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Review Article

A Review: Phytochemical and Pharmacological Properties of *Piper longum*

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ABSTRACT

Piper longum Linn. (Long Pepper), a member of the family Piperaceae, is a well-known medicinal plant widely used in traditional systems of medicine such as Ayurveda and Unani. It is valued for its potent therapeutic potential and diverse pharmacological activities. The plant contains a rich spectrum of bioactive phytochemicals, including alkaloids (piperine, piperlongumine, chavicine, piperettine), lignans (sesamin, asarinin), and flavonoids (quercetin, catechin, kaempferol), which contribute to its wide range of pharmacological effects. Pharmacological studies have demonstrated that extracts and isolated compounds of Piper longum exhibit anti-inflammatory, antioxidant, antimicrobial, hepatoprotective, antidiabetic, analgesic, anticancer, and bioenhancing activities. Among its active constituents, piperine plays a pivotal role, not only for its pharmacological properties but also for its ability to enhance the bioavailability of various drugs and phytoconstituents. This review comprehensively highlights the phytochemical composition and pharmacological significance of Piper longum, providing insight into its therapeutic applications and scientific relevance. The findings support its traditional use and encourage further research into its molecular mechanisms, clinical efficacy, and potential in novel drug formulations.

INTRODUCTION

Piper longum Linn. Commonly known as long Pepper, belongs to the family Piperaceae and has been a vital component of traditional medicine systems such as Ayurveda, Siddha, and Unani. The plant is native to the Indo-Malayan region and widely distributed across India, Sri Lanka, and Southeast Asia. It is extensively used as a spice and medicinal herb due to its diverse therapeutic potential. The fruits and roots of *Piper longum* are known for their pungent taste and aromatic nature, attributed mainly to the presence of piperine and other bioactive constituents [1].

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Phytochemical investigations have revealed that *Piper longum* contains a wide spectrum of secondary metabolites such as alkaloids (piperine, piperlongumine, piperettine, chavicine), lignans (sesamin, asarinin), flavonoids (quercetin, catechin, kaempferol), and essential oils [2,3]. These compounds are responsible for various pharmacological activities, including anti-inflammatory, antioxidant, antimicrobial, antidiabetic, hepatoprotective, antitumor, and bioenhancing effects [4,5].

The pharmacological importance of *Piper longum* has been validated by both traditional and modern scientific research, highlighting its potential in the treatment of chronic diseases related to oxidative stress and inflammation. Its chief alkaloid, piperine, also enhances the bioavailability of other drugs and phytoconstituents, making it a valuable adjuvant in herbal formulations [6,7]. Therefore, the present review aims to comprehensively discuss the phytochemical profile and pharmacological properties of *Piper longum* with scientific evidence supporting its traditional use.

Phytochemical Constituents of *Piper longum*

Piper longum (Long Pepper) is a medicinally important plant belonging to the family Piperaceae, known for its diverse array of bioactive phytochemicals responsible for its therapeutic potential. The plant contains numerous secondary metabolites distributed across its fruits, roots, and leaves.

1. Alkaloids

Piperine:

Piperine is the principal alkaloid found in the fruits and roots of *Piper longum*. It is known for its bioavailability-enhancing, anti-inflammatory, and antioxidant properties. Piperine enhances the absorption of drugs and nutrients by inhibiting hepatic and intestinal glucuronidation. It also exhibits anti-cancer, neuroprotective, and antidiabetic effects. [8]

Piperlongumine:

This alkaloid exhibits potent anti-cancer, anti-inflammatory, and anti-platelet effects. It induces apoptosis in cancer cells by increasing reactive oxygen species (ROS) levels and inhibiting NF-κB signaling. [9]

Piplartine (synonym of Piperlongumine):

It demonstrates cytotoxic, antimicrobial, and antioxidant effects, contributing to the pharmacological diversity of *Piper longum*. [10]

Chavicine:

Chavicine is a geometric isomer of piperine (trans–cis form) and one of the principal pungent alkaloids present in *Piper longum* fruits. It is an amide alkaloid responsible for the sharp, pungent flavor and characteristic aroma of long pepper. Structurally, chavicine is similar to piperine but differs in the configuration of its double bonds, which significantly influences its stability and biological activity. [11]

Pharmacologically, chavicine has been reported to exhibit antioxidant, antimicrobial, and anti-inflammatory effects. It acts by modulating oxidative stress pathways and inhibiting microbial growth by disrupting bacterial cell membranes. Upon storage or heating, chavicine gradually isomerizes back to piperine, indicating its thermolabile nature. [12]

Chavicine also contributes to the stimulation of digestive enzymes and may enhance gastrointestinal motility, which is one reason *Piper longum* is traditionally used as a digestive

stimulant. However, due to its instability, chavicine is rarely isolated in pure form and is generally studied in conjunction with other piperine derivatives. [13]

Piperlonguminine and Piperettine:

Piperettine is another important amide alkaloid isolated from the fruits and roots of *Piper longum*. It belongs to the piperidine alkaloid family and contributes to the spicy flavor and pharmacological potency of the plant. Structurally, it is characterized by the presence of a conjugated aliphatic chain linked to a piperidine nucleus, which is responsible for its biological activity. [14]

Piperettine has been reported to possess antimicrobial, analgesic, insecticidal, and cytotoxic activities. It inhibits microbial growth by interfering with the synthesis of cellular proteins and enzymes. Several studies have demonstrated that piperettine also shows anti-inflammatory and antipyretic effects, possibly through inhibition of prostaglandin synthesis and modulation of cytokine release. [15]

In traditional medicine, the presence of piperettine and related amide alkaloids is believed to enhance bioavailability and synergistic pharmacological effects when combined with other herbal constituents. Recent studies have also indicated its potential role as a natural therapeutic agent in pain management. [16]

2. Lignans

Sesamin is a lignan compound isolated from the fruits and roots of *Piper longum* as well as other plants like sesame (*Sesamum indicum*). It exhibits strong antioxidant, hepatoprotective, and antihyperlipidemic activities. Sesamin functions by scavenging reactive oxygen species (ROS) and enhancing the activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase. [17]

It has been shown to reduce lipid peroxidation, regulate cholesterol metabolism, and protect the liver from oxidative damage. Additionally, sesamin has demonstrated anti-inflammatory activity through inhibition of the NF-κB pathway and suppression of pro-inflammatory cytokines such as TNF-α and IL-6. [18]

Asarinin

Asarinin is a stereoisomer of sesamin, belonging to the same class of lignans. It has been reported to exhibit anti-inflammatory, antioxidant, and antihypertensive effects. Asarinin protects cells from oxidative stress by upregulating antioxidant defenses and modulating nitric oxide (NO) levels, which contributes to vascular protection. [19]

Studies have also shown that asarinin can reduce the production of inflammatory mediators like prostaglandins and leukotrienes, making it a potential natural compound for treating chronic inflammatory conditions. Its pharmacological actions are attributed to its ability to modulate cell signaling pathways involved in oxidative stress and inflammation. [20]

3. Flavonoids

Quercetin

Quercetin is a flavonoid widely distributed in medicinal plants including *Piper longum*. It exhibits multiple biological effects such as antioxidant, anti-inflammatory, antiallergic, and anticancer activities. Quercetin acts by scavenging free radicals, inhibiting lipid peroxidation, and modulating inflammatory pathways like NF-κB and COX-2. [21]

It also stabilizes mast cells, reducing the release of histamine and pro-inflammatory mediators. In addition, quercetin demonstrates hepatoprotective and cardioprotective effects by improving endothelial function and reducing oxidative stress in tissues. [22]

Catechin

Catechin is a polyphenolic flavonoid that occurs naturally in *Piper longum*, green tea, and cocoa. It is known for its strong antioxidant, anti-inflammatory, and antimicrobial activities. Catechin neutralizes reactive oxygen species and enhances antioxidant enzyme activity in biological systems. [23]

It exhibits cardioprotective and neuroprotective properties by preventing oxidative damage to lipids and DNA. Furthermore, catechin inhibits bacterial adhesion and enzyme activity, contributing to its antimicrobial potential. Catechin and its derivatives have also been shown to reduce inflammatory markers and modulate immune responses. [24]

Kaempferol

Kaempferol is another important flavonoid identified in *Piper longum* with broad pharmacological potential. It shows antioxidant, anti-inflammatory, anticancer, and antidiabetic properties. Kaempferol functions by inhibiting oxidative stress, downregulating inflammatory cytokines, and inducing apoptosis in cancer cells. [25]

It also helps regulate glucose metabolism and has been linked with the prevention of chronic diseases such as cardiovascular disorders and diabetes. Kaempferol exerts neuroprotective effects through modulation of signaling pathways like PI3K/Akt and MAPK, which are involved in cell survival and inflammation. [26]

4. Essential Oils

The essential oil fraction of *Piper longum* contains β-caryophyllene, limonene, sabinene, pinene, and linalool. These volatile compounds contribute to the aromatic, antimicrobial, and anti-inflammatory activities of the plant. [27]

5. Amides and Esters

Guineensine, Retrofractamide A & B, Longamide:

These compounds are known for their neuroprotective, analgesic, and cytotoxic properties. Guineensine has been reported to inhibit endocannabinoid reuptake, suggesting possible roles in pain modulation. [28]

6. Sterols and Other Phytoconstituents

β-Sitosterol, Stigmasterol, and Tannins:

Sterols like β-sitosterol and stigmasterol are known for anti-inflammatory and immunomodulatory effects. Tannins exhibit antioxidant and antimicrobial actions, contributing to wound-healing potential. [29]

Pharmacological Properties of *Piper longum* (Long Pepper)

Piper longum L. has been traditionally used in Ayurveda and Siddha systems of medicine for treating respiratory disorders, gastrointestinal ailments, inflammation, and infections. Modern pharmacological investigations have validated many of its ethnomedicinal claims, attributing its efficacy to the presence of bioactive alkaloids, lignans, flavonoids, and essential oils such as piperine, piperlongumine, sesamin, and quercetin.

1. Anti-inflammatory Activity

Several studies have demonstrated that *Piper longum* extracts possess strong anti-inflammatory effects both in vitro and in vivo. The alkaloids piperine and piperlongumine inhibit inflammatory mediators like cyclooxygenase (COX) and lipoxygenase (LOX), reducing prostaglandin (PGE2) and leukotriene synthesis. They also suppress pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6.

The anti-inflammatory effect has been evaluated using carrageenan-induced paw edema, egg albumin, and formalin-induced inflammation models in animals, where the extract showed significant reduction in edema formation comparable to standard drugs like indomethacin. [30,31]

2. Antioxidant Activity

Piper longum exhibits potent antioxidant properties, primarily due to its flavonoids (quercetin, kaempferol) and lignans (sesamin, asarinin). These phytochemicals neutralize reactive oxygen species (ROS), superoxide anions, and hydroxyl radicals, protecting cellular components from oxidative damage.

Ethanolic and methanolic extracts have shown strong DPPH and ABTS radical scavenging activity, along with increased levels of endogenous antioxidants like SOD, CAT, and GPx in tissues. Such activity contributes to the plant's protective effects against oxidative-stress–related diseases. [32,33]

3. Antimicrobial and Antifungal Activity

Extracts and essential oils of *Piper longum* show broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria such as *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis*, as well as fungi like *Candida albicans*.

The bioactive alkaloids piperettine, chavicine, and piperine disrupt microbial cell walls, interfere with enzyme systems, and inhibit nucleic acid synthesis. This supports its traditional use in the treatment of infections, colds, and throat ailments. [34,35]

4. Anticancer and Cytotoxic Activity

Piper longum has been extensively studied for its anticancer potential. Piperlongumine selectively induces apoptosis in cancer cells by increasing ROS accumulation and inhibiting anti-apoptotic proteins such as Bcl-2 and NF-κB. It has shown significant cytotoxic activity against various human cancer cell lines, including breast, lung, colon, and prostate cancers.

Piperine also inhibits metastasis, angiogenesis, and tumor progression by suppressing PI3K/Akt and MAPK signaling pathways. [36,37]

5. Analgesic and Antipyretic Activity

Studies have shown that ethanolic extracts of *Piper longum* significantly reduce pain perception and fever in animal models. The mechanism involves inhibition of prostaglandin synthesis and modulation of nociceptive neurotransmission. Piperine and piperlonguminine contribute to these effects, showing comparable efficacy to standard drugs like aspirin and paracetamol. [38]

6. Hepatoprotective Activity

Piper longum extract and its lignans (sesamin, asarinin) have shown hepatoprotective effects against chemical-induced liver damage. They enhance antioxidant enzyme levels, reduce serum transaminases (SGOT, SGPT), and prevent lipid peroxidation in hepatic tissues.

These effects are mainly attributed to the ability of piperine and sesamin to stabilize hepatocyte membranes and promote detoxifying enzyme activity. [39,40]

7. Antidiabetic Activity

Piperine and piperlongumine exhibit antidiabetic potential by improving insulin sensitivity, glucose uptake, and lipid metabolism. Animal studies have shown that *Piper longum* extract significantly reduces blood glucose levels and improves pancreatic β-cell function.

Additionally, the extract enhances the activity of key enzymes like glucose-6-phosphatase and hexokinase, and reduces oxidative stress in diabetic tissues. [41,42]

8. Immunomodulatory and Bioenhancing Activity

One of the most unique properties of *Piper longum* is its bioenhancing ability, primarily due to piperine, which increases the bioavailability of several drugs such as rifampicin, curcumin, and resveratrol by inhibiting hepatic and intestinal drug-metabolizing enzymes (CYP450, glucuronidation).

Additionally, *Piper longum* extract exhibits immunomodulatory effects by stimulating macrophage activity and enhancing antibody production, thereby improving innate and adaptive immune responses. [43,44]

9. Antimotility and Gastroprotective Activity

Traditionally used for digestive disorders, *Piper longum* shows gastroprotective effects by enhancing digestive enzyme secretion and reducing gastric mucosal damage. Piperine stimulates the release of gastric juice, bile acids, and pancreatic enzymes, improving digestion and nutrient absorption. [45,46]

CONCLUSION

Piper longum is a medicinally significant plant exhibiting a wide range of phytochemical and pharmacological properties. The plant is rich in bioactive constituents such as piperine, piperlongumine, chavicine, piperettine, sesamin, asarinin, and flavonoids, which contribute to its broad spectrum of therapeutic activities. Studies have demonstrated its anti-inflammatory, antioxidant, antimicrobial, antidiabetic, anticancer, and hepatoprotective effects, confirming its role as a promising candidate for drug development and herbal formulations.

The bioenhancing property of piperine, which improves the absorption and efficacy of various therapeutic agents, further increases the pharmacological significance of this plant. Continued research into its mechanism of action, molecular targets, and formulation development could lead to novel natural therapies derived from *Piper longum*. Hence, the plant represents a valuable link between traditional herbal knowledge and modern pharmacological science.

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