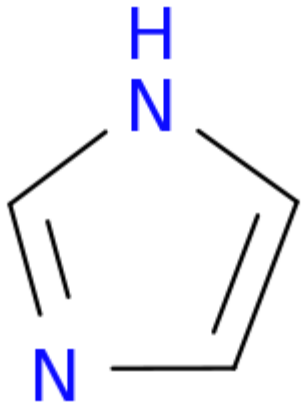
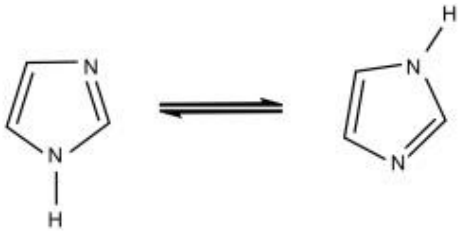
Alkaloids. Medicinal plants and raw materials containing imidazole derivatives, purine, diterpene, steroid alkaloids.

Medicinal plants containing imidazole derivatives

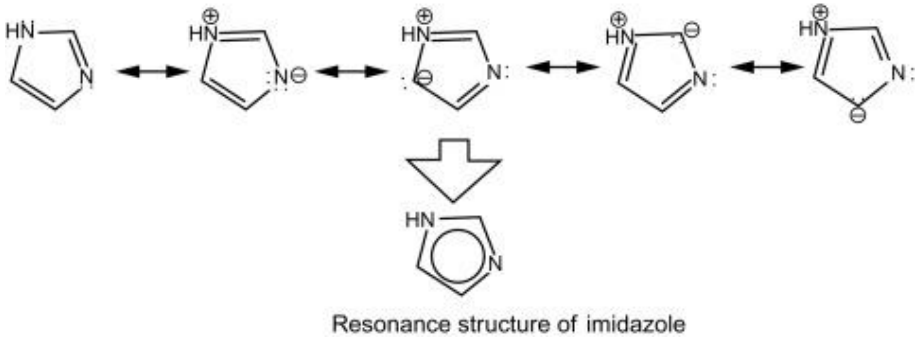
- Imidazole is a heterocyclic aromatic organic compound. This ring system is present in important biological building blocks such as histidine and histamine.



Imidazoles can act as bases and as a weak acids.
Imidazole exists in two tautomeric forms with a hydrogen atom moving between the two nitrogens.



Tautomerism of imidazole
structure at 4 and 5 position



Resonance structure of imidazole

The most important plant of this group is *Pilocarpus jaborandi.*

Medicinal raw material: Jaborandi Leaf - Jaborandi folium

Producing plants: Pilocarpus Jaborandi

Pilocarpus microphyllus

Pilocarpus pinnatifolius

Pilocarpus racemosuv

Family: Rutaceae

Pilocarpus jaborandi is a species of flowering plant in the family *Rutaceae*, native to northeast Brazil.

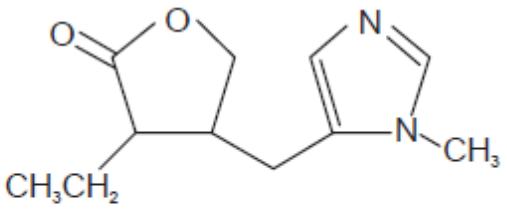
The shrub grows from 4 to 5 feet high; the bark is smooth and greyish; the flowers are thick, small and reddish-purple in colour, springing from rather thick, separate stalks about 1/4 inch long. The leaves are large compound, pinnate with an odd terminal leaflet, with two to four pairs of leaflets.

History

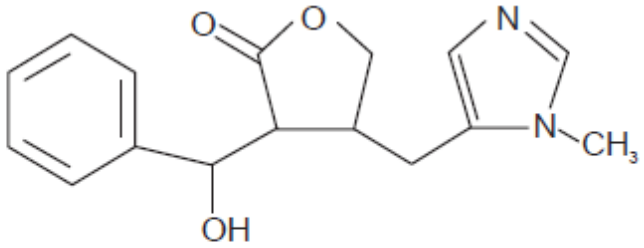
Dr. Coutinho in 1874 sent the plant to Europe from Pernambuco, hence the name Pernambuco jaborandi or *Pilocarpus jaborandi*. Later, Byasson in 1875 showed its alkaloidal nature and further Gerrard and Hardy isolated the main alkaloid ilocarpine.

Chemical Constituents

The drug contains imidazole alkaloids among, which pilocarpine is most important. Other alkaloids are isopilocarpine, pilocarpidine, pilosine, pseudopilocarpine and isopilosine. The range of total alkaloids in different species is between 0.5% and 1%.



Pilocarpine



Pilosine

Chemical Test

1. To the drug containing pilocarpine, small quantities of dilute sulphuric acid, hydrogen peroxide solution, benzene and potassium chromate solution is added and shaken, organic layer gives bluish-violet colour and yellow colour appears in aqueous layer.

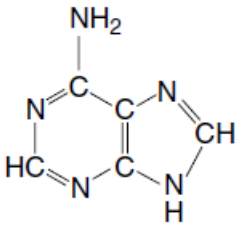
Uses

Pilocarpine is antagonistic to atropine, stimulating the nerve endings paralysed by that drug, and contracting the pupil of the eye. Its principal use is as a owerful and rapid diaphoretic. It induces also free salivation and excites most gland secretions, some regarding it as a galactagogue.

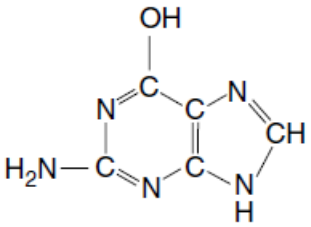
It is also used in ophthalmic practice in the treatment of glaucoma.

Medicinal plants and raw materials containing purine derivatives

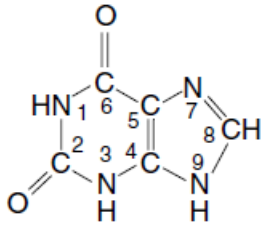
The purine nucleotides, together with the pyrimidine nucleotides, constitute vital structural units of the nucleic acids; they also function as coenzymes and as portions of complex substrate molecules. Adenine and guanine are the purines most commonly involved in these roles, but xanthine and hypoxanthine feature in their biosynthesis.



Adenine



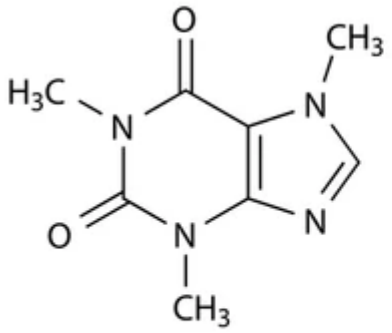
Guanine



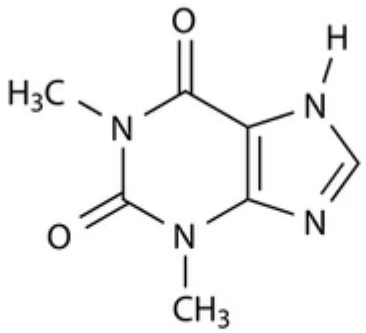
Xanthine

'Purine alkaloids' constitute secondary metabolites and are derivatives of xanthine; three well-known examples are caffeine (1,3,7-trimethylxanthine), theophylline (1,3-dimethylaxanthine) and theobromine (3,7-dimethylxanthine).

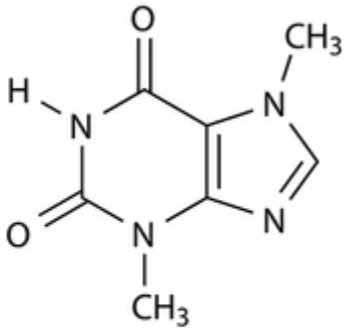
Beverages such as tea and coffee owe their stimulant properties to these substances. Caffeine stimulates the central nervous system and has a weak diuretic action, whereas theobromine acts in the reverse way.
Theophylline has generally similar properties to the above, with a shorter, though more powerful diuretic action than caffeine; it relaxes involuntary muscles more effectively than either caffeine or theobromine.
The three alkaloids are official in many countries.



Caffeine



Theophylline



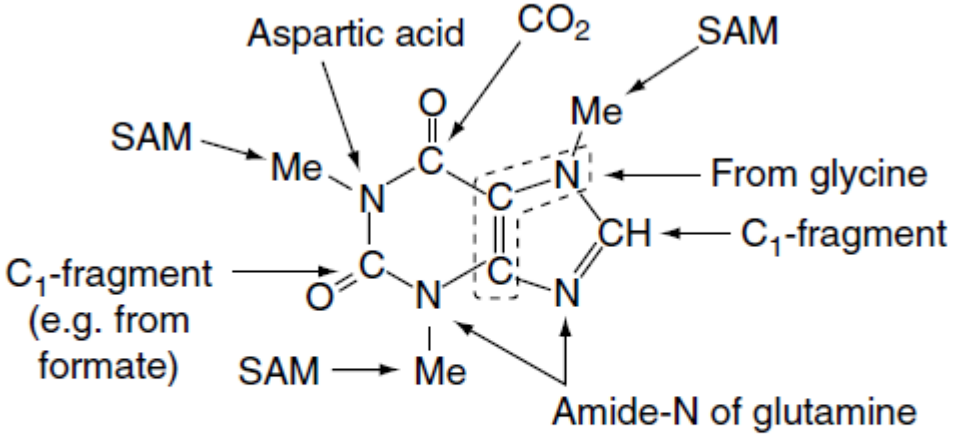
Theobromine

Biogenesis.

The ring formation of the purine alkaloids appears to follow the classical scheme for the biosynthesis of purine nucleotides with C1-moieties arising from such compounds as formates and formaldehyde.

Methylamine is also effectively incorporated into the ring system; studies by Suzuki et al. indicated that methylamine is oxidized to formaldehyde and then metabolized as a C1 compound. For caffeine, the purine bases such as hypoxanthine, adenine and guanine, and the nucleosides can also be incorporated by the plant into the molecule.

In both tea and coffee plants and in suspension cultures of Coffea arabica it has been clearly demonstrated that theobromine is methylated to caffeine. In 1979, as a result of work involving N-methyltransferases, Roberts and Waller suggested the pathway 7-methylxanthosine → 7-methylxanthine (heteroxanthin) → 3,7-dimethylxanthine (theobromine) → 1,3,7-trimethylxanthine (caffeine) which has been substantiated by later work. S-Adenosylmethionine is utilized as a donor of the methyl groups. Attempts to isolate the individual N-methyltransferase enzymes do not yet appear to have been successful due partly to their extreme lability. However progress has been made on their biochemical characterization and their time course during leaf development of Coffea arabica.



Biogenetic origin of the caffeine molecule (SAM = *S*-adenosylmethionine).

Medicinal raw material: tea tree leaves – Theae folium

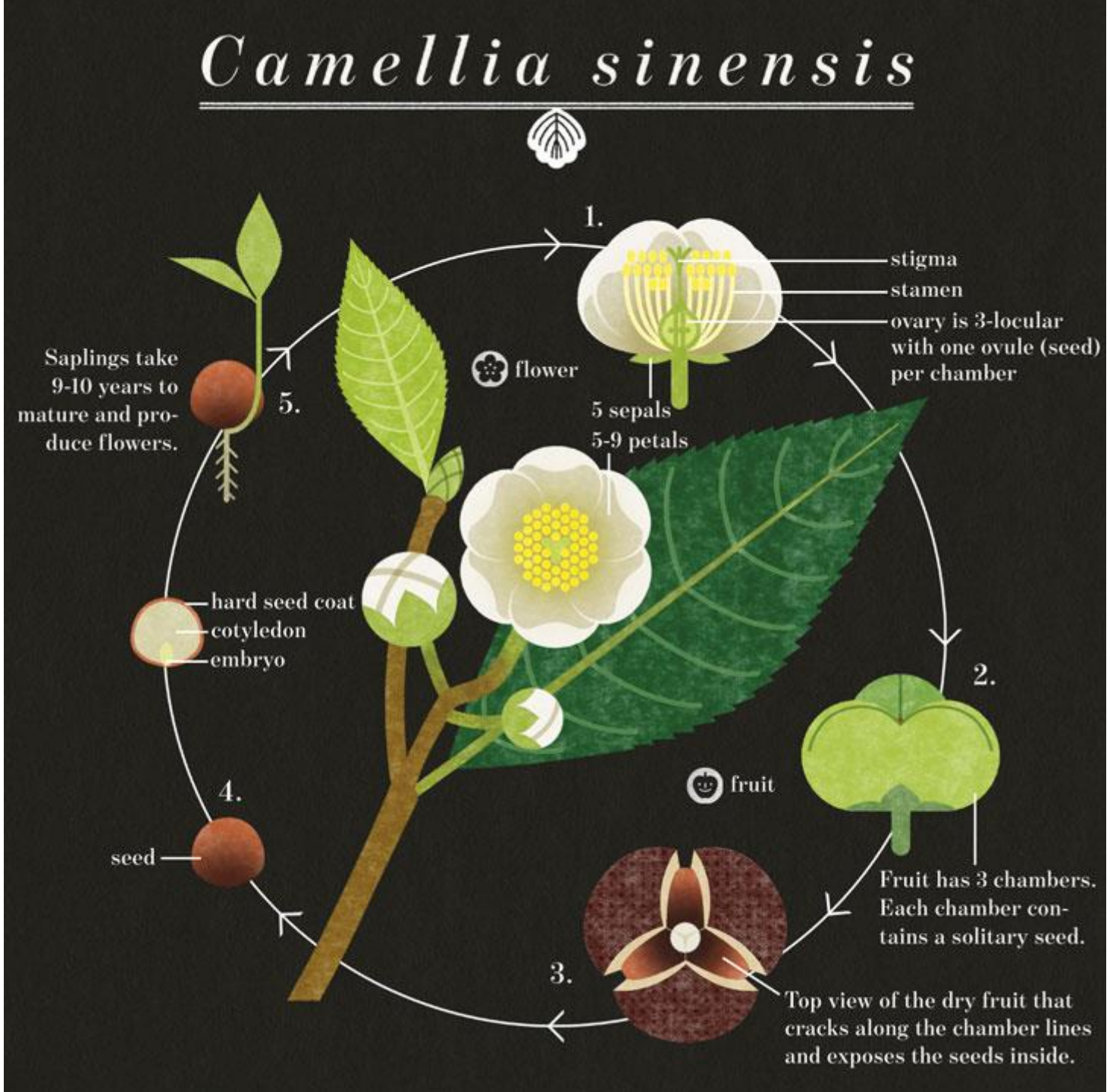
Producing plants: tea tree – Thea sinensis L.(Camellia sinensis)

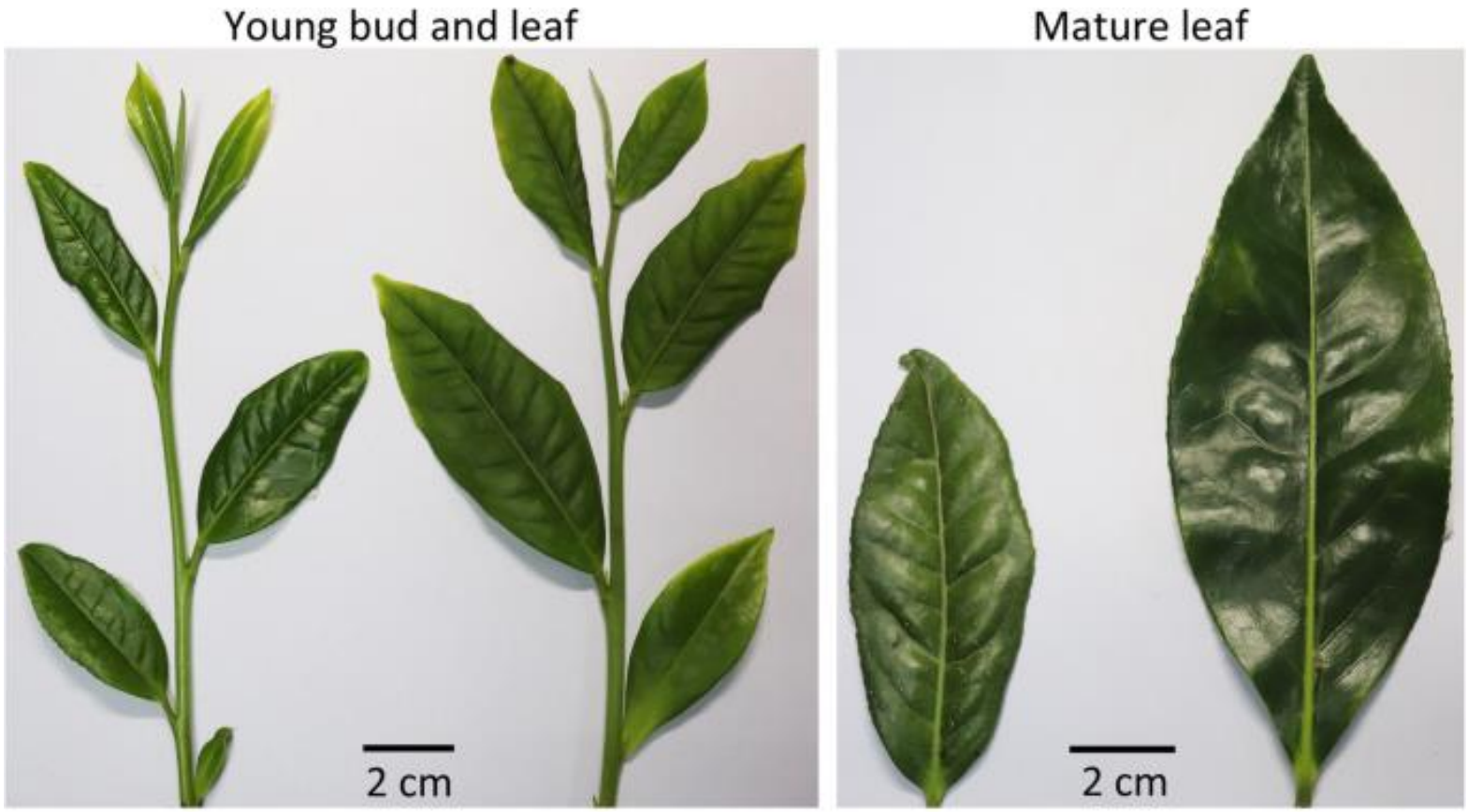
Family: Theaceae

Camellia sinensis is a species of evergreen shrub or small tree in the flowerin plant family Theaceae. Its leaves and leaf buds are used to produce the popular beverage, tea. Common names include **tea plant**, **tea shrub**, and **tea tree**

Camellia sinensis is native to East Asia, the Indian Subcontinent, and Southeast Asia, but it is today cultivated all around the world in tropical and subtropical regions. It is an evergreen shrub or small tree that is usually trimmed to below 2 m when cultivated for its leaves. It has a strong taproot. The flowers are yellow-white, 2.5–4 cm in diameter, with seven or eight petals.

The leaves are 4–15 cm in long and 2–5 cm in broad. Fresh leaves contain about 4% caffeine, as well as related compounds including theobromine. The young, light-green leaves are preferably harvested for tea production; they have short, white hairs on the underside. Older leaves are deeper green. Different leaf ages produce differing tea qualities, since their chemical compositions are different. Usually, the tip (bud) and the first two to three leaves are harvested for processing. This hand picking is repeated every one to two weeks.


Camellia sinensis
1.
stigma
stamen
ovary is 3-locular with one ovule (seed) per chamber
flower
5 sepals
5-9 petals
2.
Fruit has 3 chambers. Each chamber contains a solitary seed.
fruit
3.
Top view of the dry fruit that cracks along the chamber lines and exposes the seeds inside.
4.
seed
hard seed coat
cotyledon
embryo
5.
Saplings take 9-10 years to mature and produce flowers.


Young bud and leaf
2 cm
Mature leaf
2 cm

Constituents. Compared with black teas, green teas are abundant in catechins, because during the fermentation process of black tea (well-fermented), polyphenol oxidase results in the formation of reddish-orange colored dimeric theaflavins, and the catechins are degraded. This is in contrast to the amount of catechins in unfermented green teas, which remain unaltered.

Unfermented green tea contains the basic tea leaf. Active compounds and derivatives of camellia sinensis responding to erosive attacks on dentin polyphenols epicatechin, epigallocatechin, epicatechin gallate, and epigallocatechin gallate. Epigallocatechin-3-gallate is the major constituent of green tea, whereas theaflavins are constituents of black tea and are derived from catechins as a result of fermentation. Tea leaves also contain caffeine, theanine, myricetin, quercetin, and kaempferol, which are examples of alkaloids, amino acids, and flavonols.

Pharmacological action. Central nervous system stimulant with capillary-strengthening (flavonoid monomers and dimers), diuretic, astringent, antimicrobial, antioxidant properties.

Application. Tea is used mainly as a food product. Strongly infused, it tones and stimulates the heart and respiratory system.cardiac and respiratory functions and as an antidote to poisoning. Cuttings bushes, large leaves, partly tea grounds are used as a raw materialfor the extraction of caffeine. A significant amount of caffeine is synthetically produced. Caffeine acts on the central nervous system and the heartmuscle in an excitatory way.

Medicinal raw material: tea tree leaves – Coffeae semen

Producing plants: Coffea arabica L., Coffea liberica W.Bull ex Hiern., Coffea robusta Lind. and some other Coffea species and their varieties;

Family: Rubiaceae

Shrub or small tree, 8-10 m tall, evergreen, trunk with grey-green bark. The branches are long, flexible, spreading or drooping. Leaves are entire, smooth-edged, slightly wavy, opposite, 5-20 cm long and 1.5-5 cm wide, resting on short stalks. Flowers are white, fragrant, 3-7 in leaf axils, regular, 5-dimensional, spikelet-shaped. Blossoms and bears fruit simultaneously throughout the year. The fruit is an almost spherical or oval, dark red (cherry-like in appearance) berry with two seeds inside, surrounded by a dense leathery shell.

It grows wild in tropical areas of eastern and western Africa. Cultivated in Cuba, South America, Brazil as well as South-East Asia and Africa.

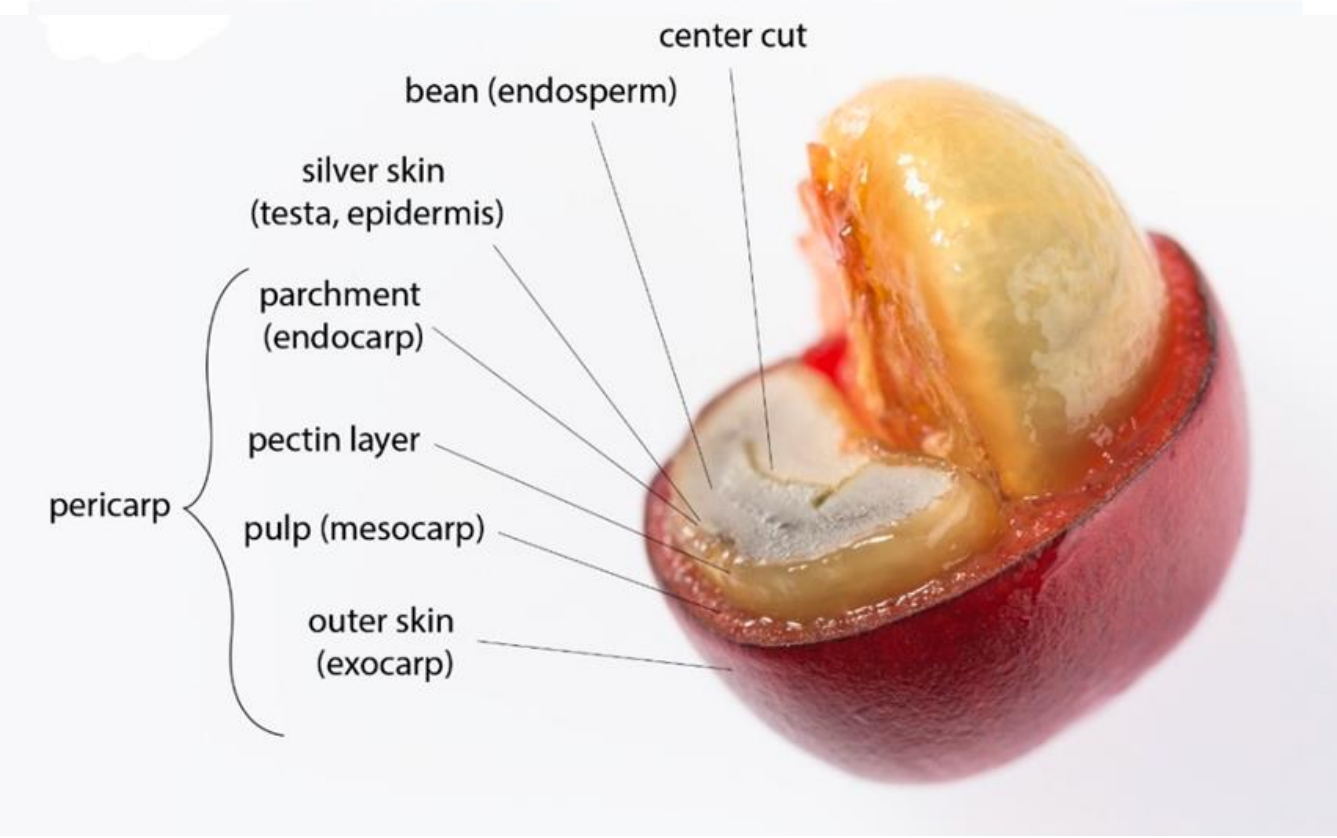
C. arabica accounts for 90% of coffee plantations. Less commonly cultivated.

C. liberica. The plant does not tolerate the heat of the tropics below 1,200-1,500 m. above sea level, so in the lower zones it is replaced by the heat-tolerant.

C. robusta. The rainfall in the cultivation area should be at least 1300 mm per year.The crop area should receive at least 1300 mm of rainfall per year; artificial irrigation is required if rainfall is insufficient.

Chemical composition. Natural coffee seeds contain alkaloidsamong which caffeine dominates, its quantity varying depending on the variety from 0.3% to 2.7%; traces of theobromine and theophylline are registeredMost of the caffeine is bound to chlorogenic acid, which is an ester of caffeic and quinic acids. The content of chlorogenic acid in the seeds ranges from 3% to 5%.Among the additional compounds associated with it are tannins (about 10%), sugars (about 8%) and fatty acids (about 8%).10%), sugars (about 8%), pentosans (6 to 7%), fatty oils, nicotinicoil, nicotinic acid and other substances.

Medicinal raw material. Harvested ripe berries are subjected to dry or wet processing. In dry processing, the berries are dried in the sun, and then the fragile pericarp is removed by machines. With wet processing, the fresh berries are passed through special machines and the pulp is washed away in a current of water.



The seeds are light grey, hard, oval, flat-convex, with a deep groove on the flat side has a deep groove. The seeds are covered with a fine 'silvery' seed coat, which rubs off during processing and the remainder is only retained in the furrows.is only retained in the furrow. Before use, the coffee seeds are roasted at 200 C.
Coffee seeds are roasted at 200 C prior to consumption, producing a brown colour and a characteristic odour.

Pharmacological action. CNS stimulant. Under the influence of caffeine the cardiac activity is increased, cerebral vessels. Brain vessels become constricted, especially in their dilatation. This is the reason why caffeine is used - and to a large extent the use of caffeine and caffeine-containing products – or Caffeine and caffeine in migraine are based on this principle, especially as caffeine enhances the effect of acetylsalicylic acid and other non-opioid analgesics.
Caffeine increases secretory activity of the stomach and also reduces platelet aggregation.

Uses. Coffee is used in the form of a drink, as a means of increasing mental and physical efficiency, as a means of primaryPre-hospital care for poisoning. Coffee is used for headaches(with migraine).

Medicinal plants and raw materials containing diterpene alkaloids.

Included in the terpenoid alkaloids are monoterpenes (e.g. skytanthine), sesquiterpenes (e.g. patchoulipyridine) and diterpenes (e.g. the alkaloids of *Aconitum*, *Delphinium* and *Taxus* spp.). Various *Taxus* spp. are considered elsewhere and aconite, which has some medicinal interest, is described below.

Medicinal raw material: Aconite root - Wolfsbane Root

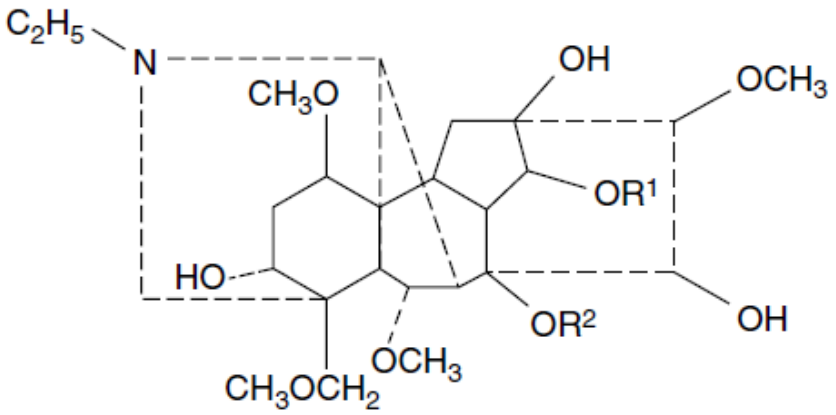
Producing plants: Aconitum napellus

Family: Ranunculaceae

A. napellus is a polymorphic aggregate extending from Western Europe to the Himalayas. Cultivated forms have deeper coloured flowers, and darker green and less narrowly divided leaves than the wild plants; the former are in considerable demand in Europe as cut flowers and to meet this demand a rapid micropropagation method using floating membrane rafts and shoot tips has been developed. The greater part of the commercial drug is derived from wild plants grown in central and southern Europe, particularly Spain.

It is an herbaceous perennial plant growing to 1 m in tall, with hairless stems and leaves. The leaves are rounded, 5–10 cm in diameter, palmately divided into five to seven deeply lobed segments. The flowers are dark purple to bluish-purple, narrow oblong helmet-shaped, 1–2 cm in tall.

Constituents. Aconite contains terpene ester alkaloids, of which the most important is aconitine.



	R^1	R^2
Aconine	H	H
Benzoylaconine	$CO{\cdot}C_6H_5$	H
Aconitine	$CO{\cdot}C_6H_5$	$CO{\cdot}CH_3$

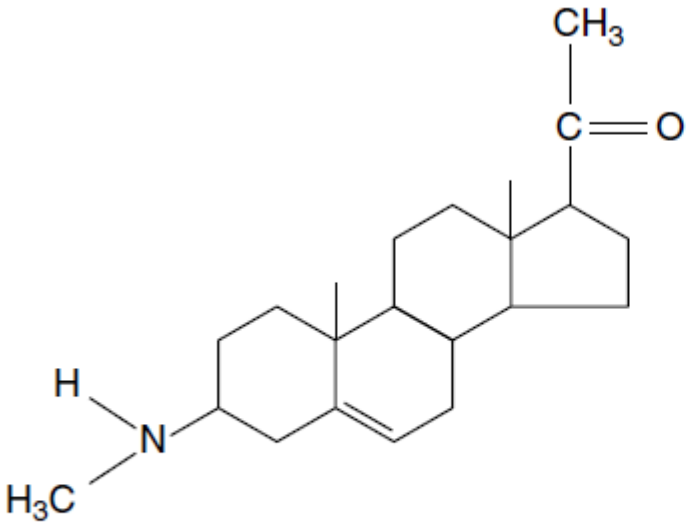
Aconite also contains other alkaloids such as mesaconitine, hypaconitine, neopelline, napelline and neoline. Hikino *et al.* isolated eight alkaloids from roots of Swiss origin, five being new to the species.

Uses. Aconite is a very potent and quick-acting poison which is now rarely used internally in the UK, except in homeopathic doses. The drug was included in the *BPC* and was formerly used for the preparation of an antineuralgic liniment.

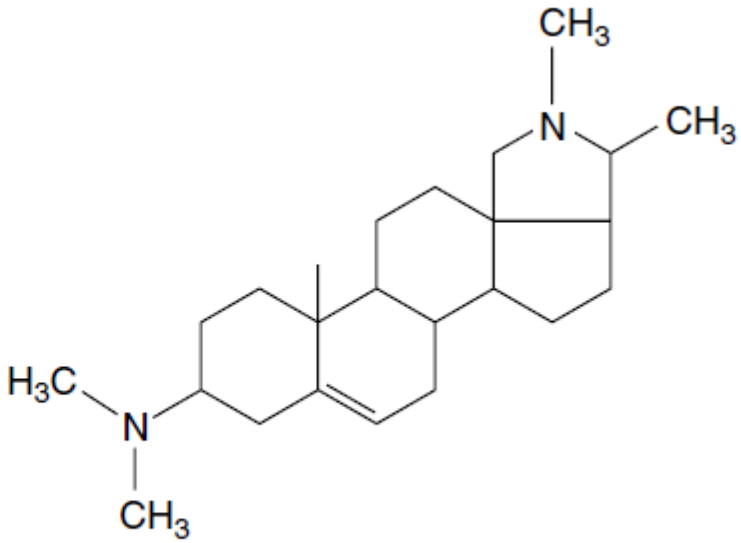
Medicinal plants and raw materials containing steroid alkaloids.

Steroidal alkaloids arise by the inclusion of a basic nitrogen at some point in the steroid molecule. Those of the C_{27} group include the *Solanum* alkaloids in relation to their potential as steroid precursors, and the *Veratrum* alkaloids, which have a similar structure. A second, C_{21} group, of which many examples are found in the Apocynaceae (*Holarrhena* and *Funtumia*) and in the Buxaceae, probably arise from pregnenolone by amination at either C-3 or C-20.

Conessine is a common alkamine of the group and represents a desirable starting material for the synthesis of some hormones (e.g. aldosterone). Whereas holaphylline has little toxicity, the quaternary diamine malouetine, which is found in the same family, is a potent curare-type poison.



Holaphylline



Conessine

Veratrums

American veratrum (Green Hellebore), *Veratrum viride* (Liliaceae), and European veratrum (White Hellebore), *V. album*, are very similar perennial herbs, whose rhizomes and roots are almost indistinguishable either macroscopically or microscopically. Some alkaloidal constituents are common to both species. The American drug is collected in the eastern parts of Canada and the USA and white hellebore in central and southern Europe.

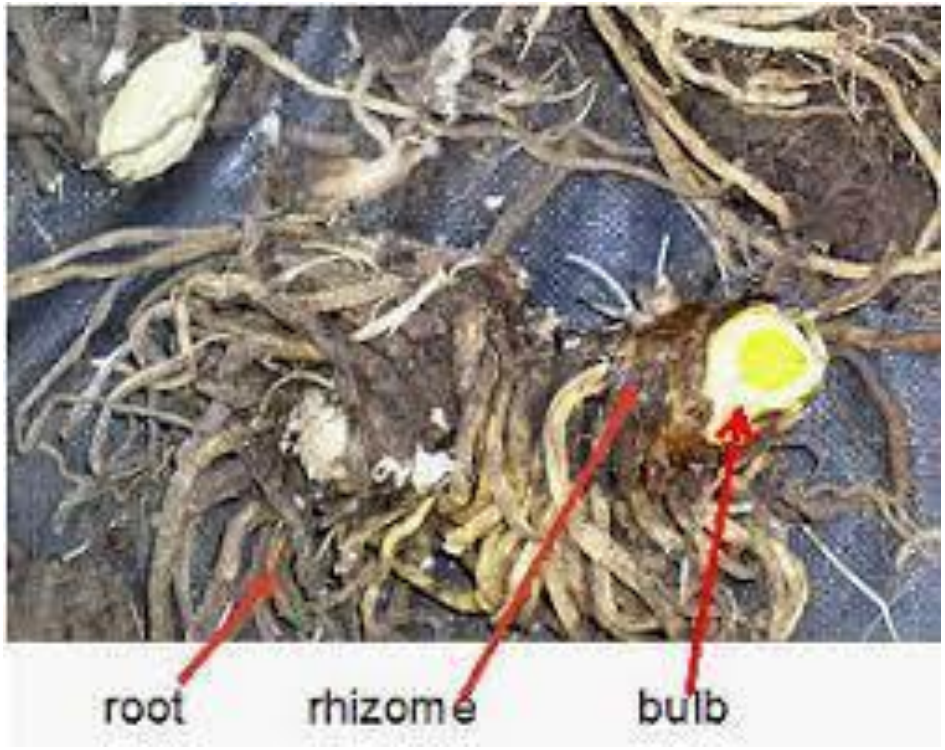
History. The North American Indians were aware of the therapeutic activity of American hellebore and it was employed by the early European settlers. Its use spread to England about 1862. In Europe the closely allied drug obtained from *V. album* had long been used. Until about 1950 veratrums, except as insecticides, were being little used. Since then they have been the subject of much research and are now employed in the treatment of hypertension.

Veratrum album is a tall herbaceous perennial plant with alternate, pleated leaves. The flowers are white, marked with green on the top portion of the stalk. The fruit is a small pod containing winged seeds. The stout, simple stems are 50–175 cm in tall. The plants have an estimated lifespan of several centuries and often achieve dominance in wild areas as they are unpalatable to grazing herbivores.

Constituents. Numerous steroidal alkaloids are present in *V. album* over 100 have been recorded and isolated.
The drug has long been used as insecticides, but its more recent importance results from those alkaloids that have hypotensive properties.

Alkaloids present in some other species, e.g. *V. californicum*, can cause serious damage to livestock grazing in locations where the plant occurs as they have teratogenic properties.
There are two distinct chemical groups of veratrum steroidal alkaloids and these are now referred to as the jerveratrum and ceveratrum groups.

Collection and preparation. The rhizome is dug up in the autumn, often sliced longitudinally into halves or quarters to facilitate drying, and sometimes deprived of many of the roots.



Macroscopical characters. The rhizome, if entire, is more or less conical and 3–8 cm long and 2–3.5 cm wide; externally brownishgrey. The roots, if present, are numerous and almost completely cover the rhizome. Entire roots are up to 8 cm long and 4 mm diameter, light brown to light orange, and usually much wrinkled (for transverse section). Commercial American veratrum is more frequently sliced than is the drug from *V. album*, and more of the roots remain attached to the rhizome. Odourless, but sternutatory; taste, bitter and acrid.

Uses. American veratrum is used for the preparation of Veriloid, a mixture of the hypotensive alkaloids. European veratrum is used for the preparation of the protoveratrines. Both drugs, and the closely related cevadilla seeds (*Schoenocaulon officinale*), are used as insecticides.

Thank You For Your Attention