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REVIEW ARTICLE

Traditional Unani and Contemporary Outlook of *Filfil daraz* (*Piper longum* L.) – A Comprehensive Review

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Abstract

The spectacular thrust and inquisitiveness of the present-day world have resulted in an incredible scientific approach regarding herbal medicine potential. The importance of herbal medicine has witnessed a tremendous expansion because of its significant effective and safe medications, especially in chronic and long-standing ailments. *Filfil daraz* (*Piper longum* L.) or long pepper, is a herb with enormous therapeutic benefits. Its beneficial actions are *Hāḍim* (digestive), *Muqawwī-i-Mi'da* (stomachic), and *Kāsir-i- Riyāḥ* (carminative). Since ages, Unani physicians used this herb for several disorders like *Balghamī khansi* (Phlegmatic cough), *Fālij* (Paralysis), *Laqwa* (Facial palsy), *Mirgi* (Epilepsy), *Niqris* (Gout), *'Irq al-Nasā* (Sciatica), and *Qūlanj* (Colitis) etc. Literature survey revealed countless important phytoconstituents namely alkaloids such as piperine, volatile oil, esters and resins. Moreover, many plant parts have shown distinct activities like analgesic, anti-microbial, anti-fungal, immunomodulatory activities in quite a lot of *in-vivo* and *in-vitro* studies. The present review delivers a comprehensive description of *Piper longum* L., its ethnobotanical uses, and recent scientific studies. New research avenues are open for future research endeavours for phytochemical studies and preclinical and clinical trials to explore its medicinal importance.

Keywords: *Piper longum* L., *Filfil daraz*, Phytoconstituents, Unani

1. Introduction

The natural reserve of medicinal plants owing to its extensive utilization by the experts of indigenous systems has captured global presence. WHO estimates around 21,000 plant species that possess potential medicinal values. The blind dependence on synthetic drugs is over, and people return to nature with hope and faith in its efficacy and safety. Herbal medicines are a potential source of therapeutics providing disease treatment and maintaining health too with their holistic approach[1]. The plant extract containing several biochemical components, which range in strength from extremely active (e.g., Digitalis leaf) to very mild (e.g., Cinnamon bark), are perpetually conventional remedies. Although swiftly mounting literature on phytochemistry exists but only a nominal percentage of the entire species have been chemically inspected. As herbal drugs catch people's interest day by day, increased knowledge of medicinal plant's potential has prompted many creative and advanced growers as well as entrepreneurs to revenue up their cultivation as a commercial venture[2]. In the current medical system, natural drug substances deliver four essential and appreciable functions, thus adequately justifying their legitimate presence in the overall therapeutic arsenal:

i. Serve as natural medicines that are helpful.
ii. Provide essential compounds that make drug molecules less toxic and more effective.
iii. Exploration of prototypes which are biologically active for new and improved synthetic drugs.
iv. Modification by sufficient biological/chemical means of inactive natural products into potent drugs[3].

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Traditional knowledge of medicinal plants is now considered to play a vital role, and there is a need for collaboration and integration of the traditional system into the mainstream system of medicine in addressing the healthcare needs.

1.1 Scientific Classification (Table 1)

Table 1. Scientific classification of *Piper longum* L.

Kingdom	Plantae
Division	Tracheophyta
Class	Magnoliopsida
Order	Piperales
Family	Piperaceae
Genus	Piper L.
Species	*Piper longum* L.

1.2 Vernaculars

The plant is known by different names in different languages, areas, and traditions, which are stated as below[4]:

Arabic	Dar Filfil
Benga	Piplamor, Piplamul, Pipli, Pipul
Burma	Peikchin, Peikkhyen, Pezinngoun
Chinese	Pi Po
English	Long Pepper
French	Poivre long
German	Langer Pfeffer
Greek	Peperi macron
Gujarati	Piper, Pipli
Hindi	Gazpipal, Pipal, Piplamul
Italian	Pepelungo
Marathi	Pimpli
Persian	Filfil daraz, Fillfil dray, Maghz pipal, Pilpil, Pipal
Sanskrit	Chanchala Chapala, Dantakapha, Eranda, Gonamika, Pippali
Telugu	Modi, Pippali, Pipallu
Urdu	Pipul
Uriya	Baihehi

1.3 Geographical Distribution

The area with high humidity and high rainfall is suitable for its growth; basically, it enjoys the shade. In India, it is found in Bengal, Bihar, Annamalai district of Tamil Nadu, and Cherapunji in Assam. It is also found in parts of East Nepal, Singapore, Sri Lanka, Indonesia, and Malaysia. It is native to the Indo-Malaya region. The plant is a slender climber spread in India's warmer regions, i.e., the Western Ghats, Assam Central Himalayas, Khasi and Miker hills, and lower hill of Bengal[5,6].

1.4 Botanical Description

Filfil daraz is a slender, aromatic, pale brown circular and elongated climber having persistent woody roots. *P. longum* L. is a dried fruit spike. Erect rootstock, dense, jointed, branched, multiple stems, 0.6-0.9 m., ascending or prostrate (not climbing) much-branched, stout, cylindrical, thickened, finely pubescent above nodes is a well-known peculiarity. Other characteristics include narrow ovate lower leaves, rather cordate with broadly rounded lobes at the base, oblong-oval upper leaves, cordate at the base, all sub-acute, whole, glabrous, thin, bullate with reticulate venation sunk above and raised below, dark green in colour and shiny above, light and dull below; 5-7.5 cm lower leaf petiole, membranous, lanceolate and obtuse. Moreover, solitary spikes, pedunculated, slender male with narrow bracts, 1.3-2.5 cm female with circular bracts, smooth, peltate; 2 stamens; 3 or 4 stigmas, short, spreading, and permanent are also found. Tiny ovoid fruit, entirely sunk in a 2.5-3.8 cm strong fleshy spike, upright, unsharpened, blackish green in colour and shiny is usually found[4–7].

2. Parts Used

Different parts of *Filfil daraz* (*Piper longum* L.) used for the medicinal purpose are -

- Fruit[8]
- Root[9]
- Leaf[10]
- Stem[11]

3. Temperament (Mizaj)

The temperament of *Filfil daraz* (*Piper longum* L.) given by different Unani scholars in literature are-

- Hot 2 and Dry 2 ([12–14])
- Hot 3 and Dry 3 ([15])

4. Chemical Constituents

Following are the isolated phytochemicals of *Piper longum* L.[16] (Table 2):

Table 2. Isolated phytochemicals of *Piper longum* L.

3β, 4α-dihydroxy-1-(3-phenylpropanoyl)- piperidine-2-one	Piperlongimin A [2E-N-isobutyl- hexadecenamide]
(2E, 4E, 14Z)-6-hydroxyl-N-isobutyleicosa-2,4,14-trienamide	2E,4E-N-isobutyl-octadecenamide
Coumaperine	Piperlongimin B [2E-octadecenoylpiperidine]
N-5-(4-hydroxy-3-methoxyphenyl)-2E- pentenoylpiperidine	2E,4E-N-isobutyl-dodecenamide
Piperolactam A	2E,4E,12E,13-(3,4-methylenedioxyphenyl)- trideca-trienoic acid isobutyl amide
1- [1-oxo-5 (3,4-methylenedioxyphenyl) -2E,4E-pentadienyl] – pirrolidine	Piperine
(R)- (-) –turmerone	Pellitorine
Octahydro-4-hydroy-3alpha-methyl-7- methylene-alpha-(1-methylethyl)-1H-indene-1- Methanol	N-[(2E,4E)-Decadienoyl]-piperidine
(+) -aphanamol I	N-Isobutyl-2E,4E-undecadienamide
Bisdemethoxycurcumin	Piperlonguminine
Demethoxycurcumin	Piperanine
Longumosides A	N-[(2E,4E)-Tetradecadienoyl] piperidine
Longumosides B	N-Isobutyl-2E,4E-hexadecadienamide
Erythro-1-[1-oxo-9(3,4-methylenedioxyphenyl)-8,9-dihydroxy-2E-nonenyl]-piperidine	Pipercallosine
	(2E,4E,12Z)-N-Isobutyl-octadeca-2,4,12- Trienamide
Threo-1-[1-oxo-9(3,4-methylenedioxyphenyl)-8,9-dihydroxy-2E-nonenyl]-piperidine	N-Isobutyl-2E, E-octadecadienamide
3β,4α-dihydroxy-2-piperidinone	(-)-alpha-cedrene
5,6-dihydro-2(1H)-pyridinone	(+)-Fargesin
Piperlongumide (1) [N-isobutyl-19-(3',4'- methylenedioxyphenyl)-2E,4E nonadecadienamide]	Piperolactam A
1-(3,4-methylenedioxyphenyl)-1E tetradecene	(+)-Sesamin
2-Phenylethanol	Bisdemethoxycurcumin
l-Zingiberene	1,4-cadinadiene
Dehydropipernonaline	Tricyclene
Pipernonatine	Alpha-Cubebene
(E)-9-(Benzo[d] [1,3] dioxol-5-yl)-1-(piperidin-1- yl) non-2-en-1-one	Piperundecalidine
1-(2E,4E,12E)-Octadecatrinoylpiperidine	3-phenylundecane
Retrofractamide B	4-[(1-Carboxy-2-methylbutyl) amino]-2(1H)- Pyrimidinone
(2E,4E,14Z)-N-Isobutyleicosa-2,4,14- Trienamide	Bicyclo [3. 2. 2] non-6-en-3-one
N-isobutyl-2E,4E-decyldecadienamide	Cedryl acetate
(2E,4E,10E)-N-11-(3,4-Methylenedioxyphenylhmdecatrienoylpiperidine	Isolongifolene epoxide

1-[(2E,4E,14Z)-1-Oxo-2,4,14-eicosatrienyl]- Piperidine	N-isobutyleicosa-2(E),4(E),8(Z)-trienamide
Guineensine	Pisatin
(2E,4E,14Z)-N-Isobutyldocosa-2,4,14- Trienamide	Tetradecahydro-1-methylphenanthrene
(2E,4E,12E)-13-(Benzo[d] [1,3] dioxol-6-yl)-1-(piperidin-1-yl) trideca-2,4,12-trien-1-one	Undulatone
(2E,4E,13E)-14-(Benzo[d] [1,3] dioxol-6-yl)-N- isobutyltetradeca-2,4,13-trienamide	Copaene
Brachyamide B	Linalool
Dihydropiperlonguminine	Sylvatine
Piperdardine	beta-Cubebene
Retrofractamide A	(-)-Caryophyllene oxide
Piperchabamide D	Hypnon
N-isobutyl-2E,4E-dodecadienamide	Moslene
Piperchabamide B	Cymol
13-(1,3-Benzodioxol-5-yl)-N-(2-methylpropyl) -(2E,4E)-tridecadienamide	Methyl hydrocinnamate
Piperchabamide C	Hexahydropyridine (PIP)
1-[(2E,4E)-1-oxo-2,4-hexadecadienyl]- Piperidine	Pisol
2,2-Dimethoxybutane (C6H14O2]	Piperonal
2-Hydroxy myristic acid (C14H28O3]	Isobutylisovalerate
β-Myrcene (C10H16]	Tridecane (TRD)
N-methyl-1- octadecanamine (C19H41N]	Pentadecane (MYS)
Piperazineadipate (C10H20N2O4]	N-Heptadecane
2-Nonynoic acid (C9H14O2]	N-Nonadecane (UPL)
Dodecanal (CH3(CH2]10CHO]	Tridecylene
ester (C24H38O4]	Heptadecene
2-Amino-4-hydroxypteridine-6-carboxylic acid	Pentadecene
(C7H5N5O3]	Nonadecene
Piperlongumine	tetradecadiene-1,13
Hydrochloric acid (HCI)	Linalool (D)
Palmitic acid	Cyclopentadecane
1,8-cineole	Beta-Bisabolene
Lawsone	Sesamol
Cis-Decahydronaphthalene	Sesamin
Piperonylic acid	p-Amino-o-cresol
8-Heptadecene	2,4-Dimethoxytoluene
9,17-OCTADECADIENAL (Z)	D-Camphor (CAM)
Cyclodecene, 1-methyl-1,4,7, -Cycloundecatriene, 1,5,9,9-tetramethyl-, Z, Z, Z-	Cis-2-Decalone
(+/-)-Isoborneol	Piperitenone
(Z)-caryophyllene	(-)-Nopinene
-cis-. beta. –Elemenediastereomer	(-)-Alpha-Pinene
N-Isobutyl-2,4-icosadienamide	Isodiprene (CHEBI:7)

(E, E, E)-11-(1,3-Benzodioxol-5-yl)-N-(2- methylpropyl)-2,4,10-undecatrienenamide	(R)-linalool
Epieudesmin (ZINC03996196)	N-(2,5-dimethoxyphenyl)-4-methoxybenzamide
Valencene	Anethole
(1S,5S)-1-isopropyl-4- methylenebicyclo [3.1.0] hexane	Isoeugenol
(5S)-5-[(1R)-1,5-dimethylhex-4-enyl]-2- methylcyclohexa-1,3-diene	(3S)-3,7-dimethylocta-1,6-dien-3-yl] propanoate
(E)-5-(4-hydroxy-3-methoxy-phenyl)-1- piperidino-pent-2-en-1-one	()-Terpinen-4-ol
(3R,8S,9S,10R,13R,14R,17R)-17-[(2R,5S)-5- ethyl-6-methylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H- cyclopenta[a]phenanthren-3-ol (ZINC03982454)	Alpha-Farnesene
Delta-elemene	Farnesene
(2R,4aR,8aR)-2-methyldecalin	alpha-humulene
(1R,5R,7S)-4,7-dimethyl-7-(4-methylpent-3- enyl) bicyclo[3.1.1] hept-3-ene	Isocaryophyllene
Calarene	p-Ocimene

Out of 159 phytochemicals identified, 26 different classes of compounds are differentiated, which are as follows[16] (Figure 1).

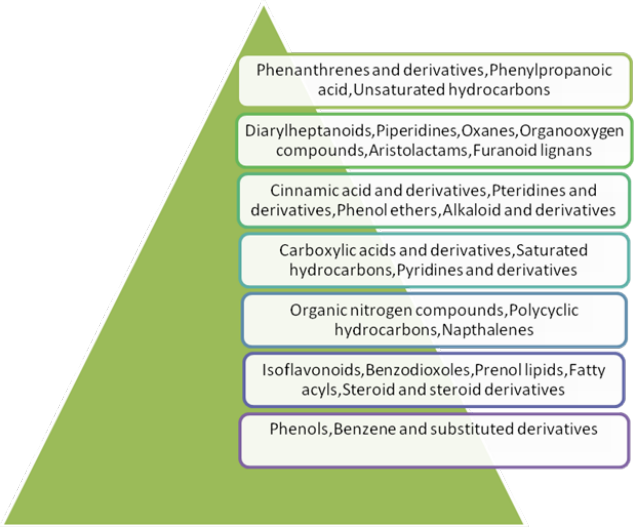

Figure 1. 26 different classes of compounds differentiated from 159 phytoconstituents identified.

5. Pharmacological Actions

Piper longum L. is being used since antiquity, and their pharmacological actions are as follows:

- *Mushtahī* (appetizer)
- *Hādim* (digestive)
- *Muqawwī-i-Mi'da* (stomachic)
- *Muqawwī-i-Bāh* (aphrodisiac)
- *Kāsir-i- Riyāh* (carminative)
- *Musakhkhin* (calorific)
- *Muhallil* (resolvent)
- *Munawwim* (sedative)
- *Muwallid-i-khūn* (haematinic)
- *Musqit-i-Janīn* (abortifacient)
- *Mushil-i-Safrā'* (cholagogue)[12,13]

6. Therapeutic Uses

Unani physicians have used this herb in *Balghamī khansi* (Phlegmatic cough), *Fālij* (Paralysis), *Laqwa* (Facial palsy), *Mirgi* (Epilepsy), *Niqris* (Gout) and *'Irq al-Nasā* (Sciatica)[13]. It is also useful in *Qūlanj* (Colitis) and pain caused by cold[15]. Numerous medicinal uses are ascribed to the fruits and roots for respiratory ailments such as cough, bronchitis, asthma, etc. Internally, it is used as carminative and locally beneficial as analgesic for relieving inflammation and muscle pain. Furthermore, it is used as snuff in cases of coma and somnolence, as a sedative in insomnia and epilepsy. It is also used as a tonic and hematinic agent; as a cholagogue in bile duct and gall bladder obstruction; as an emmenagogue and as an abortifacient agent. The beneficial effects of this herb are also recognized in dysentery and leprosy[9]. Also used to treat jaundice, to increase lactation, to help in conception[10].

Fruit: According to Unani medicine, the taste of the fruit is bitter, hot and sharp. Fruit is used as

carminative, liver tonic, general tonic, stomachic, aphrodisiac, hematinic, digestive, abortifacient, diuretic and emmenagogue agent. It is found to be helpful in liver inflammation, joints pain, lumbago, snake bite, scorpion biteand night blindness. For bronchial asthma, it is mixed with honey before its use[12]. The unripe fruit is considered to be sweetish in Ayurveda having a cooling effect and helpful in biliousness. The ripe fruits are sweetish, pungent, tonic, stomachic and laxative in nature and are generally used in asthma, bronchitis, leucoderma, chronic fevers, tumours, piles, spleen disorder, for strengthening cognition, insomnia, jaundice, diarrhoea, hiccups, tuberculous glands, leprosy, anaemia, dysentery, pain and inflammation. The role of fruit milk extract is established and showed effective decline of passive cutaneous anaphylaxis in rats and also protects against antigen-induced bronchospasm in guinea pigs[17].

Root: Usually, root is pungent and induces biliousness. The potential effects of root include its stomachic, laxative, anthelmintic, carminative and appetizer property. Various illnesses such as bronchitis, abdominal pain, spleen disorders, tumours, ascites, palsy, gout and lumbago are treated with root[4]. Oil components of the herb have been reported to inhibit the rise in triton-induced serum total cholesterol in mice. Likewise, the antifertility activity is also documented with the use of powder of root[17].

7. Therapeutic Dose

The mentioned therapeutic doses in various Unani classical textbooks are as follows:

- 1–4 Masha (1–4 gm)[13]
- 3–5 gm[14]
- 1–2 Masha (1–2 gm)[12].

8. Adulterants

Adulterated with the *Piper retrofactum* and *Piper beetle* species[18].

9. Safety Aspect

The drug is traditionally considered to be safe in the dosage mentioned[6].

10. Contraindication

According to Unani physicians, it is contraindicated in liver disorders. Furthermore, it is recommended to avoid it during headache[13].

11. Pharmacological Studies

Scientifically validated studies of *Filfil daraz* (*Piper longum* L.) are mentioned in Table 3.

Table 3. Scientifically validated studies of *Filfil daraz* (*Piper longum* L.)

Pharmacological Actions	Part and Method used	Effect
Anti-fungal activity	Whole plant (*in-vivo*)	Fungicidal activity of *P. longum* L was detected in the essential oil of the fruit against six fungi, *P. oryzae, R. solani, B. cinerea, P. infestans, P. recondita*, and *E. graminis*[19].
Anti-amoebic activity	Methanolic extract of *P. longum, P. sarmentosum* and *Q. infectoria*	*E. histolytica* of mice caecum has been studied and relative to the control animal, the incidence of caecal wall ulceration in mice receiving plant extract and metronidazole was significantly decreased[20].
Antimicrobial activity	Isolated constituents and n-hexane extract	The extract has been found to be effective for variable antibacterial actions against all bacteria evaluated[21].
Anti-asthmatic activity	Fruit extract in milk	In rats, reduced passive dermal anaphylaxis was observed and in guinea pigs against bronchospasm caused by antigens was defended[45,46]. Pediatric clinical trials showed efficacy in bronchial asthma[22].
Anti-diabetic activity	Ethanolic extract of dried fruits. Oral administration of dried fruits	Compared to the standard reference drug glibenclamide, oral dried fruit administration has demonstrated substantial anti-hyperglycemic, anti-lipid peroxidative, and antioxidant effects in diabetic rats[23].
Hypocholesterolemic activity	Unsaponifiable part of the oil of *P. longum*	In hypercholesterolaemic mice, the unsaponifiable portion of *P. longum* oil substantially lowered the overall serum cholesterol and hepatic cholesterol levels[24].

Antioxidant activity	Chloroform extract of *P. longum*	In vitro, the maximum antioxidant activity was observed when chloroform extracts were used[25].
Analgesic activity	Aqueous suspension of *P. longum* root	*P. longum* root was found to have low opioid but powerful analgesic action[26].
Anti-inflammatory activity	Decoction of the fruit	Carrageenan-induced rat paw edema was studied for anti-inflammatory activity and decoction was found to be effective[27].
Immunomodulatory activity	Alcoholic extract of the fruits of *P. longum* L.	Cytotoxic effects of alcoholic fruit extract and piperine were observed. Invitro (human PBMCs) and in vivo studies (mice) showed marked inhibition and dose-dependent reduction in lymphocyte (CD4+ and CD8+ T cells) and cytokine levels[28,29].
Anti-cancer activity	Piperine	Chemo preventive potential of oral piperine was detected on lung cancer-bearing animals. In DMBA-induced hamster buccal pouch carcinogenesis, oral ethanolic extract was found to be effective in protecting cell surface and maintaining cell membranes structural integrity[30,31].
Antidepressant activity	Ethanol extract	The strong antidepressant-like traits of piperine which is mediated through inhibiting MAO's actionwas found to be capable as antidepressant in treating depression[32].
Neuroprotective activity	Extract	Experimental glioma model in rats using C6 glioma cells was used and increased level of lipid peroxides, tissue marker enzymes lactate dehydrogenase, creatine kinase, 5'nucleotidase and acetylcholine esterase was significantly attenuated proving its anticancer and neuroprotective role[33].
Antiulcer activity	Aqueous extract of *P. longum* L., *ginger*, and *F. asafetida*	The aqueous extracts are noted to defend against gastric ulcers caused by CRS-, ASP- and P.L. in rats[34].
Bioavailability enhancement activity	Piperine	Due to its fast partitioning and better permeability of other drugs such as vasicine, indomethacin, diclofenac sodium, piperine was found to enhance the bioavailability of structural and therapeutic medicines through controlling membrane dynamics[35].
Hepatoprotective activity	Ethanol extract	Inhibition of carbon tetrachloride-induced liver fibrosis was observed with the therapy of its ethanolic extract[36].
Effect on Reproductive System	Benzene extract of *P. longum* with methanol extract of E. ribes	Pregnancy inhibition in 80 percent of animals was identified with its extract[37].
Spermicidal activity	Hexane extract of *P. longum*	*In-vitro* study revealed significant drop in sperm viability in the treated group when compared to control establishing robust contraceptive spermicidal activity[38].
Effect on the cardiovascular system	Chloroform extract	ACAT activity was dose-dependently inhibited by guineensine, extracted from chloroform extract. The isolated chloroform extract from the fruits of *P. longum* results in isolation of a new alkamide and four familiar alkamide. The factor responsible for the potential treatment of obesity and type 2 diabetes was found to be inhibition of acyl CoA: diacylglycerol acyltransferase done by alkamide[39,40].
Effect on the respiratory system	Fruit Pet. ether extract	In mice, the extract displayed antagonizing property when morphine-induced respiratory depression was taken into account[41].
Clinical trial in irritable bowel syndrome	Powder of fruit	Significant efficacy was noted in forty patients of various subjective parameters of IBS along with marked changes in laboratory results[42].
Clinical study on prostate cancer cell	Alkaloid *Piper longum*ine	In human prostate cancer cells, rapid diminution was observed in androgen receptors[43].
Anticancer activity of prostate cancer cells	Pipernonaline	Sub-G1 accumulation and G1/S phase transition of PC-3 cells was induced and pipernonaline showed apoptotic activity via reactive oxygen species production[44].

12. Conclusion

The present world is in crisis for various novel diseases with no cure in modern science, consequently leading to a surge in demand for alternative treatment. Alternative and traditional medicine has incredible potential as far as disease management is concerned due to their high efficacy, safety, and economic merits, and the high time has come to gain benefits from them. This paper demonstrates the diverse and enormous use of *P. longum* in Unani medicine, especially in respiratory and neurological illnesses. It adds new impetus through the description of its chemical constituents and several preclinical and clinical trials, thus making it eligible as therapeutic aid in healthcare system. The information collected through this paper can be well utilized in research of the pharmacological action and various secondary metabolites of *Piper longum* L. Although it has been used for a long time, some of its actions mentioned in the Unani literature needs to be validated by scientific research. The practice of using the herb extensively as single drug and a component in many compound formulations proves its importance. This paper will support in understanding innumerable facets of *Piper longum* L. in a nutshell and help correlate its actions with chemical constituents. This may be helpful in designing further studies on *Piper longum* L. to investigate new uses and possible actions thereafter.

13. Conflict of Interest

None

14. References

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