Chapter 3

Plant profiles of

Camellia sinensis (L.) Kuntze,
Nigella sativa Linn. &
Piper longum Linn.
Chapter 3

Plant Profiles

Camellia sinensis (L.) Kuntze
(Theaceae)

Plant description

The plant Camellia sinensis (syn. Thea sinensis, or C. thea) is an evergreen shrub indigenous to Assam (India) and parts of China and Japan. In its native state, it grows to a height up to 9 m, but in cultivation it is pruned to 1.2-1.5 m (Duke, 2001). The leaves of the tea plant are used both as a social and medicinal beverage since 3000 B.C. Traditional medicinal systems worldwide have recommended the green tea to ameliorate headaches, bodyaches, digestion, enhancement of immune defences, detoxification, as an energizer and to prolong life (John, 1997; Leung, 1980; Anonymous; 2000).

Taxonomical description

Super division  Spermatophyta
Division  Magnoliophyta
Class  Magnoliopsida
Subclass  Dilleniidae
Order  Theales
Family  Theaceae
Genus  Camellia
Species  sinensis

Vernacular names

Hindi  Chaay
Sanskrit  Syamaparni
Urdu  Chaay
Arabic  Shay
Gujrati  Cha
Bengali  Cha
Tamil  Tey
Malyalam  Tey
Kannada  Teyaku
Oriya  Cha
Punjab  Cha

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Morphological characters

The lanceolate leaves are dark green, alternate, exstipulate, lanceolate to obovate, up to 30 cm long, 2-5 cm broad, pubescent, sometimes becoming glabrous, serrate, acute or acuminate; flowers 1-3, in axillary or subterminal cymes, deflexed, 2-5 cm broad, aromatic, white or pinkish, actinomorphic, sepals and petals 5-7, pedicels 5-15 mm long; stamens numerous; ovary 3-carpellate, each carpel 4-6 ovulate; capsules depressed-globose, brownish, lobate, 2 cm broad, valvate, with 1-3 subglobose seeds in each lobe; approximately 500 seeds/kg (Duke and Atchley, 1984; Kokate et al., 2005).

Fig 3.1: Leaves of Camellia sinensis

Cultivation

C. sinensis is an evergreen plant and grows in tropical to sub-tropical climates. In addition to tropical climates (at least 50 inches of rainfall a year), it also prefers acidic soils. Many high quality tea plants grow at elevations up to 1500 m, as the plants grow more slowly and acquire a better flavor. Only the top 1-2 inches of the mature plant are picked up. These buds and leaves are called flushes, and a plant will grow a new flush every seven to ten days during the growing season. Tea plants will grow into a tree if left undisturbed, but cultivated plants are pruned to waist height for ease of plucking. Two principal varieties are used, the small-leaved China plant (C. sinensis sinensis) and the large-leaved Assam plant (C. sinensis assamica) (Anonymous, 2000; Trease and Evans, 1985).
Geographical distribution

Tea is native to China where it grows wild. The Chinese determined that the leaves changed the flavor and taste of the water when they boiled and used to prevent sickness. Tea plant cultivation in China began about 4,000 years ago but it wasn't until the 8th century A.D. that outsiders (the Japanese) discovered it. Europeans finally introduced tea during the 17th century and the British spread its use by implementing new growing areas such as India. Tea also played an important role in the development of the United States—its taxation led to the Boston Tea Party, one of the issues that triggered the War of Independence. Americans further influenced tea use both by inventing tea bags and by starting the practice of drinking iced tea at the St. Louis World's Fair in 1904. The word "tea" can refer to the beverage, the leaves used to make the beverage and the magnolia-related evergreen shrub from which the leaves come. All tea plants belong to the same species but varying climates and soils combine in different ways to create a plethora of distinctive leaves. The processing of these leaves is responsible for the individual characteristics of each tea (Tapan et al., 2004; Anonymous, 2000).

Processing

The types of tea are distinguished by the processing they undergo. Tea leaves soon begin to wilt and oxidize if not dried quickly after picking. The leaves turn progressively darker because chlorophyll breaks down and tannins are released. This process, enzymatic oxidation, is called fermentation in the tea industry although no true fermentation happens (that is, the process isn't microorganism-driven). The next step in processing is to stop the oxidation process at a predetermined stage by heating, which deactivates the responsible enzymes. With black tea this is done simultaneously with drying. White black, green and oolong tea are the main types produced during processing (Reiko et al., 2005; Robert and Patrick, 2006; Balentine et al., 1997; Yamamoto et al., 1997).

White tea

It consists of young leaves (new growth buds) that have undergone no oxidation and buds shielded from sunlight to prevent formation of chlorophyll. White tea is produced in lesser quantities than most other styles, and can be correspondingly more expensive than tea from the same plant processed by other methods. It is less known in countries outside
of China, though this is changing with increased western interest in organic or premium teas.

**Green tea**

The oxidation process is stopped after a minimal amount of oxidation by application of heat, either with steam, or by dry cooking in hot pans. Tea leaves may be left to dry as separate leaves or they may be rolled into small pellets to make Gunpowder tea. This process is time consuming and is typically done with pekoes of higher quality. The tea is processed within one to two days of harvesting.

**Oolong**

Oxidation is stopped somewhere between the standards for green tea and black tea. The oxidation process takes two to three days. In China, semi-oxidized teas are collectively grouped as blue tea (literally: blue-green tea), while the term "oolong" is used specifically as a name for certain semi-oxidized teas.

**Black tea/Red tea**

The tea leaves are allowed to completely oxidize. Black tea is the most common form of tea in southern Asia African countries. The Chinese call it red tea because the actual tea liquid is red. Westerners call it black tea because the tea leaves used to brew it are usually black. The oxidation process will take between two weeks and one month. Black tea is further classified as either orthodox or as CTC (Crush, Tear, Curl, a production method). Unblended black teas are also identified by the estate they come from, their year and the flush (first, second or autumn).

**Tea Processing Chart** (http://www.teazonline.com/tea-production.htm)
Traditional uses

Today tea is consumed by more people and in greater quantity than any beverage except water. The flavor of tea is due to volatile oils, its stimulating property is due to caffeine, and its astringency is due to the tannin content (reduced in black teas by the fermentation process). In all parts of the world, tea like beverages are made from the leaves or flowers of a wide variety of other plants, often for their medicinal properties (Duke, 2001; Yamamoto et al., 1997; Mahmood et al., 2010)

Phytoconstituents reported

Tea leaves have more than 700 chemical constituents, among which flavanoids, amino acids, vitamins (C, E, K), caffeine and polysaccharides are important to human health (Christiane et al., 2001; Tsung, 2006; Chiehming et al., 2000; Naghma and Mukhtar, 2007). Following is the list of major phytoconstituents from C. sinensis leaves:

1. Catechins (30-42% dry weight)
   a. Epigallocatechin gallate-EGCG (11%)
   b. Epicatechin gallate-ECG (2%)
   c. Gallocatechin gallate-GCG (2%)
   d. Epigallocatechin-EC (10%)
   e. Gallocatechin
   f. Catechin

2. Theaflavin
   a. Theaflavin-3'-gallate
   b. Theaflavin-3'-galIate
   c. Theaflavin-3,3'-digallate

3. Thearubigens
4. Theogallin (2-3%)
5. Proanthocyanidin
6. Flavonols (5-10%)
   a. Quercetin
   b. Kaempferol
   c. Rutin
Chemical structures of major flavonols and polyphenols from *Camellia sinensis*

- **Quercetin**
- **Kaempferol**
- (-)-Epigallocatechin-3-gallate
- (-)-Epicatechin-3-gallate
- (-)-Epigallocatechin
- (-)-Epicatechin
7. Methylxanthines (7-9%)
   a. Caffeine (3-5%)
   b. Theobromine (0.1%)
   c. Theophylline (0.02%)

8. Amino acids
   a. Theanine (4-6%)

9. Organic acids (4-5%)
   a. Caffeic acid
   b. Quinic acid (2%)
   c. Gallic acid

10. Volatiles (0.02%)
    a. Linalool
    b. δ-Cardinene
    c. Geraniol
    d. Nerolidol
    e. cis-Jasmone

Bioactivities reported

Anti-Alzheimer activity: Choi et al (2001) showed that EGCG protected against beta-amyloid-induced neurotoxicity in cultured hippocampal neurons, an effect attributed to its antioxidant properties. In addition, Levites et al (2003) recently showed that EGCG regulated the processing of APP, through PKC activation, to the non-amyloidogenic soluble APP (sAPP), thus preventing the formation of the neurotoxic beta-amyloid.

Anti-cancer activity: Studies in animal models have demonstrated that green tea and EGCG could inhibit carcinogenesis at all stages, viz. initiation, promotion and progression (Chung et al., 2003). This multifaceted inhibition of the tumorigenic process was attributed to a combination of antioxidative, antiproliferative and pro-apoptotic effects (Gouni-Berthold and Sachinidis, 2004).

Anti-malarial activity: A crude extract of green tea as well as two of its main constituents EGCG and ECG strongly inhibited Plasmodium falciparum growth in-vitro. Both these catechins were found to potentiate the antimalarial effects of artemisinin without interfering with the folate pathway (Sannella et al., 2007).
Anti-diabetic activity: An aqueous solution of green tea polyphenols (GTP) was found to inhibit lipid peroxidation (LP), scavenge hydroxyl and superoxide radicals *in-vitro*. Concentration needed for 50% inhibition of superoxide, hydroxyl and LP radicals were 10, 52.5 and 136 mg/ml, respectively. Administration of GTP (500 mg/kg BW) to normal rats increased glucose tolerance significantly at 60 min. GTP was also found to reduce serum glucose level in alloxan diabetic rats significantly at a dose level of 100 mg/kg BW. Continued daily administration (15 days) of the extract 50 and 100 mg/kg BW produced 29 and 44% reduction in the elevated serum glucose level produced by alloxan administration (Sabu *et al.*, 2002).

Anti-hepatitis activity: The efficacy of a natural green tea extract (GTE) against HBV in a stably expressed HBV cell line HepG2-N10 was examined. The expression of viral antigens, HBsAg and HBeAg were determined by using enzyme linked immunosorbent assay (ELISA). Quantitative real-time-PCR (Q-PCR) was used for the determination of extracellular HBV DNA and intracellular replicative intermediates and nuclear covalent closed circular DNA (cccDNA). HBV mRNAs were also analyzed by reverse transcription PCR (RT-PCR). Results showed that the 50% effective concentration of GTE on HBsAg, HBeAg, extracellular HBV DNA and intracellular HBV DNA were 5.02, 5.68, 19.81, and 10.76 g/ml, respectively while the concentration of GTE with the inhibition percentage of 50% on proliferating cells was 171.8 g/ml. Similar analysis of the principal component of GTE, EGCG had relative weaker efficacy compared to GTE (Jun *et al.*, 2008).

Anti-microbial activity: Extract of black, white, green and red and rooibos tea had an inhibitory effect against *Bacillus cereus*. The second most sensitive strain was *Micrococcus luteus*, followed by *Pseudomonas aeruginosa*. In contrast *Escherichia coli* were only inhibited very weakly for white and green tea extracts (Almajano *et al.*, 2008).

Anti-oxidant activity: The antioxidant activity of black tea theaflavins and catechin derivatives in canola oil was examined. Oxidation was conducted at 95 °C by monitoring the oxygen consumption and decrease in the linoleic and α-linolenic acids of canola oil. All were tested at a concentration of 0.5 mM. Catechins, including (-)-epicatechin, (-)-epicatechin gallate, (-)-epigallocatechin and (-)-epigallocatechin gallate (EGCG), were more effective than theaflavins, namely, theaflavin-1, theaflavin-3-gallate, theaflavin-3'-
gallate and theaflavin-3,3'-digallate, against the lipid oxidation of canola oil (Ya-Lun et al., 2004; Reza et al., 2007).

**Anti-Parkinson's activity:** EGCG, administered orally in doses as low as 25 mg/kg, prevented loss of dopaminergic neurons in the substantia nigra and preserved striatal levels of dopamine (Choi et al., 2002). Recently, Mandel et al. (2004) also showed that EGCG prevented the accumulation of iron and alpha-synuclein in MPTP-treated mice. These effects have been attributed to the antioxidant activity and iron-chelating properties of EGCG, respectively. Although several in-vitro studies have also implicated other pathways of neuroprotection, such as the enhancement of PKC phosphorylation and inhibition of pro-apoptotic genes, particularly at low EGCG concentrations, these effects have yet to be established in vivo.

**Anti-stroke activity:** EGCG has been shown to afford protection against neuronal damage after ischemia in gerbils, when administered systemically at 50 mg/kg immediately after excitotoxic ischemic insult. At this dose, EGCG was also found to exhibit a significant antioxidant effect in rats and protected against neurological deficit and infarction due to the focal ischemia, when administered 24 h after a transient cerebral occlusion (Choi et al., 2002).

**Anti-tumour activity:** Green tea components have enhancing effect on doxorubicin (DOX) induced antitumor activity. Components, such as caffeine, theanine, EGCG and flavonoids have inhibitory effects on the DOX efflux from Ehrlich ascites carcinoma cells. It is suggested that EGCG and flavonoids may enhance DOX induced antitumor activity and increase the DOX concentrations in tumors through the inhibition of DOX efflux (Yasuyuki et al., 2000).

**P-gp inhibiting activity:** Green tea polyphenols (GTPs) at a dose of 30 mg/ml inhibited the photolabeling of P-gp by 75% and increased the accumulation of rhodamine-123 (Rh-123) 3-fold in the multidrug-resistant cell line CHRC5, indicating that GTPs interacted with P-gp and inhibited its transport activity (Julie et al., 2002).

**Safety profile**

Generally, green tea has little or no side effects at least up to 10 cups/day. However because it contains caffeine, excessive amounts may cause heart related problems (Robert and Patrick, 2006).
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Plant Profiles

*Nigella sativa* Linn.
(Ranunculaceae)

**Plant description**

*Nigella* is a genus of 14 species of annual plants belonging to the family Ranunculaceae. It is native to southern Europe, North Africa and Southwest Asia. Several species are grown as ornamental plants in gardens, popular for their seed capsules (Daniel and Maria, 2000). *Nigella sativa* commonly known as black cumin and *Kalonji* in Hindi is an annual flowering plant, indigenous to southwest Asia. The plant is common in the Mediterranean region but now found widely in India (Jammu and Kashmir, Himachal Pradesh, Bihar, Assam and Punjab). The herb is cultivated in Bengal and north-east India (Anonymous, 2001)

**Taxonomic description**

- **Kingdom**: Plantae
- **Division**: Magnoliophyta
- **Order**: Ranunculales
- **Family**: Ranunculaceae
- **Genus**: *Nigella*
- **Species**: *sativa*

**Vernacular names**

- **Hindi**: Kalonji, kalajira, mugrela
- **English**: Small Fennel, Black Cumin
- **Sanskrit**: Kalonji, Kalajira, Kalajaji, Mugrela, Upakuncika
- **Gujrati**: Kalonji-jiram
- **Bengali**: Kalijira, mungrela
- **Tamil**: Karunjiragam
- **Telgu**: Nellajeelakaira
- **Kannad**: Karejirage
- **Malyalam**: Karunchiragam
- **Urdu**: Kalonji
Morphology
It is a small prostrate annual herb about 45 cm high with 2-3 slender pinnatisect leaves, 2-4 cm long cut into linear and oblong segments. Flowers are pale, blue on solitary long peduncles, seeds are trigonous and black in color. The plant has a rather stiff, erect, branching stem, bears deeply-cut grayish-green leaves and terminal grayish-blue flowers, followed by odd, toothed seed vessels, filled with small compressed seeds, usually three-cornered, with two sides flat and one convex, black or brown externally white and oleaginous with a strong agreeable aromatic odor, like that of nutmegs, and a spicy, pungent taste. The flowers are delicate, and usually colored pale blue and white, with 5-10 petals (Fig 3.2). The fruit is a large and inflated capsule composed of 3-7 united follicles, each containing numerous seeds. Seeds are angular, dark gray in color. It has a pungent bitter taste and a faint smell of strawberries (Dwivedi, 2003; Kirtikar and Basu, 2000a).

Fig 3.2: *Nigella sativa* (whole plant, flower and seeds).

History
Although the archeological evidence about the earliest cultivation of *N. sativa* is still scanty, but there are reports showing that *N. sativa* seeds have been found in several sites from ancient Egypt, including Tutankhamen's tomb. Although its exact role in Egyptian
culture is unknown, it is known that items entombed with a pharaoh were carefully selected to assist him in the after life (Dwivedi, 2003).

Traditional uses

*N. sativa* has been used for medicinal purposes for centuries, both as herb and pressed into oil, in Asia, Middle East and Africa. It has been traditionally beneficial for a variety of conditions and treatments related to respiratory health, stomach and intestinal disorders, kidney and liver function, circulatory and immune system support, and for general well-being. In Islam, it is regarded as one of the greatest forms of healing medicine available. In the Unani system of medicine, *N. sativa* is considered as a valuable remedy for a number of diseases. The seeds have been traditionally used in the Middle East and Southeast Asian countries to treat ailments including asthma, bronchitis, rheumatism and related inflammatory diseases, to increase milk production in nursing mothers, to promote digestion and to fight parasitic infections. Its oil is beneficial to treat skin conditions such as eczema and boils and to prevent cold symptoms (Dwivedi, 2004; Dwivedi et al., 2007). The seeds are useful as flavoring to improve digestion and produce warmth, especially in cold climates. They are scattered in the folds of woollen fabrics to preserve them from insect damage. In India the seeds are consumed as a carminative and stimulant to ease bowel and indigestion problems and are given to treat intestinal worms and nerve defects to reduce flatulence and induce sweating. Dried pods are sniffed to restore a lost sense of smell. *Nigella* seeds are carminative, aromatic, stimulant, diuretic, anthelmintic, galactagogue and diaphoretic. They are taken as a condiment in curries. A tincture prepared from the seeds is useful in indigestion, loss of appetite, diarrhoea, dropsy, amenorrhoea and dysmenorrhoea and as remedy for worms and skin eruptions. Externally the oil is applied as an antiseptic. To arrest vomiting, the seeds are roasted and given internally (Dwivedi, 1999; Dwivedi et al., 2006; Khare, 2004).

Phytoconstituents reported

Phytochemical analysis of black cumin gave the following values: total ash, 3.8-5.3; ash insoluble in HCl, 0.0 - 0.5; volatile oil, 0.5-1.6; ether extract (fatty oil), 35.6 - 41.6; and oleic acid 3.4 – 6.3 % (Anonymous, 2001).
Chemical structures of phytoconstituents reported from *Nigella sativa*

Thymoquinone

Dithymoquinone

Thymol

Thymohydroquinol

Nigellicine

Nigellimine and Nigellimine N-oxide

Methylmonadeca-15, 17-dienoate
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Fatty acids
The seeds contained numerous esters of structurally unusual unsaturated fatty acids mainly with terpene alcohols. Saturated fatty acids (palmitic, stearic acid) amount to about 30% or less (Dwivedi et al., 2007).

Essential oil
In the essential oil thymoquinone was identified as the main component (up to 50%) besides p-cymene (40%), pinene (up to 15%), dithymoquinone and thymohydroquinone. Other terpene derivatives were present only in trace amounts: carvacrol, carvone, limonene, 4-terpineol, citronellol. Furthermore, the essential oil contains significant...
amounts of fatty acid ethyl esters. On storage, thymoquinone yielded dithyminonestrene and higher oligocondensation products (Cevdet and Semih, 1993).

Alkaloids
Isoquinoline and imidazole derived alkaloids have been isolated from seeds of *Nigella* cultivated in Pakistan (Atta-ur-Rahman *et al.*, 1985a, 1985b). Furthermore, traces of alkaloids were found which belong to two different types: isoquinoline alkaloids were represented by nigellimine and nigellimine-N-oxide, and pyrazole alkaloids include nigellidine and nigellicine (Cevdet and Semih, 1993).

Saponins
Steroidal triterpenic saponins have been reported from the seeds of *N. sativa*. It also contained prosaponins which contained three additional sugar units. Both saponin and prosaponin occurred as glycosides (Akbar *et al.*, 1988).

Lipids
*Nigella* seeds are covered with a thick waxy cuticle giving it a shining appearance. The petroleum ether extract of its seeds revealed the presence of novel lipid that are mainly esters of higher fatty acids as methyl nonadecenoate, pentyl hexadecenoate and pentyl pentadecenoate (Mehta *et al.*, 2008).

Bioactivities reported
**Anthemintic activity:** *N. sativa* was found to have an anthemintic activity against tapeworm comparable to that of piperazine (Agarwal *et al.*, 1979).

**Anti-diabetic activity:** Significant hypoglycemic activity has been reported in the seeds of *Nigella* and is thought to be due to the essential oil present. Clinical studies have confirmed these results and supported that the antidiabetic action of the plant extract (Anwar-ul-Hasan *et al.*, 2004; Al-Hader *et al.*, 1993).

**Anti-fertility activity:** The anti-fertility activity of *N. sativa* in male rats has been established as shown by an inhibition of spermatogenesis and a significant reduction in sialic acid content of the testis, epididymis, seminal vesicles and prostate (Ali and Blunden, 2003). A reversible inhibition of spontaneous smooth muscle contraction and inhibition of uterine smooth muscle contraction induced by oxytocin stimulation have been observed (Aqel and Shahin, 1996).
Anti-inflammatory activity: Asthma and arthritis are chronic inflammatory disorders involving a variety of inflammatory mediators and different pathways. The fixed oil and thymoquinone from the seeds were found to inhibit eicosanoid generation in leucocytes and membrane lipid peroxidation and a significant reduction in rat paw oedema and a reduction in granuloma pouch weight were also observed. Nigellone in low concentration was effective in inhibiting the histamine release from the mast cells, which supported an antiasthmatic role for the plant (Houghton et al., 1995). The essential oil produced significant analgesic activity using chemical and thermal noxious stimuli methods such as acetic acid-induced writhing, hot plate and tail flick tests (Al-Ghamdi, 2001).

Anti-malarial activity: Intraperitoneal and oral administrations of ethanol, chloroform and aqueous seed extracts (50, 100, 200 and 400 µl/ kg) of N. sativa, were screened in the 4-day suppressive assays for their anti-malarial properties against Plasmodium berghei in mice (Abdulelah et al., 2007).

Anti-microbial activity: N. sativa exhibited strong antimicrobial activity against Salmonella typhi, Pseudomonas aeruginosa and others. The essential oil was effective against Gram positive and Gram negative bacteria. However, sensitivity against Gram positive bacteria such as Staphylococcus aureus and Vibrio cholerae was found to be stronger. Bacteria like Staphylococcus aureus, S. pyrogenes and S. viridans are more susceptible to N. sativa. In an in-vitro study, the volatile oil showed activity comparable to ampicillin. The activity of the volatile oil also extended to drug-resistant strains of Shigella spp, Vibrio cholerae and Escherichia coli and was found to have a synergistic action with streptomycin and gentamycin (Salem, 2005).

Anti-oxidant activity: N. sativa seed oil and its main constituent inhibited peroxidation in ox brain phospholipids liposomes (Houghton et al., 1995).

Antitussive activity: The antitussive activity of thymoquinone, a constituent of N. sativa seeds, has been reported using the nebulized solution of citric acid 20 % in guinea pigs (Hossein et al., 2008).

Cytotoxic activity: Cytotoxic and immunopotentiating effects of N. sativa have been established. The long chain fatty acids are thought to contribute to the antitumour activity. The extract showed a modulatory effect in cisplatin-induced toxicity in mice and a protective effect against cisplatin-induced falls in haemoglobin levels and leucocyte
counts (Salem, 2005). *In-vitro* and *in-vivo* anti-cancer effect of *N. sativa* seed extracts has been evaluated (Ait-Mbarek et al., 2007).

**Hepatoprotective activity:** Thymoquinone, one of the active constituents of *N. sativa*, possessed hepatoprotective activity. An *in-vitro* study showed the protective effect against tert-butyl hydroperoxide (TBHP)-induced oxidative damage to hepatocytes. The activity was demonstrated by a decreased leakage of alanine transaminase and aspartic transaminase (Salem, 2005).

**Immunomodulatory activity:** Recently, well-designed studies confirmed the immunomodulatory effects of the whole extract of *N. sativa* seeds and their protein components *in-vitro* (Haq et al., 1995 and 1999; Mansour, et al., 2001).

**Other activities:** Thymoquinone showed comparable activity against *Aspergillus niger* although in relatively higher concentrations (Abdul-Rahman et al., 2007). The anticonvulsant effects of thymoquinone, the major constituent of *N. sativa* seeds, were investigated using pentylenetetrazole and maximal electroshock induced seizure models (Hosseinzadeh and Parvardeh, 2004). Other reports include hypocholesterolaemic, anti hypertensive and galactagogue effects. The seeds are considered carminative, stimulant, diuretic, emmenagogue, galactagogue, whereas their oil is applied externally for skin eruptions (Kirtikar and Basu, 2000a). *N. sativa* has been used for thousands of years in the Middle East for allergies, asthma, and for treating immune disorders. It increases the number of mammary cells in laboratory animals. Great research has been done on *N. sativa* in regards to its anti-cancer properties, especially breast cancer with promising results (Sharma et al., 2009). The seed oil has been reported to possess antibacterial and CNS depressant effects (Morsi, 2000; Nair, 2005; Rathee et al., 1982).

These activities have been attributed to fixed oil, volatile oil or their components.

**Safety profile**

No health hazards or side effects are known with the proper administration of designated therapeutic dosages. Seeds of *N. sativa* have a long history of use for food and medicinal purposes. No adverse or side effects have been reported when used within the recommended dosage, although dermatitis has been reported (Sharma et al., 2009).
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**Piper longum** Linn.

*(Piperaceae)*

Piperaceae family contains approximately 2,000 species which are widely distributed and commonly used in tropical and subtropical regions as food, spice, traditional medicines and pest control agents (Nair and Burke, 1990; Shultes and Raffauf, 1990). *P. longum* commonly known as long pepper, sometimes called Javanese, Indian or Indonesian long pepper, is a flowering vine cultivated for its fruits which is usually dried and used as a spice and seasoning. Long pepper is a close relative of *P. nigrum* giving black, green and white pepper, and has a similar, though generally hotter, taste. The word pepper itself is derived from the Sanskrit word for long pepper, *Pippali*. The Aryans were the first exporters of both kinds of pepper from the tropical forests of South Asia. (Pongboonrod, 1976, Saralamp et al., 1996).

**Taxonomic description**

- **Kingdom**: Plantae
- **Division**: Angiosperms
- **Class**: Magnolids
- **Order**: Piperales
- **Family**: Piperaceae
- **Genus**: *Piper*
- **Species**: *longum*

**Vernacular names**

- **Hindi**: Gazpipal, Pipli
- **Sanskrit**: Chanchala, Chapal
- **Urdu**: Pipul
- **Arabic**: Darfilfil
- **Gujrati**: Piper, Pipli
- **Bengali**: Piplamul, Piplamor
- **Tamil**: Argadi, Atti, Kalidi
- **Telgu**: Modi, Pipalli, Pipallu
- **Punjab**: Darfilfil, Filfildaraz

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*Jamia Hamdard*
Morphology
It is a small shrub with a large woody root and numerous creeping, jointed stems, thickened at the nodes. The leaves are alternate, spreading, without stipules and blade varying greatly in size. The lowest leaves are 5-7 cm long, whereas, the uppermost 2-3 cm long. The inflorescence is a cylindrical, pedunculate spike. The flowers are in solitary spikes. The female flower is up to 2.5 cm long and 4-5 mm in diameter, the male flowers being larger and more slender. The fruits, berries are in fleshy spikes 2.5-3.5 cm long and 5 mm thick, oblong, blunt and blackish green in color. The mature spikes collected and dried, form the commercial *pippali* and the root is known as *pippalimula*. The fruit of the pepper consists of many minuscule fruits, each about the size of a poppy seed, embedded in the surface of a flower spike. The fruits contain the alkaloid piperine, which contributes to their pungency (Kirtikar and Basu, 2000b)

![Image of Piper longum fruits](image)

Fig. 3.3: *Piper longum* fruits

Geographical distribution
The plant grows all over India, in evergreen forests and is cultivated in Assam, Tamilnadu and Andhra Pradesh. It is considered a native of South Asia and is found both wild as well as cultivated, throughout the hotter parts of India from central to the northeastern Himalayas. The herb also grows wild in Malaysia, Singapore, Bhutan and Myanmar (Anonymous, 2003).
Traditional uses
The dried fruit spikes are extensively used for flavouring a variety of foods. They are considered to have stimulant, carminative, laxative and stomachic properties. The berries are also given with honey to treat asthma, coughs and sore throats. The root is a stimulant and is also used to cure gout, rheumatism and lumbago. The whole plant is considered by tribal people in India to be useful in splenic disorders, cholera, dysentery, asthma, cough and bronchitis (Anonymous, 1987).

Medicinal uses
The fruits are aromatic, stimulant, carminative and prescribed to relieve constipation, gonorrhea, paralysis of the tongue, diarrhea, cholera, chronic malaria and viral hepatitis. *P. longum* is most commonly ingested to prevent respiratory infections such as stomachache, bronchitis, diseases of the spleen, cough, tumors, and asthma. When applied topically, it soothes and reduces muscular pains and inflammation. In Ayurvedic medicine, it is said to be a good rejuvenator. *P. longum* helps to stimulate the appetite and it dispels gas from the intestines. An infusion of *P. longum* root is used after birth to induce the expulsion of the placenta. It is used as sedative in insomnia and epilepsy. Also as cholangogue in obstruction of bile duct and gall bladder (Pei, 1983). The fruit and root are widely utilized in Ayurveda for the preparation of many recipes. It is given as a remedy to mitigate respiratory and digestive irregularities and in malarial disease. It is a part of *Trikatu* (three pungent herbs). Individually long pepper is consumed in correcting for digestive disturbances and minor respiratory ailments. *Trikatu* is an important constituent in many Ayurvedic formulations. Research studies suggest that intake of *Trikatu* enhances bioavailability of the substances administered along with them. (Anonymous, 1979; Antarkar and Vaidya, 1983)

Phytoconstituents reported
Alkaloids and amides
The fruit contains a large number of alkaloids and related compounds, the most abundant of which is piperine, together with methyl piperine, piperlongumine, pipernonaline, pipерундекалидине, piperettine, asarinine, pellitorine, piperlongumidine, retrofractamide A, peregumidiene, brachystamine-B, a dimer of desmethoxypiplartine, N-isobutyl-decadienamide, brachyamide-A, brachystine, pipercide, dehydropipernonaline piperidine,
Chemical structures of phytoconstituents reported from *Piper longum*
piperderidine longamide, tetrahydro piperine, tetrahydropiperlongumine and trimethoxy
cinnamyl-piperidine have been found in the roots (Chatterjee and Dutta, 1966;
Madhusudhan and Vandana, 2001; Byeoung-Soo et al., 2002).

Esters
The fruits contain tridecyl-dihydro-p-coumarate, eicosanyl-(E)-p-coumarate and Z-12-
octadecenoic-glycerol-monoester (Sarvesh et al., 2005).

Lignans
Sesamin, pulviatilol, fargesin and others have been isolated from the fruits (Parmar et al.,
1997).

Volatile oil
The essential oil of the fruit is a complex mixture, the three major components of which
are (excluding the volatile piperine) caryophyllene and pentadecane (both about 17.8%)
and bisaboline (11%). Others include thujene, terpinolene, zingiberene, p-cymene, p-
methoxyacetophenone and dihydrocarveol (Madhavi et al., 2009).

Bioactivities reported
Anti-amoebic activity: The fruits were tested for their efficacy against Entamoeba
histolytica in-vitro and experimental caecal amoebiasis in-vivo. Both the ethanolic extract
and isolated piperine produced an improvement of 90% and 40%, respectively, in rats
with caecal amoebiasis (Ghoshal and Lakshmi, 2002).

Anti-asthmatic activity: Studies have been carried out to validate the traditional claims
of Ayurveda for antiasthmatic activity of P. longum. An extract of the fruits in milk
reduced passive cutaneous anaphylaxis in rats and protected guinea pigs against antigen
induced bronchospasm (Dahanukar, et al., 1984).

Anti-bacterial activity: The essential oil of P. longum showed antibacterial action
against a number of bacterial strains although a 50% ethanolic extract of the fruits did not
show any effect. 3'-Piperlonguminine was found to have potent activity against Bacillus
subtilis while piperine was more effective against Staphylococcus aureus (Abbas et al.,
2007).

Anti-inflammatory activity: A marked anti-inflammatory activity of a decoction of P.
longum fruits has been reported using carrageenan-induced rat oedema (Lee et al., 1984).
Antioxidant activity: The antioxidant activity of the methanolic extract was assessed by 1-diphenyl-2-picrylhydrazyl (DPPH) method; it showed potential antioxidant activity (Nooman et al., 2008).

Anti-platelet effects: The inhibitory effects of four acidamides, piperine, pipernonaline, piperoctadecalidine, and piperlongumine, isolated from the fruits of *P. longum* on washed rabbit platelet aggregation were examined. All of the four tested acidamides showed dose-dependent inhibitory activities on washed rabbit platelet aggregation induced by collagen, arachidonic acid (AA), and platelet-activating factor (PAF), except for that induced by thrombin. Piperlongumine, in particular, showed stronger inhibitory effects than other acidamides to rabbit platelet aggregation induced by collagen, AA and PAF (Parka et al., 2007).

Bio-availability enhancement: Piperine has been shown to enhance the bio-availability of structurally and therapeutically diverse drugs, possibly by modulating membrane dynamics, due to its easy partitioning and increasing permeability. The effect of Trikatu, a compound Ayurvedic preparation containing *P. longum* as one of the major ingredients, was tested in combination with other drugs. The study reported that Trikatu increased their bio-availability either by promoting rapid absorption from the gastrointestinal tract or by protecting the drug from being metabolized during its first passage through the liver after being absorbed, or by combination of both mechanisms (Johri and Zutshi, 1992).

Fungicidal activity: Fungicidal activity of *P. longum* fruit-derived materials toward six phytopathogenic fungi, *Pyricularia oryzae*, *Rhizoctonia solani*, *Botrytis cineria*, *Phytophthora infestans*, *Puccinia recondita*, and *Erysiphe graminis*, was tested using a whole plant method *in-vivo*. It was comparable to synthetic fungicides (chlorothalonil and mancozeb) and four commercially available compounds (eugenol, piperine, piperlongumine, and piperettine) derived from *P. longum* (Sung-Eun et al., 2001).

Hepatoprotective activity: Piperine exerted significant protection against tertiary butyl hydroperoxide and carbon tetrachloride induced hepatotoxicity, by reducing both *in-vitro* and *in-vivo* lipid peroxidation. A fruit extract was assessed in rodents for its hepatoprotective action against CCl4 induced acute, chronic and reversible damage and chronic irreversible damage, using morphological, biochemical and histopathological assessment parameters. The extract improved the regeneration process by restricting
fibrosis, but offered no protection against acute damage or against cirrhotic changes (Christina et al., 2006).

**Hypocholesterolaemic activity:** Methyl piperine significantly inhibited the elevation of total serum cholesterol, and the total cholesterol to HDL-cholesterol ratio, in rats fed with a high cholesterol diet. The unsaponifiable fraction of the oil of *P. longum* also significantly decreased total serum cholesterol and hepatic cholesterol in hypercholesterolaemic mice (Jin et al., 2009).

**Immunomodulatory activity:** Tests such as haemaglutination titre (HA), macrophage migration index (MMI) and phagocytic index (PI) in mice has demonstrated the immunostimulatory action of *P. longum* fruits. The effect was more prominent at lower doses (225 mg/kg) and was marginally reduced when the dose was increased. In another study, it was found to offer protection against externally induced stress. A famous Ayurvedic preparation containing long pepper, *Pippali Rasayana*, was tested in mice infected with *Giardia lamblia* and found to produce significant activation of macrophages (Choudhary, 2006).

**Insecticidal activity:** Two alkaloids isolated from *P. longum*, pipernonaline (LD₅₀=125 mg/l) and piperoctadecalidine (LD₅₀=95.5 mg/l), showed insecticidal activity towards *Myzus persicae* Sulzer (Aphididae). Piperoctadecalidine (LD₅₀=246 mg/l) but not pipernonaline showed acaricidal activity against *Tetranychus urticae* (Tetranychidae) (Byeoung-Soo et al., 2002; Ian et al., 2008).

**MAO inhibitory activity:** Methylpiperate, guineensine, and piperlongumunine were isolated from the fruits of *P. longum* and evaluated for their MAO inhibitory activities in mouse brain (Seon et al., 2008).

**Stimulant effects:** Piperine isolated from *P. longum* showed a central stimulant action in frogs, mice, rats and dogs and increased the hypnotic response in mice. It antagonised respiratory depression induced by morphine or pentobarbitone in anaesthetised dogs and a petroleum ether extract of the fruits antagonised morphine-induced respiratory depression in mice. A comparative study conducted with piperine and nalorphine, for effects against morphine-induced respiratory depression and analgesia, found that both reversed respiratory depression but unlike nalorphine, piperine did not antagonise morphine induced analgesia in rats (Singh et al., 1973).
Safety profile
Since it is so widely used in cooking and traditional medicine, it is generally assumed to be safe in moderate doses. However, as the fruits are reported to have contraceptive activity in experimental models, its use during pregnancy and lactation should be avoided. Piperine may interfere with enzymatic drug biotransformations, resulting in the inhibition of hepatic arylhydrocarbon hydroxylase (AHH) and UDP glucuronyltransferase, and alter the pharmacokinetic parameters of barbiturates and phenytoin. A single oral dose of 3 g/kg body weight in experimental animals, and chronic toxicity studies with 100 mg/kg body weight for 90 days, revealed no untoward effects. In the evaluation of antifertility activity, long pepper at a dose of 1 g/kg body weight was found to be an effective contraceptive agent without toxic or teratogenic effects (Inder et al., 2007; Govindarajan, 1977).
References


Chapter 3

Plant Profiles


*Ph. D Thesis* 49  *Jamia Hamdard*


Chapter 3


