positions; their structure includes eight disulfide bridges. Thaumatin is readily soluble in water and soluble in dilute alcohols.
Properties : Thaumatin is a potent sweetener : its activity can be detected at a concentration of 10^{-8} M. The sweet sensation induced by thaumatin is slightly delayed; it persists for 15-20 minutes (with a licorice aftertaste), hence its applications in products such as chewing gums or breath fresheners. It is not toxic, not carcinogenic, and it enhances aromas and flavors at low doses. At higher doses, it is an intense sweetener.

Other Protein Sweeteners

Monellin ***Dioscoreophyllum cuminsii*** **fructus**
Menispermaceae

Miraculin ***Synpesalum dulcificum*** **fructus**
Sapotaceae

Dioscoreophyllum cuminsii

Synsepalum dulcificum

Lectins

Lectins, from the latin lego, legere (lectum) = to read, to choose, to select… are uninduced proteins or glycoproteins able to bind to saccharide residues on cell membranes, in a specific and reversible fashion, without displaying enzymatic activity. Most lectins of higher plants are located in the seeds. Many lectins have the ability to agglutinate red blood cells – they are referred to as phytohemagglutinins – and several among them do so with blood group specificity. Some lectins are mitotic; a few can differentiate between normal and tumor cells; some are highly toxic.

VEGETABLES THAT ARE TOXIC DUE TO LECTINS

Although lectins are often toxic only by the parenteral route, some are not destroyed by the enzymes of the digestive tract (e.g. ricin of castor seeds).

Intoxication by ingestion of this type of poison manifests itself 2-3 hours after consumption, by vomiting and hemorraghic diarrhea, loss of fluids, and a state of shock.

Lectins are in fact denatured by cooking.

Ricini semen castor hint yağı bitkisi tohumu

Ricinus communis **Euphorbiaceae**

Ricin interferes with protein synthesis by enzymatically inactivating the 28S ribosome subunit in eucaryotic cells and causing the hydrolysis of an adenyl residue. Ricin is responsible for the toxicity of the castor bean.

The minimal lethal dose is on the order of 0.4 µg/kg in the rat (by parenteral route). The toxicity also manifests itself by the oral route: castor seed intoxications result in nausea, headaches, bloody diarrhea, dehydration, liver necrosis, loss of conciousness.

Visci albi herba **mistletoe** **ökse otu**

Viscum album **Viscaceae**

Viscum album is a semiparasite which grows affixed by roots modified into suckers, on various species of deciduous trees. The leafy stems of the plant contain triterpenoids, sterols, amines (choline, histamine, tyramine) and phenolic compounds: phenolic acids (particularly in C6-C3), lignans (eleutheroside E, glycoside of syringaresinol), syringin and flavonoids (especially glycosides of quercetin). The specific proteins that have received attention are viscotoxins and lectins. Viscotoxins A_2, A_3, and B have a molecular weight near 5000 daltons (they include 46 amino acids), and are resistant to heat and proteases. Lectins ML I (or viscumin), ML II, and ML III are glycoproteins. Their toxicity is considerable (100 µg/kg in the rat by the intraperitoneal route).

Pharmacological Activity : The cytotoxic activity of mistletoe (Visci albi herba) and of its preparations on various cell lines is due to the protein fractions. Lectins are perticularly cytotoxic (inhibition on human leukemia cells at concentrations of 1-3 ng/ml); note also some immunogenic effects. Viscotoxins are also cytotoxic; but much less intensely; they have a cytolytic effect. Tradition attributes to the drug also hypotensive properties.

Uses : Taking into consideration cytostatic and immunostimulating properties that have been observed experimentally, various German pharmaceutical companies market mistletoe-based products that they promote as antitumor agents (fermentation products, extracts titrated for lectins). The German Commission E monograph mentions the cytostatic and immunostimulating properties observed in animals and lists the following uses : as palliative therapy for malignant tumors via non specific immunostimulation.

Enzymes

Carica papaya	**papaya tree**	**papaya**	**Caricaceae**
Papayae latex			

The fruit of this species, the papaya, is rich in sugars, vitamins, and volatile compounds. It contains a «mixture of enzymes possessing proteolytic and esterase activities from the thickened latex obtained by incision of the fruits shortly before maturity, designated «papaya latex». In therapeutics, a purified fraction, chymopapain, is often used for the treatment of sciatica due to a herniated lumbar disc.
The drug, that is Papayae latex, is collected after incision of the unripe fruits; the latex, which coagulates rapidly, is recovered by scraping and dried in the sun or artificially, at a temparature lower than 50 ^{o}C.

Chemical Composition : Crude papain is commonly purified by the normal protein separation techniques (alternating precipitations and dissolutions) and by the classic techniques of affinity chromatography. It consists of a mixture of papain, chymopapains, and papayaproteinase Ω. Papain is a protein of 212 amino acids with a molecular weight of about 23.000 dalton; the chain is folded in two labels at the junction of which is the active site. It is an endopeptidase activated by thiols and reducing moieties, resistant to heat, with an optimal pH ranging from 5 to 7; it is inactivated by metal ions, oxidants, and reagents which react with thiols.

Pure cymopapain is a protein of 218 amino acids of structure and properties closely resembling those of papains.

Properties and Uses

1. Chymopapain : because of its proteolytic properties, chymopapain can be injected into an intervertebral disc to cleave the proteoglycans that constitute the nucleus pulposus, this is chemonucleolysis, a form of therapy for a herniated lumbar disc with root compression that is refractory to proper conventional medical treatment. It has been thought that intradiscal injection of radioopaque fluids prior to intradiscal **chymopapain** therapy might have some inhibitory effect on its enzyme **activity** and, thus, disc nuclear dissolution. The contraindications, the risk of anaphylactic shock, the neurotoxicity of the enzyme in case of intrathecal subsequent to a technical error, and the requirement for strict asepsis all explain why the technique may only be applied by highly trained personnel and only in the hospital setting. Cymopapain is currently available lyophilized in combination with sodium cysteinate.

2. Papain : Papain, alone or in combination, is promoted as therapy for digestive disorders, and in dietetics, as a substitute enzyme to relieve gastric or duodenal insufficiency and for the symptomatic treatment of dyspepsia. It is used locally in the formulation of adjunct treatment products for disorders limited to the buccal and oropharynx mucous membranes, for post-operative care, and for accidental buccal lesions ; as a wound healing and cleansing agent, it is often combined with an antibiotic or with lysozyme. It can also be used in contact lens cleaning liquids.

Ananas comosus **pineapple ananas Bromeliaceae**

Ananasi fructus

The pineapple fruit is rich in soluble mono- and disaccharides (up to 15%), in organic acids, and in vitamins. Its color is due to carotenoids and its flavor to a complex mixture in which oxygenated aliphatic compounds predominate. The ripe fruit and the stem contain a proteolytic enzyme, bromelain. The bromelain from the stems is a mixture of basic glykoproteins of molecular weight between 18.000 and 28.000 daltons, in which the protein moiety not very different from that of papain. The bromelain from the fruits is an acidic protease. Bromelains are proteases with thiol groups, activated by reducing agents, and inhibited by oxidants and metals.

Pharmacological Activity : The antiinflammatory and **antiexudative** properties of bromelain on various experimental models have been the subject of numerous publications: they might be linked to an interaction of the enzyme with the metabolism of eicosanoids; note also anti-platelet aggregation and fibrinolytic activity.

Bromelains are promoted as a treatment for post-traumatic and post-operative edemas (per os 500.000 U/day, enteric coated tablets). They are sometimes combined with antibiotics. The were also used as ingredients of pharmaceuticals for the symptomatic treatment of dyspepsia.

Ficus ssp. (*Ficus carica, F. insipida*) ficus incir Moraceae

Ficus carica

Ficus insipida

A certain number of species of the genus *Ficus* provide ficin, a proteolytic enzyme closely related to papain and bromelain. By incising the trunk a latex is collected and coagulates rapidly; filtered and dried, it constitutes crude ficin. Ficin is a mixture of proteases which possesses an activity close to that of papain. It is used in food technology (meat tenderizing). The ficus pseudo-fruit may be used in the symptomatic treatment of constipation.

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