Available online through
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ISSN 2321 - 6328

Review Article

UNVEILING PIPPALI: A CRITICAL REVIEW OF ITS MEDICINAL SIGNIFICANCE IN AYURVEDA AND BEYOND

Harish Kumar Singhal [1*], Prem Prakash Vyas [2], Neetu [3]
[1] Professor & HOD, P. G. Department of Kaumarbhritya, Postgraduate Institute of Ayurveda, Dr. S. R. Rajasthan Ayurved University, Jodhpur, Rajasthan, India
[2] Principal, MJF Ayurved Medical College, NH52, Harota, Chomu, Rajasthan, India
[3] Ayurvedic Medical Officer, State Ayurved Hospital, Rohana, Dist- Muzaffarnagar, India
*Corresponding Author Email: drharish_md@yahoo.co.in

Article Received on: 20/05/25 Accepted on: 18/07/25

DOI: 10.7897/2321-6328.133404

ABSTRACT

Pippali (Piper longum) is a revered herb in Ayurvedic medicine, traditionally employed for managing respiratory, digestive, and metabolic disorders. Despite its extensive documentation in classical texts such as the *Charaka Samhita, Sushruta Samhita*, and *Bhava Prakasha Nighantu*, a critical appraisal of its pharmacological potential through the lens of modern science remains essential. This review synthesizes insights from *Ayurvedic* literature and contemporary databases (PubMed, Scopus, Google Scholar), focusing on the phytochemistry, pharmacological actions, and clinical relevance of *Pippali*. Key bioactive constituents, notably piperine, exhibit potent antioxidant, anti-inflammatory, antimicrobial, and bio-enhancing effects. While traditional uses align with modern pharmacological findings, the majority of evidence stems from preclinical studies, with limited clinical validation. The review highlights the urgent need for standardized formulations, toxicological profiling, and rigorous clinical trials. Bridging traditional knowledge with scientific research may unlock *Pippali*'s full potential as a *Rasayana* and integrative therapeutic agent.

Keywords: Ayurvedic medicine, Evidence-based Ayurveda, *Pippali*, Piper longum, Piperine pharmacology, Rasayana, Toxicology

INTRODUCTION

Ayurveda, the ancient system of Indian medicine, has long emphasized the therapeutic potential of herbs in promoting health and managing disease. Among these, *Pippali* (*Piper longum*), commonly known as long pepper, holds a distinctive place due to its wide spectrum of medicinal applications. Described in classical *Ayurvedic* texts as a *Rasayana* (rejuvenator) and a potent *Deepana-Pachana* (digestive stimulant), *Pippali* has traditionally been used to treat respiratory ailments, digestive disorders, and metabolic imbalances.

Piper longum Linn belong to Piperaceae[1] family which is commonly known as *Magadhi, Krishna, Vaidehi, Chapala, Kana, Upkulya, Ushana, Shoundi, Magadhi, Krishna, Vaidehi, Chapala, Kana, Upkulya, Shoundi, Kola, Pippali, Shyamahava, Teekshantandula,[2] Shyama,[3] Krakara, Katubeeja, Kaurangi, Tilatundula, Dantphala, Magadhudbhava, Ushna, Smritiyahava,[4] Magdha, Karni, Vishwa,[5] Krishanphala, Vrasya, Katukandarasa, Bahubeeja, Kali, Krtmangala[6]* in the different *Ayurveda* textbook. According to *Chakra Samhita,* it come under *Kasahara,[7] Hikkanighrahana, Shrirovirechana,[8] Vamana,[9] Truptighna,[10] Deepaniya,[11] Shoolaprashamana[12]* while *Acharya Sushruta* mentioned this in *Pippalyadi,[13] Urdhwabhaghara,[14] Shirovirechana.[15]* But *Acharya Bhava Prakasha* mentioned *Piper longum Linn[16]* under *Panchakola,[17] Shadushana,[17] Haritakyadi[16] Gana.* It is an aromatic cylinder climber. Its stems are creeping, jointed, attached to the other plants while climbing. Leaves 5 -9 cm X 3 - 5 cm, subacute, entire glabrous, cordate at the base. Flowers lies in pendulate spikes, straight, male larger and slender, female 1.3 -2.5 cm X 4-5 mm diameter. Fruits are of yellowish orange, aboid, sunk in flashy spike.[18] Flowering occurs in rainy seasons and fruits in autumn. It is widely distributed in the hotter parts of the India from central Himalayas to Assam, and Mickey hills. It is also found in forest of western ghats from Konkan to Kerala. Essential oil, mono and sequisterpenes, carrophyllene, piperine, piplartine, piperlongumine, piperlonguminine, pipernonaline, piperundecalidine, pipercide, sesamin, B-sitosterol, four aristolactams, 4, 5– dioxoaporphines[18] are the chemical constituents found in it.

Modern scientific investigations have begun to validate many of these traditional uses, with studies highlighting *Pippali*'s bioactive constituents, such as piperine, responsible for its antioxidant, anti-inflammatory, immunomodulatory, and bio enhancing effects. Despite this growing interest, there remains a significant gap between traditional *Ayurvedic* knowledge and contemporary scientific validation.

This critical review aims to bridge that gap by analyzing the medicinal significance of *Pippali* through a comprehensive lens evaluating classical *Ayurvedic* references, phytochemical profiles, and pharmacological studies. In doing so, it seeks to present a balanced perspective that honors the depth of traditional wisdom while assessing the herb's relevance and applicability in modern healthcare settings.

The current study set out to gather works cited in old textbooks that were supported by new research findings. To do this, well-known databases such as PubMed and Medline from 1980 to the present were consulted.

Pharmacodynamic Properties

Table 1: Pharmacological Properties of Fresh *Pippali*

Nighantu (Ay.Text)	*Rasa*	*Virya*	*Vipaka*	*Guna*	*Doshaghnata*
P.N[19]	*Madhura*	*Sheeta*	-	*Guru*	*Vatakapha Vardhaka, Pittasamaka*
S.N[20]	*Madhura*	*Sheeta*		*Guru Snigdha*	*Kaphavardhaka*
B.P.N[21]	*Madura*	*Sheeta*	-	*Snigdha, Laghu*	*Kapha Vardhaka, Pittashamaka*
K.N[22]	*Madhura*	*Sheeta*	*Madhura Dry Pippali*	*Guru, Singdha*	*Kaphakaraka*
M.P.N[23]	*Madhura*	*Sheeta*	*Madhura*	*Guru, Singdha*	*Kaphpvardhaka*

P.N. – Priya Nighantu, S.N.- Sodal Nighantu, B.P.N.-Bhav Prakash Nighantu, K.N. – Kaiydev Nighantu, M.P.N.- Madan Pala Nighantu

Table 2: Pharmacological Properties of Dry *Pippali*

Nighantu (Ay.Text)	*Rasa*	*Virya*	*Vipaka*	*Guna*	*Doshaghnata*
P.N[19]	*Katu*	*Anushna Sheeta*	*Madhura*	*Laghu, Snigdha, Tikshna*	*Dry Pippali- Kapha Vata Shamaka*
R.N[24]	*Katu, Tikta*	*Ushna*	-	*Snigdha*	*Kaphanashaka*
S.N[20]	*Katu*	*Ushna*	*Madhura*	*Snigdha, Laghu*	*Pittavirodhani, Vatakaphashamaka*
D.N[25]	*Katu*	*Madhura*	*Sheeta*	*Snigdha*	*Tridoshahara*
B.P.N[21]	*Katu*	*Unaushana*	*Madura*	*Snigdha, Laghu*	*Pittavardhaka Vatakaphashamaka*
K.N[22]	*Katu*	*Istaushna*	*Madhura*	*Singdha*	*Kaphavatanashaka, Pittavardhaka*
M.P.N[23]	*Katu*	*Ati-Ushana*	*Madhura*	*Snigdha, Laghu*	*Kaphavatahara, Pittavardhaka*
N.A.[26]	*Katu*	*Sheeta*	*Madhura*	*Snigdha*	*Vatakaphahara*

P.N. – Priya Nighantu, R.N.- Raj Nighantu, S.N.- Sodal Nighantu, D.N.- Dhanwantri Nighantu, B.P.N.-Bhav Prakash Nighantu, K.N. – Kaiydev Nighantu, M.P.N.- Madan Pala Nighantu, N.A.- Nighantu Adarsha

Therapeutic Properties: *Deepana, Vatanulomana, Shoolaprashamana, Mridurechana, Krimighna, Yakrituttejaka, Raktashodhaka, Balya, Rasayana*[27] *Aamvatanasaka, Kasa, Prameghana, Gulma, Plihagna,*[23] *Vrisaya, Rasayana, Rechana*[22]

Indications: *Agnimandya, Aruchi, Ajirna, Udarashoola, Gulma, Vibandha, Yakritvikara, Pleehavriddhi, Krimiroga, Pandu, Jeernajawara, Medhya,*[28] *Kasa, Udarroga, Shwasa*[29] *Jwara, Krimi, Hridya Roga, Vrishya, Trishana,*[25] *Vata Vikara, Kshaya*[24]

Pharmacological activity of *Piper longum*

Antimicrobial Activity

Piper longum possesses broad-spectrum antimicrobial activity. It has been found effective against various gram-positive and gram-negative bacteria, as well as fungi. Its essential oils and extracts inhibit microbial growth by disrupting microbial cell membranes and inhibiting protein synthesis. Researchers examined the antibacterial and antifungal effects of several solvent extracts from P. longum against various harmful bacteria and fungi. In addition to its use, Singh and Rai claim that P. longum can be a promising source of antimicrobial compounds that could be employed against specific antibiotic-resistant bacteria.[30]

Hepatoprotective Activity

Experimental models have shown that *Piper longum* can protect the liver from toxin-induced damage. It helps in reducing serum liver enzyme levels and restoring hepatic histology, largely due to its antioxidant and anti-inflammatory effects. P. longum and piperine have hepatoprotective effects by reducing the rate of lipid peroxidation and raising reduced glutathione levels when used with anti-TB medications.[31,32]

Antioxidant Activity

Piper longum exhibits strong antioxidant potential, helping to scavenge free radicals and reduce oxidative stress. Studies have shown that its extracts enhance the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase.[33]

Anabolic Effect

In the *Pippali Rasayna* formulation, Singh and Guru (1972) discovered an anabolic effect which significantly increased body weight and the ratios of serum albumin and globulin.[34] Singh et al. discovered analeptic action in the alkaloids in 1973.[35] Tripathi et al. (1989) saw a thyrogenic reaction in long pepper.[36] The tissue's oxygen absorption and thyroid peroxidase activity were significantly improved, and the basal metabolic rates increased. A preliminary study conducted on the effect of alcoholic extract of *Pippali* Rasayana is significant increase in body weight, serum albumin and globulin ratio were also observed.

Immunomodulatory Activity

Pippali longum enhances both cellular and humoral immune responses. It has been observed to stimulate macrophage activity and increase levels of immunoglobulins, supporting its role in boosting overall immunity.[37] In mice infected with Giardia lamblia, a well-known Ayurvedic remedy containing long pepper (*Pippali rasayana*) was examined, and it was discovered to activate macrophages as demonstrated by an enhanced macrophage movement index and phagocytic index, showing immune-stimulatory action.[38]

Anti-inflammatory

Pippali longum has demonstrated significant anti-inflammatory effects by inhibiting the production of pro-inflammatory mediators like TNF-α, IL-6, and prostaglandins.[39] Piperine, a major alkaloid, modulates the NF-κB signaling pathway, thereby reducing inflammation in chronic condition. Piperine and piper extracts have anti-inflammatory effects via inhibiting the production of prostaglandins and leukotrienes and, consequently, COX-1.[40]

Bioavailability enhancer

In an experimental study to understand the absorption dynamics of *piperine* in intestine on oral absorption, intestinal everted sacs were used as an experimental model. Cycloheximide treatment and exclusion of Na+ salts from incubating medium were the variables used. Absorption half-life, absorption rates, absorption clearance and apparent permeability co-efficient were computed

from the data. Data thus obtained suggested that *piperine* is absorbed very fast across the intestinal barrier. It may act as a polar molecule and form polar complex with drugs and solutes. It may modulate membrane dynamics due to its easy partitioning, thus helping in efficient permeability across the barriers.[41] *Pippali* is a powerful stimulant for both the digestive and the respiratory systems and has showed a rejuvenating effect on lungs. It plays an important role in aiding the thermogenic response, i.e. the release of metabolic heat energy. This effect is the result of increased thyroid hormone level in the body. *Pippali* a typical Ayurvedic complementary component whose benefit is to increase the bioavailability and enhance absorption of the other active ingredients.[42]

Antidiarrheal activity

Anti diarrheal activity of piperine, the principle alkaloid of *Piper longum* and *Piper nigrum* L. (Piperaceae) was investigated against diarrhoea induced by castor oil, magnesium sulphate and arachidonic acid in rats. Piperine significantly inhibited diarrhoea produced by above laxatives and aperients at a dose of 8 and 32 mg/kg p.o. dose. It further inhibited castor oil induced enter pooling explaining prostaglandin inhibiting effect. An ethanol extract of the *Piper longum* fruit showed antiamoebic activity both in vitro and in vivo, curing 90% of rats with caecal amoebiasis.[43] An Ayurvedic herbal medicine prepared from *Piper longum* and *Butea monosperma* and prescribed for the treatment of chronic dysentery and worm infestations was tested for anti-giardial and immunostimulatory activity in mice infected with *Giardia lamblia* trophozoites. The preparation produced up to 98% recovery from the infection and induced significant activation of macrophages as evidenced by increased macrophage migration index and phagocytic activity.[44,45]

Renal protective

Gallic acid and piperine, when administered individually, showed moderate efficacy in ameliorating beryllium-induced biochemical disturbances. However, their combined administration resulted in a complete reversal of these alterations and associated oxidative stress. The findings indicate a synergistic interaction between gallic acid and piperine, enhancing their protective effects against beryllium-induced hepatorenal toxicity and oxidative damage.[46]

Anti-diabetic Activity

The herb exhibits hypoglycemic effects by enhancing insulin secretion, improving insulin sensitivity, and reducing oxidative stress in pancreatic β-cells. This supports its traditional use in managing metabolic disorders.[47]

Gastroprotective Activity

Traditionally used for digestive ailments, *Piper longum* has shown efficacy in treating ulcers and promoting digestive enzyme secretion. It helps maintain gastrointestinal mucosal integrity and reduces gastric acidity.[48]

Toxicity

Standard therapeutic doses of Piper longum are generally well tolerated. In experimental studies, administration of P. longum powder boiled in milk and water at a dose of 1 g/kg orally in rats resulted in no mortality, indicating a favorable safety profile. However, acute toxicity evaluations of its isolated constituents revealed varying lethal dose (LD_{50}) values in mice: piperine at 56.2 mg/kg, piperlongumine at 110.1 mg/kg, and piperlonguminine at 115.3 mg/kg when administered orally.[49] *Piper longum* and its active constituent piperine were well tolerated by guinea pigs up to doses of 2000 mg/kg and 850 mg/kg respectively. However, the ether extract of *Piper longum* was found to be toxic at a dose of 1200 mg/kg in guinea pigs.[50]

Anticancer Activity

Compounds such as piperlongumine have shown promising anticancer activity in preclinical models. They induce apoptosis, inhibit angiogenesis, and suppress tumor growth by modulating oxidative stress and cellular signaling pathways.[51,52]

Neuroprotective Activity

Piper longum has demonstrated neuroprotective effects in models of neurodegenerative diseases. It improves memory, reduces neuronal damage, and modulates neurotransmitter levels, suggesting potential benefits in disorders such as Alzheimer's and Parkinson's disease.[53]

DISCUSSION

Pippali (*Piper longum* Linn.), commonly known as long pepper, is a treasured medicinal herb extensively used in Ayurveda since antiquity. Recognized as one of the constituents of *Trikatu* (along with *Shunthi* and *Maricha*), it plays a vital role in digestive, respiratory, and rejuvenative formulations. Ayurvedic texts such as *Charaka Samhita* and *Sushruta Samhita* describe *Pippali* as a powerful *Deepana* (appetizer), *Pachana* (digestant), *Rasayana* (rejuvenator), and *Vata-Kapha Hara* (pacifier of *Vata and Kapha* doshas).[54] These traditional properties underline its use in conditions such as asthma (*Shwasa*), cough (*Kasa*), indigestion (*Ajeerna*), and metabolic disorders like *Prameha* (diabetes) and obesity.

Modern research has increasingly validated the pharmacological attributes of *Pippali*, revealing a wide array of bioactive compounds such as piperine, piperlongumine, and essential oils. Among these, piperine has received considerable attention due to its potent bioenhancing capabilities. It is known to inhibit drug-metabolizing enzymes such as CYP3A4 and P-glycoprotein, thereby increasing the bioavailability of numerous drugs and nutrients.[55] This property makes *Pippali* particularly valuable in enhancing the efficacy of herbal formulations and modern pharmaceuticals.

Scientific studies have also demonstrated the diverse pharmacological actions of *Pippali*. It exhibits antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, neuroprotective, antidiabetic, and immunomodulatory effects.[56,57] Its antioxidant activity helps in mitigating oxidative stress, which plays a pivotal role in the pathogenesis of chronic diseases. The hepatoprotective action of *Pippali* has been reported in experimental models of drug-induced liver injury, showing significant restoration of liver enzymes and histopathological architecture.[58] Moreover, its immunomodulatory effect supports its traditional use in *Rasayana* therapy aimed at enhancing vitality and disease resistance.

The synergistic potential of *Pippali* is particularly noteworthy. When combined with other herbs or compounds, it enhances therapeutic outcomes more effectively than when used alone. For example, piperine has been shown to significantly increase the bioavailability of curcumin, resveratrol, and various anti-tubercular drugs, making it a potent natural adjuvant.[59] In Ayurveda, this quality is referred to as *Yogavahi*, highlighting its ability to potentiate the effects of co-administered substances. This makes *Pippali* highly relevant in the context of integrative and personalized medicine.

Despite its widespread traditional and experimental support, *Pippali* is underrepresented in large-scale clinical trials. Standardization of dosage, extract type, and formulation remains a challenge. Moreover, long-term safety data is limited, particularly regarding its use in high doses or in vulnerable

populations such as children and pregnant women.[60] Hence, further research is essential to establish evidence-based protocols and safety guidelines for its use in contemporary clinical practice.

CONCLUSION

Pippali stands as a bridge between classical Ayurvedic knowledge and emerging biomedical research. Its broad therapeutic spectrum, bioavailability-enhancing property, and adaptogenic actions make it a valuable botanical in both traditional and integrative healthcare systems. With focused efforts on standardization, clinical validation, and sustainable cultivation, *Pippali* holds promise as a globally recognized therapeutic agent rooted in ancient wisdom yet aligned with modern medical demands.

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Cite this article as:

Harish Kumar Singhal, Prem Prakash Vyas and Neetu. Unveiling *Pippali*: A critical review of its medicinal significance in Ayurveda and beyond. J Biol Sci Opin 2025;13(3):22-26.
http://dx.doi.org/10.7897/2321-6328.133404

Source of support: Nil; Conflict of interest: None Declared