Review Article

CHEMISTRY AND PHARMACOLOGY OF *PIPER LONGUM* L.

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ABSTRACT

Earthen hemisphere is gifted with varieties of large number of medicinal herbs. Herbs are natural remedies for the disease with higher safety profile and efficacy. The country like India has got variety of climatic conditions and seasons favorable for growth of many species of plants. Amongst the large number of herbal drugs existing in India, very few have been studied systematically so far. The list of drugs is very meticulous and diversified hence extensive efforts are required for their correct recognition. *Piper longum* is a highly valuable drug and is one of the essential ingredients in the most of the compound preparations included in Ayurvedic literature. Further, the use of the plant as a bioavailability enhancer has immensely increased its importance in the field of Ayurveda. Hence, an attempt has been made to address the chemistry and pharmacology of the plant *P. longum.* Commonly the plant *P. longum* is known as long pepper, species of the genus *Piper* belonging to family *piperaceae* of the unique order piperales of the verticillate of dicotyledones.

Keywords: *Piper longum, Piperaceae*, piperine.

INTRODUCTION

Plants have been the source of medicines since thousands of years. Species of the genus *Piper* are among the important medicinal plants used in various systems of medicine[1, 2]. *Piper longum* L. (Piperaceae), commonly known as "long pepper", is widely distributed in the tropical and subtropical regions of the world, throughout the Indian subcontinent, Sri Lanka, Middle Eastern countries and the Americas. It is said that the Roman emperors valued it even more highly than black pepper due to its high commercial and economical importance.

Synonyms: *Piper latifolium Hunter, P. saramentosum Wall. , Chavica roxburghii Miq, C.*

Vernacular names: *English*: Long pepper, *Hindi*: Pippali, *Sanskrit*: Pipali

Habitat: The native of plant is considered to be South Asia and is found both wild as well as cultivated, throughout the hotter parts of India from central to the north-eastern Himalayas. The herb also grows wild in Malaysia, Singapore, Bhutan, Myanmar and elsewhere[1].

Ayurvedic properties:
Rasa: Katu (pungent)
Guna: Laghu (light), snigdha (unctuous), tikshna (sharp)
Veerya: Anushnashita (slight cold)
Vipaka: Madhur (sweet)
Dosha: Pacifies *kapha* and *vata*

Botanical description:

It is having slender, aromatic, perennial climber, with woody roots and numerous wide ovate, cordate leaves. The inflorescence is a cylindrical, pedunculate spike, the female flower is up to 2.5 cm long and 4-5 mm in diameter but the male flower is larger and slender. The fruits are small, ovoid berries, shiny blackish green, embedded in fleshy spikes[3].

PHARMACOGNOSTICAL CHARACTERISTICS:

Flowering plant

Unripe fruit

Dried mature fruits

Plant of *Piper longum* L.

ROOT

Bisht[4] had described complete pharmacognosy of the root and stem of *P.longum* Winton and winton[5] had described the morphological and microscopical characters of *P. longum* roots. Joshi[6] had studied the structure and development of the ovule and Embryo sac of *P. longum*. The root in a transverse section showed thick walled parenchyma, simple or compound starch grains, lignified and striated stone cells, resinous cells in the cortex, perivascular fibres in the phloem, and radical strips of xylem which meet at the center. Pith was found to be absent. The stem had a secretory cavity in the center. The cortex showed starch grains as well as resinous and some stone cells. The phloem was capped by perivascular fibres and xylem arranged in V-shaped groups[7]. The detailed microscopical study of root of *Piper longum* is shown in Figure -1.

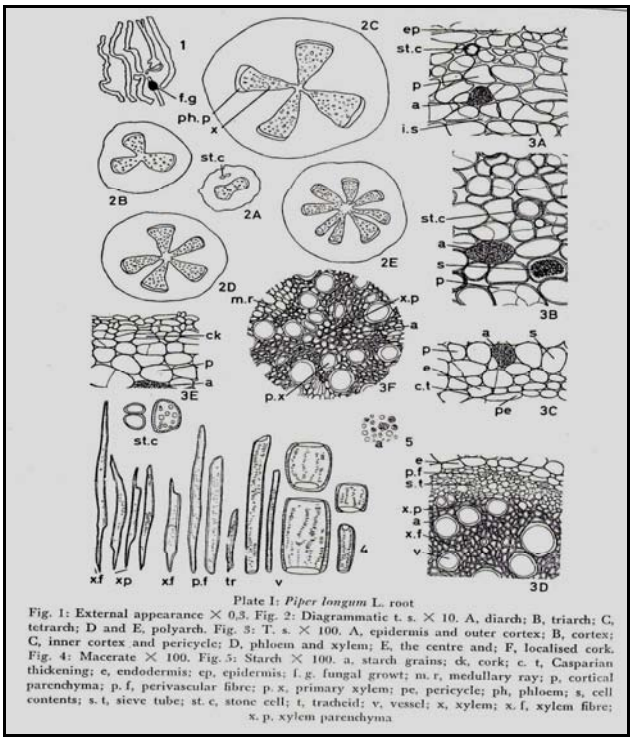


Plate I: *Piper longum* L. root

Fig. 1: External appearance × 0.3. Fig. 2: Diagrammatic t. s. × 10. A, diarch; B, triarch; C, tetrarch; D and E, polyarch. Fig. 3: T. s. × 100. A, epidermis and outer cortex; B, cortex; C, inner cortex and pericycle; D, phloem and xylem; E, the centre and; F, localised cork. Fig. 4: Macerate × 100. Fig. 5: Starch × 100. a, starch grains; ck, cork; c. t, Casparian thickening; e, endodermis; ep, epidermis; f. g. fungal growt; m. r, medullary ray; p, cortical parenchyma; p. f, perivascular fibre; p. x, primary xylem; pe, pericycle; ph, phloem; s, cell contents; s. t, sieve tube; st. c, stone cell; t, tracheid; v, vessel; x, xylem; x. f, xylem fibre; x. p, xylem parenchyma

Figure 1: Piper longum L. root

FRUIT

Mehra and Puri[8] described the fruiting spike of *P. longum* as black, cylindrical, irregular, up to 2 to 5 cm long, and compact. The fruits are one seeded with three-layered pericarp. Winton and winton[5] described the morphological and microscopical characters of *P. longum* fruits. Endocarp is wavy in outline, which is a distinguishing character. Das Gupta and Dutta[9] while giving details of anatomy of the fruits, described the fruit let of *P. longum* as thick-walled with heavy brown contents in the outermost layer, mesocarp with thickened cells, endocarp and seed coat fused to form a deep zone with hyaline content in the outer layers, and orange-red pigment.

STEM

Atal and Banga[10] reported detail pharmacognosy of the stem pieces of *P.longum*. The detailed microscopical study of stem of *Piper longum* is shown in Figure -2.

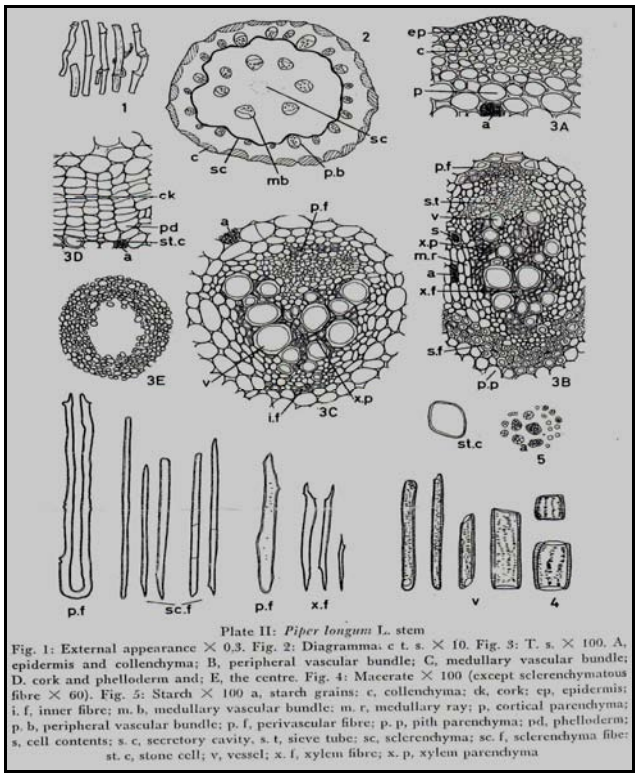


Plate II: *Piper longum* L. stem

Fig. 1: External appearance × 0.3. Fig. 2: Diagramma. c t. s. × 10. Fig. 3: T. s. × 100. A, epidermis and collenchyma; B, peripheral vascular bundle; C, medullary vascular bundle; D. cork and phelloderm and; E, the centre. Fig. 4: Macerate × 100 (except sclerenchymatous fibre × 60). Fig. 5: Starch × 100 a, starch grains; c, collenchyma; ck, cork; ep, epidermis; i. f, inner fibre; m. b, medullary vascular bundle; m. r, medullary ray; p, cortical parenchyma; p. b, peripheral vascular bundle; p. f, perivascular fibre; p. p, pith parenchyma; pd, phelloderm; s, cell contents; s. c, secretory cavity, s. t, sieve tube; sc, sclerenchyma; sc. f, sclerenchyma fiber; st. c, stone cell; v, vessel; x. f, xylem fibre; x. p, xylem parenchyma

Figure 2: Piper longum L. stem

Traditional uses:

Parts used: Immature spikes, roots and seeds

Dried unripe fruits are used as an alternative to tonic. Decoction of immature fruits and roots is used in chronic bronchitis, cough and cold. Roots and fruits are also used as anti-dote in snake biting and scorpion sting[11]. An equal part of powdered seeds of *Embelia ribes*, fruit of *P. longum* L. and borax powder has been used as an Ayurvedic contraceptive[12]. *P. longum* L. has been used in traditional remedies as well as in the Ayurvedic system of medicine against various disorders[13, 14].

Ethanoveterinary use: A decoction of the roots is given for swellings of the joints of cattle in the north-western Himalayan regions.

PHYTOCHEMISTRY:

The Chemical Constituents of Pepper:

Piperine is the major and active constituent of long pepper (*Piper longum*). The piperine content is 3-5% (on dry weight basis) in *P. longum.*

Isolation and extraction of Piperine from Piper species:

Piperine can be isolated from the oleoresin of *P. nigrum* or *P. longum.* The powdered fruits of the plant are extracted with dichloromethane at room temperature with stirring for 12 hours. The extract is filtered, concentrated in vacuum, and then the residue is purified on an alumina column. Pure piperine can also be obtained by crystallization from ethanol, which may be required for food and/or medicinal usages. Piperine is obtained directly from the crude residue in lesser amounts by extraction in alcohol, filtration and successive crystallization.

Properties of piperine[15]:

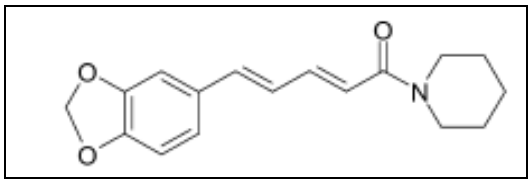
*Chemical names:

a. 1- piperoyl piperidine

b. (E, E) 1-[5-(1, 3-Benzodioxol-5-yl)-1-oxo-2, 4-pentadienyl] piperidine

*Molecular weight: 285.33

*Percentage composition: C= 71.55%, H=6.71%, N=4.91% and O=16.82%.

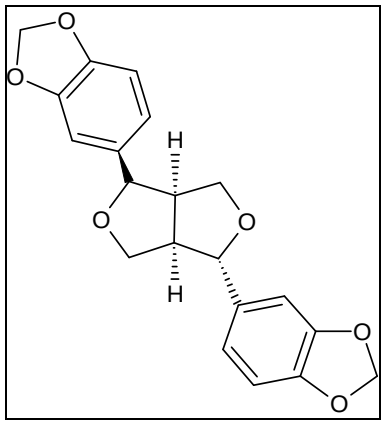


Piperine

The fruits gave positive tests for the presence of volatile oil, starch, protein and alkaloids, saponins, carbohydrates, and amygdalin and negative test for tannins[9]. Sylvatine and dieudesmin were present in the seeds of *P. longum* [16]. Fatty acids of crushed seeds were reported to be palmitic, hexadecenoic, stearic, linoleic, oleic, higher saturated acids, arachidic, and behenic acids[17].

Alkaloids and amides

The fruit of *P. longum* contains a large number of alkaloids and related compounds, the most abundant of which is piperine, together with methyl piperine, iperonaline, piperettine, asarinine, pellitorine, piperundecalidine, piperlongumine, piperlonguminine, refractomide A, pregumidiene, brachystamide, brachystamide-A, brachystine, pipercide, piperderidine, longamide and tetrahydropiperine, terahydro piperlongumine, dehydropipernonaline piperidine, piperine, terahydropiperlongumine and trimethoxy cinnamoyl-piperidine and piperlongumine have been found in the root of *P. longum* [18-28] .



(+)-Asarinine

Lignans

Sesamin, pulvuatilol, fargesin and others have been isolated from the fruit of *P. longum* [19, 20, 22, 29].

Esters

The fruit of *P. longum* contains tridecyl-dihydro-p-coumaarate,eicosanyl-(E)-p-coumarate and Z-12-octandecenoic –glycerol-monoester[19,20,22,28].

Volatile oil

The essential oil of the fruit *P. longum* 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 thujine, terpinoline, zingiberine, p-cymene, p-methoxy acetophenone and dihydrocarveol[19, 20, 22, 28, 30-32]. Long pepper contains less essential oil than its relatives (about 1%), which consists of sesquiterpene hydrocarbons and ethers (bisabolene, β-caryophyllene, β-caryophyllene oxide, each 10 to 20%; α-zingiberene, 5%), and saturated aliphatic hydrocarbons such as 18% pentadecane, 7% tridecane, 6% heptadecane[33].

The volatile constituents and microbiological studies on *Kaempheria galanga, Hibiscus abelmoschus*, and *Piper longum* revealed presence of over 15 components which were further identified by GC-MS of the volatile oil of *Piper longum*. The variations in the piperine content with maturity were also monitored. The *P. longum* and *H. abelmoschus* seed oil had only antibacterial activities[34]**.** By using a systematic bioassay guided fractionation method pipataline, pellitorine, sesamin, brachystamide B and guineensine active principles were isolated. A reversed-phase high-performance liquid chromatography method was developed to quantify these active principles in the plant material [35]. In the chromatogram of *P. longum* fruits, retrofractamides B and D, and N-isobutyl-2E, 4E-octadecadienamide can be detected. The HPLC-chromatogram of *P.longum* showed a homogeneous distribution of numerous peaks, with piperine and pellitorine as the predominant compounds[36]. A simple and convenient HPTLC method was developed for standardization of the plant material using the two major constituents, pellitorine and dihydropiperlonguminine, as

markers at 260 nm[37]. The hexane extract of dried fruits of *P. longum* on fractionation afforded a new alkamide, isodihydropiperlonguminine and two phenyl propanoic acid derivatives. The structures of these compounds were established based on spectroscopic evidence and synthesis[38]. Thymoquinol and 6-Hydroxydopamine were also identified in *Piper longum*[39].

MEDICINAL AND PHARMACOLOGICAL ACTIVITIES:

Insecticidal and acaricidal activity:

The essential oil of the fruits showed insecticidal and insect-repellant activity [40].Toxicities of two piperidine alkaloids, pipernonaline and piperoctadecalidine, isolated from *P. longum* were determined against five species of arthropod pests. Both of the alkaloids showed insecticidal activity [41].

Antifungal activity:

The essential oil of the fruits showed fungicidal activity of *P. longum* L. The fruit-derived materials was tested towards six phytopathogenic fungi, *Pyricularia oryzae*, *Rhizoctonia solani*, *Botrytis cineria*, *Phytophthora infestans*, *Puccinia recondita*, and *Erysiphe graminis* using a whole plant in vivo method [42-44]. A piperidine alkaloid, pipernonaline, was isolated from the hexane fraction of *P.longum* showed a potent fungicidal activity against *P. recondita* with 91% and 80% control values at the concentration of 0.5 and 0.25 mg ml^{-1}, respectively[45].

Antiamoebic activity:

The anti-amoebic effects of crude methanol extract of *Piper longum* fruit, *Piper sarmentosum* root and *Quercus infectoria* nut gall against *Entamoeba histolytica* infecting the caecum of mice were studied. The severity of caecal wall ulceration was reduced in mice which received the plant extract and metronidazole as compared to the control animals[46].The activities of *n*-hexane, dichloromethane and methanol extracts from five anti-diarrheic Thai medicinal plants, *Acacia catechu* (Fabaceae) resin, *Amaranthus spinosus* (Amaranthaceae) whole plant, *Brucea javanica* (Simaroubaceae) seed, *P. longum* (Piperaceae) fruit and *Quercus infectoria* (Fagaceae) nut gall were tested against the in vitro growth of fresh isolates of the intestinal protozoan parasite *Blastocystis hominis*. All extracts showed inhibitory activity with reference to metronidazole[47]. Both the root and fruit of *P. longum* possess antiamoebic activity approximately to the same extent[48]. The ethanolic extract, hexane fraction, *n*-butanol soluble fraction exerted in vitro amoebicidal action at 1000 micrograms/mL and the chloroform fraction showed the same at 500 micrograms/mL. The ethanolic extract and piperine, a pure compound, from this plant material cured 90% and 40% of rats with caecal amoebiasis respectively [49, 46].

Antimicrobial activity:

Various extracts of *P. longum* were prepared and evaluated against bacterial pathogens, such as *S. albus, S. typhi, P. aeruginosa, E. coli* and *B. megaterium* and one fungus, *A. niger.* Compared to streptomycin all the extracts exhibited a good antibacterial activity[50]. The isolated constituents and n-hexane extract were found to show varying degree of antibacterial activity against all the tested bacteria. However, the aqueous extract did not show antibacterial activity against the tested bacteria[51].

Effect on respiratory system:

Isolated piperine showed a central stimulant action in frogs, mice, rats and dogs along with increased hypnotic response in mice. It antagonized respiratory depression induced by morphine or pentobarbitone in anesthetized dogs[52]. A petroleum ether extract of the fruits antagonized morphine-induced respiratory depression in mice[53]. A comparative study conducted with piperine and nalorphine, for effects against morphine-induced respiratory depression and analgesia, revealed that both reversed morphine-induced respiratory depression but, unlike nalorphine, piperine did not antagonize morphine-induced analgesia in rats[54]. Petroleum ether extract of *P. longum* produced respiratory stimulation in smaller dose but higher dose cause convulsion in laboratory animals. This may be due to presence of some medullary stimulant factors in the extract[55, 56]. The crude extract of *P. longum* as well as piplartine, one of its alkaloids, suppressed the cilliary movements of the esophagus of the frog, which may be due to the suppression of cough reflex[57].

Antiasthmatic activity:

An extract of the fruits in milk reduced passive cutaneous anaphylaxis in rats and protected guinea pigs against antigen-induced bronchospasm[55, 56].

Effect on cardiovascular system:

Bioassay-guided isolation of chloroform extract of the fruits of *P. longum* is using an in vitro DGAT inhibitory assay, lead to isolation of a new alkamide together with four known alkamides. Pharmacological inhibition of acyl CoA: diacylglycerol acyl transferase by alkamides emerged as a potential therapy for the treatment of obesity and type 2 diabetes[58]. Guineensine, isolated from chloroform extract inhibited ACAT activity in a dose-dependent manner[59]. An amide namely dehydropipernonaline having coronary vaso-relaxant activity was isolated from the fruit of *Piper longum* [60]. Methanolic extract from dried fruits, roots and nutgalls of *Piper longum*, *Piper sarmentosum, Quercus infectoria* respectively, were examined for their spasmolytic activities using isolated rat or guinea pig ileum and compared with a reference anti-diarrheal drug such as loperamide and an L-type calcium channel blocker such as verapamil. All extracts and both drugs suppressed the contraction in rat ileum showing the same potency for P. *longum* and *P. sarmentosum* which was more than seen for Q. *infectoria*[61].

The effects of the several extracts of *Piper longum* on rabbit platelet function were examined. The ethanol extracts inhibited platelet aggregation induced by U46619

in a concentration-dependent manner and by thrombin weakly. It was concluded that *P. longum* contains a constituent(s) that inhibits platelet aggregation as a non-competitive thromboxane A2 receptor antagonist[62]. Four acidamides, piperine, pipernonaline, piperoctadecalidine, and piper longumine, isolated from the fruits of *P. longum* 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[63]. A pilot study was carried out on the breast development in female wistar rats using an indigenous herbal preparation by topical application containing *Piper longum* that showed an increase in the appetite[64].

Antidiabetic activity:

The antihyperglycemic and antilipidperoxidative effects of ethanolic extract of *Piper longum* dried fruits in alloxan-induced diabetic rats were studied [65]. The blood glucose level, carbohydrate metabolizing enzymes and the status of lipid peroxidation and antioxidants were assayed using specific colorimetric methods. Oral administration of dried fruits has shown significant anti-hyperglycemic, anti-lipidperoxidative and antioxidant effects in diabetic rats comparable to that of the standard reference drug glibenclamide[66].

Hypochoesterolaemic 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[67]. The unsaponificable fraction of the oil of *P. longum* also significantly decreased total serum cholesterol and hepatic cholesterol in hypercholesterolaemic mice[68].

Antioxidant activity:

A combination of spices (*Piper nigrum*, *Piper longum* and *Zingiber officinale*), herbs (*Cyperus rotundus* and *Plumbago zeylanica*) and salts make up *Amrita Bindu* were tested for anti-oxidant activity. The analysis revealed the antioxidant potential of the ingredients in the following order: *Piper nigrum* > *Piper longum* > *Cyperus rotundus* > *Plumbago zeylanca* > *Zingiber officinale*[69].

Analgesic activity:

P. longum root for opioid type analgesia using rat tail-flick method and for NSAID type analgesia using acetic-acid writhing method by using pentazocine and ibuprofen as drug controls. An aqueous suspension of *P. longum* root powder was given orally to mice and rat. The study accomplished that *P. longum* root had weak opioid but potent NSAID type of analgesic activity[70].

Anti-inflammatory activity:

The fruit decoction showed anti-inflammatory activity against carrageenin induced rat paw edema[71].

Immunomodulatory activity:

The immunoregulatory potential of *P. longum* and piperinic acid, one of its active constituent, in Balb/C mice (*in vivo*) and human PBMCs (*in vitro*) models showed a dose dependent decrease of lymphocytes (CD4+ and CD8+ T cells) and cytokine levels in sensitized Balb/C mice with a marked inhibition[72]. Alcoholic extract of the fruits of *P. longum* and its component piperine was studied for their immunomodulatory and antitumor activity. Alcoholic extract of the fruits and piperine were found to be cytotoxic[73]. An aqueous extract of *P. longum* fruit powder showed 100% giardicidal activity[13]. *P. longum* was found to offer protection against externally induced stress. A famous Ayurvedic preparation containing long pepper in pippli rasyana was tested in mice infected with Giardia lamblia and found to produce significant activation of macrophages, as shown by an increased MMI and phagocytic activity[74].

Anti-cancer activity:

Piper longum is reported to exhibit significant anti-tubercular activity [75, 76]. The effect of piperine on the inhibition of lung metastasis induced by B16F-10 melanoma cells was studied in C57BL/6 mice. Simultaneous administration of the compound with tumor induction produced a significant reduction (95.2%) in tumor nodule formation along with reduced lung collagen hydroxyproline, uronic acid and hexosamine content in the piperine-treated animals. Piperine, an alkaloid present in plants such as *P. nigrum* and *P. longum* showed significant anti-metastasis activity[77]**.** Piperine has chemopreventive effects when administered orally on lung cancer bearing animals[78]. Piperlonguminine showed an inhibitory effect on α-MSH-induced tyrosinase synthesis[79]. It was found that oral administration of ethanolic extract protected the cell surface and maintained the structural integrity of the cell membranes during DMBA induced hamster buccal pouch carcinogenesis[80]. The two active principles, ethyl 3', 4', 5'-trimethoxycinnamate and piperine were isolated and characterized from the combined hexane and chloroform extracts of *Piper longum.* The extracts significantly blocked the adhesion of neutrophils to endothelium in a time- and concentration-dependent manner[81]. Piplartine and piperine alkaloidal amides were isolated from *Piper*. It showed cytotoxic activity towards several tumor cell lines[82]. The study clearly demonstrated that piperine has the anti-oxidative, anti-apoptotic, and restorative ability against cell proliferative mutagenic response and phenotypic alterations by piperine, suggesting its therapeutic usefulness in immunocompromised conditions[83].

Anti-depressant activity:

Treatment with piperine (6.25–25 µM) for 72 h reversed the (corticosterone) CORT-induced reduction of BDNF mRNA expression in cultured hippocampal neurons[84]. A bioassay-guided isolation of the ethanol extract from the fruits of *P. longum* yielded a known piperidine alkaloid, piperine having potent antidepressant-like properties which are mediated in part through the inhibition of MAO activity, and therefore represent a promising pharmacotherapeutic candidate as an antidepressant agent[85].

Antiulcer activity:

The water decoction of ginger making up one of the constituents of *Mahakasyaya drugs* along with water decoction of *P. longum* and colloidal solution of *Ferula asafoetida* has been reported to protect against CRS-, ASP- and PL- induced gastric ulcers in rats[86]. Piperine, an alkaloid of long peppers, inhibited gastric emptying (GE) of solids/liquids in rats and gastrointestinal transit (GT) in mice in a dose and time dependent manner. GE inhibitory activity of piperine is independent of gastric acid and pepsin secretion[87].

Effect on Reproductive system:

The benzene extract of *P. longum* in combination with methanol extract of *Embelia ribes* berries lead to inhibition of pregnancy in 80% of animals[88]. The exposure to pippaliyadi does not have any adverse effect on the postnatal development and reproductive performance of the F_1 progeny[89]. Piperine showed marked increase in serum gonadotropins and a decrease in intratesticular testosterone concentration, despite normal serum testosterone titres[90]. The crude extract of *Piper longum* and its hexane fraction exhibited 100 and 86% efficacy respectively in female rats[91]. The reproductive toxicity of piperine was studied in Swiss albino mice. Piperine increased the period of the diestrous phase, which seemed to result in decreased mating performance and fertility. The results showed that piperine interferes with several crucial reproductive events in a mammalian model[92]**.** An ayurvedic contraceptive — pippaliyadi vati, containing equal parts of powdered seeds or fruit berries of *Embelia ribes*, fruit of *P. longum* and borax powder was fed orally to two groups of pregnant rats and humans to study embryotoxicity and teratogenicity. The fetuses of mothers fed with pippaliyadi had low birth weights and were smaller in length with less weight gained during gestation[93].

Bioavailability enhancement:

Piperine was found to enhance the bioavailability of structurally and therapeutically diverse drugs, possibly by modulating membrane dynamics due to its easy partitioning and increase in permeability of other drugs such as vasicine, indomethacin, diclofenac sodium etc.[94,95]. It was suggested that piperine might be inducing alterations in membrane dynamics and permeation characteristics, along with induction in the synthesis of proteins associated with cytoskeletal function, resulting in an increase in the small intestine absorptive surface, thus assisting efficient permeation through the epithelial barrier[96, 97]. The study showed that piperine enhances the serum concentration, extent of absorption and bioavailability of curcumin in both rats and humans with no adverse effects[98].

Hepatoprotective activity:

The fruit extract improved the regeneration process by restricting fibrosis, but offered no protection against acute damage or against cirrhotic changes in rodents[99]. Treatment with the ethanol extract of *P. longum* inhibits liver fibrosis induced by carbon tetrachloride (CCl_4)[100]. Piperine exerted a significant protection against *tert*-butyl hydroperoxide and carbon tetrachloride hepatotoxicity by reducing both *in vitro* and *in vivo* lipid peroxidation, enzymatic leakage of GPT and AP, and by preventing the depletion of GSH and total thiols in the intoxicated mice. Piperine showed lower hepato-protective potency than silymarin[101].

Safety profile:

Since, it is 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. In the evaluation of antifertility activity, long pepper at a dose of 1gm/kg body weight was found to be an effective contraceptive agent without toxic or teratogenic effects[102]. Acute and chronic oral toxicity studies on the ethanolic extracts of common spices *Cinnamomum zeylanicum* bark and *P.longum* fruits were carried out in mice showed no significant acute or chronic mortality compared to the control during this study[103]. The radio protective property of an ethanolic extract of *P. longum* fruits reduced the elevated levels of glutathione pyruvate transaminase (GPT), alkaline phosphatase (ALP), and lipid peroxidation (LPO) in liver and serum of radiation treated mice. The extract administration also increased the reduced glutathione (GSH) production to offer the radioprotection[104]. Piperine might interfere with enzymatic drug biotrasformations resulting in the inhibition of hepatic aryl hydrocarbon hydroxylase (AHH) and UDP-glucuronyltransferase and altered the pharmacokinetic parameters of barbiturates and phenytoin[103, 105,106].

CONCLUSION

Here, an attempt was made to address chemistry and pharmacology of the *P. longum.* Therefore, the review of plant *Piper longum* revealed that it has got a variety of pharmacologically and medicinally significant constituents, which are being utilized in the field of Ayurveda. It is a plant of high commercial and economical importance and its use as a bioavailability enhancer can be explored in various formulations. The above review provides information of its phytopharmacolgy, which may

be useful for further study of Ayurvedic drugs of folk medicinal practice of present era.

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