

A Review on Medicinal Plant *Piper cubeba* L. and Its Pharmaceutical Properties

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Abstract

Plants are regarded as the richest research for many potential drugs. Medicinal plants have been used for the treatment of various diseases since ancient time. The bioactive compounds like different phytochemicals are extracted from various parts of the medicinal plants, as they serve as traditional herbal drugs. These drugs are well recognized in modern medication system due to natural products, much safer, effective in curing various diseases and it have less side effects. The secondary metabolite like tannine, saponin, flavonoids, alkaloids and phenolic compounds are widely used in pharmaceuticals. Therefore, some plants are usage as medicine for curing different diseases. *Piper cubeba* (Kabab Chini) is tropical medicinal plants which are common in Indonesia and different parts of the world. It has been reported that *Piper cubeba* is potential medicinal plant which has various phytochemicals and its uses in antimicrobial, anti-inflammatory, antibacterial, antioxidant, anti-cancerous, hepatoprotective, nephroprotective and antileishmanial activity. Thus, the aim of this review of literatures is to describe the phytochemicals and pharmaceutical attributes of *Piper cubeba*, which possess a broad range in biological activities.

Keywords

Piper cubeba, Kabab Chini, Medicinal plant, Pharmaceutical properties

1. Introduction

Piper cubeba L., is a flowering vine which are commonly known as Java Pepper or Kabbab Chini and belong to family Piperaceae, genus *Piper*, and it cultivated for fruits and essential oil. The two largest genera are *Piper* and *Peperomia*, each containing about one thousand of the species in which about 30 species are medicinal in Asia-Pacific [1, 2]. One such therapeutically significant medicinal plant *Piper cubeba* has more than 700 species which distributed in the tropical and subtropical regions of the world [3]. This is a very variable species which cultivated mostly in Java and Sunatra. Efforts have been made to cultivate it in India, especially in Mysore of Karnataka state, but not or on a commercial scale [4]. *Piper cubeba* is a climbing shrub with cylindrical, smooth zigzag, striate stem somewhat thickened at the node. These species are mostly shrub, climbing herbs or tree and are widely distributed in tropical regions such as Asia, Central and Western Africa, South and Central America, and Pacific Ocean islands [5]. *Piper cubeba* inhabits Java, Sumatra, Southern Borneo, Moluce and other isles in the Indian Ocean. It is mostly grown in Java and Sumatra; hence some time known as 'Java pepper' but also from some African countries, cubeb pepper is exported. It is cultivated in some of the West Indian island [6]. *Piper cubeba* is a native plant of Indonesia [4, 7, 8, 9]. Effort have been made to cultivate it in India, most in Mysore but not on a commercial scale cubeb can be easily grow by planting at the foot of the shade trees in coffee plantation. The fruits are collected when fully grown but still green, and dried in the sun light when they become black and wrinkled [10]. The fruit of *Piper cubeba* wrinkled, rounded (5-7 mm in diameter), light brown to dark brown with 7 mm long stalk, pericarp red to slightly brown, testa fused with pericarp, fruit hard and stony albumen white and oily, occur aromatic in characteristic, test pungent and slightly bitter [11, 12]. *Piper* are used

for many purposes such as spices, foods, fish poison, fish bait, insecticides, hallucinogen, oils, perfumes, ornaments and for medicines [13, 14]. *Piper cubeba* use in the Western Medicine which can be traced to the middle ages [15]. In Indonesia, *Piper cubeba* is valued as a medicinal plant and used in Indonesian traditional medicine to treat dysentery, gonorrhoea, syphilis, diarrhoea, asthma, enteritis and abdominal pain [16].

2. Phytochemicals constituents

The bioactive compounds from *Piper* species have played a substantial role as therapeutic agents in drug discovery [17]. The phytochemicals of *Piper* species is pigeonholed by the production of typical chemical compounds such as benzoic acids, amides and chromenes, as well as terpenes, phenylpropanoids, lignans, other phenolics and a series of alkaloids [18, 19]. Piperine is an abundant alkaloid in the barrier of this species [20]. Sabinene, β - elemene, and cubebol are the principal components of essential oil *Piper cubeba* [21]. Dried fruits powder of *P. cubeba* contain essential oil monoterpenes, sabinene, α -thujene, β -elemene, careen, 1, 4-cineol and 1, 8-cineol; sesquiterpenes: b-caryophyllene, copaene, α - and β - cubebene, d-cadinene, cubebol and germacene; and some lignans including the dibenzylbutyrolactone lignin i.e. (-) cubebin [22, 23]. A lignin profile of *P. cubeba* from Indonesia has revealed 13 lignans found in the fruits, 15 in the leaves and only five lignans in the stalk. Twenty four lignans have so far been reported from *Piper cubeba* [24, 25, 26, 27, 28]. The chemical structures of lignans are very biodiversed comprising of furanofuran lignans commonly found in the genus *Piper* such as cubebin, hinokinin, yatein, isoyatein, and neolignans with a curious structure such as kadsurin A and piperenone [29, 30]. The other chemical constituents in essential oil of *Piper* include alloaromadendrene, α -muurolene, α -phellandrene, α -pipene, α -terpinene, α -terpineol, asrone, β -pinene, β -bisabolene, bicyclosesquiphellandrene, calamene, cesarone, cubebic acid, cubenol, cubebinolide, epicubenol, g-humulene, g-terpinene, gum, ledol, limonene, myrcene, linalool, nerolidol, ocimene, resinoids, sabinol, and safrole [22]. Prabhu and Mulchandai, [25] have been isolated some lignans which are from *Piper cubeba*, and neolignans have been isolated by Badheka et al. [26, 27].

3. Pharmacological activity

The fruit of *Piper cubeba* are frequently used as a spice and have also been used for the treatment of various disease like asthma, abdominal pain, diarrhoea, dysentery, syphilis, gonorrhoea and enteritis [16] has also inhibitory effects on hepatitis C virus protease Some biological activities of essential oils of *Piper cubeba* is anti-parasitic [31], antimicrobial [32] and insecticidal activities [33] have been reported. *Piper cubeba* and their different products are scientifically proved for various pharmacological activities.

3.1. Antimicrobial activity

The extracts of *Piper cubeba* have antimicrobial activity against the selected bacteria and fungi [22]. The essential oil of *P. cubeba* has antibacterial activity against *B. pumilus*, *B. subtilis*, *C. diphtheria*, *Vib. Cholere*, *Sal. Typhi*, *Stre. Pyogenes*, *Ps. Solanacearum*, *E. coli*, *Staph. aureus*, *Sal. Typhi*, *Sal. Paratyphi*, *Pestalotia* species [12] and against *B. Pumilus*, *S. faecalis* and *P. solanacearum* [34]. The different extract of fruit powder of *P. cubeba* including alcoholic, aceton, chloroformic and water extract have antibacterial activity against gram negative *Escherichia coli*, *Pseudomonas aeruginosa* and gram positive *Staphylococcus aureus* [35]. The fruit oil of *Piper cubeba* showed significant antifungal activity against *Aspergillus fumigates* *A. flavus*, *Curvularia plunata*, *Trichoderma vird*, *Alternaria tenuis penicillum funiculosum*, *Penicillium javanicum*, *P. striatum* and *Fusarium solani* [36]. The cubeb oil is isolated from *P. cubeba* which are effectively used against *Bacillus typhosus* and influenza virus [4].

3.2. Anti-inflammatory activity

Piper species could serve as alternatives to synthetic anti-inflammatory drugs, as research has demonstrated that synthetic anti-inflammatory drugs such as NSAIDs and steroids are often associated with adverse effects [37, 38] when compared to natural compounds. Choi and Hwang, [36] has been reported that methanolic extract of fruits powder of *Piper cubeba* have anti-inflammatory activity. Several species of *Piper cubeba* were found to have anti-inflammatory activities [39]. The essential oil of *Piper cubeba* is uses in painful and inflammatory conditions [40]. Anti-inflammatory activities of *Piper cubeba* has been studied using chemically-induced edema and arthritis in *in vivo* [36]. Desouza et al. [41] have reported that active component of cubebin which isolated from *Piper cubeba* and its have anti-inflammatory activities. The phytochemical cubebin has potential anti- inflammatory activity [42].

3.3. Antibacterial activity

The fruit powder of *Piper cubeba* was extracted in alcoholic, chloroformic, aceton and water which evaluated for antibacterial activity against gram (-) *Pseudomonas aeruginosa*, *Escherichia coli* and gram (+) *Staphylococcus aureus* in which all extract of *Piper cubeba* showed antibacterial activity [43]. Khan and Siddiqui [44] have reported that ex-

tract of *Piper cubeba* shows antibacterial activity against *Salmonella typhi*, *Staphylococcus albus*, *Bacillus megaterium*, *Pseudomonas aeruginosa* and *Escherichia coli*. While the chloroform extract has antibacterial activity on both gram positive and gram negative at effect (12 mm) on *E. coli*, 10 mm on *P. aeruginosa* and 11 mm on *S. aureus* [44]. The essential oil of *Piper cubeba* has antibacterial activity against *Bacillus subtilis*, *Vib. cholera*, *Sal. Typhi*, *Streptococcus faecalis*, *Strep. Pyogenes*, *B. pumilus*, *Ps. Solanacearum*, *B. utilis*, *E. coli*, *Staph. Aureus*, *Sal. typhi*, *Sal. paratyphi* and *Pestalotia spp* [9].

3.4. Antioxidant activity

Piper species, commonly used in diet and traditional medicine, were assessed for their antioxidant potential. Muchandi et al. [45] have studied that methanol extract of *Piper cubeba* exhibited high potential of DPPH free radical scavenging activity. The ethanolic extracts of *Piper cubeba* have high antioxidant activity [46]. Aboul-Enein et al. [47] have studied and examined that *Piper cubeba* has antioxidant action viz. magnitude and have capabilities to search free radicals, hydroxyl radical (HO) and superoxide anion radical in different type of systems. Choi and Hwang [48] investigated that *Piper cubeba* is effective on plasma antioxidant system and lipid levels in rat. In rats result in increase in antioxidant enzyme activity and HDL-cholesterol, and a decrease in malondialdehyde. In *in vitro* ethanolic extract of fruit powder of *Piper cubeba* has potent antioxidant capabilities like DPPH scavenging (93.88%), nitric oxide (89.06%) and hydroxyl radical (87.69%) and scavenging activity at a concentration of 200 µg/mL [49, 50]. The ethanolic extract of *Piper cubeba* has high amount of alkaloids, glycosides, tannins, phenolics and other chief secondary metabolites which have potent antioxidant activity. In living system, some enzymes such as glutathione peroxidase, superoxide dismutase and catalase the certain endogenous antioxidant such as α -tocopherol, ascorbic acid, β -carotene and uric acid, since the endogenous antioxidants acting as intracellular defensive cells which from free radicals damage and extensive lyses [46].

3.5. Anti-cancerous activity

The ethanolic extract of *Piper cubeba* significantly inhibits the growth induced by β -estradiol in MCF-7, breast cancer cell line in human [51]. Yam et al. [52] have reported that ethanolic extract P9605 inhibited proliferation in androgen-dependent LNCaP human prostate cancer cell by reducing DNA synthesis and inducing apoptosis. This antigrowth effect was less pronounced in androgen independent PC-3 prostate cancer cell lines. The fraction from *Piper cubeba* exhibited cytotoxic activity against breast cancer [39] cells and normal breast cells and it also have lower toxicity against normal fibroblast cell. The bioactive compounds of crude extracts from *Piper* species have been widely reported to have inhibitory effects on tumour cell lines and could be potential sources of new anticancer drugs [53, 54, 55, 56]. They have effects on cancer cells and can serve as chemopreventive against in malignant growth [57, 58]. The cytotoxic effect of *Piper cubeba* fraction inhibited cell growth and appears to have induced apoptosis in MCF-7, MDA-MB-468, MDA-MB-231 and L929 cells [59]. Alkaloids and amides are the main constituents of *Piper* species that suppress the growth of cancer cell lines [60]. The phytochemicals of lignans isolated from essential oil of *P. cubeba* and its have anticancerous activity in metabolic pathways, however, through the induction of cell death by apoptosis [61, 62, 63, 64]. The derivatives of lignin in *in vitro* have anticancer activity against six human cancer cell lines (i.e. HT29, HCT196, A549, K562, Kb and SiHa) [65].

3.6. Hepatoprotective activity

Piper species have gastrointestinal and hepatoprotective effect [66]. The ethanol extract of *Piper cubeba* fruits attenuated CCl₄ (Carbon tetra chloride) which induced serum marker enzymes and total protein [22]. The histology of animal liver section treated with ethanolic extracts of *Piper cubeba* showed the presence of normal hepatic cords, absence of necrosis and fatty infiltration [67] which further testifies the hepatoprotective activity. The extract of *Piper cubeba* fruit reduced the levels of SGPT (Serum Glutamic Pyruvate Transaminase) and SGOT (Serum Glutamic Oxaloacetic Transaminase), which stabilized and repaired plasma membrane and hepatic tissue when damage was induced by CCl₄ [68, 69, 70].

3.7. Nephroprotective activity

The fruit powder of *Piper cubeba* was given orally in the form of suspension at dose of 800 mg/kg and 100 mg/kg in pre-treated and post treated rat model against gentamycin induced nephrotoxicity, serum urea and serum creatinine was significantly decreased. The nephroprotective effect was assessed on the basis of biochemical estimation and histopathological examination of the treated kidney [71]. It is used to treat genitourinary disease, kidney and bladder calculi [72].

3.8. Antileishmanial activity

The methanol, ethyl acetate and acetone and n-hexane extracts of *Piper cubeba* in *in vitro* have potent antileishmanial activity against *Leishmania donovani* [73]. Piplartine and cubebin in *in vitro* at 100 µm showed significant antileishmanial.

4. Conclusion

Medicinal plants may serve as a potentially useful in therapy of various diseases. *Piper cubeba* (Kabab chini) is commonly used in traditional medicine for various disorders. The exploration of present review article established the scientific evidence of *P. cubeba* and its phytochemicals constituents and pharmaceutical properties like antimicrobial, anti-inflammatory, antibacterial, antioxidant, anti-cancerous, hepatoprotective, nephroprotective and antileishmanial activity. This has opened new vistas for further research in vital activities.

Conflict of Interest

The author declares no conflict of interest.

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