CHAPTER-II
PLANT PROFILE

*Piper nigrum*

Figure-2.1 Unripe Fruits of *Piper nigrum*
Figure-2.2 Sterile *Piper nigrum* Plant

Figure-2.3 Ripen Fruits of *Piper nigrum*

**Vernacular Name**

Sans.- Maricha, Ushana, Hapusha
Hindi, Beng.- Kalimirch, kalamorich, Golmorich
Mar.- Kalimirch, Mire
Guj.- Kalamari, Kalomirich
Tel.- Miriyala tige
Tam.- Milagu
Kan.- Kare menasu
Mal.- Kurumulaku, Nalla mulaku

**Biological source**

Black pepper consists of the dried, fully developed unripe fruits of *Piper nigrum* L. belonging to family Piperaceae.

A branching, climbing perennial shrub, mostly found cultivated in hot and moist parts of India, Ceylon and other tropical countries. Branches stout, trailing and rooting at the nodes; leaves entire, 12.5-17.5 by 5.0-12.5 cm, very variable in breadth, sometimes glaucous beneath, base acute rounded or cordate, equal or unequal; flowers minute in spikes, usually dioecious, but often the sample bears 2 anthers, and the male, a pistilode; fruiting spikes very variable in lengths and robustness, rachis glabrous; fruits ovoid or globose, bright red when ripe; seeds usually globose, testa thin, albumin hard. Several types of pepper (Balamcotta, Cheria Kaniakadan, Cherakodi, Chumala, Doddaga, Kalluvalli, Karimunda, Karimcotta, Karivilanchi, Kottanadan, kumbhakodi, Kuthiraval, Malligesara, Narayakodi, Perumkodi, Tattisara, Uthuranceotta and Wokalamorata etc.) are known in cultivation and their precise identification is rather difficult, since some of them go by different names in different regions. Generally, the choice of a type depends on its yield and resistance to diseases and pests. The characteristics of important types of pepper grown in various regions are different. It stated that a high yielding type should have long spikes, with good-sized fruits compactly set all over. Generally the Travencore types are hardy; their shoots strike roots easily and make
rapid growth. Some of them are more short-lived than the types of other regions, but bear profuse crops. Almost all types cultivated at present are selections from wild plants.\textsuperscript{207}

Pepper fruits are used mainly after drying as black pepper or after processing into white pepper. In parts of Kerala fresh green pepper is sometimes used for preparing pickles. Black and white peppers are used as major condiments employed for seasoning freshly cooked and prepared foods. In U.S.A. and other western countries they are used mainly for preserving meat. The whole fruits are added to pickles, certain sausages, etc. Black pepper is mostly used for its characteristic delicate penetrating aroma and pungent, biting taste. White pepper has a similar flavour but is less pungent. On grinding white pepper yields a product with low ash and fibre contents with very little pungency.

Pepper owes its characteristic pungency and aroma to its oleoresin which can be obtained by extracting the crushed, not fully ripe fruits with volatile solvents. In modern European medicine black pepper is rarely prescribed, except indirectly, as an ingredients of some combined preparations. In modern Indian medicine is much employed as an aromatic stimulant in cholera, weakness following fevers, vertigo, coma, etc, as a stomachic in dyspepsia and flatulence, as an antiperiodic in malarial fever and as an alternative in paraplegia and arthritic diseases. Externally, it is valued for its rubefacient properties and as a local application for sore throat, piles and some skin diseases.\textsuperscript{185}

Pepper, particularly its oleoresin, has bacteriostatic and fungistatic properties. The oleoresin at 0.1% concentration inhibits the growth of \textit{Micrococcus pyrogens var. aereusus} and \textit{Aspergillus versicolour}. Alcoholic extracts of the spice are active against \textit{Micrococcus pyrogens var. aereusus} and \textit{Escherichia coli}. Aqueous extracts of pepper did not show any activity, probably due to low concentrations of oleoresins extracted from the spice by water. Pepper in concentration of 0.1% or less, lower the phagocytic activity of leucocytes. Extracts of pepper are found to have a hypercoagulative effect in vitro; they lessen the clotting time by accelerating the thrombin activation and lowering the heparin levels in clotting system.\textsuperscript{192} Pepper
retards the development of rancidity in oil and fats, frozen ground pork, beef and lard. This activity has been attributed to the presence of tocopherols in the oleoresin (total, 0.54%; α-tocopherol, 0.1%). The small concentrations of pepper commonly used may however, not be sufficient to prevent deterioration of foods.  

**Composition**

Analysis of a sample of green pepper (after discarding the stalks) gave; moisture 70.6; protein, 4.8; fat, 2.7; carbohydrates, 13.7; fibre, 6.4; and mineral matter, 1.8%; calcium, 270; phosphorous, 70; iron, 2.4; thiamine, 0.05; riboflavin, 0.04; nicotinic acid 0.2; and ascorbic acid, 1 mg/100 gm; carotene (as vitamin A), 900 I.U/100 g.

The characteristic aromatic odour of pepper is due to the presence of a volatile oil in the cells of the pericarp. On steam distillation crushed black pepper yields 1.0-2.6% (up to 4.8%) of the oil, the yield depending greatly upon the age of the dried fruits subjected to distillation. The oil of pepper consists chiefly of the terpenes, l-phenandrene, caryophyllene, and perhaps dipentene. The characteristic odour of the oil has been attributed to the presence of small amounts of oxygenated compounds, among which piperonal, dihydrocarveol, caryophyllene oxide, cryptone and an alcohol have been identified. The oil samples from various regions also contain a number of mono and sesquiterpenes ex. 1,8 cineole, p-cymene, carvone, b-bisabolene.

The alkaloid piperine (C_{17}H_{19}O_{3}N, m.p. 129-130°) is considered to be the major constituent responsible for the biting taste of black pepper; it is absent in leaves and stems of pepper plant.

Piperine is an alkaloid found naturally in plants belonging to the *Piperaceae* family, such as *Piper nigrum* L, commonly known as black pepper, and *Piper longum* L, commonly known as long pepper. Piperine is the major pungent substance in these plants and is isolated from the fruit of the black pepper and long pepper plants. Piperine comprises 1 to 99% of these plants. The term black pepper is used both for the plant *Piper nigrum* and the spice that is mainly in the fruit of the plant.
Piperine is a solid substance essentially sparingly soluble in water, readily soluble in alcohol and on hydrolysis splits into piperidine and piperic acid. It is a weak base that is tasteless at first, but leaves a burning aftertaste. Piperine belongs to the vanilloid family of compounds, a family that also includes capsaicin, the pungent substance in hot chili peppers. Its molecular formula is C\textsubscript{17}H\textsubscript{19}NO\textsubscript{3}, and its molecular weight is 285.34 Daltons. Piperine is the trans-trans stereoisomer of 1-piperoylpiperidine. It is also known as (E, E)-1-piperoylpiperidine and (E, E)-1-[5-(1, 3-benzodioxol-5-yl)-1-oxo-2, 4-pentadienyl] piperidine. It is represented by the following chemical structure:

![Chemical structure of Piperine]

Black pepper and long pepper have been used in Ayurvedic medicine for the treatment of various diseases. One such preparation is known by the Sanskrit name trikatu and consists of black pepper, long pepper and ginger. Another preparation, known by the Sanskrit name pippali, consists of long pepper. It is thought that piperine is one of the major bioactive substances of these Ayurvedic remedies. Black pepper has also been used in traditional Chinese medicine to treat seizure disorders. A derivative of piperine, antiepilepsirine, has also been used in China to treat seizure disorders. Some recent research suggests that piperine may enhance the bioavailability of some drugs and nutritional substances. The pungent alkaloids occurring in pepper in small amounts are pipericine, piperanine, piperamides, pipericide, guineensine, samentine, propenyl phenols viz., eugenol, myristicine, safrole, chavicine, piperidine and piperettine.
Chavicine a resinous isomer of piperine is said to be the most biting ingredient of pepper and on hydrolysis yields piperidine and isochavicinic acid (an isomer of piperic acid). The other constituents reported in black pepper are methyl caffeic acid piperidide and an optically active β-methyl pyrroline.

**Actions and Pharmacology**

**Actions**

Piperine may have bioavailability-enhancing activity for some nutritional substances and for some drugs. It has putative anti-inflammatory activity and may have activity in promoting digestive processes.

**Mechanism of Action**

Piperine has been demonstrated to increase the serum levels and lengthen the serum half lives of some nutritional substances, such as coenzyme Q₁₀ and beta-carotene. The mechanism of this action is unknown. It is speculated that piperine may act as a so-called thermo nutrient and increase the absorption of certain nutritional substances from the gastrointestinal tract by producing a local thermogenic action. There is no evidence for this.

Piperine has also been found to increase the serum levels and lengthen the serum half lives of some drugs, such as propanolol and theophylline. The mechanism is thought to be by inhibition of certain enzymes involved in the biotransformation of the affected drugs. Piperine has been found to be a nonspecific inhibitor of drug and xenobiotic metabolism. It appears to inhibit many different cytochrome P450 isoforms, as well as UDP-glucuronyltransferase and hepatic arylhydrocarbon hydroxylase and other enzymes involved in drug and xenobiotic metabolism.

The mechanism of piperine's putative anti-inflammatory activity may be accounted for, in part, by piperine's possible antioxidant activity. There are a few studies suggesting that piperine may inhibit lipid peroxidation. Piperine has been shown
to stimulate the secretion of the digestive enzymes like pancreatic amylase, trypsin, chymotrypsin and lipase in rats. However, piperine appears to have this activity when administered with other spice bioactives, such as capsaicin and curcumin, and not when administered by itself.

**Pharmacokinetics**

The pharmacokinetics of piperine in humans remain incompletely understood. In rats, piperine is absorbed following ingestion, and some metabolites have been identified: piperonylic acid, piperonyl alcohol, piperonal and vanillic acid are found in the urine. One metabolite, piperic acid, is found in the bile.

**Indications and Usage**

Piperine, in appropriate doses, may be useful in increasing the bioavailability of some drugs and nutrients. There is very preliminary evidence suggesting that piperine may aid in the digestion of food. There is also preliminary evidence that it may have some anticonvulsant, anticarcinogenic and anti-inflammatory properties. On the other hand, there is also preliminary evidence that it might be carcinogenic and cytotoxic in some circumstances and that it might interfere with reproductive processes and have negative effects on sperm.

There are *in vitro*, animal and human studies demonstrating that piperine can significantly increase the bioavailability of numerous drugs and some nutritional supplements. Reportedly, it has demonstrated this effect with some antimicrobial, antiprotozoal, antihelmintic, antihistaminic, non-steroidal anti-inflammatory, muscle-relaxant and anticancer drugs, among others. It has also increased the bioavailability of coenzyme Q₁₀, curcumin and beta-carotene.

In humans given 2-gram doses of curcumin alone, levels of curcumin in serum were undetectable to very low one hour post-administration. Concomitant
administration of 20 mg of piperine was said to significantly increase absorption and bioavailability (by 2000%). Similar results were reported in rats.

In a double-blind crossover study, 5 mg of piperine daily for 14-day periods resulted in significant increase in serum beta-carotene levels. The same dose of piperine produced similar results in another study, this one involving coenzyme Q10.

The claim that piperine may aid in the digestion of food is based on some experimental animal data showing that dietary piperine seems to enhance pancreatic amylase lipase, trypsin and chymotrypsin activity.

The claim that piperine may have some anticonvulsant activity comes, in part, from China, where the substance is used in an effort to treat some forms of epilepsy. In mice, piperine injected intraperitoneally inhibited clonic convulsions induced by kainate. It did not significantly block seizure activity induced by L-glutamate, N-methyl-D-aspartate or guanidinosuccinate.

In a rat intestinal model, piperine was said to provide protection against oxidative changes induced by a number of chemical carcinogens. In another study, this one in vitro, piperine reportedly reduced the cytotoxicity of aflatoxin B1 in rat hepatoma cells.

Piperine exhibited significant anti-inflammatory activity in carageenan-induced rat paw edema and in some other experimental models of inflammation. In one animal study, piperine reduced liver lipid peroxidation, acid phosphatase and edema induced by carageenan.

On the negative side, piperine has shown some evidence of being mutagenic and potentially carcinogenic under some circumstances. It has reportedly given rise to mutagenic products on reaction with nitrites. This causes concern since nitrites and piperine may be consumed simultaneously. Risk might increase with high-dose piperine supplementation. In another study, piperine appeared to enhance the bioavailability of
aflatoxin B1 in rat tissues. And in yet another study, piperine was found to be cytotoxic to cultured brain neurons. Piperine was said to be non-mutagenic, however, in a study examining effects of the substance on the germ cells of Swiss albino mice.

In a recent study utilizing albino rats, piperine, given at doses of 5 and 10 mg/kg body weight for 30 days, resulted (at the 10-mg/kg dose level) in significant reduction in the weights of testes and accessory sex organs as well as severe damage to seminiferous tubules. The 5 mg/kg dose resulted in partial degeneration of germ cells.

Decreased mating performance, decreased fertility and anti-implantation activity, along with some other adverse reproductive events, were observed in mice given very high doses of piperine.

Contraindications

Piperine is contraindicated for those who are hypersensitive to any component of a piperine-containing preparation.

Precautions

Pregnant women and nursing mothers should avoid piperine supplementation. Piperine at doses generally higher than 15 mg daily may affect the metabolism of a wide range of drugs and xenobiotics. In some cases, doses lower than 15 mg daily may affect the metabolism of these substances.

Piperine may form mutagenic and possibly carcinogenic substances with nitrites. Those who eat processed food containing nitrites and nitrates as food preservatives should exercise caution in the use of piperine supplements.

Adverse Reactions

The typical dose of piperine in nutritional formulas is 5 milligrams, and doses of 15 milligrams daily are rarely exceeded. No adverse reactions have been reported with
these doses. Piperine, if exposed to the tongue, is tasteless at first but leaves a burning after taste.

**Interactions**

**Drugs**

Piperine, usually at a dose of 20 mg or greater, has been shown to inhibit the metabolism of the following drugs: propranolol, theophylline, phenytoin, sulfadiazine, rifampicin, isoniazid, ethambutol, pyrazinamide and dapsone. This list is not inclusive. Piperine is a nonspecific inhibitor of drugs and xenobiotics. Most drugs metabolized via cytochrome P450 enzymes would likely be affected by piperine.

**Nutritional Supplements**

Piperine at a dose of 5 mg daily has been found to enhance the absorption of beta-carotene and coenzyme Q_{10}. At a dose of 20 mg daily, it has been found to enhance the absorption of curcumin. Piperine may also enhance the absorption of vitamin B_6, vitamin C and the mineral selenium in the form of L-selenomethionine.

**Dosage and Administration**

Piperine is available in stand-alone supplements and in combination products. A typical dose is 5 mg daily. Doses higher than 15 mg daily should be avoided.
Zingiber officinale

Figure-2.4 Fresh Ginger

Figure-2.5 Ginger Rhizome with a Bud
Figure-2.6 Ginger Rhizome with Plant
Figure-2.7 Ginger Plant with Flower

**Vernacular Name**

Sans.- Adraka (fresh), Shunthi (dried), Shringaveran, Sringaaran, Nagara

Hindi- Adi, Adrak (fresh), Sonth (dried)

English- Ginger

Beng.- Ada

Mar.- Alha, Aale (fresh), Sunth, Shuntya (dried)

Oriya- Ada, Adraka

Assamese- Ada

Tel.- Allam, Allamu, Allamu chettu, Shonti

Tam.- Ingee, Inji
Ginger is the dried rhizome of *Zingiber officinale* Rose., scraped to remove the darker outer skin and dried in sun. The drug is belonging to family Zingiberaceae.

A herbaceous, rhizomatous perennial, reaching up to 90cm. in height under cultivation. Rhizomes are aromatic, thick-lobed, pale yellowish, differing in shape and size in the different cultivated types. The herb develops several lateral shoots in clumps which begin to dry when the plant matures. Leaves narrow, distichous, sub-sessile, linear-lanceolate, 17.0cm. x 1.8cm., dark green, evenly narrowed to form a slender tip, flowers in spikes, greenish yellow with a small dark purple or purplish black tip.

Several commercial types are recognized in cultivation. They are generally named after the localities where they are grown. The types with less fibre, which varies from 1.7-9.0%, have higher demand. The prominent types include: Khuruppampadi, Thadupuzha, and Wynaad manatoddy (all from Kerala), Narsapattam (AP), and Maran (Assam).

Ginger is marketed both in the peeled and unpeeled condition, the peeled as scraped ginger and unpeeled as unscraped ginger. In scraped ginger the epidermal layer of the fresh ginger is scraped off with the help of a sharpened bamboo-splinter and then washed in water and dried in the sun for 7-10 days. The procedure is uniformly turned during drying. As the essential oil is contained in the epidermal cells, excessive or careless scraping results in the loss of this oil and depreciates the quality of the spice.

In trade, ginger is known after the country of shipment. The following types are recognized: Jamaican ginger- it is considered to be the best quality of ginger and was in great demand in U.S.A. and European countries. The rhizomes are
unbleached and are devoid of outer suberized layers. Unbleached Jamaican ginger occurs in branched pieces known as ‘races’ or ‘hands’. The pieces are from 7-12cm. or more in length and up to 2.0cm. in thickness. Externally, the ginger is pale-yellowish brown to yellowish-orange. The fracture is short and uneven, mealy, fibrous and resinous. It is pleasantly pungent and aromatic. Inferior grade of Jamaican ginger is known as Ratoon ginger is also marketed. Indian ginger is considered only second to Jamaican in quality. There are two main types of Indian ginger: (i) Cochin ginger, which comes from central Kerala, peeled type, and light brown to yellowish grey externally; (ii) Calicut ginger, from Malabar, is orange or reddish brown resembling African ginger, but the periderm is usually removed; it is inferior to Cochin ginger in quality. Another type, Calcutta ginger, possibly as Calicut ginger, is grayish brown to grayish blue externally. Indian ginger is more starchy and almost as pungent as Jamaican ginger, but is less agreeable in odour. Indian ginger has a faint lemon like odour due to presence of small quantity of citral.

According to Indian standard specifications, ginger (whole) shall be the rhizomes of *Z. officinale* in pieces irregular in shape and size, not less than 20mm. in length or in small cut-pieces, pale brown in colour and fibrous with peel not entirely removed. The ginger pieces may be lime bleached. The material must not have musty odour or rancid-bitter taste and shall be free from insects. African ginger- this ginger is mostly unpeeled, much of the ventral and dorsal surfaces bear patches of wrinkled curved of an earthy-brown colour. It is darker than Cochin ginger in bulk, and appears discoloured due to lack of care during the preparation. The fracture is short or short-fibrous, odour strongly aromatic and taste pungent. Chinese ginger- it is white and free from fibre. It is inferior in aroma to the Jamaican ginger and consists of rhizomes which are not fully ripe. The absence of fibre in the rhizome makes this type very suitable for pickling. Besides the above mentioned ginger some types are derived from species other than *Z. officinale*; the Japanese ginger is obtained from *Z.mioga* Rosc. and Martinique ginger from *Z. zerumbet* Rosc.
The chemical composition of ginger varies according to the type and agro-climatic conditions under which it is grown. The characteristic pleasant and aromatic odour of ginger is due to an essential oil, which can be separated from the rhizome by steam distillation. Unscraped gingers are preferred over scraped gingers for extraction of oil as the epidermal cells contains numerous oil containing cells. The yield of oil from freshly ground, unscraped, dry ginger varies from 1.5 to 3.0% (av.2.0%). The oil contains sesquiterpene hydrocarbons (50% or more), sesquiterpene alcohols, moterpenoids and associated compounds; the occurrence of esters of acetic and caprylic acids and a trace of phenol has been reported. The predominant sesquiterpene hydrocarbon is zingiberene (α- and β-zingiberene); other sesquiterpenes present in the oil are ar-curcumene (17.7%), farnesene (9.8%) and relatively smaller amounts of β-bisabolene, γ-selinene, β-elemene and β-sesquiphellandrene. The sesquiterpene alcohol, zingiberol (C_{15}H_{26}O) which is a mixture of β-eudesmol stereoisomers, occurs in the oil. Two other isomeric alcohols and a crystalline diol (m.p.126\degree) have been reported. The monoterpene hydrocarbons present in the oil include camphene, α- and β-pinene, cumene, myrcene, limonene, p-cymene and β-phellandrene.\textsuperscript{207,213} The oxygenated monoterpenes and associated compounds present are 2-heptanol, 2-nonanol, n-nonanal, n-decanal, methyl heptenone; 1,8-cineole, borneol, borneol acetate, linalool, geranial and neral.\textsuperscript{194}

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\begin{align*}
\text{Gingerol} & \quad \text{Cinnamate pathway} \quad \text{Polyketide or acetate pathway}
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The sesquiterpene hydrocarbons present in the oil are reported to be weakly odourous. The monoterpenoids and associated compounds have a relatively strong odour and some of them may be responsible for the characteristic aroma of the oil. The pungent principles of ginger are oxymethyl phenols. Commercial preparations of the oleoresin contain gingerol, shogaol and zingerone; small quantities of paradol are also reported to be present. The various pungent principles are interrelated. The proportions of the different constituents in the oleoresin vary. Freshly prepared oleoresin contains gingerol as main constituents (1/3 of the weight of the oleoresin), whereas commercial samples which have been stored for long periods contain mainly shogaol. It has been suggested that shogaol and zingerone don’t naturally occur in the fresh rhizome, and that they are present in the commercial preparations of the oleoresin is due to chemical changes brought during the preparation and storage of the oleoresin. Both shogaol and zingerone are less pungent than gingerol and the quality of oleoresin can be judged by the gingerol content. Oleoresins of poor quality and off-flavour contain high levels of shogaol and zingerone.

Ginger contains small quantities of glucose, fructose and sucrose; raffinose is probably present in traces. The principal carbohydrate is starch. Besides starch the rhizomes are reported to contain pentosans. The free amino acid present in the ginger include glutamic acid, aspartic acid, serine, glycine, threonine, alanine, glutamine, arginine, γ-aminobutyric acid, valine, phenylalanine, asparagine, lysine, cystine, histidine, leucine, proline and pipecolic acid.

**Actions and Pharmacology**

**Indication**

Magnesium, calcium and phosphorus function together in bone formation, muscle contraction, and nerve transmission. The high content of these minerals in ginger makes it a useful candidate for muscle spasms, depression, hypertension, muscle weakness, convulsions, confusion, personality changes, nausea, lack of coordination and gastrointestinal disorders.
The high content of potassium in ginger will protect the body against bone fragility, paralysis, sterility, muscle weakness, mental apathy and confusion, kidney damage, and damage to the heart. In addition to the role of potassium in blood pressure regulation, it also regulates heartbeat.

Ginger has a high content of antioxidants. This makes it a free radical scavenger. This means, it has antimitagenic and anti-inflammatory properties.229

In a study, acetone extract of ginger at 100 mg/kg p.o. significantly inhibited serotonin (5-HT) induced hypothermia. The active responsible was found to be shogaol. Shogaol, [6]-dehydrogingerdione, [8]- and [10]-gingerol were also found to have an anticathartic action.

The pungent constituents of ginger release substance P from sensory fibres. The released substance P in turn either stimulates cholinergic and histaminic neurons to release Ach and histamine, respectively, or produces direct muscle contraction by activating M and H1 receptors correspondingly. It is proposed that after being excited by substance P, M and H1 receptors are inactive temporarily and unable to be excited by agonists, therefore, ginger juice exhibits anticholinergic and antihistaminic action. Ginger juice produces antimotion sickness action possibly by central and peripheral anticholinergic and antihistaminic effects.

**Mechanism of Action**

Ginger possesses antiemetic, anti-inflammatory, analgesic, and cardiotonic properties. Ginger is a cholagogic agent that promotes the flow of bile into the intestine, especially through contraction of the gallbladder. Pharmacologically active components of the oleoresin include gingerols, a class of structurally similar cardioactive compounds, and shogaols. *In vitro*, gingerols produce concentration-dependent inotropic effects through activation of sarcoplasmic reticulum calcium adenosine triphosphatase (SR Ca2+ATPase).191
Antiemetic Actions

Ginger's mechanism of action for the prevention of motion sickness and nausea is not clear. In animal studies, ginger produced antispasmodic effects and exhibited anticholinergic and antihistaminic action. Ginger increases salivation and stimulates intestinal motility through increased tone and peristalsis of the intestine in humans. However, the results of a double-blind randomized crossover trial of healthy volunteers demonstrated no measurable effect on gastric emptying. Galanolactone, a diterpenoid constituent of ginger, demonstrated activity as a 5HT3 antagonist in vitro. Receptors for 5HT3 are located on intestinal vagal nerve terminals and in the chemoreceptor trigger zone.

Anti-inflammatory Actions

Ginger inhibits thromboxane synthetase and is a prostacyclin agonist. Prostaglandins induce vasodilation and increase tissue permeability, which, in turn, promote the influx of fluids and leukocytes. Ultimately, the classic symptoms of inflammation result: swelling, redness, warmth, and pain. It is believed that at least one of the mechanisms by which ginger produces its anti-inflammatory effects is through the inhibition of prostaglandin and leukotriene biosynthesis. Through this dual inhibition of eicosanoid biosynthesis, ginger decreases capillary permeability, thus reducing swelling and the influx of inflammatory mediators.

Analgesic Actions

The analgesic property of ginger is thought to be mainly a result of peripheral actions but direct effects on the CNS are possible. By inhibiting prostaglandin synthesis, ginger decreases the perception of pain.
Antiplatelet Activity

Several pungent constituents of ginger, Zingiber officinale are reported to inhibit arachidonic acid (AA) induced platelet activation in humans.\(^{190}\) The constituent (8)-paradol is the most potent inhibitor of COX-1 and exhibits the greatest anti-platelet activity versus other gingerol analogues.\(^{190}\) The mechanism of ginger-associated platelet inhibition may be related to decreased COX-1/thromboxane synthase enzymatic activity.\(^{190}\)

Clinical Pharmacology

Gingerol (one of the ginger's active ingredient) demonstrate a number of diverse properties such as antipyretic, analgesic, antitussive, cardiotonic, and sedative activities. This herb also possesses hypoglycemic and positive cardiac inotropic activities. Ginger can help to improve appetite and digestion, increase bile and reduce gastric secretions. Ginger can stimulate vasomotor and respiratory centers. This is partially the reason for ginger's usefulness in treatment of disequilibrium.

Medicinal Uses/Indications

Antinauseant (e.g. motion sickness, morning sickness, chemotherapy, indigestion, postoperative nausea and vomiting)
- Carminative
- Cardiotonic
- Anti-inflammatory
- Anthelmintic, fungicidal, antibacterial

Adverse Reactions

Possible CNS depression - with large overdoses
- Arrhythmias - with large overdoses
- Bleeding abnormalities
- Questionable reports of mutagenic or antimutagenic properties
**Contraindications**

- Should be used with caution in patients taking anticoagulant therapies.
- Due to ginger's cardiotonic effects, exercise caution for patients with cardiovascular disorders.
- Patients with gallstones should not use ginger until further evaluation.
- Theoretically, ginger might interfere with increased or decreased blood pressure.
- Theoretically, large doses of ginger might cause hypoglycemia
- Contraindicated in pregnant females

**Interactions and Depletions**

- Use in post-operative patients requires close monitoring due to ginger's potent actions in preventing platelet aggregation and clot formation.
- Use caution in patients currently taking antihyperglycemic and antihypertensive therapy
- Theoretically, ginger might interfere with antacids, sucralfate, H2 antagonists, or proton pump inhibitors
- Effects of barbiturates might be enhanced by concomitant administration of ginger
- Cyclophosphamide-induced vomiting could be prevented theoretically by prior administration of ginger
Glycyrrhiza glabra

Figure-2.8 Glycyrrhiza root

Figure-2.9 Glycyrrhiza (G. glabra) flowers
Figure-2.10 Russian Liquorice, Glycyrrhiza echinata

Vernacular Name

Sans.- Madhuka, Yashti-madhu
Pers.- Bikhemahak
Hindi- Mulhatti, Jethi-madh
Beng.- Jashtimadhu, Jaishbomodhu
Biology Source

Glycyrrhiza consists of the dried unpeeled roots and rhizome of *Glycyrrhiza glabra* L. var. typica or of *G. glabra* var. *glandulifera* or of other varieties of *G. glabra* yielding a yellow and sweet wood belonging to family Leguminosae. It contains not less than 4% of glycyrrhizinic acid.

A genus of perennial herbs and under shrubs distributed in the subtropical, warm and temperate region of the world, chiefly in the Mediterranean countries and China. *Glycyrrhiza glabra* Linn. and its varieties constitute the principal sources of liquorice official in the pharmacopoeias. None of the liquorice-yielding species occurs in India. But cultivation of *G. glabra* on an experimental scale has been undertaken in several places. The drug is imported into India on a considerable scale from Asia Minor, Iraq, Persia and other Central Asian countries.

*G. glabra*, the principal source of commercial drug is hardy herb or under shrub attaining a height up to 6ft.; leaves multifoliolate, imparipinnate; flowers in axillary spikes, papilionaceous, lavender to violet in colour; pods compressed, containing
reniform seeds. The underground part in some varieties consists of a rootstock with a number of long, branched stems; in others the rootstock, which is stout, throws off a large number of perennial roots. The dried, peeled or unpeeled underground stems and roots constitute the drug, known in the trade as liquorice.

Roots and underground stems after harvesting are cut into pieces and dried slowly under cover. A portion of the harvested material may be decorticated before drying to give peeled liquorice of commerce. During the drying process the moisture content is reduced from about 50% to 10%. A yield, under favourable conditions, of 60 md. Per acre, of which about 75% is marketable has been reported.231

**Spanish Liquorice-** *G. glabra* var. *typica* Regel and Herd collected chiefly in Sicily and Spain. The drug consists of peeled or unpeeled pieces of underground stems mixed with a few pieces of roots, 6-8 inch or more in length and 1/4-3/4 inch in diameter. Unpeeled pieces are dark reddish or purplish brown in colour and longitudinally wrinkled. The fracture is fibrous in the bark and splintery in the wood. Peeled pieces are smooth and yellow. The drug has a faint characteristic odour and a sweet taste almost free from bitterness. It commands a high price in the market as it is sweetest of the liquorice varieties.

**Russian Liquorice-** is derived from *G. glabra* var. *glandulifera* Waldst. Kit. It is collected in the Southern Russia chiefly from wild plants. It consists mainly of roots and some pieces of rootstock; bigger pieces are longitudinally split. Unpeeled pieces are up to 10 inches in length and 2 inches in diameter with a somewhat purplish and frequently scaly bark; the taste, although sweet, is accompanied by a perceptible, but not strong, bitterness and acridity. Russian liquorice is exported in peeled form and pieces which are excessively acrid are excluded.

**Persian Liquorice-** is derived from *G. glabra* var. *violacea* Boiss. and is collected chiefly in the Tigris and Euphrates valley in Iraq. It is usually thicker than other varieties and marketed in an unpeeled state.212,213

Liquorice of commerce is soft, flexible and fibrous, internally of a light yellow colour, with a characteristic sweet pleasant taste. It is tonic, expectorant, demulcent and mild laxative. It is used for allaying coughs and catarrhal affections. It is also useful in
irritable conditions of the mucous membrane of urinary organs. Liquorice extract is a constituent of cough syrups, throat lozenges and pastilles and it is employed in the form of aromatic syrups and elixirs for masking the taste of nauseous medicines. The extract is reported to exert a healing effect on gastric ulcers; it is spasmolytic and stimulates hydrochloric acid secretion. Extract medication, however may lead to the development of oedema. The extract is reported to be useful also in the treatment of Addison’s disease. In the form of powder, liquorice is used in the preparation of pills, either to give them a proper consistence or to prevent their adhesion. Liquorice is used in indigenous medicine in the form of decoction, infusion or as lozenges. It is also chewed with pan (betel leaves). Externally it is applied with ghee and honey for cuts and wounds.¹⁸⁵

**European liquorice,** on the other hand, is a plant with a rich historical tradition. In Europe it is found in dry open habitats in the south and east, and has been cultivated throughout the continent where it is naturalized in almost all countries, except Scandinavia. Liquorice was always harvested from the wild until the first European plantings of the herb were established almost a thousand years ago. The first century Roman naturalist Pliny mentions that liquorice is native to Sicily. Theophrastus notes the sweet flavour of the roots and says it is used for asthma, dry cough, and all diseases of the lungs. Though not native to Germany, it was well-known there by the eleventh century and extensively grown in Bavaria by the end of the sixteenth century. Cultivation is recorded in Spain by the thirteenth century. Edward the First of England placed a tax on liquorice imports in the year 1305 to finance the repair of the London Bridge. Liquorice stick is the sweet, earthy- flavoured underground stem of the plant, which may travel up to twenty feet from the main root. Cut into sections about 8 inches long, these underground stems or stolons are widely available in the herb market. They can be chewed to impart their sweet flavour. Napoleon chewed liquorice sticks and that’s what is said to have turned his teeth black.

**American Liquorice**—only one species is native to the United States, *Glycyrrhiza lepidota.* Our wild liquorice has a broad range from western Ontario to Washington, south to Texas, Mexico and Missouri. Eastward, there are scattered
populations. It is a plant of prairies, meadows and the western shore. It has never been
developed as a commercial source of liquorice. Surprisingly, the plant is little studied.
The Teton Dakota used the leaves for treating sores on the backs of horses. The leaves
were chewed and applied as a poultice. Toothaches were treated by chewing the root,
holding a piece of the root in the mouth. The root was also used for treating fever in
children. It has a strong bitter taste, which then becomes sweet. In Texas, it is called
amolillo, which refers to the foaming produced by stirring the root in water. In Texas
folk tradition, the root tea was used to reduce fever in women after childbirth and to
help expel the placenta. Other than a few relatively obscure folk uses of the plant by
European settlers and indigenous groups, the plant is little known in the United States.

**Chinese liquorice** mainly comes from *Glycyrrhiza uralensis*. It is found in dry
grassy plains, and sunny mountainsides from much of northern China, especially the
Asian steppes to the west. Most of the supply comes from Northwest China. While it is
the main species used in Asia, European liquorice also occurs in wild desert regions, dry
plains, grassy plains with salty alkaline soil, and fallow wastelands that were once used
for producing rice, wheat, and millet in northwest China. These two species along with
another Chinese native, *Glycyrrhiza inflata*, are official drug plants in Chinese
Pharmacopoeia. The Chinese call liquorice gan-cao, which means "sweet herb." An
ancient Chinese herb, it is mentioned in one of the earliest Chinese herbals attributed to
the Divine Plowman Emperor, Shen Nong, surviving from the first century. The work is
known as *Shen Nong Ben Cao Jing*. Virtually all of the important Chinese medicinal
herbs of today were mentioned in this important work, which has never been translated
into English.

In Chinese medicine, liquorice is one of the more widely used herbal drugs.
Unlike European herbal medicine, in which herbs are often used alone, in traditional
Chinese medicine most herbs are used in prescriptions with 3 or more herbs, sometimes
10 herbs, or even 50 or 100 herbs in a single prescription. According to the theories of
traditional Chinese medicine, the prescriptions are separated into the monarch or main
drug, minister drugs, assistant drugs, and guide drugs. The monarch drug is the "king"
of the prescription and has the primary effect on the health condition. Many "assistant" drugs cooperate with a major ingredient in a prescription to produce a better effect on one particular organ or condition. The minister drug helps to synergistically increase the effect of the monarch drug. The "guide drug" is added to enhance the effectiveness of other ingredients, reduce toxicity or improve taste. Liquorice is used in many Chinese herbal prescriptions as a guide drug to enhance the activity of other ingredients, reduce toxicity, as well as improve flavour. It is said that liquorice is used in as many as half of all traditional Chinese medicine prescriptions.

Substitutes and Adulterants

Manchurian Liquorice: *G. uralensis* Fisch. is reported to be the source. It resembles Russian liquorice in appearance. The barks are pale chocolate brown in colour and exfoliate readily. It contains only a small percentage of sugar and gives a rather pungent extract. Roots and rhizomes of some plant genera are also used as substitutes and adulterants of liquorice. The roots of *Abrus precatorius* are known in the trade as Indian liquorice.²⁰⁷,²¹²

Chemical Constituents

The principal constituent of liquorice to which it owes its characteristic sweet taste is glycyrrhizin which is present in different varieties in a concentration of 2-14%. This principle is not found in the aerial parts of the plant. Spanish liquorice contains 6-8% glycyrrhizin, while Russian liquorice contains 10-14%; the concentration of bitter principle is much less in Spanish liquorice. Liquorice from plants experimentally grown in Srinagar was found to contain 3.6% of glycyrrhizin.²¹³ Other constituents present in the liquorice are: glucose (up to 3.8%), sucrose (2.4-6.5%), mannite, starch, asparagine, bitter principles, resins (2-4%), a volatile oil (0.03-0.035%) and colouring matter. The yellow colour is due to the anthoxanthin glycoside, isoliquiritin which undergoes partial conversion to liquiritin during drying and storage of roots. Isoliquiritin gives on hydrolysis isoliquiritigenin while liquiritin gives liquiritigenin as aglycone. Both isoliquiritin and liquiritin are bitter with a sweet after taste and stimulate the salivary glands. Commercial samples contain 2.2% of isoliquiritin. A steroid estrogen, possibly estriol is also reported to be present in liquorice. The presence in the inner bark of a haemolytically active saponin has been reported. The Chinese liquorice contains a
substance (C_{20}H_{12}O_{9}; \text{ m.p., } 202-204^{\circ}) which is hydrolysed by acid to lapachol derivatives.\textsuperscript{198}

Glycyrrhizin occurs in liquorice as the calcium or potassium salt of the trihydroxy acid, glycyrrhizic acid (C_{41}H_{62}O_{16}; \text{ m.p., } 205^{\circ}). It is nearly 50 times as sweet as cane sugar and its sweetness is perceptible even in a dilution of 1:20,000. A solution of glycyrrhizin in hot water gelatinizes on cooling. On hydolysis it yields glycyrrhetic acid (C_{30}H_{46}O_{4}) and mannuronic acid. Glycyrrhetic acid appears to exist in two forms (m.p., 283 and 296\textsuperscript{0}) and is a triterpene related to oleanolic acid. It has a haemolytic action, though glycyrrhizic acid does not cause haemolysis.\textsuperscript{199}

**Actions and Pharmacology**

Liquorice contains the glycoside, glycyrrhizin which has a similar structure and activity as the adrenal steroids. Liquorice has an anti-inflammatory activity similar to cortisone and has been found useful for arthritis and allergies. In addition liquorice has
been used for mild Addison's disease and other adrenal insufficiencies, such as hypoglycemia. Liquorice also acts like the hormone, ACTH, causing sodium retention, potassium depletion, and water retention. Excess consumption of liquorice can lead to the classic symptoms of hypertension, with edema, increased blood pressure, potassium loss, and muscular weakness. The deglycyrrhizinated (DGL) form is most often used to avoid the hypertensive side effects of the glycyrrhetic acid in whole liquorice. Liquorice and DGL have a mild laxative effect and can protect the intestinal lining by increasing the production of mucous, thus alleviating heartburn and ulcers. Liquorice and DGL also have a demulcent action and have been used for coughs and other bronchial complaints.

**Modern Research**

If we look at use of liquorice from a western perspective, we see that its use has changed little over 3,000 years. It is considered demulcent, expectorant, and stimulates mucous secretions of the trachea. Other well-documented activities include significant anti-inflammatory effects, a protectant effect on the liver against toxic substances and antiallergic activity.

As a very important medicinal plant on a worldwide basis, the chemistry and pharmacology of European and Chinese liquorice have been well studied. Up to 24 percent of the root weight is glycyrrhizin, the plant's major active component. Glycyrrhizin (also known as glycyrrhizic acid) is an extremely sweet glycoside, which foams in water. Glycyrrhizin is said to be from fifty to two hundred times sweeter than sugar, hence the sweet taste associated with liquorice root. Liquorice root itself has a very sweet musty flavour, rather than the "anise" flavour we have come to associate with liquorice.

Studies have shown that glycyrrhizin stimulates the secretion of hormones by the adrenal cortex. Some researchers have suggested it as a possible drug to prolong the action of cortisone. Glycyrrhizin has a similar chemical structure to corticosteroids released by the adrenals, and further studies have suggested that it might one day prove
useful in improving the function of hormonal drugs, or be used as an aid in helping to reduce withdrawal symptoms from dependency on some corticosteroid hormones. Glycyrrhizin has also shown estrogenic activity in laboratory animals, and is experimentally anti-inflammatory, antirheumatic, and antibacterial. In China, liquorice root is used as an antacid.

**Liquorice and Ulcer**

One of the better known folk uses of liquorice in Europe has been in the treatment of gastric ulcers. Based on this historical use, in European herbal medicine, liquorice has been widely used in the treatment of gastric ulcers. Modern use began in 1946, when a Dutch physician, F. E. Revers demonstrated that liquorice was the active ingredient in a domestic medicine used in Netherland, then reported good results obtained in the treatment of stomach ulcers in 32 patients. In the 1950s new research showed that liquorice-derived compounds can raise the concentration of prostaglandins in the digestive system that promote mucous secretion from the stomach, as well as produce new cells in the stomach lining. It was also shown that liquorice prolongs the life span of surface cells in the stomach and has an antipepsin effect. The combined effect leads to the healing of ulcers. A recent study from Iranian researchers used aspirin coated with liquorice and found that it helped to protect against ulcers induced by aspirin, reducing the size and number of ulcers.

**Liquorice the Down Side**

About 20 percent of patients treated with liquorice in the 1950s experienced side effects such as water retention, upper abdominal pain, headache, shortness of breath, and stiffness. At first scientists thought this was an allergic reaction. Treatment with antihistamines brought no relief. The symptoms usually disappeared when the dose was reduced, though sometimes it was necessary to stop liquorice use all together. Similar symptoms have been reported from ingestion of large amounts of liquorice-containing candy, as well as by users of tobacco products flavoured with liquorice. This
indication of side effects left medical practitioners with little interest in using liquorice in the past thirty years.

More experience has been accumulated in the clinical use of liquorice. Recognized side effects of prolonged use of liquorice can include hypertension, water retention, sodium retention and loss of potassium. Therefore, the German health authorities warn that liquorice should not be used for more than four to six weeks in therapeutic doses, without medical advice. During this period of time, a diet rich in potassium (such as bananas and dried apricots) is recommended. The potassium loss can also produce interactions with other drugs. The water loss-producing effects of conventional thiazide diuretics can be increased. In addition, if the individual is on digitalis glycoside heart medications (derived from foxglove), the potassium loss can actually increase the effect of the digitalis glycoside drugs by up to 50%. Since the toxic and effective doses of digitalis glycosides are in close balance, physicians should be aware of this potential drug interaction. In addition, various European health authorities, including the German and French health agencies warn that liquorice should not be used in cases of high blood pressure, potassium deficiency in the blood, or chronic liver inflammation and liver cirrhosis.

According to the German health authorities, the dose of liquorice is about 1 teaspoonful of the cut and sifted root (equivalent to 2-4 g), in a cup of boiling water. After the water is poured over the root, it is allowed to simmer for an additional five minutes. It is then cooled and filtered. One cup of the tea is taken after a meal. Use is limited to four to six weeks without a physician prescribing further use.

**New Potential**

Scientists have shown that liquorice has an effect on the adrenals, helping to stimulate glucocorticoid production. In excess, this leads to the side effects now recognized for liquorice. Recognizing these effects described for and related to liquorice, Riccardo Baschetti of Padova, Italy, sent a letter to the *New Zealand Medical Journal* reporting his own success in treating his own case of chronic fatigue syndrome.
with liquorice root. Citing the work of Dr. Mark Demitrack of the University of Michigan Medical Center who had published a number of papers related to mild glucocorticoid insufficiency in chronic fatigue syndrome patients who don't have symptoms of Addison's disease. If his theory is correct, it occurred to him that liquorice consumption, which potentiates glucocorticoid hormone action, might be useful in chronic fatigue syndrome. His chronic fatigue syndrome had persisted for 20 months with unsatisfactory results with various treatments. He then started taking liquorice at a dose of 2.5 g/500 ml/d in milk. After a few days of liquorice therapy, his physical and mental stamina returned (though his lymph nodes did not reduce significantly in size). The author warned that the symptoms of depression are similar to chronic fatigue syndrome, and that liquorice could be detrimental to depressed patients. Physicians, he warned, should make sure that patients have chronic fatigue syndrome and not depression before trying this regimen. It is important to note that this report is only the experience of one individual and is not a cure for chronic fatigue syndrome. Rather, it provides a significant research lead, and possible approach that other practitioners may wish to monitor in patients using liquorice.

Liquorice is more than a flavour. While in small doses over a short period of time, liquorice can help in reducing ulcers, and is used traditionally as a cough suppressant, expectorant, and other uses, its future perhaps lies in taking what is currently known about the herb, and applying that to new applications. We shall see what the future will bring.
Commiphora mukul

Figure-2.11 Commiphora mukul plant

Vernacular Name

Arabic- Mogla, Moql, Mokhil, Aphalatana

Bengali- Guggul, Mukul

English- Salai tree, Gum-gugul, Indian Bedellium

Gujarati- Gugal, Gugara

Hindi- Duk, Tei

Marathi- Guggala, Gulag

Sanskrit- Guggula, Kou-shikaha

Tamil- Gukkulu, Gukkal

Telugu- Maishakshi, Gukkulu

Oriya- Gokula

Biological Source

Guggul is a gum-resin obtain by incision of the bark of Commiphora mukul (H. & S.) belonging to family Burseraceae.
Shrubby, 1.2-1.8m. high; young parts glandular-Pubescent; branches knotty and crooked, divaricate, usually ending in a sharp spine. Leaves 1-3-foliolate; leaflets subsessile (the terminal up to 20 by 8 mm.), rhomboid-ovate, serrate-toothed in the upper part (the tapering base entire), smooth, and shining, the lateral leaflets when present less than half the size of the terminal ones. Flowers in fascicles of 2-3; pedicels very short. Calyx campanulate, glandular-hairy; lobes 4-5, triangular, as long as the tube. Petals brownish red, broadly linear, nearly thrice the length of the calyx, reflexed at the apex. Stamens 8-10, alternately long and short, half the length of the petals. Disk 8-10 lobed, the alternate sinuses deeper and in these are inserted the shorter stamens. Ovary oblong-ovoid, attenuated into the style. Drupes red when ripe, 6-8 mm. diameter, ovoid, acute; epicarp 4 valved; pyrenes ovate, acute, readily splitting into 2.

Gum guggul is brown to pale yellow or dull green in colour; agreeable, aromatic and balsamic odour with characteristic bitter taste. 0.5 to 1.0-2.5cm. in diameter; they occur rounded or irregular mass or agglomerated tears. Tears are somewhat transparent, with waxy surface and brittle in nature, gummy to touch and are normally with fractured surface. When triturated with water it forms milky emulsion and partly soluble in alcohol. It burns in fire and melts in the sun.

**Chemical Constituents**

The resin is fractionated, first by mixing it with ethyl acetate, a common, moderately-non polar organic solvent, to yield a soluble fraction (~45%) and an insoluble fraction around 55%. The soluble fraction contains the active guggul lipid components and the insoluble fraction contains the carbohydrate residues, which are toxic. The soluble portion is further sub-fractionated into acid (4%), basic (1%), and neutral (95%) fractions. The acid fraction contains the anti-inflammatory components (i.e., ferulic acid, phenols, and other nonphenolic aromatic acids), while the neutral fraction contains the lipid-active components. The neutral fraction is further divided into ketonic (12%) and nonketonic (88%) sub-fractions, with the active components residing in the ketonic fraction. The inactive sub-fraction contains lignin, diterpenes, and fatty alcohols. The active ketonic fraction consists of C$_{21}$ and C$_{27}$ sterols, mainly Z-
and E-guggulsterones, and other esters. Gugulipid is a standardized neutral fraction extract of *Gum guggul* that contains a minimum of 50mg. guggulsterone per gram of extract.\textsuperscript{226} It has been speculated, but not proven, that the other components of the neutral extract exert a synergistic effect with the guggulsterone; a more likely rational is that it is cheaper to market the neutral fraction than further purify the guggulsterone from the mixture. Guggul contains several constituents and minerals as in Table-2.1

**Table-2.1 Chemical Constituents Present in Different Parts of the Plant**

<table>
<thead>
<tr>
<th>Chemical Constituents</th>
<th>Parts of the plant containing the constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)-SESAMIN</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>10-BETA-HYDROXY-PREGN-4-EN-3-ONE</td>
<td>Gum</td>
</tr>
<tr>
<td>16-ALPHA-HYDROXY-PREGN-4-EN-3-ONE</td>
<td>Gum</td>
</tr>
<tr>
<td>20(R)-HYDROXY-PREGN-4-EN-3-ONE</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>20(S)-HYDROXY-PREGN-4-EN-3-ONE</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>20-ALPHA-HYDROXY-PREGN-4-EN-3-ONE</td>
<td>Gum</td>
</tr>
<tr>
<td>3-(4-HYDROXY-3-METHOXY-PHENYL)-PROPANOIC-ACID-DOCOSANE-1-2-3-4-TETRAOL-1-YL-ESTER</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>3-(4-HYDROXY-3-METHOXY-PHENYL)-PROPANOIC-ACID-EICOSANE-1-2-3-4-TETRAOL-1-YL-ESTER</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>3-(4-HYDROXY-3-METHOXY-PHENYL)-PROPANOIC-ACID-HENEICOSANE-1-2-3-4-TETRAOL-1-YL-ESTER</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>3-(4-HYDROXY-3-METHOXY-PHENYL)-PROPANOIC-ACID-HEPTADECANE-1-2-3-4-TETRAOL-1-YL-ESTER</td>
<td>Resin, Exudate, Sap</td>
</tr>
</tbody>
</table>

*table contd.*
<table>
<thead>
<tr>
<th>Chemical Constituents</th>
<th>Parts of the plant containing the constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-(4-HYDROXY-3-METHOXY-PHENYL)-PROPANOIC-ACID-NONADECANE-1,2,3,4-TETRAOL-1-YL-ESTER</td>
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</tr>
<tr>
<td>3-(4-HYDROXY-3-METHOXY-PHENYL)-PROPANOIC-ACID-OCTADECANE-1,2,3,4-TETRAOL-1-YL-ESTER</td>
<td>Resin, Exudate, Sap</td>
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<tr>
<td>3-(4-HYDROXY-3-METHOXY-PHENYL)-PROPANOIC-ACID-HEXADECANE-1,2,3,4-TETRAOL-1-YL-ESTER</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>ALLO-CEMBROL</td>
<td>Shoot</td>
</tr>
<tr>
<td>ALLYL-CEMBROL</td>
<td>Shoot</td>
</tr>
<tr>
<td>ALUMINUM</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>AMINO-ACIDS</td>
<td>Plant</td>
</tr>
<tr>
<td>BETA-SITOSTEROL</td>
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<tr>
<td>CALCIUM</td>
<td>Inflorescence</td>
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<tr>
<td>CEMBRENE-A</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>CHOLESTEROL</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>CHOLESTEROL</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>CIS-GUGGULSTEROL</td>
<td>Gum</td>
</tr>
<tr>
<td>CIS-GUGGULSTEROL</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>CIS-GUGGULSTERONE</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>CIS-GUGGULSTERONE</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>CIS-GUGGULSTERONE</td>
<td>Plant</td>
</tr>
<tr>
<td>COMMIPHORA-MUKUL-KETO-STEROID</td>
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<tr>
<td>COMMIPHORA-MUKUL-KETO-STEROID</td>
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</tr>
<tr>
<td>COMMIPHORA-MUKUL-STEROID</td>
<td>Gum</td>
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<tr>
<td>COMMIPHORA-MUKUL-STEROL</td>
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</tr>
<tr>
<td>COPPER</td>
<td>Inflorescence</td>
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Table contd..
<table>
<thead>
<tr>
<th>Chemical Constituents</th>
<th>Parts of the plant containing the constituents</th>
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<tbody>
<tr>
<td>EICOSANE-1-2-3-4-TETROL</td>
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<tr>
<td>ELLAGIC-ACID</td>
<td>Flower</td>
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<tr>
<td>FERULIC-ACID</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>GUAIAVERIN</td>
<td>Flower</td>
</tr>
<tr>
<td>GUGGUL</td>
<td>Plant</td>
</tr>
<tr>
<td>GUGGULIPID</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>GUGGULLIGNAN-I</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>GUGGULLIGNAN-II</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>GUGGULSTEROL-I</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>GUGGULSTEROL-I</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>GUGGULSTEROL-II</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>GUGGULSTEROL-II</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>GUGGULSTEROL-III</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>GUGGULSTEROL-III</td>
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</tr>
<tr>
<td>GUGGULSTEROL-IV</td>
<td>Gum</td>
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<tr>
<td>GUGGULSTEROL-V</td>
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<tr>
<td>GUGGULSTEROL-VI</td>
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</tr>
<tr>
<td>HYPEROSIDE</td>
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<tr>
<td>IRON</td>
<td>Inflorescence</td>
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<tr>
<td>MAGNESIUM</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>MUKULOL</td>
<td>Resin, Exudate, Sap</td>
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<td>MYRICYL-ALCOHOL</td>
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<td>NONADECANE-1-2-3-4-TETROL</td>
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<td>OCTADECANE-1-2-3-4-TETROL</td>
<td>Inflorescence</td>
</tr>
<tr>
<td>PELARGONIDIN-3-5-DI-O-GLUCOSIDE</td>
<td>Flower</td>
</tr>
<tr>
<td>PELARGONIN</td>
<td>Flower</td>
</tr>
<tr>
<td>QUERCETIN</td>
<td>Flower</td>
</tr>
<tr>
<td>QUERCETIN-3-O-BETA-D-GLUCURONIDE</td>
<td>Flower</td>
</tr>
<tr>
<td>QUERCITRIN</td>
<td>Flower</td>
</tr>
<tr>
<td>TRANS-GUGGULSTERONE</td>
<td>Inflorescence</td>
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<tr>
<td>TRANS-GUGGULSTERONE</td>
<td>Resin, Exudate, Sap</td>
</tr>
<tr>
<td>TRANS-GUGGULSTERONE</td>
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Actions and Pharmacology
History and Folk Use

Guggul plays an important role in the Indian medical system Ayurveda in formulas for rheumatoid arthritis and lipid disorders. Early beliefs (2,600 years ago) also assigned a weight-reducing effect and a cardiovascular protective effect to guggul, in addition to its anti-inflammatory and lipid-lowering effects. This led to studies of guggul lipid's hypolipidemic effect on both cholesterol and triglycerides. Guggul was approved in India as a lipid-lowering drug in 1986.

What is Gugulipid?

Gugulipid is the purified standardized extract of crude Gum guggul (oleoresin). The active components of gugulipid are Z-guggulsterone and E-guggulsterone. Other components of gugulipid include various diterpenes, sterols, steroids, esters, and fatty alcohols.

Gugulipid is preferred to crude Gum guggul because it is safer and more effective. In early studies, Gum guggul was linked with mild side effects such as skin rashes, gastrointestinal irritation and diarrhoea. In contrast, no side effects have been reported with gugulipid. Apparently, the insoluble irritants of Gum guggul are removed in the production of the soluble gugulipid.

This just one example of how science is advancing in the efficacy of herbal therapy. Through careful scientific study, researchers developed a safer and superior form of natural plant medicine.
Pharmacology

An ancient medicinal plant from India shows promise in the fight against heart disease. The mukul myrrh tree (*Commiphora mukul*) secretes a resinous material called *Gum guggul*. The classic Ayurvedic medical text, the “Sushruta Samhita,” describes guggul’s role in the treatment of obesity and other lipid (fat) disorders.\(^{225}\)

Comprehensive scientific studies have investigated the clinical effectiveness of *Gum guggul* in disorders of lipid (fat) metabolism. Specifically, researchers have studied this extract’s ability to support healthy cholesterol and triglyceride levels and promote weight loss. As a result of this research, scientists have developed a natural substance-gugulipid-that appears to be safer than many other cholesterol-lowering agents, including niacin.\(^{227}\)

Gugulipid lowers serum level of triglycerides and cholesterol by stimulating the liver to increase the uptake of the lipoproteins VLDL and LDL, respectively. Gugulipid has also been shown to increase blood levels of HDL, providing a cardio protective benefit; therefore, guggul lipid would be most beneficial in treating Type IIb and IV hyperlipoproteinemias. In animal studies, guggul lipid reversed the deposition of pre-existing atherosclerotic plaques, promoted fibrinolysis, inhibited platelet aggregation and functioned as a free-radical scavenger, all serving a cardio protective function.\(^{228}\)

Gugulipid's anti-inflammatory action is thought to be due to inhibition of delayed hypersensitivity reactions. The sterol is approximately equivalent to ibuprofen and 1/5 the effect of hydrocortisone.

Gugulipid is a fairly nontoxic product, having an LD\(_{50}\) in rats is 1.6 g/kg. In doses used for clinical efficacy, there may be mild skin rashes or gastrointestinal upset/diarrhoea. It is safe to use during pregnancy and does not adversely affect liver or kidney function, hematological tests or blood sugar levels in diabetic patients.
Clinical studies

Gugulipid’s impact on cholesterol and triglycerides is quite startling. When the diet is supplemented with guggul lipid, cholesterol levels typically drop 14 to 27 percent in four to twelve weeks, while triglyceride levels drop 22 to 30 percent. Those are extremely significant reductions.

The effect of guggul lipid on serum cholesterol and triglycerides compares favourably to that of lipid-lowering drugs. Clofibrate and cholestyramine lower cholesterol levels from 6 to 12 percent and 20 to 27 percent respectively, but are associated with some degree of toxicity. In contrast, no side effects have been reported with guggul lipid. In addition to the excellent safety demonstrated in human studies, guggul lipid has been shown to be nontoxic in safety studies on laboratory animals.

Actions

The Ethyl acetate extract of Commiphora mukul was found to confer significant protection to albino rats against the development of experimental atherosclerosis. The drug not only prevented deteriorating changes in serum cholesterol, triglycerides, and plasma fibrinogen level but also favourably increased plasma fibrinolytic activity.200

The oleoresin fraction of guggul possesses significant anti-arthritic and anti-inflammatory activities, the minimum effective dose being 12.5 mg. /100 g. body weight. The crude aqueous extract of the oleo gum resin was found to suppress acute rat-paw edema induced by carrageenan. Gum guggul also had a suppressive action against the granuloma pouch test. In adjuvant arthritis, the extract suppressed the secondary lesions very effectively without having any significant action on the primary phase. Side effects such as gastric ulceration, loss of weight and mortality were negligible in the animals treated with the extract as compared to those treated with betamethasone.201 Guggul is also known as Indian bdellium. This oleo-gum-resin has properties similar to myrrh as a powerful purifying agent. The rejuvenating action assists in the general well-being of all the tissues of the body but it works specifically
on the nervous system, genito-urinary system, digestive system, and the skin. As other oleo-resins, guggul will increase leukocytes in the blood which will stimulate phagocytosis. As it is excreted by the skin, mucous membranes and the kidneys, it will disinfect their secretions. This makes it effective in assisting the body’s natural defense systems in fighting the infection. Gum guggul is particularly useful in chronic conditions but may also be used in acute infections. Gum guggul can be mixed with other herbs that may be taken for particular conditions such as laryngitis, bronchitis, pneumonia, whooping cough, cystitis, and sinus infections.

This herb may be used in purifying the body from toxins, fat, and tumors. Over the years, it has become well-known in the lowering of blood cholesterol levels. Gum guggul may be also used as part of a weight reduction program.

As it assists the body in removing toxins, gum guggul is highly effective in treating arthritis. In Ayurveda, arthritis is caused by toxins and an increased vata in the joints and tissues. Guggul improves digestion, thereby the food is more completely digested and the body will produce fewer toxins (ama). Ama means "undigested food" and is made when something has disrupted the digestion process. This may be due to the unconscious eating habits, wrong choice of food, or digestive problems. Guggul also plays a role in assisting the body in removing the stored toxins that may have formed in the joints and brought about the arthritis. Therefore, this herb will address the causes of the arthritis on several levels. It is also used as thyroid stimulant, fungicidal, demulcent, aperient, stomachic, bitter, immune system stimulant, diaphoretic, stimulating expectorant, diuretic, carminative, antispasmodic and emmenagogue. Gum guggul has no action on the unbroken skin, but on the abraded skin and on mucous membranes, it acts as an astringent and antiseptic. Two main areas of investigation have been guggul's hypolipidemic action and anti-inflammatory effect. Purified guggul steroid mixture completely inhibits ADP-adrenaline or serotonin-induced platelet aggregation. The aqueous extract of the resin guggul significantly inhibited both the maximal edema response and the total edema response during 6 hours of carrageenan-induced rat paw edema. Oral administration of ethyl acetate extract of C. mukul in albino rats
significantly prevented rise in serum cholesterol and serum triglyceride level, caused by atherogenic diet. *C. mukul* was also found to confer significant protection against atherogenic diet induced atherosclerosis. The essential oil of *C. mukul* was tested for efficacy against *Aspergillus flavus, A. fumigatus, A. sulphureus, Mucor fragilis* and *Thizopus stolonifer*. *C. mukul* was fungistatic or fungicidal to one or other of the moulds, depending on the concentrations.

**Indications**

Gum guggul is astringent, anti-inflammatory and antiseptic. When taken internally it acts as a bitter, stomachic and carminative, stimulating the appetite and improving digestion. It causes an increase in leukocytes in the blood and stimulates phagocytosis. Gum guggul acts as a diaphoretic, expectorant and diuretic, and is said to be uterine stimulant and emmenagogue. The resin is used in the form of lotion for indolent ulcers and as a gargle in chronic tonsillitis, pharyngitis and ulcerated throat.

Guggul is used to treat hypercholesterolemia, inflammation, edema, pyorrhoea, chronic tonsilitis, chronic dyspepsia, colitis, catarrh of the bowels, tubercular ulceration, fever, anemia, neurasthenia, debility, laryngitis, bronchitis, pneumonia, whooping cough, cystitis, gonorrhoea, rheumatism, nervous disease, urinary disorders, atherosclerosis, hemiplegia, diabetes, hypertension, ischaemic heart disease, obesity, arthritis and skin disease.

**Interactions**

Guggul can be problematic for people being treated for thyroid conditions. Since guggul stimulates production of thyroid hormone, it may alter the dosage requirements for thyroid replacement medication. It can also reduce the availability and effectiveness of the heart medications propranolol and diltiazem. Patients should consult a health care practitioner before taking guggul along with any other herbs or medications.
Usual Dosages

The usual clinically effective dosage of guggulsterones is 25 mg tid for lipid-lowering effects. For a preparation containing 5% guggulsterones, this translates to an effective dose of 500 mg gugulipid tid.

Contraindications, Toxicity, Cautions and Safety

Purified guggul may be taken for a long time without ill effect. For more than 2,000 years, healers in India have used a tree resin as a folk medicine to treat a variety of ailments. Modern researchers now find it effective in controlling high cholesterol.

The tree is known in India as guggul. Its sap contains a compound that blocks the action of a cell receptor, called FXR, which helps to regulate body's cholesterol level, said David D. Moore, a molecular biologist at the Baylor School of Medicine in Houston. He is co-author of a study that appeared Friday in Science Express, the electronic version of the journal Science. "Our results suggest that other compounds that could affect FXR could also control cholesterol," Moore said. "This mechanism is completely different from the action of statin drugs," which are taken by million to control cholesterol.

Clinical Studies

Clinical trial with purified guggul has been carried out in 35 patients of rheumatoid arthritis in order to assess its antirheumatic activity, dose requirement, resistance development, side effects, and effects on hematology (ESR). From the results obtained it has been indicated that guggul acts as a digestive and analgesic agent without the toxic or side effects.203 Twenty patients of hyperlipidemia were administered 4.5 g. of purified gum guggul in two divided doses daily for 16 weeks. Serum cholesterol and serum triglyceride levels decreased at the end of the 4th to 8th
weeks. HDL cholesterol showed a gradual increase while VLDL and LDL cholesterol showed significant decrease at all time points.  

An ancient Ayurvedic remedy proven to lower cholesterol (lowers bad LDL and raised good HDL cholesterol), suggested as a protection against heart attacks and strokes.

Ayurvedic literature is full of praises for guggul and its divine actions, from healing bone fractures and inflammations to treating cardiovascular disease, obesity and lipid disorders. In Tibetan medicine, the plant is used for skin disease, anemia, edema, salivation and heaviness of stomach. Guggul is used for ulcers, tonsillitis, sore throat, hay fever, nasal catarrh, laryngitis and bronchitis. Gum from the guggul plant is used in the treatment of rheumatism, neurological disorders, obesity, syphilis, urinary disorders and thyroid conditions.

Guggul has also been proven helpful for regulating cholesterol levels. The plant’s lipid lowering properties have been noted among practitioners of Ayurvedic medicine, and modern scientific research is validating these observations. Cholesterol disorders plague millions of Americans and can lead to two of the nation’s primary life-threatening illnesses which are heart disease and stroke. Unfortunately, the drugs most commonly used to treat cholesterol disorders often produce unpleasant side effects. Including liver damage, cancer, and gallstones. Guggul works to balance conditions of both low and high cholesterol whether brought on by diet, lack of exercise, chronic stress, or genetic predilection. Gum guggul does not create any of the harmful side effects associated with drugs commonly used for cholesterol disorders.

Scientists have been studying the hypolipidemic activity of guggul for over 20 years. It began with animal trials in the late 1960s, and because of its success, quickly progressed to human clinical studies. Guggul proved extremely effective in regulating cholesterol, triglycerides, and phospholipids in both types of research. Extracts of
Guggul have been shown to lower the serum cholesterol level in chicks, and have shown similar effects in rabbits, rats and domestic pigs.

Another study performed in India in the late 1970s researched the long-term effects of lipid regulating substances on humans. The two substances compared were clofibrate, an effective and frequently used hypolipidemic drug, and an ether extract of guggul resin. The guggul extract (1.5 grams/day) was taken orally by 41 of 51 subjects suffering from elevated cholesterol & triglycerides. The remaining 10 took clofibrate (2.0 grams/day). Cholesterol and triglyceride levels fell significantly, progressively, and equally in both groups. However, the guggul extract was gentler on the body as a whole, producing only mild diarrhoea in five of the subjects. No additional side effects and no biochemical abnormalities in the guggul cases were noted. The clinical profiles of the subjects in this study were varied. Some subjects were asymptomatic while others were experiencing acute discomfort as a result of illnesses such as diabetes mellitus, vascular disease and gout. In fact, six were suffering from acute cases of skin santhomatosis; three of these were placed in the guggul group and three in the clofibrate group. The three treated with guggul showed complete regression of skin lesions after 40 weeks, while only one person taking clofibrate experienced such regression. The other two taking clofibrate remained symptomatic during the course of the study.

In a study done of 25 patients suffering from hemiplegia - paralysis of one side of the body - 12 of the patients recovered completely after being treated with guggul for three months. Other studies have reported a significant reduction in body weight among animals and humans treated with guggul gum. However, the effects of guggul on body weight vary, and may be attributed to the variation in the samples of the guggul gum resin used in the studies.

Guggul has been used traditionally in Ayurveda to treat arthritis due to its anti-inflammatory properties. In one study, three compound Ayurvedic preparations with guggul as a main ingredient were tested for anti-inflammatory activity in rats. All three preparations showed a significant anti-inflammatory effect.
Studies have also shown guggul to be effective in countering hypertension and ischaemic heart disease. Guggul can be used as a prophylactic to prevent these diseases, as studies of the plant have shown its effectiveness in reducing plaque formation in the arteries.

It is believed that the lipid regulating effects of guggul result from its thyroid regulating action, and its combined effects of inhibiting the biosynthesis of cholesterol's thyroid hormones. Z-guggulsterone, a ketosteroid and a component of guggul, is such an agent. The plant is especially useful where T3 (triiodothyronine) values of the thyroid are low. Guggul's thyroid stimulating property also explains the traditional use of the plant for thyroid related problems. Ayurvedic medicine for centuries has prescribed guggul because of its healing actions which today's technologically equipped scientists are only just discovering.

Increased levels of catecholamines, dopamine and beta-hydroxylase found after taking guggul suggest another possible mechanism of lowering lipid levels in the blood. The high affinity binding anion exchange of guggul has also been suggested to contribute to its hypolipidemic activity.
Allium sativum

Figure-2.12 Garlic cloves

Figure-2.13 Garlic plants
Figure-2.14 Garlic heads

Figure-2.15 Garlic flower cluster
Vernacular Name

Arabic- Fum, Thoum, Thum  
Assamese- Naharu  
Bengali- Rasun, Lashan, Lashun  
Chinese- Syun tauh, Suen tau  
English- Garlic  
Greek- Skordo  
Gujarati- Lasan  
Hindi- Lahsan  
Kannada- Bellulli, Ulli, Lashuna  
Malayalam- Vellulli, Velutha ullah  
Marathi- Lasunas  
Sanskrit- Lashuna  
Tamil- Vallai pondu, Vellai poondu  
Telugu- Velluli tella-gadda  
Oriya- Rasuna  
Punjabi- Lasun, Lasan  
Urdu- Lahnun, Lassun

Biological Source

Garlic is the ripe bulb of *Allium sativum* Linn. Belonging to family Liliaceae.

A hardy perennial, 60 cm in height, native to Central Asia and cultivated all over India. Bulbs made up of cloves [An interesting comment can be made about the term “clove of garlic”. The English word “clove” has two culinarily relevant meanings, which one
should never confuse: A sub element of a bulb (as in “a clove of garlic”) and an aromatic spice from the Moluccas. Both meanings are related. Here, it should be noted that German Knoblauch and English clove are etymologically related and both hint on the “cleavability” of garlic bulbs. Garlic cloves are referred to as “Zehen” (toes) in German. ]

Leaves long, flat, acute, sheathing the lower half of the stem; scape slender, smooth shining; spathes long, beaked, enclosing heads bearing solid bulbils; flowers small, white, prolonged into leafy points.

Garlic (Allium sativum) is a perennial plant in the family Liliaceae and genus Allium, closely related to the onion, shallot, and leek. It does not grow in the wild, and is thought to have arisen in cultivation, probably descended from the species Allium longicuspis, which grows wild in South-western Asia. Garlic has been used throughout all of recorded history for both culinary and medicinal purposes.

The portion of the plant most often consumed is an underground storage structure called a head. A head of garlic is composed of a dozen or more discrete cloves, each of which is a botanical bulb, an underground structure comprised of thickened leaf bases. Each garlic clove may often be composed of just one leaf base, unlike onions, which almost always have multiple layers. The above-ground portions of the garlic plant are also sometimes consumed, particularly while immature and tender.

Garlic has a powerful pungent or "hot" flavour when raw, which mellows considerably when it is cooked. Raw or cooked, garlic is noted for its strong characteristic odour, and for giving those who eat it a distinctive breath odour as well. Some cultures accept the odour of garlic more than others. Northern European cuisines, for example, use garlic only modestly and tend to cook it for long periods of time to diminish its strength.

Because of its wide cultivation, the origins of garlic are not fully certain. It is related to onions and lilies, and cultivated in the same manner as the shallot. The domesticated garlic plant does not produce seeds, but is grown from bulbs. These bulbs are the part of the plant most commonly eaten, though some cooks also use the early spring shoots. These shoots are often pickled in Russia and states of the Caucasus and eaten as an appetizer. A common error made by novice cooks is to misinterpret the word "clove" as
meaning the entire garlic head (naturally occurring cluster of cloves, depending on the species) rather than one of its segments, thereby wildly exaggerating the amount of garlic in a recipe.

A garlic head is generally four to eight centimeters in diameter, white to pinkish or purple, and is composed of numerous (8 - 25) discrete bulbs. The foliage comprises a central stem 25 - 100 cm tall, with flat or keeled (but not tubular) leaves 30 - 60 cm long and 2 - 3 cm broad. The flowers are produced in a small cluster at the top of the stem, often together with several bulblets, and surrounded by a papery basal spathe; each flower is white, pink or purple, with six tepals 3 - 5 millimetres long. The flowers are commonly abortive and rarely produce any seeds due to lack of sexual reproduction and therefore the varietal improvement has to be secured through bulb selection.

The garlic plant has long, narrow, flat, obscurely keeled leaves. The head (compound bulb) has flaky, mostly white outer layers of skin like that of an onion. Inside are 8-25 cloves, or smaller bulbs. From these, new bulbs can be produced by planting out in late winter or early spring.

**Garlic Flower Head**

Like other members of the onion family, garlic actually creates the chemicals that give it a sharp flavour when the plant's cells are damaged. When a cell of a garlic clove is broken by chopping, chewing, or crushing, enzymes stored in cell vacuoles trigger the breakdown of several sulfur-containing compounds stored in the cell fluids. The resultant compounds are responsible for the sharp or hot taste and strong smell of garlic. Some of the compounds are unstable and continue to evolve over time. Among the members of the onion family, garlic has by far the highest concentrations of initial reaction products, making garlic much more potent than onions, shallots, or leeks. Although people have come to enjoy the taste of garlic, these compounds are believed to have evolved as a defensive mechanism, deterring animals like birds, insects, and worms from eating the plant.

A large number of sulfur compounds contribute to the smell and taste of garlic. Diallyl disulfide is believed to be an important odour component. Allicin has been found to be the compound most responsible for the spiciness of raw garlic. This chemical opens
thermo TRP (transient receptor potential) channels that are responsible for the burning sense of heat in foods. In the process of cooking garlic removes allicin, thus mellowing its spiciness.

**Garlic Varieties**

**Subgroups of Stiffneck Garlies**

There are several distinctive sub groupings of stiffneck garlies based on the colour, sheen, and shape of bulbs and cloves. Rocamboles perform best at latitudes greater than 40 degrees north. In wet, mild winters they often bulb poorly if at all or fail to form cloves. These are arguably the highest flavoured of all garlies, peel most easily, and thus are preferred by cooks. The plants are short and squat with broad, spreading leaves. The flower stalks make 1-3 tight coils (360 degrees) and then resume their vertical growth. Other varieties form coils that shoot off at random angles. The bulb wrappers are a light streaked purple. The cloves are rounded and plump with high soluble solids and number 6-11. The clove colour is usually brown, often a rich mahogany with a purple splash. Rocamboles mature midseason to late and have the shortest storage life of all stiffnecks (2-4 months). Varieties of note - Russian Red – large, thick, nearly round bulbs with a copper hue and purple blotches. 8-12 cloves per bulb. The taste is fiery but quickly turns sweet and buttery. Spanish Roja – the standard when judging true garlic flavour. Cloves vary from teak to brown in colour; bulb wrappers are purple streaked. Rich, spicy flavoured bulbs mature in midseason and store 4-6 months. May produce poorly in mild wet winter areas. German Red – produces large bulbs with deep red colour and 8-12 cloves. Fiery, spicy rich garlic flavour does best in cold winter climates. Matures mid season. Kilamey Red – high yields, late maturation, one of the better Rocamboles for mild, wet winter areas. Similar in appearance to German Red and Spanish Roja. Sustained heat, rich garlicky-butter after taste.

**Porcelain Group**

This is an eye-catching group of stiffnecks. Porcelains have almost pure white bulb wrappers with a reflective sheen and feature tall, symmetrical bulbs with 5-8 cloves. The cloves are a plump, crescent shape with an elongated paper tail at the top.
The clove skins are usually light brown to pink with some rose or red streaking. Clove size sometimes rivals Elephant garlic. The cloves are easily separated from the bulb and easy to peel. The vigorous plants can reach 4-5 feet in height with the seed stalk extending up another 2-3 feet. These are the longest storing of all stiffneck types (5-8 months). Varieties of note – Music – indeed it is music to the garlic lover’s eyes and mouth. White skinned with a touch of pink blush. 5-6 large cloves per bulb. Highest yielding variety with a long storage life (7-9 months). A medium heat index that sticks around in the back of the mouth. Georgian Crystal – native to the republic of Georgia. Large pure white, satin bulb wrappers cover light brown, red streaked tall cloves that peel easily. 5-6 cloves per bulb. Mild, almost sweet flavour, even raw. Georgian Fire – very similar to Georgian Crystal except it has a strong kick that shows off well in salsa.

Purple Striped and Marbled Group

These two very similar groups of stiffneck garlics indeed have purple stripes on the bulb wrappers and a smooth satin sheen. The slender bulbs are not as tall as Porcelain types and contain 5-6 cloves with a distinctive paper tail. The taste of the purple stripes is moderately fiery initially but mellows quickly. This group roasts well. Varieties of note – Chesnok Red – large bulbs, 6-10 easy-to peel cloves. One of the best roasting and cooking garlics as it holds its shape and flavour. White bulb wrappers with purple streaks. Stores 4-6 months.

A Garlic Primer

Red Rezan – bulb colour is a glazed purple with a hint of gold or copper and a satiny finish. Moderate storage (4-5 months). High flavour but not overwhelming. Purple Glazer – similar to Red Rezan but with fatter cloves. Originally from the Republic of Georgia. Brown Tempest – satiny bulb wrappers with faint, fine purple stripes. Light brown, rose-tinged cloves are short and plump, 6-9 cloves per bulb, 5-6 month storage. Fiery with a buttery after taste. Siberian – perhaps the most outstanding of the purple stripe group. Large, white, purple-striped bulbs, 7-8 cloves are wrapped by light pink bluish-red bulb wrappers. Korean Red – extremely large, tall bulb with
intense red to almost black-red colouring. 4-8 cloves. Longest storage of stiffnecks (up to 9 months). Hot, lingering taste.

**Subgroups of Softneck Garlic**

**Artichoke Type**

These have a lumpy, spreading bulb that vaguely resembles an artichoke flower. Varieties of note – Inchellium Red – the best for roasting. 9-20 uniform cloves, bulbs often greater than 3 inches in diameter. High soluble solids give this variety a denser, heavier feel and more edible portion than other garlics. Stores 6-9 months. Mild but lingering buttery taste.

**Silverskin Types**

These softneck garlics are more demanding about climate conditions and soil fertility. Because of their silver-white exteriors, clean appearance and long, thin necks, they are excellent for breeding varieties.

Nichol’s Silverskin – the whitest of all silver skin types.

Silver White – highly productive in both coastal and hot interior climates, with a large bulb.

Nootka Rose – from the San Juan Islands off Washington State’s Olympic Peninsula; 5 clove layers with up to 35 cloves, streaked red, large bulbs with strong flavour.

**Asiatic Types**

While genetically softnecks, these unique garlics combine large bulbs with the single layer clove arrangement, false flower stalk, purple or marbled colour, and plump cloves of ‘Tzan’ ‘Georgian Fire’ ‘Dushambe’ ‘Creole Red’ ‘Asian Tempest’ and productive. Lumpy off-white bulbs with pink-tinged cloves. Tight bulb wrappers, 7-10 month storage. Mild flavoured, slightly sweet, tame taste. Many small unusable cloves in center of bulb.

Machashi – good-sized flat, uniform bulbs. Cloves often occur in a single layer and are thus user friendly. Silky buttery aftertaste follows initial tongue-tingling fire.

Simoneti – a large, uniform bulb with a rosy patina on bulb wrappers, with pink cloves. Very productive, with a mellow taste.
Polish White or New York Polish – a monstrously big, uniform-shaped bulb; often the largest softneck type. Extremely cold hardy and does well in mild winter areas. Only 10-13 large cloves. Initially hot, but tones down quickly with a “sticks around” buttery sensation on the lips.

**Creole Types**

Genetically, these are softnecks that bolt early and appear stiffneck-like in ‘California Late’ variety.

**Chemical Constituents**

Garlic contains 0.1-0.36% of a volatile oil composed of sulfur-containing compounds: allicin, diallyl disulfide, diallyl trisulfide, and others. The garlic oil is obtained by steam distillation of the crushed fresh bulbs. These volatile compounds are generally considered to be responsible for most of the pharmacological properties of garlic. Other constituents of garlic include: alliin (S-allyl-L-cysteine sulfoxide), S-methyl- L-cysteine sulfoxide, protein (16.8%, dry weight basis), high concentrations of trace minerals (particularly selenium), vitamins, glucosinolates, and enzymes (alliinase, peroxidase, and myrosinase). Allicin is mainly responsible for garlic’s pungent odour. It is formed by the action of the enzyme alliinase on the compound alliin. The essential oil of garlic yields approximately 60% of its weight in allicin after exposure to alliinase. The enzyme is inactivated by heat, which accounts for the fact that cooked garlic produces neither as strong an odour as raw garlic nor nearly as powerful physiological effects.
### Table 2.2 Components of Garlic

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<th>Nutrients</th>
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<td>Stigmasterol</td>
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**Actions and Pharmacology**

**Pharmacology**
- Effects have been most attributed to allicin, ajoene and other organo-sulfur constituents e.g. S-allyl cysteine.
- Dried powdered garlic contains approximately 1% alliin which is broken down to allicin when the garlic bulb is crushed or cut. (Allicin gives the garlic odour). Further conversion yields ajoene.
- Aged garlic (to reduce the odour) or steam-distilled garlic (to produce garlic oil) denatures allicin and thus decreases activity. Aged garlic and garlic oil do not contain significant amounts of alliin or allicin and as a result do not have as much physiologic activity as fresh garlic or garlic powder.

**Mechanism of Action**
- Garlic's lipid lowering effects are thought to be due to diallyl disulfide, a decomposition product of allicin, which might lower cholesterol levels by acting as a HMG-CoA reductase inhibitor (statin).
- Garlic powder and aged garlic have been found to increase fibrinolysis and decrease platelet aggregation. Raw garlic has more potent antiplatelet effects than cooked garlic.

**Clinical Studies**
- According to reports published in JAMA tested garlic oil for cholesterol lowering and showed no effect. Garlic oil does not contain allicin, however, which is the active ingredient in garlic powder.
- One recent meta-analysis found 13 trials which met inclusion criteria. Garlic significantly reduced total cholesterol by a mean of 16 mg/dl. Several of these studies had serious methodological flaws, however.
- Another recent meta-analysis also found that garlic led to small reductions in total cholesterol at 1-3 months (range 1-25 mg/dl), but not at 6 months. Parallel reductions were seen in LDL with no change in HDL.
• The magnitude of cholesterol lowering seen in these trials is only a fraction of the lipid lowering typically found with statin drugs.
• Trials have reported much more mixed effects on blood pressure and no effects on serum glucose.

Adverse Effects
• By far the most common and bothersome side effect is malodorous breath and body odour, both of which are quite pronounced at the doses needed to see significant cholesterol lowering effects.
• Methods of preparation designed to lessen malodour also lessen effectiveness.
• Other possible adverse effects are heartburn, flatulence, nausea, and diarrhoea.

Contraindications/Cautions
• High doses of garlic can cause prolonged bleeding so repeated high doses should be avoided for 2 weeks prior to surgery.

Important Drug/Herb Interactions
• Warfarin: anticoagulant activity may be enhanced.
• Cytochrome P450 3A4: may cause induction of this enzyme resulting in enhanced metabolism and so decreased effectiveness of many drugs including cyclosporine with subsequent organ transplant rejection. Antiviral HIV drugs such as protease inhibitors with subsequent development of viral resistance.

Formulation and Dosage
• Garlic powder: 0.4-1.2 grams daily divided into three doses.
• Aging of preparations designed to reduce odour also likely to reduce efficacy.

Although garlic has a wide range of well-documented effects, its most important clinical uses are in the areas of infection, cancer prevention, and cardiovascular disease.

Antimicrobial Activity
Garlic has been shown to have broad-spectrum antimicrobial activity against many genera of bacteria, viruses, worms and fungi as summarized in several works.
These findings support the historical use of garlic in the treatment of a variety of infectious conditions.

**Antibacterial Activity**

As far back as 1944, studies have demonstrated that both garlic juice and allicin inhibited the growth of *Staphylococcus, Streptococcus, Bacillus, Brucella* and *Vibrio* species at low concentrations. In more recent studies using serial dilution and filter paper disk techniques, fresh and vacuum-dried powdered garlic preparations were found to be effective antibiotic agents against many bacteria. In these studies, the antimicrobial effects of garlic were compared to commonly used antibiotics, including penicillin, streptomycin, chloramphenicol, erythromycin and tetracyclines. Besides confirming garlic's well-known antibacterial effects, the studies demonstrated its efficacy in inhibiting the growth of some bacteria which had become resistant to one or more of the antibiotics.  

**Antifungal Activity**

Garlic has demonstrated significant antifungal activity in many *in vitro* and *in vivo* studies. From a clinical perspective, inhibition of *Candida albicans* has the most significant as both animal and *in vitro* studies have shown garlic to be more potent than nystatin, gentian violet and six other reputed antifungal agents. In one study at a major Chinese hospital, garlic therapy alone was used effectively in the treatment of cryptococcal meningitis, one of the most serious fungal infections imaginable.

**Anthelmintic Effects**

Garlic extracts have been shown to have anthelmintic activity against common intestinal parasites, including *Ascaris lumbricoides* (roundworm) and hookworms.

**Antiviral Effects**

Garlic's antiviral effects have been demonstrated by its protection of mice from infection with intranasally inoculated influenza virus and by its enhancement of neutralizing antibody production when given with influenza vaccine. The *in vitro* virus-killing effects of fresh garlic, allicin, and other sulfur components of garlic was determined against *Herpes simplex* type 1 and 2, *Parainfluenza virus* type 3, *Vaccinia*
virus, *Vesicular stomatitis* virus, and *Human rhinovirus* type 2. The order for virucidal activity was: ajoene>allicin>allyl methyl thiosulfinate>methyl allyl thiosulfinate. Ajoene was found in oil macerates of garlic but not in fresh garlic extracts. No antiviral activity was found for alliin, deoxyalliin, diallyl disulfide, or diallyl trisulfide. Fresh garlic extract was virucidal against all viruses tested. Virucidal activity of commercial products was dependent upon their preparation processes. Those products producing the highest level of allicin and other thiosulfinates had the best virucidal activity.

**Immune Enhancing and Anti-cancer Effects**

Garlic possesses important immune enhancing and anticancer properties. The famous Greek physician Hippocrates prescribed eating garlic as treatment for cancers. Animal research and some human studies suggest this advice may have been well-founded. Several garlic components have displayed significant immune enhancing as well as anticancer effects. Human studies showing garlic's immune enhancing and anticancer effects are largely based on epidemiological studies. These studies show an inverse relationship between cancer rates and garlic consumption. In China, a study comparing populations in different regions found that death from gastric cancers in regions where garlic consumption was high was significantly less that in regions with lower garlic consumption. Garlic extracts and allicin have displayed potent antitumor effects in animal studies. Human studies have shown garlic inhibits the formation of nitrosamines (powerful cancer causing compounds formed during digestion).

**Anti-inflammatory Effects**

Garlic extract has demonstrated significant anti-inflammatory activity in experimental models of inflammation. This activity is probably a result of garlic's inhibition of the formation of inflammatory compounds.

**Hypoglycemic Action**

Garlic (and onions) has often been used in the treatment of diabetes. Allicin has been shown to have significant hypoglycemic action. This effect is thought to be due to increased hepatic metabolism, increased release of insulin and/or insulin-sparing effect. The latter mechanism appears to be the major factor, as allicin and other sulfhydryl
compounds in garlic and onions compete with insulin (also a disulfide protein) for insulin-inactivating compounds, which results in an increase in free insulin.

**Miscellaneous Effects**

Garlic possesses diuretic, diaphoretic, emmenagogue, and expectorant action. It is also a carminative, anti-spasmodic and digestant, making it useful in cases of flatulence, nausea, vomiting, colic and indigestion.

**Clinical Applications**

Although garlic has long been used in infectious conditions, a use supported by its antimicrobial and immune enhancing properties. The primary clinical use of garlic has focused on its role in cardiovascular disease. Specifically, garlic is recommended primarily for its ability to lower cholesterol and blood pressure in the attempt to reduce the risk of dying prematurely from a heart attack or stroke. The majority of studies showing a positive effect of garlic and garlic preparations in reducing the risk of cardiovascular mortality are those which use products which deliver a sufficient dosage of allicin. Since allicin is the component in garlic that is responsible for its easily identifiable odour, several manufacturers have developed highly sophisticated methods in an effort to provide the full benefits of garlic without odour. These "odourless" garlic products concentrate for alliin because alliin is relatively "odourless" until it is converted to allicin in the body. Products concentrated for alliin and other sulfur components and stabilized in enteric-coated capsules provide all the benefits of fresh garlic but are more socially acceptable. In addition to the use of garlic preparations, garlic consumption as a food should be encouraged, despite its odour, in patients with high cholesterol levels and high blood pressure. Garlic and garlic preparations should also be encouraged in patients with diabetes, candidiasis, asthma, infections (particularly respiratory tract infections) and gastrointestinal complaints.

**Cholesterol Lowering Activity**

Foremost in garlic's ability to offer significant protection against heart disease and strokes is due to its ability to lower blood cholesterol levels. According to the results from numerous double-blind, placebo-controlled studies in patients with initial cholesterol levels greater than 200 mg/dl, supplementation with commercial
preparations providing a daily dose of at least 10 mg alliin or a total allicin potential of 4,000 mcg can lower total serum cholesterol levels by about 10% to 12%; LDL cholesterol will decrease by about 15%; HDL cholesterol levels will usually increase by about 10%; and triglyceride levels will typically drop 15%. Although the effects of supplemental garlic preparations on cholesterol levels are modest, the combination of lowering LDL and raising HDL can greatly improve the LDL to HDL ratio, a significant goal in the prevention of heart disease and strokes. In addition, garlic preparations standardized for alliin content exert several other beneficial effects in preventing heart disease and strokes. In addition to taking a garlic supplement, individuals with high cholesterol levels should eat more garlic and onions as increased dietary intake of garlic and onion can also lower cholesterol levels. In 1979 population study, researchers studied three populations of vegetarians in the Jain community in India who consumed differing amounts of garlic and onions. Numerous favourable effects on blood lipids, as shown in the table 2.3, were observed in the group that consumed the largest amount. Blood fibrinogen levels were highest in the group eating no onions or garlic. The study is quite significant because the subjects had nearly identical diets, except in garlic and onion ingestion.

Table 2.3 Effect of Garlic and Onion Consumption on Serum Lipids under Carefully Matched Diet.

<table>
<thead>
<tr>
<th>Garlic/Onion</th>
<th>Cholesterol</th>
<th>Triglyceride</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>208 mg/dl</td>
<td>109 mg/dl</td>
</tr>
<tr>
<td>10/200 g/wk</td>
<td>172 mg/dl</td>
<td>75 mg/dl</td>
</tr>
<tr>
<td>50/600 g/wk</td>
<td>159 mg/dl</td>
<td>52 mg/dl</td>
</tr>
</tbody>
</table>

Hypertension

Garlic has demonstrated hypotensive action in both experimental animals and humans with hypertension. A meta-analysis of published and unpublished randomized controlled trials of garlic preparations was conducted to determine the effect of garlic on blood pressure relative to placebo. A total of 415 subjects were included in the analysis. All trials used a dried garlic powder standardized to contain 1.3% alliin at a
dosage of 600 to 900 mg daily (corresponding to 7.8 and 11.7 mg of alliin or approximately 1.8 to 2.7 g of fresh garlic daily). The meta-analysis concluded that garlic preparations designed to yield allicin can lower systolic and diastolic blood pressure over a one to three month period. The typical drop from pooled data was 11 mmHg in the systolic and 5.0 mmHg in the diastolic. This degree of blood pressure reduction in hypertensives can be quite significant. It is estimated that if the blood pressure lowering effects of garlic can be maintained, the risk of stroke may be reduced by 30-40% and the risk of heart attack by 20-25%.

Platelet Aggregation Inhibition

Excessive platelet aggregation is strongly linked to atherosclerosis, heart disease, and strokes. Garlic preparations standardized for alliin content as well as garlic oil have demonstrated significant inhibition of platelet aggregation. In one study, 120 patients with increased platelet aggregation were given either 900 mg/day of a dried garlic preparation containing 1.3% alliin or a placebo for 4 weeks. In the garlic group, spontaneous platelet aggregation disappeared, the microcirculation of the skin increased by 47.6%, plasma viscosity decreased by 3.2%, diastolic blood pressure dropped from an average of 74 to 67 mmHg, and fasting blood glucose concentration dropped from an average of 89.4 to 79 mg/dl.

Fibrinolytic Activity

Epidemiological studies have suggested that fibrinogen is a major primary risk factor for cardiovascular disease. Fibrinogen is an "acute phase" protein involved in the clotting system. However, it plays many other important roles including several which promote atherosclerosis, such as acting as a co-factor for platelet aggregation, determining the viscosity of blood, and stimulating the migration and proliferation of smooth muscle cells of the artery walls. Early clinical studies stimulated detailed population studies on the possible link between fibrinogen levels and cardiovascular disease. The first such study was the Northwick Park Heart Study in the U.K. This large study involved 1,510 men aged 40 to 64 years who were randomly recruited and tested for a range of clotting factors, including fibrinogen. A stronger association was found between cardiovascular deaths and fibrinogen levels than for cholesterol. This
association has been confirmed in five other prospective epidemiological studies. The clinical significance of these findings can be summarized as follows:

1. Fibrinogen levels should be determined and monitored in patients with, or at high risk for, coronary heart disease or stroke.

2. Garlic and other natural therapies which promote fibrinolysis (e.g., omega-3 oils, bromelain, capsicum, etc.) may offer significant benefit in the prevention of heart attacks, strokes, and other thromboembolic events. Garlic preparations standardized for alliin content as well as garlic oil, and both fried and raw garlic have been shown to significantly increase serum fibrinolytic activity in humans. This increase occurs within the first six hours after ingestion and continues for up to 12 hours.

**Prevention of LDL-Oxidation**

There is growing evidence that lipoprotein (LDL) oxidation plays a significant role in the development of atherosclerosis. Accordingly, substances which prevent oxidation of LDL slow down atherosclerosis. Antioxidants like vitamin E, vitamin C, and beta-carotene have all been shown to offer protection against LDL oxidation and heart disease. Garlic is known to exert antioxidant activity, but until recently, there were no studies examining its effects on LDL oxidation. Healthy human volunteers given 600 mg/day of a garlic preparation providing 7.8 mg alliin for two weeks had a 34% lower susceptibility to lipoprotein oxidation compared to controls. These results are quite significant given the short amount of time they took to produce coupled with the importance of reducing lipoprotein oxidation.

**Dosage**

The modern use of garlic features the use of commercial preparations designed to offer the benefits of garlic without the odour. The marketplace is swamped with garlic products with each manufacturer claiming their product is the best. Preparations standardized for alliin content provide the greatest assurance of quality. However, consumers must be aware of the subtle techniques manufacturers of garlic products use to disguise the quality of their products. Based on a great deal of clinical research, the dosage of a commercial garlic product should provide a daily dose equal to at least
4,000 mg of fresh garlic. This dosage translates to at least 10 mg alliin or a total allicin potential of 4,000 mcg.

Toxicity

For the vast majority of individuals, garlic is nontoxic at the dosages commonly used. For some, however, it can cause irritation to the digestive tract, while others are apparently unable to effectively detoxify allicin and other sulfur-containing components. Prolonged feeding of large amounts of raw garlic to rats results in anemia, weight loss and failure to grow. Although the exact toxicity of garlic has yet to be definitively determined, side effects are rare at the dosage recommended above.

History and Folk Use

Garlic has been used throughout history for the treatment of a wide variety of conditions. Its usage predates written history. Sanskrit records document the use of garlic remedies approximately 5,000 years ago, while the Chinese have been using it for at least 3,000 years. The Codex Ebers, an Egyptian medical papyrus dating to about 1550 B.C., mentions garlic as an effective remedy for a variety of ailments, including hypertension, headache, bites, worms, and tumors. Hippocrates, Aristotle and Pliny cited numerous therapeutic uses for garlic. In general, garlic has been used throughout the world to treat coughs, toothache, earache, dandruff, hypertension, atherosclerosis, hysteria, diarrhoea, dysentery, diphtheria, vaginitis, and many other conditions. Garlic's antibiotic activity was noted by Pasteur in 1858. Garlic was used by Albert Schwietzer in Africa for the treatment of amebic dysentery, and as an antiseptic in the prevention of gangrene during the two world wars.

Scientific Evidence for Garlic

Atherosclerosis

Preliminary evidence suggests that garlic may help prevent atherosclerosis, the most common cause of heart attack and strokes. Garlic preparations have been found to slow hardening of the arteries in animals, reducing the size of plaque deposits by nearly 50%. In a double-blind, placebo-controlled study that followed 152 people for 4 years, standardized garlic powder at a dosage of 900 mg daily significantly slowed the development of atherosclerosis as measured by ultrasound. Unfortunately, this study
suffered from some statistical problems that make its results less than fully reliable. An observational study of 200 people measured the flexibility of the aorta, the main artery exiting the heart. 51 participants who took garlic showed more flexibility, indicating less atherosclerosis. However, because this was not a double-blind trial, its results prove little.

**Heart Attack Prevention**

In one study, 432 people who had suffered a heart attack were given either garlic oil extract or no treatment over a period of 3 years. The results showed a significant reduction of second heart attacks and about a 50% reduction in death rate among those taking garlic.

**High Cholesterol**

A number of studies published in the 1980s and 1990s found evidence that garlic preparations can reduce high cholesterol. However, several more recent and generally better-designed studies have found no benefit. The accumulating impact of these results has tended to reduce enthusiasm for using garlic as a cholesterol lowering agent. One recent study suggests that garlic can work, providing it's the right form of garlic. This 12 week, double-blind, placebo-controlled trial of 46 people with high cholesterol tested a special enteric-coated garlic product. The results showed significant improvement in levels of total cholesterol and LDL cholesterol. Besides using an enteric coating, researchers in this trial used almost twice the dose of allicin generally administered in clinical trials. This may explain the positive results.

**Hypertension**

Numerous studies have found weak evidence that garlic lowers blood pressure slightly, perhaps in the neighborhood of 5 to 10% more than placebo. However, all of these studies suffered from significant flaws, and most were performed on people who did not have high blood pressure. At present, it is not clear whether garlic actually has any effects on blood pressure. One study followed 47 subjects with an average starting blood pressure of 171/101 over a period of 12 weeks, half were treated with 600 mg of garlic powder daily standardized to 1.3% alliin, while the other half were given placebo. The results showed a statistically significant drop of 11% in the systolic blood pressure.
and 13% in the diastolic pressure. In comparison, blood pressure fell in the placebo group by 5% and 4%, respectively. However, this study suffers from a significant problem: the average starting blood pressure of the placebo and the treated groups were quite different, making comparisons unreliable.

Cautions

When garlic is used in combination with other lipid-lowering agents e.g., atorvastatin [lipitor], fluvastatin [lescol], pravastatin [pravachol], simvastatin [zocor], gemfibrozil [lupid], fenofibrate [tricor], niacin [niaspan], hypoglycemic agents e.g., insulin, glyburide, glipizide, troglitazone [rezulin], glimeripide [amaryl], chlorpropamide [diabenese], tolbutamide [orinase], or antihypertensive agents, their effects may be increased.

Garlic can also be used to decrease platelet aggregation; thus, combined use with anticoagulants may increase the risk of bleeding. Isolated reports have suggested that garlic may increase international normalized rations (INRs). However, none of these potential drug interactions has been adequately documented.

The potential for irreversible inhibition of platelet aggregation warrants stopping its use at least 7 days prior to surgery, especially if postoperative bleeding is of particular concern or if other platelet inhibitors are used.

Culinary Use

Garlic is most often used as a seasoning or a condiment. When crushed or finely chopped it yields allicin, a powerful antibiotic and anti-fungal compound (phytoncide). It also contains alliin, ajoene, enzymes, vitamin B, minerals, and flavonoids.

Garlic is widely used in many forms of cooking for its strong flavour, which is considered to enhance many other flavours. Depending on the form of cooking and the desired result, the flavour is either mellow or intense. It is often paired with onion, tomato, and/or ginger. In culinary preparation, it is necessary to remove the parchment-
like skin from individual cloves before chopping. Lightly crushing the cloves with the ball of the hand or flat of a knife makes this job much easier.

When eaten in quantity, garlic may be strongly evident in the diner’s sweat and breath the following day. This is because garlic's strong smelling sulfur compounds are metabolized forming allyl methyl sulfide. Allyl methyl sulfide (AMS) cannot be digested and is passed into the blood. It is carried to the lungs and the skin where it is excreted. Since digestion takes several hours, and release of AMS several hours more, the effect of eating garlic may be present for a long time.

The well-known phenomenon of "garlic breath" is alleged to be alleviated by eating fresh parsley. This is therefore included in many garlic recipes. However since garlic breath results mainly from digestive processes placing compounds such as AMS in the blood, and AMS is then released through the lungs over the course of many hours, eating parsley is at best a temporary fix. Because of its strong odour, garlic is sometimes called the "stinking rose".

Hardneck garlic varieties feature a seedpod that grows atop a leafless stalk known as a "scape". Immature scapes are tender and edible. They are also known as "garlic spears", "stems", or "tops". Scapes generally have a milder taste than cloves. They are often used in stir frying or prepared like asparagus.

Some scientific research indicates that garlic can have some health benefits, such as diminishment of platelet aggregation; a meta-analysis showing significant (12%) lipid lowering of cholesterol, triglycerides, and low-density lipoprotein (LDL)-cholesterol; treatment of hyperlipidaemia; the significant inhibition of atherosclerosis via the use of aged garlic extract Kyolic; and the protective nature of chronic garlic intake on elastic properties of aorta in the elderly. Regular and prolonged use of therapeutic amounts of aged garlic extracts lower blood homocysteine levels, and prevent some complications of diabetes mellitus. It may have some cancer fighting properties because it is high in diallyl sulphide (DADs), believed to be an anticarcinogen.

In modern naturopathy, garlic is used as a treatment for intestinal worms. Garlic cloves continue to be used by aficionados as a remedy for infections (especially chest
problems), digestive disorders, and fungal infections such as thrush. They are claimed to be an effective long-term remedy for cardiovascular problems reducing excessive blood cholesterol levels, atherosclerosis, the risk of thrombosis, and hypertension but these claims are disputed, as there has been no clinical trial that has demonstrated any such benefits. Whole cloves used as suppositories are sometimes used as a home remedy for Candidiasis (yeast infections). Garlic is also alleged to help regulate blood sugar levels, and so can be helpful in late-onset diabetes, though people taking insulin should not consume medicinal amounts of garlic without consulting a physician. In such applications, garlic must be fresh and uncooked, otherwise the allicin will be lost.
Trigonella foenum-graecum

Figure-2.16 Fenugreek plant

Figure-2.17 Fenugreek (plants with ripening fruits)
Figure 2.18 Fenugreek flower

Figure 2.19 Fenugreek seeds

Vernacular Name

<table>
<thead>
<tr>
<th>Language</th>
<th>Name</th>
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<tbody>
<tr>
<td>Arabic</td>
<td>Hulba, Hilbeh</td>
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<td>Assamese</td>
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<td>Beng.</td>
<td>Methi</td>
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<td>Chinese</td>
<td>Hu lu ba</td>
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<td>Greek</td>
<td>Trigonella, Moschositaro</td>
</tr>
<tr>
<td>Guj.</td>
<td>Methro, Methini</td>
</tr>
<tr>
<td>Hindi</td>
<td>Methi (seeds); Kasoori methi</td>
</tr>
<tr>
<td>Japanese</td>
<td>Koruha, Henu-guriku, Fenu-guriku</td>
</tr>
<tr>
<td>Kan.</td>
<td>Mente, Mentya</td>
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<tr>
<td>Mal.</td>
<td>Venthiam, Uluva</td>
</tr>
<tr>
<td>Mar.</td>
<td>Methi</td>
</tr>
</tbody>
</table>
Biological Source

The drug consists of the dried ripe seeds of *Trigonella foenum-graecum* Linn., (Sub family- Papilionaceae) belonging to family Leguminosae.

Annual growing to 0.6m by 0.4m at a fast rate. It is hardy to zone 6. It is in flower from June to August, and the seeds ripen from August to September. The scented flowers are hermaphrodite (have both male and female organs) and are pollinated by insects. It can fix nitrogen. The plant prefers light (sandy), medium (loamy) and heavy (clay) soils. The plant prefers acid, neutral and basic (alkaline) soils. It cannot grow in the shade. It requires dry or moist soil. Found widely in Kashmir, Punjab and the upper Gangetic planes; and widely cultivated in many parts of India. Two fairly distinct types of plants are recognized: the dwarf type, grown for culinary purposes; and the tall growing type known as Metha in Punjab grown for fodder. Leaves pinnate, 3-foliolate: leaflets 2.0 -2.5 cm long, oblanceolate- oblong, obscurely dentate; flowers white or yellowish white, one or two, axillary; pods 3-15 cm long 10-20 seeded; seeds greenish brown, 2.5-5.0 x 2.0-3.5mm. Oblong with a deep groove across one corner giving the seeds a hooked appearance.

Composition

Fenugreek seeds contains water 6.2%, protein 2%, fat 23.2%, carbohydrate 8% and fibre 10%. Fenugreek seeds contain only minute quantities of an essential oil. In the essential oil, 40 different compounds were found, furthermore, n-alkanes, sesquiterpenes, alkanoles and lactones were reported.
The dominant aroma component in fenugreek seeds is a hemiterpenoid γ-lactone, sotolone (3-hydroxy-4,5-dimethyl-2(5H)-furanone), which is contained in concentrations up to 25ppm. It supposedly forms by oxidative deamination of 4-hydroxy-isoleucine. Sotolone has a spicy flavour and was also found a key flavour. Toasted fenugreek seeds owe their altered, more nutty flavour to another type of heterocyclic compounds, the so-called pyrazines.

Fenugreek leaves were found to contain small amounts of sesquiterpenes (cadinene, α-cadinol, γ-eudesmol and α-bisabolol). Among the non-volatile components of fenugreek seeds, the furostanol glycosides are probably responsible for the bitter taste; among the several more compounds yet identified, sterols and diosgenin derivatives and trigonellin (N-methyl-pyridinium-3-carboxylate, 0.4%) are most worth noting.

**Actions and Pharmacology**

Fenugreek seed has been used for stomach upset, swelling (inflammation) of the upper air passages or throat, appetite, for lowering blood sugar, and for softening the stool. It also has been used as a gargle to relieve sore throat, and as an external dressing for swelling (local inflammation).

Fenugreek is much used in herbal medicine, especially in North Africa, the Middle East and India. It has a wide range of medicinal applications. The seeds are very nourishing and are given to convalescents and to encourage weight gain, especially in anorexia nervosa. The seeds should not be prescribed medicinally for pregnant women since they can induce uterine contractions. Research has shown that the seeds can inhibit cancer of the liver, lower blood cholesterol levels and also have an antidiabetic effect. The seed and leaves are anticholesterolemic, anti-inflammatory, antitumor, carminative, demulcent, emollient, expectorant, febrifuge, galactogogue, hypoglycaemic, laxative, parasiticide, restorative and uterine tonic. The seed yields
strong mucilage and is therefore useful in the treatment of inflammation and ulcers of
the stomach and intestines. Taken internally, a decoction of the ground seeds serves to
drain off the sweat ducts. The seeds very nourishing and body-building and is one of the
most efficacious tonics in cases of physical debility caused by anaemia or by infectious
diseases, especially where a nervous factor is involved. It is also used in the treatment
of late-onset diabetes, poor digestion, insufficient lactation, painful menstruation, labour
pains etc. The seeds freshen bad breath and restore a dulled sense of taste. Externally,
the seeds can be ground into a powder and used as a poultice for abscesses, boils,
ulcers, burns etc, or they can be used as a douche for excessive vaginal discharge.
Compounds extracted from the plant have shown cardiotonic, hypoglycemic, diuretic,
antiphlogistic and hypotensive activity. One of its constituent alkaloids, called 'trigonelline', has shown potential for use in cancer therapy. The seed contains the
saponin diosgenin, an important substance in the synthesis of oral contraceptives and
sex hormones.

Fenugreek given in a dose of 2.5 g twice daily for 3 months to healthy
individuals did not affect the blood lipids and blood sugar (fasting and post prandial). However, administered in the same daily dose for the same duration to CAD patients
also with NIDDM, fenugreek decreased significantly the blood lipids (total cholesterol
and triglycerides) without affecting the HDL cholesterol. When administered in the
same daily dose to NIDDM (non-CAD) patients (mild cases), fenugreek reduced
significantly the blood sugar (fasting and post prandial). In severe NIDDM cases, blood
sugar (both fasting and post prandial) was only slightly reduced. The changes were not
significant. Fenugreek administration did not affect platelet aggregation, fibrinolytic
activity and fibrinogen.

Fenugreek seeds contain a high percentage of mucilage a natural gummy
substance present in the coatings of many seeds. Although it does not dissolve in water,
mucilage forms a thick, gooey mass when exposed to fluids. Like other mucilage
containing substances, fenugreek seeds swell up and become slick when they are
exposed to fluids. The resulting soft mass is not absorbed by the body, but instead
passes through the intestines and also triggers intestinal muscle contractions. Both actions promote the emptying of intestinal contents. Therefore, fenugreek is a mild but effective laxative.

In addition, fenugreek seeds contain chemicals that slow down the time that food takes to go through the intestinal tract. As one result, sugars are absorbed from foods more slowly and blood sugar levels may not rise as high or fluctuate as much as usual. Fenugreek may further affect blood sugar levels by decreasing the activity of an enzyme that is involved in releasing stored sugar from the liver into the blood. Also, fenugreek contains an amino acid called 4-hydroxyisoleucine, which appears to increase the body's production of insulin when blood sugar levels are high. For many individuals, higher insulin production decreases the amounts of sugar that stay in the blood. In some studies of animals and humans with both diabetes and high cholesterol levels, fenugreek lowered cholesterol levels as well as blood sugar levels. However, no blood-sugar lowering effect was seen in non-diabetic animals. Similarly, individuals with normal cholesterol levels showed no significant reductions in cholesterol while taking fenugreek.

Some evidence suggests that fenugreek may also have other medical uses. It may reduce the amounts of calcium oxalate in the kidneys. Calcium oxalate often contributes to kidney stones. In animal studies, fenugreek also appeared to lessen the chance of developing colon cancer by blocking the action of certain enzymes. It may have some ability to protect the liver against damage from alcohol and other chemicals, but much further research is needed to prove or disprove all these possible uses of fenugreek.

Topically, the gelatinous texture of fenugreek seed may have some benefit for soothing skin that is irritated by eczema or other conditions. It has also been applied as a warm poultice to relieve muscle aches and gout pain.

The protective effect of a polyphenolic extract of fenugreek seeds (FPEt) against ethanol (Ethanol)-induced toxicity was investigated in human Chang liver cells. Cells
were incubated with either 30 mM Ethanol alone or together in the presence of seed extract for 24 h. Assays were performed in treated cells to evaluate the ability of seeds to prevent the toxic effects of ethanol. Ethanol treatment suppressed the growth of Chang liver cells and induced cytotoxicity, oxygen radical formation and mitochondrial dysfunction. Reduced glutathione (GSH) concentration was decreased significantly while oxidized glutathione (GSSG) concentration was significantly elevated in Ethanol-treated cells as compared with normal cells. Incubation of FPEt along with Ethanol significantly increased cell viability in a dose-dependent manner, caused a reduction in lactate dehydrogenase leakage and normalized GSH/GSSG ratio. The extract dose-dependently reduced thiobarbituric acid reactive substances formation. Apoptosis was observed in ethanol-treated cells while FPEt reduced apoptosis by decreasing the accumulation of sub-G₁ phase cells. The cytoprotective effects of FPEt were comparable with those of a positive control silymarin, a known hepatoprotective agent. The findings suggest that the polyphenolic compounds of fenugreek seeds can be considered cytoprotective during ethanol-induced liver damage.

For millennia, fenugreek has been used both as a medicine and as a food spice in Egypt, India, and the Middle East. Present interest in fenugreek focuses on its potential benefits for people with diabetes or high cholesterol. Numerous animal studies and preliminary trials in humans have found that fenugreek can help support healthy blood sugar and serum cholesterol levels in people with diabetes.

In a study conducted in India, 25 newly diagnosed patients with type 2 diabetes were randomly divided into two groups. Group received 1 gram a day of fenugreek seed extract and group 2 received usual care (dietary control, exercise) and placebo capsules for two months. Serum triglycerides decreased and HDL increased significantly in group 1 as compared to group 2. In addition, fenugreek seeds improved blood sugar control and decreased insulin resistance in those with mild type-2 diabetic patients.

Studies in rodents indicate that fenugreek has immune stimulating, antioxidant and anti-tumor properties, and protects the liver against alcohol toxicity. Administration of fenugreek seed extract with ethanol to rats prevented the enzymatic leakage and the
rise in lipid peroxidation. The seeds exhibited appreciable antioxidant property in vitro which was comparable with that of reduced glutathione and vitamin E. Further, examination of liver and brain revealed that, extract of fenugreek seeds could offer a significant protection against ethanol toxicity. Fenugreek also has anti-ulcer properties.

Fenugreek seeds have been used in traditional medicines as a remedy for diabetes. Rich in protein, fenugreek seeds contain the unique major free amino acid 4-hydroxyisoleucine (4-OH-Ile), which has been characterized as one of the active ingredients in fenugreek for blood glucose control. Current use of fenugreek in foodstuff has been limited to its role as a flavoring agent, and not as an ingredient to help mitigate the blood glucose response for people with diabetes. As part of a safety evaluation of novel ingredients for use in blood glucose control, the potential genotoxicity of a fenugreek seed extract, containing a minimum of 40% 4-OH-ILE, was evaluated using the standard battery of tests (reverse mutation assay; mouse lymphoma forward mutation assay; mouse micronucleus assay) recommended by US Food and Drug Administration for food ingredients. Fenugreek extract was determined not to be genotoxic under the conditions of the tested genetic toxicity battery. The negative assay results provide support that addition of fenugreek seed extract to foodstuffs formulated for people with diabetes is expected to be safe. A wide safety margin is established, as anticipated fenugreek doses are small compared to the doses administered in the assays.

Diosgenin, a steroid saponin of Trigonella foenum-graecum (Fenugreek), inhibits azoxymethane-induced aberrant crypt foci formation in F344 rats and induces apoptosis in HT-29 human colon cancer cells. Recent studies suggest that fenugreek and its active constituents may possess anticarcinogenic potential. There is preventive efficacy of dietary fenugreek seed and its major steroidal saponin constituent, diosgenin, on azoxymethane-induced rat colon carcinogenesis during initiation and promotion stages. Diosgenin seems to have potential as a novel colon cancer preventive agent.
Mechanism of Action

Mechanism of action of an orally active hypoglycemic principle isolated from water extract of seeds of Trigonella foenum graecum (fenugreek) was investigated in alloxan induced subdiabetic and overtly diabetic rabbits of different severities. The active principle was orally administered to the subdiabetic and mild diabetic rabbits (five in each group) at a dose of 50 mg/kg body weight for 15 days. The fenugreek treatment produced significant attenuation of the glucose tolerance curve and improvement in the glucose induced insulin response, suggesting that the fenugreek hypoglycemic effect may be mediated through stimulating insulin synthesis and/or secretion from the beta pancreatic cells of langerhans. Prolonged administration of the same fenugreek dose of the active principle for 30 days to the severely diabetic rabbits lowered fasting blood glucose significantly, but could elevate the fasting serum insulin level to a much lower extent, which suggests an extra-pancreatic mode of action for the active principle. The fenugreek effect may also be by increasing the sensitivity of tissues to available insulin. The fenugreek hypoglycemic effect was observed to be slow but sustained, without any risk of developing severe hypoglycemia. Fenugreek also has a favorable effect on hypertriglyceridaemia.

Indications and Uses

Fenugreek has a long history of medical uses in Ayurvedic and Chinese medicine, and has been used for numerous indications, including labor induction, aiding digestion, and as a general tonic to improve metabolism and health. Preliminary animal and human trials suggest possible hypoglycemic and antihyperlipidemic properties of oral fenugreek seed powder. Adjunct use of fenugreek seeds improves glycemic control and decreases insulin resistance in mild type-2 diabetic patients.

The fenugreek diet significantly reduces fasting blood sugar and improves the glucose tolerance test. There was a 54 per cent reduction in 24-h urinary glucose excretion. Serum total cholesterol, LDL and VLDL cholesterol and triglycerides were...
also significantly reduced. The HDL cholesterol fraction, however, remained unchanged.

**Side Effects**

As a commonly eaten food, fenugreek is generally regarded as safe. The only common side effect is mild gastrointestinal distress when it is taken in high doses. Animal studies have found fenugreek essentially non-toxic. Stomach upset may occur when a large quantity of fenugreek has been used.

**Precautions**

The liquid preparations of this product may contain sugar and/or alcohol. Caution is advised if you have diabetes, alcohol dependence or liver disease. Fenugreek is not recommended for use during pregnancy.
Asphaltum punjabium (Shilajit)

Figure-2.20 Shilajit

**Common Name:** Mineral Pitch

Shilajit means "something that has won over rocks." Shilajeet or Shilajit (Mineral Pitch in English) is a herbo-mineral drug ejected out of fissures in iron rich rocks, during hot weather. Commonly found in the Himalayas, at altitudes between 1000-5000 m, from Arunachal Pradesh in the East to Kashmir in the West. It is also found in other countries, e.g. Afghanistan (Hindukush), Bhutan, China, Nepal, Pakistan, Tibet (Himalayan belt) and the USSR (Tien Shan, Ural).

It gives bright flame when burn. It is soluble in turpentine. It is a product of high degree of coalification and grade into Kerogen shale and finally petroleum. It is fluidized and transformed into liquid product rich in humic acid due to vegetal matter derived from roots. Other important sources of humus are the litter and latex of plants. Variation in the quality of shilajit humus (both chemical and biological) is, therefore, conceivable. The other factors that cause variations in shilajit humus are: (i) altitude and the nature of shilajit-bearing rocks; (ii) atmospheric conditions (e.g. alternate wetting and drying); (iii) pH and moisture content of the rock source; and (iv) activity of the rhizospheric microorganisms and their exo-enzymes. The stability of the humus reserve depends on one or more of these factors. Shilajit samples collected from different places, as expected, exhibit variations in chemical characteristics and bioactivities. Furthermore, the hazards of collection of shilajit and the scanty amount generally
available in any one locale prompt unscrupulous traders to adulterate it with rock soil, plant debris and quercus gums. It was, therefore, thought imperative to determine certain standards of shilajit on the basis of bioactivity-directed investigation of its chemical constituents. Shilajit is a rare drug in nature and this is the reason it is high value drug. In India, it is mostly collected from Himalayan range.

It is called as "panacea" by Charaka, the most respected of Ayurvedic texts. According to Ayurveda it is hot, bitter and reduces kapha mostly, but is beneficial for vata and pitta as well. It is an adaptogen or rasayana. It is called yogavahi, which means it strengthens and enhances all other herbs and processes in the body. It is used in immune disorders, chronic fatigue, urinary tract disorders, memory, reduces tumors, nervous disorders, and sexual dysfunction. It is a known free radical scavenger, anti-stress agent and a powerful adaptogen.

Although the process is not fully understood, it is believed that the porous fulvic and humic acids in shilajit carry herbal compounds deeply into the tissues of the body. These porous carrying cavities also hook toxins and escort them out of the body. This process is rare and is known a yogavahi or bioavailability enhancer.

Chemistry

The chemical character of shilajit was the observation that shilajit, from different regions, contained a large variety of organic compounds that can be broadly grouped into humic and nonhumic substances. The nonhumic substances, in soil-sediment humus are low molecular weight organic compounds that are characterizable by chemical and spectroscopic methods. The humic substances, by contrast, do not exhibit any specific physical and chemical characteristics (e.g. sharp m.p., consistent elemental composition, consistent pH, well-defined IR and NMR spectra), normally exhibited by characterizable organic compounds. Humic substances are produced by interaction of plants, algae, mosses, and microorganisms. During the bioactivity-directed investigation of shilajit samples, from different countries, some striking similarities were observed in respect of their contained low molecular weight bioactive
compounds. Several phenylpropanoid acetate derived aucuparins, oxygenated biphenylcarboxylates, isolated and characterized as their permethylated derivatives (1-3), and oxygenated dibenzo-or -pyrones (3-5) were found to occur ubiquitously, albeit in different amounts, in all authentic samples of shilajit.\textsuperscript{281,282}

Over eighty different plant species were reported in and around the shilajit rocks in Kumaon itself.\textsuperscript{283} One species which was consistently found to be present in shilajit-bearing rocks, throughout the Eastern and the Western Himalayas, was a rich latex producing plant, \textit{Euphorbia royleana} Boiss. (Euphorbiaceae). Some other latex and resin producing common species, in these regions, are the legumes, e.g. \textit{Trifolium}, (family, \textit{Anacardiaceae}), \textit{Ficus} (Moraceae), and \textit{Juniperus} (Cuprassaceae). \textit{Trifolium ripens} (Leguminosae), collected from different places in the Himalayan belt, yielded several phenylpropanoid-acetate-derived metabolites including (1) to (2). \textit{E. royleana} (latex and debris), putrefied by shilajit rhizospheric microorganisms, yield the three other important shilajit marker compounds (5-5) along with several other equivalent metabolites. \textit{Succedanea} (\textit{Anacardiaceae}), several phenolic lipids of the type (2) an ditriterpenoids (both free and conjugated,- oligoglycosides) of the tirucallane types (11-12). Enzymatic hydrolysis of a major triterpenoid saponin fraction, with hesperidinase, followed by column chromatography (Silica gel using n-butanol saturated with water) of the sapogenin fraction afforded a mixture of 24(Z)-3-hydroxytirucalla- 7,24- dien-26-oic acid and 24(2)-3 p -hydroxytirucalla-8,24-dien-26-oic acid. From the aqueous hydrolysate, L-arabinose, L-rhamnose, D-xylose and D-glucose were isolated, as their alditol acetates, and identified by GLC. In case of shilajit, from different regions, both E- and Z-isomers of the triterpenoid sapogenins and the phenolic constituents were isolated and characterized.

Pharmacology

Pharmacological and immunological screening of these compounds, individually and in combination, established their significant contribution to the therapeutic efficacy of shilajit. Among the other organic compounds contributing to the bioactivity of shilajit, humic and fulvic acids, from shilajit humus, are noteworthy. Studies have shown shilajit to have positive adaptogenic properties on improving memory, handling
stress as well as antiinflammatory properties. It has shown to dramatically lower recovery time in muscle, bone and nerve injuries along with powerful immunomodulating or immune-stimulating properties.

Clinical Applications

Clinical applications of shilajit in Ayurveda, as a rasayan, are well documented. The effects of shilajit, as reported in the Ayurvedic literature, seem to suggest its influence on endocrine, autonomic, and brain functional changes. The discovery that these changes can be mediated by cytokines, released by activated immunologic cells, has opened up possibilities for similar mechanism of action of shilajit. Certain combinations of the phenolic and triterpenoid constituents and the fulvic acid of shilajit produced significant effects against restraint stress-induced ulcers. The mechanism of anti-ulcerogenic actions of shilajit is based on their effects on mucin contents, and on the concentrations of DNA and protein in the gastric juice. The combinations provided significant resistance to mucosa against the effects of ulcerogens and also prevented the shedding of mucosal cells. The anti-allergic action of these compounds was successfully tested against antigen and histamine releasing substances that induced degranulation of mast cells. The anti-stress activity of these compounds was suggested by their augmentation of murine swimming endurance exercises. Shilajit and its combined constituents also elicited and activated, in different degrees, murine peritoneal macrophages and activated splenocytes of tumour-bearing animals at early and later stages (unresponsive) of tumour growth. Shilajit from USSR, and its corresponding combined fractions, acted essentially as cell-growth factors in both normal and tumour cells by maintaining membrane integrity. The results obtained till now are sufficiently impressive to warrant expectation that more extensive and comprehensive studies on shilajit and its constituents would validate the Ayurvedic rasayan, shilajit, as more effective than several currently available clinically efficacious immunomodulators.
Uses

In folk medicine, shilajit has been used to treat diverse clinical conditions ranging from peptic ulcer to bone healing. Shilajit increases the carbohydrate/protein ratio and decreased gastric ulcer index, indicating an increased mucus barrier, antiinflammatory effect in carrageenan-induced acute pedal oedema, granuloma pouch and adjuvant-induced arthritis in rats. It is also used as aphrodisiac. Its anti-ageing properties have also been reported.

Contraindication

It is contraindicated in kidney stones.