

PIPER LONGUM (PIPPALIMOOL): A REVIEW ON MEDICINAL IMPORTANCE AND HEALTH CARING ACTIVITIES

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ABSTRACT

Medicinal principles are present in different parts of the plant like root, stem, bark, heartwood, leaf, flower, fruit or plant exudates. These medicinal principles are separated by different processes; the most common being extraction. Extraction is the separation of the required constituents from plant materials using a solvent. Medicinal plants are known as the 'backbone of the traditional medicinal system. More than 3.3 billion people in developing countries rely on medicinal plants to treat various diseases. One such plant is *Piper longum* is also known as Javanese, long pepper, pippalimool (the root of *Piper longum* Linn.). The root is useful in bronchitis, stomach ache, diseases of spleen and tumours. Fruit is useful in *vata* and *kapha*, asthma, bronchitis, abdominal complaints, fever, leucoderma, urinary discharges, tumours, piles, insomnia and tuberculosis. There are some reported experimental studies that showed the pharmacological activities of *P. longum* such as neuroprotective, anti-inflammatory, analgesic, antibacterial, antidiabetic, antiulcer and many more. The extract of *P. longum* fruit showed effective antibacterial activity against selected bacteria or microbes, the plant extracts exhibit significant antibacterial activity when tested against different bacterial pathogens such as *Staphylococcus albus*, *Pseudomonas aeruginosa*, *E. coli*, *Bacillus megaterium* and *Salmonella typhi*.

KEYWORD: *Piper longum*, pippalimool, Phytochemistry, Antibacterial, Antimicrobial activity.

INTRODUCTION

Herbs are staging a comeback and herbal 'renaissance' is happening all over the globe. The herbal products today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment. Although herbs had been prized for their medicinal, flavouring and aromatic qualities for centuries, the synthetic products of the

modern age surpassed their importance, for a while. However, the blind dependence on synthetics is over and people are returning to them at urals with hope of safety and security.

Piper longum

Long pepper is a slender aromatic climber whose spike is widely used in ayurvedic and unani systems of medicine particularly for diseases of respiratory tract. *Pipalarishta*, *Pippalyasava*, *Panchakola*, *Pippalayadilauha*, and *Lavana bhaskar churan* are common ayurvedic preparations made out of the dry spikes of female types. Its roots also have several medicinal uses. Root and fruit are used in gout and lumbago. The infusion of root is prescribed after parturition to induce the expulsion of placenta. The root and fruit decoction are used in acute and chronic bronchitis and cough. It contains the alkaloid piperine which has diverse pharmacological activities, including nerve depressant and antagonistic effect on electroshock and chemo shock seizures as well as muscular in coordination.

Distribution

The plant Long pepper is a native of Indo-Malaya region. It was very early introduced to Europe and was highly regarded as a flavor ingredient by the Romans. The Greek name "*Peperi*", the Latin "*Piper*" and the English "*Pepper*" were derived from the Sanskrit name "*Pippali*". It grows wild in the tropical rain forests of India, Nepal, Indonesia, Malaysia, Srilanka. In India, it is seen in Assam, West Bengal, Uttar Pradesh, Madhya Pradesh, Maharashtra, Kerala, Karnataka and Tamil Nadu. It is also cultivated in Bengal, Chirapunchi area of Assam, Akola-Amravati region of Maharashtra, Anamalai hills of Tamil Nadu, Orissa, Uduppi and Mangalore regions of Karnataka. Bulk of Indian long pepper comes from its wild growth in Assam, Shillong and West Bengal, supplemented by imports from Sri Lanka and Indonesia (Viswanathan, 1995).

Taxonomy

Piper longum Linn., is a member of Piperaceae family. The plant is a glabrous perennial under shrub with erect or scandent nodose stem and slender branches; the latter are often creeping or trailing and rooting below or rarely scandent reaching a few meters height. Leaves are simple, alternate, stipulate, and petiolate or nearly sessile; lower ones broadly ovate, cordate; upper ones oblong, oval, all entire, smooth, and thin with reticulate venation; veins raised beneath. It flowers nearly throughout the year. Inflorescence is spiking with unisexual small a chlamydeous densely packed flowers and form very close clusters of small grayish green or darker grey berries. Female spikes with short thick stalk varying from 1.5 to 2.5 cm in length and 0.5 to 0.7 cm in thickness.

A number of geographical races are available in different agro climatic regions of India; the most popular being Assam, West Bengal and Nepal races. *Piper officinarum* DC; syn. *Chavica officinarum* Miquel, *Piper pepuloides* and *Piper chaba* Hunter are the other related species of importance.

Long pepper was considered one of the major Indian exporters for nearly 2400 years. Theophrastus categorized pepper in two divisions i.e. round one and another one which is long. This plant is mainly utilized as a spice and as a drug in Europe during the medieval period and in the 19th century. It is the source of the drugs Pippali and Pippalimulam. The fruit of *P. longum* has been used as a flavor since ancient times and is used as a preservative in pickles, food items, medicine and traditional drinks (Subramaniam *et al*, 2021). It is an aromatic climber and is widely distributed in the tropical and subtropical regions of the world. It is mainly used for cooking purposes as a spice. Medicinally, the plant is reported as a good remedy to cure menstrual pain, gonorrhoea, sleeping problems, tuberculosis, respiratory tract

infections, arthritic conditions and chronic gut-related pain (Mehta *et al*, 1998). In Ayurveda, Unani, Siddha the roots and fruits of *P. longum* are used to treat fever, asthma, hemorrhoid infection, bronchial stress, abdominal pain, inflammation, jaundice diarrhea and antidote to snake bite.

The main active constituent present in the *P. longum* plant is piperine which is reported to have CNS depressant, analgesic, antipyretic, antioxidant, (Wakade *et al*, 2008) anti-inflammatory, (Ratner 1991) and hepatoprotective properties. (Gurumurthy *et al*, 2012). In Ayurveda, it comes under panchakola, Shudhashana and is considered a great remedy for dipaniya (stomachic), pachaniya (digestive). From various clinical studies, it was reported that pippali shows significant effects against bronchial asthma in children (Dahanukar *et al*, 1984).

Botanical Description

Piper longum is a small, perennial climber, an aromatic shrub that belongs to the Piperaceae family. The roots of the plant are woody, wide ovate with cordate leaves. The stem is creeping, jointed and thickened at the nodes. The leaves are spreading, alternate, without stipules and with blades that varies greatly in size. The lowest leaves are 5- 7 cm long and the uppermost leaves are 2-3 cm long. Flowers are cylindrical with solitary spikes. The fruits are small, ovoid that grow in fleshy spikes, blunt, oblong, blackish-green with length 2.5-3.5 cm and 5 mm width. The mature spikes are long, cylindrical, and oblong. The berries are red or black with aromatic odor and pungent taste that is collected and dried as the commercial form of pippali. The root radix is known as pippalimula (Manoj *et al* 2004).

Phytochemical Constituents

The main active constituents present in *P. longum* plant are alkaloids which include piperine, piper longuminine, piper longumine and methyl-3,4,5- tri methoxycinnamate (Chatterjee A, Dutta CP. 1966). The fruit part consists of volatile oil (1%), protein, starch, alkaloids, saponins, carbohydrates and amygdalin, a waxy alkaloid Nisobutyldeca-trans-2-trans-4-dienamide, alkaloids piperine, calcium, phosphorus, iron and a terpenoid substance. Lignans and esters such as sesamin, (Atal CK.1966). pulvuatilol, fargesin, Z-12-octadecenoic-glycerolmonoester, tridecyl-dihydro-p-coumarate and eicosanyl- (E)-p-coumarate were also isolated from the fruit part of the plant (Tabuneng *et al* 1983). The root part of the plant contains piperlongumine or pipartinine, piperine and dihydro stigmasterolas arinine, pellitorine, refractomide A, brachystine, pipericide, piperderidine, piperundecalidine, iperonaline, methyl piperine, terahydropiper longumine, dehydropiper nonaline piperidine, trimethoxy cinnamoyl-piperidine and piperlongumine, (Parmar *et al*, 1998, Lee *et al*, 2001). The dried spikes of the plant consist of 0.7% essential oil with a spice odor. The essential oil of the plant contains sesquiterpenes, caryophyllene and hydrocarbons. Other chemical constituents present are sesamine, dihydro stigmasterol, piperacide, piperundecalidine, pipernonaline, dieudesmin and sitosterol. The seed part of the plant contains sylvatine and dieudesmin.

Medicinal applications of *Piper longum*

Piper longum is used in various formulations such as pain balm, relief balm, cough syrups, heart and geri /stress care and joint care balm. Some important formulations include Trikatu, Vardhamanas Pippali rasayana, Talisapatradi churna, pippalyedyesava, kanakasava, balacaturbhadrika, shringyadi churna, amritarishta (amrutharishtam), Gudapippalyadi choorna, shiva gutika, Abhayaristam, Draksaristam, Chayavanaprasam, Pippalyasavam and Kaishore guggulu, Pancakola Curna, Dasamula taila, Dasam ulastapalaka ghrta, Asvagandhadyarista, Amrtariasta, Ayaskrti, Gudapippali (Sivarajan and Balachandran 1994).

Antibacterial, Antimicrobial and Anti-amoebic

The ethyl acetate extract of *P. longum* fruit showed effective antibacterial activity against selected bacteria or microbes using the agar well diffusion method (Chauhan *et al*, 2019). In another study, the plant extracts exhibit significant antibacterial activity when tested against different bacterial pathogens such as *Staphylococcus albus*, *Pseudomonas aeruginosa*, *E. coli*, *Bacillus megaterium* and *Salmonella typhi*. The methanolic extract of the *P. longum* fruit showed significant antimicrobial activity by inhibiting the severity of cercal wall ulceration in mice caused by *Entamoeba histolytica* (Sawangjaroen *et al*, 2004). The root and fruit extract of the plant showed significant antiamoebic activity against amoebiasis almost to the same extent. In another study, ethyl acetate and petroleum ether extract of *P. longum* showed antimicrobial activity against various microorganisms (Nabi *et al*, 2013).

Antidiabetic activity

The ethanolic extract of *P. longum* plant was demonstrated for the antidiabetic activity in diabetic rats. It was found that the oral administration of the extract restores the blood glucose level which ultimately stimulates the liver activities to maintain the normal homeostasis of blood glucose level (Ali *et al* 2007). Another study was conducted on streptozotocin-induced diabetic rats where an aqueous extract of the plant showed significant antidiabetic rat at a dosage of 200 mg/kg b.w. after 6 h of the treatment with the extract (Reddy KR. 2018).

Neuroprotective

The dichloromethane fraction of *P. longum* and *P. nigrum* was examined for the therapeutic effect of neuron injury after apoplexy using a middle cerebral artery occlusion model in rats. The extract was administered orally in the rat model for 14 days. The model exhibits a significant increase in PSD95, phosphorylated CaMK II (p-CaMK II), calmodin (CaM) and N-methyl D-aspartate receptor subtype 2B (NR2B) (Kumar *et al*, 2018).

Immunomodulatory

The alcoholic extract of *P. longum* was demonstrated to identify the Immunomodulatory action of the extract. The rat model was injected with the alcoholic extract of fruit and piperine constituent. A significant increase of the WBC counts and plaque-forming cells contributing antibodies production was observed which ultimately stimulate the hematopoietic system indicating stem cell proliferation and overall immune system (Bezerra *et al*, 2008).

Anti-tumor

The piperine and piplartine constituent of the plant was studied for the antitumor activity in the mice model. A significant reduction of tumor weight was observed in piplartine and piperine-treated animals. The alcoholic extract of *P. longum* and piperine at the dosage of 10 mg and 1.14 mg restricts the solid tumor development in mice induced with Dalton's lymphoma as cites cells and increases the life span of the mice model. The piperine component showed cytotoxicity in Dalton's lymphoma as cites and Ehrlich as cites carcinoma cells at the dosage of 250 mg/ml (Pradeep CR & Kuttan G. 2002). The piperine constituent inhibits the lung metastasis induced by B16F-10 melanoma cells when studied in C57BL/6 mice, thus showed chemo preventive effects when administered orally. The oral administration of the ethanolic extract showed a protective effect on the cell surface and maintains the structural integrity of the cell membrane during DMBA induced hamster buccal pouch carcinogenesis (Manoharan *et al* 2008). The previous studies demonstrated that the piperine constituent exhibits anti-apoptotic, antioxidative and restorative ability against cell proliferative mutagenic response (Pathak N & Khandelwal S. 2008).

Antioxidant

The determination of the antioxidant potential of the extract is based upon the radical scavenging activity of DPPH free radical. The phenolic compounds and flavonoids exhibit antioxidant activity against free radical-induced oxidative damage. Also, petroleum ether extract and piperine constituents of roots showed a significant reduction in the lipid peroxide level and maintain glutathione content (Natarajan *et al*, 2006). In another, *in vitro* study, it was found that the ethanolic extract of Pipali leaves showed the highest radical scavenging activity i.e. 63.84 ± 0.05 and showed less toxicity. Hence the extract showed significant antiviral, hepatoprotective and anticancer activities (Parida R and Dhal Y, 2011).

Antiplatelet

The piperine, piperonaline, piper longumine and piper octadecalidine constituents of pipali fruit were demonstrated for the antiplatelet activity against washed rabbit platelet aggregation. The inhibition of washed platelet aggregation induced by collagen, platelet-activating factor and arachidonic acid was observed in a dose-dependent manner (Iwashita *et al*, 2007).

Antifertility

The antifertility activity of the benzene extract of the *P. longum* plant was studied using a female rat model. It was found that the oral administration of the plant extract in combination with *E. ribes* berries showed 80% inhibition in the pregnancy rate in the female rat model. The hexane extract of *P. longum* possesses an immobility factor that reduced the sperms motility by disturbing the outer layer of sperm cells (Sarwar *et al*, 2015).

Anti-asthmatic

The *P. longum* fruit extract exhibited broncho relaxation with 83% inhibiting activity in histamine-induced broncho spasm model in guinea pig at a dosage of 200 mg/kg. It was also reported that the petroleum ether extract exhibited significant anti asthmatic activity against the mice model. The anti allergic activity of the extract was also demonstrated using milk-induced leukocytosis in mice and passive paw anaphylaxis in rats. The extract showed a significant protective effect in histamine-induced bronchospasm in haloperidol-induced catalepsy and passive paw anaphylaxis (Kaushik *et al*, 2012).

Anthelmintic

The methanolic, chloroform and n-hexane extract of the *P. longum* fruit showed *in vitro* ovicidal, larvicidal and adulticidal activity against strongyle, ova, larvae and adult amphistomes at the dosage of 1.95 mg/ml respectively. It showed complete larval mortality at the highest concentration of 500 mg/ml within 6 hours and a 50 % mortality rate at the lowest concentration. The chloroform extract exhibited less anthelmintic activity against L3 larvae with IC₅₀ of 12.47 mg/ml (Koorse *et al*, 2018).

Anti-snake venom

P. longum ethanolic fruit extract was examined for the anti-snake venom activity against Russell's viper venom in embryonated fertile chicken eggs, rats and mice. The extract showed noticeable inhibition of venom lethal action, venom defibrino genating action, paw edema, hemorrhagic activity, mast cell degranulation, necrotizing action, catalase activity and creatine kinase assay at a dosage of 250 mg/kg, 500 mg/kg and 750 mg/kg (Shenoy *et al*, 2013).

Acaricidal

The acaricidal activity of the aqueous and ethanolic extract of *P. longum* was examined using a three-host ixodid tick, *Hyalomma anatolicum*. The alcoholic extract of the plant showed maximum acaricidal activity with the minimum lethal dosage of 50 (LC50) and lethal concentration 95 (LC95) values respectively (Singh *et al*, 2017).

Antiulcer

P. longum extract was investigated for antiulcer activity. It was found that the administration of the extract to foot shock-induced stress animals protected ulcer severity up to 90% as compared with doxycycline (Yadav *et al*, 2015).

CONCLUSION

The *P. longum* plant has a significant importance and utilized both as a spice and medicine since ancient times. In Ayurveda medicinal system, there are about 135 ayurvedic formulations where *P. longum* is used as a major ingredient. In the traditional medicinal system, the plant is used to cure and treat for numerous diseases such as epilepsy, pleural effusion, spleen disorders, dementia, diarrhea, dysentery, insomnia and many more. There are some reported pharmacological activities of the *P. longum* plant such as antiulcer, anti-inflammatory, anticancer, neuroprotective and others. Besides that still, the plant needs more attention from researchers as the data on the pharmacological properties of this plant is not much explored. This plant claims to treat various diseases as per the literature study but there are no reported pieces of evidence available that showed its effective results. So, the plant needs more explorations and experimental and clinical studies are needed in future.

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