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PIPER LONGUM LINN.: AN IN-DEPTH REVIEW OF ITS BOTANICAL CHARACTERISTICS, PHYTOCHEMICAL CONSTITUENTS AND DIVERSE PHARMACOLOGICAL ACTIVITIES

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Abstract: Piper longum Linn., commonly known as Indian long pepper, is an important medicinal plant historically rooted in the Ayurveda and Unani systems of medicine, applied to manage respir-atory, gastrointestinal, inflammatory, and metabolic disorders. Over the past few years, scien-tific attention has increased toward its varied phytochemical composition and broad-spectrum pharmacological effects. The plant contains a wide array of bioactive constituents; Scientific investigation has identified over 159 phytochemicals, predominantly alkaloids such as piper-ine and piperlongumine, along with lignans, flavonoids, and volatile oils that contribute to itstherapeutic potential. Experimental evidence indicates that P. longum shows significant bioavailability-enhancing, antioxidant, anti-inflammatory, anticancer, hepatoprotective, and neuroprotective actions. Additionally, advanced analytical techniques such as HPLC, GC-MS and FTIR have contributed to the standardisation and identification of its active constituents and assist to validate its therapeutic claims. Even with promising preclinical findings, there is lack of clinical validation and comprehensive mechanistic studies. This review offers current overview of the botanical features, traditional uses, phytochemistry, pharmacological efficacy, and research gaps related to P. longum, highlighting its importance as a valuable source for the development of phytopharmaceutical agents in future.

Key words: *Piper longum*, piperine, piperlongumine, pharmacological activity, phytochemistry, medicinal plant

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INTRODUCTION

Piper longum Linn. is a perennial aromatic climbing plant belonging to Piperaceae family, widely known for itstraditionally medicinal use and economic importance.The plant is indigenousto the Indo-Malayan region and has been widely used in Ayurveda, Siddha, and Unani medical system (Ara *et al*., 2021; Khushbu *et al*., 2011). It has been reported that Roman emperorsvalued it even more highly than black pepper (Zaveri *et al.*, 2010). The dried fruits and roots of this plant are commonly used for managing respiratory problems, digestive issues, inflammatory conditions, and neurological disorders (Ara *et al*., 2021).The medicinalsignificance of *P. longum* is primarilyassociated with its chemically diverse secondary metabolites, especially alkaloids such as piperine and piperlongumine (Sinha *et al*., 2025).Scientific interest in these compounds has increased because of their ability to regulate various biological pathways, thereby resulting in a wide range of pharmacological effects (Choudhary and Singh, 2018). Among these, the ability of piperine to enhance bioavailability has received notableattention due to its ability to improve the absorption and effectiveness of co-administered therapeutic agents (Khushbu *et al*., 2011; Siddiqui *et al*., 2023).

Furthermore, along with its traditional applications, recent pharmacological studies indicate that *P. longum* has significant antioxidant, anti-inflammatory, anticancer, hepatoprotective, and neuroprotective activities (Zaveri *et al*., 2010). Despite these promising outcomes, its clinical efficacy, safety profile, and molecular mechanisms remain inadequately investigated. The present review aims to provide an overview of current information regarding the botany, phytochemistry, traditional uses, pharmacological properties, analytical advancement, and research limitations of *P. longum*, thereby establishing a scientific basis for its future therapeutic use.

Botanical description

Piper longum Linn. is a slender, perennial, aromatic climbing plant, classified under the Piperaceae family, a large group, containing around 3,610 identified species(Biswas *et al*., 2022). It has been labelled under different botanical synonyms, such as *Piper latifolium* Hunter and *Chavica roxburghii* Miq (Zaveri *et al*., 2010).

The plant is occurred extensively throughout tropical and subtropical regions of South and Southeast Asia.*Piper longum* flourishes in humid, tropical, and subtropical evergreen forests which provide partially filtered sunlight and sufficient rainfall. It can be grow in the wild and under cultivation in the many regions, especially in India, Nepal, Sri Lanka, Indonesia, and Malaysia. Assam, West Bengal and the West Ghats are the common regions in India where it grows under favourable conditions. Piper longum is often referred to as a slender climbing shrub with a creeping root system (Kumar *et al*., 2011). Its composition includes:

Roots

The root system typically wraps around the node and helps to anchor the plant to its host tree. The roots contain thick-walled parenchyma cells, starch granules (either simple or compound), lignified stone cells with striations and resin cells in the cortex as well as perivascular fibres within the phloem. Regions of the root that connect with the xylem and have a radial arrangement join to form the center of the root. The roots have also been found to contain the following chemical compounds: piperine, piperlongumine (piplartine), and dihydrostigmasterol (Khushbu *et al*., 2011; Zaveri *et al*., 2010).

Stem

The stems have a jointed and slightly swollen appearance at the nodes and can be described as slender, aromatic, stout and appearing in many colour variations from reddish brown through to grey. Structurally they can be most easily distinguished from one another by their distinctively arranged internodes, swollen nodes, small rootlets and root scars present on the stems. One distinguished feature of the stem is that it has an inner cavity for secretory material located in the center (Khushbu *et al*., 2011; Zaveri *et al*., 2010).

Leaves

The arrangement of leaves alternates between the spreading type to be with no stipules. The size of the leaf blade can range dramatically. The lower leaf blades typically range between 5-9 cm long by approx 5cm across and usually have an ovate to cordate shape with broad round lobes situated at their base; while also possessing sub-acute ends, smooth surfaces (no hair). The upper leaf blades tend to be much smaller generally around 2-3cm long and have a more membranous type texture that is darker green in color with an acuminate type tip and cordate or obliquely shaped base. The aromatic odor released from the leaf when crushed is due in part to some degree of oil contained within young twigs which have downy covers (Chaveerach *et al*., 2006; Yadav *et. al.,*2020).

Flowers

The plant has flowers that're either male or female and they grow on their own in straight spikes. These flowers usually come out during the season or right after it (Yadav *et al*., 2020).

Fruits (Spikes)

The fruits grow in spikes. They are small and shaped like eggs. They can be yellowish-orange or shiny blackish green. They are stuck in a stem. The fruits are shaped like cylinders, a bit round and not too sharp. They smell really good. But they do not taste good. They are bitter and make tongue numb. Spikes outside of the fruits has three layers (Kumar *et al.,* 2011). The inside layer has an edge, which is very special. The little fruits have walls with brown stuff inside a middle layer with thick cells and a hard inside layer that is stuck to the seed. This inside layer has a zone, with clear and orange-red colors (Khushbu *et al.,* 2011; Peter, 2006).

Traditional uses

Piper longum has been used for centuries as a medicinal plant in various traditional medicine systems, Ayurveda, Siddha and Unani, etc. Piper longum is an important medicinal plant used in traditional medicine practices throughout large parts of countries such as India, China, and Malaysia, as well as throughout most South East Asian nations (Ara *et al*., 2021; Khushbu *et al*., 2011; Kumar *et al.,* 2011). Piper longum has appeared in literature relating to medicinal plants over the past several thousand years, and its extensive references in ancient Ayurvedic texts ('Caraka Samhita', 'Susruta Samhita') bear witness to its longstanding use in traditional healing (Yadav *et al.*, 2020; Ramawat and Goyal, 2008).

Piper Longum (PL) is an herb that has been used for centuries to treat many different ailments. Some of these ailments include:

General tonic and rejuvenant

In Ayurvedic medicine, PL is a Rasayana (rejuvenator) and enhances vitality and strength (Khushbu *et al*., 2011).

Respiratory disorders

PL has been shown to be effective in treating coughs, bronchitis/asthma, and colds. There have been numerous studies showing that PL is especially effective in treating childhood asthma (Ara *et al*., 2021).

Gastrointestinal disorders

PL is used as a stimulant, carminative, laxative, anti-diarrheal, and anti-dysenteric. It is often used for loss of appetite, abdominal issues, flatulence, and parasitic infections (Khan, 2015).

Neurological conditions

Historically, PL was used to treat paralysis, gout, lumbago, insomnia, dementia, and seizures. In cases of insomnia or seizure activity, a decoction of the root was given as a sedative; as snuff, it was used to promote consciousness/sleepiness. Additionally, it has been reported to improve cognitive function/memory (Sharma *et al*., 2020; Sinha *et al*., 2025; Yadav *et al.*, 2020).

Reproductive Health

Piper longum is considered to have aphrodisiac, emmenagogue, and abortifacient properties. Traditionally, a decoction made from the root has been used to assist with placenta expulsion following childbirth. Its use during pregnancy or lactation is not recommended due to its effect in experimental studies as an anti-fertility agent. (Godara *et al*., 2018; Kumar *et al*., 2011; Yadav *et al*., 2020)

Other Traditional Uses

The fruit and the root of Piper longum have other traditional medicinal uses. The fruit is used externally as a treatment for fever, leucoderma, urinary discharges, tumors, piles, spleen disease, jaundice, hiccups, tuberculosis of the gland, leprosy, and as an antidote for snakebites and scorpion venom. (Khushbu *et al*., 2011) The root is the medicinal part of the plant in the Unani system of medicine, serving as both a liver tonic and diuretic. (Khushbu *et al*. 2011). In the Konkan region, hot roasted fruits are pounded and mixed with honey to treat rheumatism. (Yadav *et al.,* 2020) In northwestern Himalayan regions, a decoction of the root is given to cattle with swollen joints (Zaveri *et al.*, 2010). Piper longum is one of the main ingredients used in the traditional Indian system of medicine known as Ayurveda's Trikatu formula (which includes black pepper [Piper nigrum], long pepper, and ginger [Zingiber officinale]), often prescribed for the treatment and management of obesity. Piper longum is also an ingredient in many classical Ayurvedic formulations, including Pippali Rasayana, Amrtariasta, and Cyavanaprasa Avaleha (Yadav *et al.* 2020).

Phytochemical Constituents

Among all parts of the plant, Piper longum has been found to be rich in phytochemical constituents. Alkaloids, Lignans and Volatile oils are the main phytochemical constituents found in it (Akbar *et al.,* 2014).

Alkaloids

Alkaloids are the key active compounds found in plants (Yadav et al., 2022), and piperine is by far the predominant and most abundantly active alkaloid in piper longum having an approximate dry weight of 3-5% contributing to its pungent/spicy taste as documented (Zaveri *et al* 2010). Laboratory-tested, in vitro isolatable, two alkaloids in piper longum include piperlongumine or piplartine piperlonguminine (Yadav *et al.,* 2021). The other alkaloids isolated from piper longum include methylpiperine, pipernonaline, piperettine, pellitorine, dehydropipernonaline, guineensine, and tetrahydropiperine. There are also a number of miscellaneous aristolactams in piper longum that include cepharadione A, B and C; aristolactam AII; norcepharadione; piper-lactam A; piper-lactam B; and 4,5-dioxoaporphine. Recently reported compounds from whole plant extracts include pipahyaine and coumaperine and characteristic plant amides from those extracts include (Z)-12-octadecenicacid 1-alpha-glycerol monoester and N-5-(4-hydroxy-3-methoxyphenyl)-2E-pentenoyl piperidine. Piper longumin (i.e., piper longumine) is found in the roots at levels of 0.20% - 0.25% and piper longumin is found at levels of 0.020% (Bao *et al*., 2014; Kumar *et al*., 2011).

Lignans

Seeds and fruits contain various types of lignans (sesamin, sylvatin, diaeudesmin, pluviatilol and fargesin). Lignans vary greatly from one species of plant to another (Khushbu *et al*., 2011; Kumar *et al*., 2011).

Volatile oil

Essential oil found in dried stems contains approximately 0.7% of the a compound that has a hot odor that is similar to pepper and ginger oils. The essential oil complex contains both long-chain hydrocarbons, mono- and sesquiterpenes. The major components of this essential oil include caryophyllene (major), alpha pinene, beta pinene, limonene, terpinolene, zingiberine and pentadecane. Analysis also shows different constituents of essential oil found in various parts of the plant (fruit leaf roots, stem, etc.). The majority of the beta-pinene constituent comes from the fruit, root and stem of the plant while a higher concentration of sesquiterpene is found in the leaves (Varughese *et al.,* 2016; Yadav *et al*., 2020).

Other constituents

Other constituents of the plant include esters (tridecyl dihydrop-coumarate, eicosynyl-(e) p-coumarate, and z-12-octadecenoic-glycerolmonoester), fatty acids (palmitic, hexadecenoic, stearic, linoleic oleic, linolenic, and arachidic acids), amino acids (fruit contained l-tyrosine, l-cysteine hydrochloride, d-serine and l-aspartic acid) and flavonoids and phenolic compounds (caffeic acid, quercetin, kaempferol and apigenin 7,4'-dimethyl ether) will also be obtained from the whole plant. In addition to these other constituents there are also carbohydrates starch and proteins found in the fruit of this plant (Akbar *et al.,* 2014 Khushbu *et al*., 2011; Yadav *et al*., 2020).

According to numerous studies done in the modern era, many traditional uses of Piper longum have been verified and some previously unknown pharmacological uses have been uncovered.

The following are some examples:

Analgesic properties

The powdered form of P. longum was shown to have relatively high levels of analgesia through non-steroidal anti-inflammatory drugs. The level of analgesia increases based on the amount administrated and the frequency of dosing (Ara *et al.,* 2021; Vaghasiya *et al*., 2007).

Anti-asthmatic properties

The use of fruit extracts in conjunction with milk resulted in the significant reduction of the passive cutaneous anaphylaxis response in rats and provided protection against an allergic reaction (i.e. allergen-induced bronchospasm) in guinea pigs

(Choudhary and Singh, 2018; Kaushik *et al*., 2012; Khushbu *et al.*, 2011).

Anticancer properties

Extracts of P. longum and particular individual components (e.g. piperine and piperlongumine) show promising levels of cytotoxicity against multiple types of cancer cell lines (e.g. Dalton's lymphoma, Ehrlich ascites carcinoma, prostate cancer, breast cancer, lung cancer and rectal cancer) (Choudhary and Singh, 2018; Sinha *et al*., 2025). All extracts have inhibited various steps in the cell cycle, caused apoptosis and inhibited the activity of the transcription factor as well as inhibited the pathways associated with cancer through the reduction of oxidative stress and inflammation (Jin *et al*., 2014; Khushbu *et al.*, 2011; Sinha *et al*., 2025).

Anti-diabetic activity

The Extracts of P. longum created a suppression of alpha-glucosidase-I and also exhibited activity in diabetic animal models (induced by alloxan/streptozotocin), promoted hepatic function to maintain homeostasis of blood glucose levels, and exhibited insulin by stimulating secretion of insulin from the pancreas (Ara *et al*., 2021; Sinha *et al.,* 2025; Yadav *et al*., 2020).

Anti-hyperlipidemic activity

Methyl piperine and the unsaponifiable fractions of piperine in the P. longum oil decreased both the total blood cholesterol and hepatic cholesterol levels in hypercholesterolaemic animal models (Kumar *et al*., 2013; Zaveri *et al*., 2010).

Anti-inflammatory activity

The decoctions and extracts of P. longum fruit were significant for their anti-inflammatory activity against carrageenan induced footpad oedema in the rat model, related to molecules such as piperine, which decrease COX and prostaglandin pathways, and neutralize pro-inflammation (e.g. cytokines like IL-1 and TNF-alpha) (Ara *et al.*, 2021).

Anti-microbial activity

The essential oil from P. longum demonstrated antimicrobial activity with numerous bacteria including active against Bacillus subtilis (with Piperlongum oil) and Staphylococcus aureus (with piperine) (Ara *et al*., 2021; Kumar *et al*., 2011; Sinha *et al*., 2025; Vaghasiya *et al*., 2007).

Antioxidant Activity

P. longum extract has demonstrated significant antioxidant capacity through free radical scavenging, through free radical scavenging, through lipoperoxidation reduction and through retention of glutathione. This antioxidant activity is probably due to the antioxidant properties of phenolic substances and flavonoids which are present in *P. longum* (Akbar *et al*., 2014; Khushbu *et al*., 2011; Sinha *et al.*, 2025; Yadav *et al.*, 2020).

Bioavailability Enhancement Effect

Piperine has been found to improve the absorption of drugs with low bioavailability by increasing their permeability (possibly by altering the dynamics of the cellular membrane), as a result of its ability to freely pass through cellular membranes. Therefore, it can advantageously serve as a therapeutic adjuvant to improve the bioavailability of "poorly bioavailable" drugs (Harwansh *et al*., 2014; Zaveri *et al*., 2010).

Cardioprotective Activity

P. longum has been shown to provide cardioprotection. Coronary vasorelaxation has been demonstrated by amides found in P. longum, such as dehydropipernonaline (Chaudhary *et al*., 2013; Kumar *et al.*, 2011; Zaveri *et al*., 2010).

Hepatoprotective Activity

Piperine and extracts of its fruit exhibit potent hepatoprotective activity against chemical-induced hepatic toxicity, including, but not limited to, ter-butyl hydroperoxide and carbon tetrachloride, primarily through reduction of lipid peroxidation and prevention of fibrosis (Khan, 2015; Kumar *et al*., 2011; Yadav *et al.,* 2020).

Modulatory effects on immune system

The use of the fruits of the Piper longum plant is said to have a stimulatory effect on the immune system, both specific and non-specific immune system stimulation by enhancing macrophage activity and providing protection from stress brought on by environmental toxins. Piperine has been shown to lower levels of inflammation and raise levels of antioxidants (Sunila and Kuttan, 2004).

Insect repellents and larvicidal activity

Essential oils and alkaloids from Piper longum exhibit both insecticidal and larvicidal activities against a variety of insect pests and mosquito species (*Aedes aegypti*, *Culex quinquefasciatus*) (Khushbu *et al*., 2011).

Neuro-protective and anti-depressant effects

Alkaloids (piperine, piperlongumine) of Piper longum are thought to protect dopaminergic neurons in animal models of Parkinson's disease; reduce oxidative stress levels and increase dopamine levels. Piperine may also have potential uses as an antihypertensive drug because of its capacity to act as a monoamine oxidase inhibitor and reverse reductions in BDNF and mRNA levels caused by stress. Piperine may also enhance cognitive abilities and improve spatial memory (Akbar *et al*., 2014; Yadav *et al*., 2020).

Analytical advances

Contemporary analytical methods have significantly contributed in the standardization of Piper longum Linn. and the identification of its active metabolites.

Methods such as HPLC, GC-MS, and FTIRare extensively used for profiling alkaloids and volatile compounds, ensuring extract quality, and support pharmacological i studies

Research gaps and future perspectives

Piper longum Linn. is still lacking in a number of important areas despite important preclinical discoveries. Clinical research assessing its effectiveness, dose optimization, long-term safety, and herb-drug interactions is currently few. Furthermore, there hasn't been enough research done on the pharmacokinetics and tissue distribution of different active ingredients.

Future investigation should emphasis on mechanistic research, controlled clinical trials, and the use of omics-based methods to elucidate the molecular basis of its pharmacological activity.

These studies will be crucial for interpreting the traditional use and experimental data into reliable clinical practice.

CONCLUSION

Piper longum Linn. stands out as a valuable medicinal species, extensively used in traditional medicine and possessing pharmacological benefits. Its diverse phytochemical profile, particularly the occurrence of bioactive alkaloids such as piperine and piperlongumine, contributes in a various biological effects including improvementin drug bioavailability, antioxidant activity, anti-inflammatory action and anticancerproerties.

Although the available preclinical data are promising, clinical validation still remains insufficient to support its broad therapeutic application. Further research intended at standardize, understanding mechanisms of actionand clinical verification is crucial to fully exploit its therapeuticefficacy and enable its use into evidence-based phytopharmaceutical development.

Tabel 1. Major Phytochemicals Reported in *Piper longum linn*. and their Biological Significance

Phytochemical Class	Major Compounds Identified	Biological Significance
Alkaloids	Piperine, Piperlongumine, Piperlonguminine, Pellitorine	Bioavailability enhancement, anticancer, anti-inflammatory, neuroprotective activities
Lignans	Sesamin, Sylvatin, Diaeudesmin	Antioxidant and hepatoprotective properties
Flavonoids	Quercetin, Kaempferol	Free radical scavenging, anti-inflammatory activities
Terpenoids	Caryophyllene, α-Pinene, β-Pinene	Antimicrobial, antioxidant, anti-inflammatory effects
Phenolic Compounds	Various phenolic acids	Antioxidant potential and cellular protection
Fatty Acids	Palmitic acid, Myristic acid	Structural and metabolic roles
Volatile Oils	Essential oil fractions	Aroma, antimicrobial and therapeutic properties

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