ETHNOBOTANY AND THERAPEUTIC POTENTIAL OF KABAB CHINI (PIPER CUBEBA)

Dr. Qazi Zaid Ahmad*, Aziz Ur Rahman and Tajuddin

Department of Saidla, Faculty of Unani Medicine, AMU, Aligarh-202002, UP, India.

ABSTRACT
Kabab chini (Piper cubeba) the dried ripe berries of Piper cubeba commonly known as Cubeb which has been used in traditional medicines for various disorders. Such as urogenital diseases, gonorrhoea, dysentery, syphilis, abdominal pain, diarrhoea, enteritis and asthma. It has been described in the classical Unani literature in detail and various actions such as Mudirre baul (diuretic), Mufattit wa Mukhrije Hasat (lithotriptic), Dafeye taffun (antiseptic), Muqa-wwiye Kulyah (kidney tonic), Mohafize Kulyah (nephroprotective), etc. have been ascribed to it. In recent years the Kabab chini (Piper cubeba) has been studied by a number of scientists to validate the acclaimed medicinal properties along with pharmacognostical and phytochemical properties. So an attempt has been made for review of the work carried out by scientific community along with an overview on ethnobotanical and ethnopharmacological description.

KEYWORDS: Mudirre baul, Mufattit wa Mukhrije Hasat, Dafeye taffun etc.

INTRODUCTION
Kabab Chini is the dried ripe berries of Piper cubeba. Piper is the nominate genus of the family Piperaceae. A pan tropical family composed of five to eight or more genera. The two largest genera are Piper and Peperomia, each containing about one thousands species, thirty species are medicinal in Asia-Pacific.[1,2]

Members of the genus Piper are used for many purposes, such as foods and spices, fish bait, fish poison, hallucinogen, insecticides, oils, ornaments, perfumes and for many medicines.[3,4]
The berries of *Piper cubeba*, commonly known as Cubeb, have been extensively used as a condiment, particularly in the tropics. Old Arabian and Persian Physician are said to have used the fruit in genito-urinary diseases. Its use in the Western Medicine can be traced to the middle ages.\[^5\] In Indonesia *Piper cubeba* is valued as a medicinal plant and used in Indonesian traditional medicine to treat gonorrhoea, dysentery, syphilis, abdominal pain, diarrhoea, enteritis and asthma.\[^6\]

**Historical Aspect**

In the 4th century BC, *Theophrastus* mentioned *komakon*. Guillaume Budé and Claudius Salmasius have identified *komakon* with cubeb, probably due to the resemblance which the word bears to the Javanese name of cubeb, *kumukus*. This is seen as a curious evidence of Greek trade with Java in a time earlier than that of *Theophrastus*.\[^7\]

In India, Sanskrit texts included cubeb in various remedies. *Charaka* and *Sushruta* prescribed a cubeb paste as a mouthwash, and the use of dried cubebs internally for oral and dental diseases, loss of voice, halitosis, fevers, and cough.\[^8\] In the *Raja Nirghanta* which was written 600 years ago cubebs appear in the name of *kankola*.\[^8\] Unani physicians use a paste of the cubeb berries externally on male and female genitals to intensify sexual pleasure during coitus. Due to this attributed property, cubeb was called "*Habb-ul-Uruus*".\[^9\]

Cubeb was introduced into medicine by the Arab physician of the middle ages. *Masoodi* in 10th century stated them to be a production of Java. The author of pharmacographia draw attention to the fact that the action of Cubebs upon the urogenital organs, though known to the old Arabian physicians were unknown to modern European writers on materia medicas at the commencement of the present century.\[^8\] Nicholas Culpeper wrote in the *London Dispensatorie* that cubebs were "hot and dry in the third degree, they cleanse the flegm of head and strenghthen the brain, they heat the stomach and provoke lust".\[^10\] *The National Botanic Pharmacopoeia* printed in 1921 tells that cubebs were "an excellent remedy for flour albus or whites.\[^11\]

**Etymology**

The Greek physician and botanist *Dioscorides* author of *Kitab ul Hashaish* as cited by Razi, mentioned it by the name of *kasifiyoon* and the some other Unani physicians named it *Safra’anioon* and *Maharioon* and in Greek it was famous by the name of *Qarqisoon*, Jalinoos mentioned it in his book “*Kitabul Advia al Mugablatu lil Adwa*” by the name of
The word cubeb entered European language via Arabic, Al-kababah, which, however, is of unknown origin but Zakaria Razi mentioned in his book Al-Havi that the Hunain named it Kababah.[12] Kababah is Arabic word and it is also known in Arabic by "Habb-ul-Uruus" and in Unani by the name of Qaqoon, Qarqasyoon, Qraqisoon, and in Roman language by the name of Diflyoon.[13,14]

Vernacular Names
Arabic: Kabaaba, Kababah, "Habb-ul-Uruus"
Chinese: Biji, Bicheng qie Czech
English: Jawa peppercorn, Jawanese pepper, Tailed Pepper
Hindi: Kabab-chini, Sital chini
Indonesian Cabé jawa, Kamukus
Japanese: Kubeba, Kubebu
Korean: Chaba huchu, Jaba huchu, Kubepu Kyubebu
Persian: Kubabah, Kababah
Russian: Perets Kubeba, Yavanskij perets, Perets kubebe
Turkish: Hint biberi tohomu, Java biberi, Kübabe,
Urdu: Kabab chini.[12,13,14,15]

Habitat and Distribution
Piper cubeba (Piperaceae) inhabits Java, Sumatra, Southern Borneo, Molucc 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 (SierraLeone, Congo), cubeb pepper is exported. It is cultivated in some of the West Indian islands.[16] Efforts have been made to cultivate it in India, mostly in Mysore but not on a commercial scale. Cubeb can be easily grown 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 when they become black and wrinkled.[17]

Description of Drug in Unani Literature
Morphology
The morphology has been described in detail by certain Unani physicians. Zakaria Razi mentioned in Al-Havi that the fruit of Kababah is similar to black pepper. Pungent and bitter in taste with pleasant odour and its property are similar to that of Fuwwah and Darchini but Darchini is more efficacious.[12] Ishaq bin Imran mentioned that its "Habb-ul-Uruus" and its
properties are just like pepper, it has a tail or pedicle on its base which is whitish yellow in colour. Ibn Haitham ascribed that it has two types.

1. Long
2. Short

The long type is "Habb-ul-Uruus" and the shorter one is known as Flanja. Hunain and other translaters cited that the Bitrique told about the Greek name of Kabab chini is Qarqisoon and Hunain named it Kababah. Jalinoos mentioned in his book Kitab al Advia al that the Qarqisoon is the thin pieces of wood as Darchini, while the kababah found in the form of fruit (Habb) however may be these thin pieces of wood from this fruit.\[12,14\] Abu Haneefah ascribed that the tree of Kababah just as tree of Aas and the leaves are thin as compared to leaves of Raihan, the flower is whitish yellow and grown into the hard soil. The fruit is globular or oval shaped and the diameter is about 1/6 inch long blackish brown in colour, wrinkled surface and having stalk or tail on its back side, beneath the wrinkled surface hard and brown covering having seeds when fruit is full riped. It possesses pungent and some what bitter taste with a strong characteristic aromatic odour. The stalked berries are a little bit larger than pepper corns, having a furrowed surface. Most berries are hollow. They are sold whole and should be crushed or ground before usage. The powder of Kababah is reddish brown having characteristic sharp and pleasant odour.\[18\]

Amanullah khan mentioned in his book “Ganj Bad Award” that the kababah has three varieties:

1. Habashi
2. Chini
3. Hindi

The difference between them according to their shape or morphology is that the variety of kababah which belongs to China has small fruit as compare to other species, a little longer than the black pepper having a stalk on their head, hollow and light in weight. The fruit of kababah habashi is bigger and heavier than the Chinese variety. It is filled internally and one of the corners is white and has characteristic pleasant odour while the taste of both is similar. The variety which belongs to India is rounded, bigger and heavier than the variety of China, after crushing it gives the characteristic aroma and internally white in colour and it does not have the stalk.\[12,14,18\]
Hakim Momin khan described in his book, Tohfat ul Mominin that the fruit of kababah is just as Habbe Balsan. Its aroma is also similar to the same fruit, blackish in colour, the pulp is white and the tree is similar with the tree of Maurid and in India its small variety is found which is known as Flanja.[19] Hakim Ali bin Husain Ansari mentioned about the Kababah, (Habbul-Uruus) that it has the property of Fuwwah.[20]

Daud Zarair Antaki mentioned in his book that the tree of kababah is similar to the tree of Aas and has two types:

1. **Kabir**: It is just like Habbe balsan having white pulp.
2. **Saghir**: It is known as Falanjah and is of better quality which has pleasant odour. Its efficacy tends to remain up to 10 years.[21]

**Mizaj (Temperament)**
Hot and dry in second degree.[8]

Masih bin Hakam said that it has both the hot and cold temperaments but the heatness dominantes.[18,22]

**Af’aal (Pharmacological Actions)**
Kabab chini (Piper cubeba) is described extensively in classical Unani literature, and various actions of the plant have been discussed. Some pharmacological actions are as follows:

Munaqq-e- kulyah wa masanah (Cathartic for kidney and bladder), Mudirr-e- baul (Diuretic), Mukhrj-e- sang-e- gurdah wa masanah (Lithotriptic), Mufattih-e- sudad (Deobstruent), Mulattif (Demulcent), Habis-e- ishal (Astringent), Dafa-e- taaffun (Anti septic), Mufattih-e- sudad-e- jigar (Deobstruent), Muqavvi-e- jigar (Hepatotonic) Muhallil (Anti inflammatory), Mutayyib-e- dahan (Mouth Refreshner), Muharrik (Stimulant), Nafe-e Zeeq un nafas (Anti asthmatic), Kasir-e-riyah (Carminative), Musakkin (Sedative), Muqawwi-e me’adah (Gastrotonic).[12,14,18,21]

**Medicinal uses**
Qurooh lissa mutaffnah (Septic gingivitis), Qulae dahan mutaffina (Septic stomatitis)
Quroohe majara baul (Uro-genital ulcer), Yarqan (Jaundice), Qurooh lissa (Gums ulcer), Fasade maedah wa tahal (Disorders of stomach and spleen), Riyah wa hasaat (Gases and calculi), Waram (Inflammation), Khafqan (Palpitation), Hasate gurdah wa masana (Kidney and Bladder calculi), Suda’ (Headache), Quroohe fam (Mouth/oral ulcer), Buae dahan
(Halitosis) Sudda-e- jigar (Hepatic obstruction), Amraz Alate Tanasul wa Baul (Genito urinary disease), Iltehabe Masana (Cystitis), Suzak (Gonorrhoea), Zaheer (Dysentery), Waj’ul Mafasil (Rheumatism), Sual (Cough) Qurooh (Ulcers), Ehtebase Baul (Retention of urine). \cite{12,14,18,21}

**Mazarrat (Adverse effect)** Headache, Indigestion. \cite{18,21}

**Musleh (corrective)** In case of adverse effect of Kabab chini the following drugs are used as musleh (corrective).

Mastagi (*Pistacia lentiscus*)

Sandal safaid (*Santalum album*)

Gule surkh177,164,175 (*Rosa damascus*)

**Miqdare khoorak (Dose)**

3 - 4½ gm (powder form)

1 to 3 gm \cite{19}

4 gm \cite{23}

5 gm \cite{24}

9 gm (decoction) \cite{12}

5-20 drops (Roghan). \cite{12,18}

**Important Farmulations**

- Jawarish Zarooni
- Laboobe Sagheer,
- Majoone Seer Alvi Khan
- Majoone Antaki
- Sufoofe Shora murakkab
- Sufoofe Indrijulab
- Sinoone mujallli
- Zuroore Qula’ Abyaz
- Zuroore \cite{23,24}

**Description of the Drug in Modern literature**

**Classification**

**Taxonomy**

Kingdom : Plantae.
In field collection Piperaceae can be recognized by three main features.

- Articulate stem
- Asymmetric or cordate leaves
- And axillary spikes of little round berry like fruits.

**Macroscopic features**

*Piper cubeba*, a climbing shrub with cylindrical, smooth zigzag, striate stem some what thickened at the node. Fruit wrinkled, rounded, 5-7 mm in diameter, light brown to dark brown, about 7 mm long stalk attached, pericarp red to slightly brown, testa fused with pericarp, fruit hard and stony albumen white and oily, odour aromatic and characteristic, taste pungent and slightly bitter.[24,25] The fruit is almost globular (diameter 3-6 mm.) with a slender stalk like portion (length, upto 7 mm.) attached to its base, hence the Cubeb is also known as Tailed pepper. The pericarp is dusky red to slightly brown, rarely grayish in colour.[26] In size and form Cubeb resembles black pepper, but they are readily distinguished from it by being furnished with stalk, from which circumstance they have received the name of tailed pepper. They are spherical in form, and about the size generally of black pepper, or small pea; their colour is blackish or grayish.[16] It climbs to 10 feet high, it has heart- to lance shaped leaves up to 6 inch and 4 inch flower spike.[17] The distinguishing feature being the short pedicle or stalk attached to the base of the cubeb. The stalk is 4-7 mm long.[23]

**Leaves:** Alternate, on short stout petiole, blade about 6 inches long, lanceolate or oval oblong, tapering to the acute apex, usually somewhat unequal at the base, quite entire, slightly wavy, glabrous on both surfaces, somewhat coriaceous, deep green rather paler and prominent vein beneath.[16,23]

**Flower:** Unisexual, dioecious, minute, sessile, each with a bract at the base, densely crowded in small, cylindrical, stalked, solid spike coming of opposite the leaves; the mail spikes
slender, tapering, shortly stalked, about an inch long, the female shorter, blunt, thick and fleshy, on longer stalks.\textsuperscript{[16,23]}

**Fruit:** Globular smooth, about ¼ inch long, with a blunt apiculous and tapering below into a stalk –like base, which a little longer than round extremity, projecting horizontally from the axis and together forming a lax raceme ( many of the ovaries becoming abortive) about 2 inches long.\textsuperscript{[16,23]}

**Other species of \textit{Piper} which are commonly being used as substitute or adulterants**

\textit{Piper} species yielding fruits of similar nature are: \textit{P. ribesioides} Wall. and \textit{P. sumatrana} DC. Which are considered possibly as large forms of \textit{P. cubeba}. Fruits of other species of \textit{Piper} like \textit{P. crassipes}, Korth., \textit{P. cannaum}, Blume. and \textit{P. baccatum}, Blume are reported to be used as substitutes or adulterants. Fruits obtained from \textit{P. clusii} DC. and \textit{P. guineense}, DC. are also used as substitutes, they are often called false Cubebs and are obtained from Africa. Fruits of \textit{Litsea cubeba}, Pers. are also used as substitute. Adulteration of true cubebs with similar fruits from other \textit{Piper} spp. can be detected by visual examination, or under the microscope, or by treatment with sulphuric acid with which the true fruits develop a bright red color.\textsuperscript{[25]} Trade standards require that a given lot of cubebs should contain, shrivelled and immature fruits >10; stems, >5; foreign organic matter, > 2; and acid-insoluble ash, >2%, each 100 gm of the cubebs should yield not less than 13 ml of volatile oil.\textsuperscript{[25]}

Leaves and Flowers of Kabab chini (\textit{Piper cubeba}).

Fruits and flower of Kabab chini \textit{Piper cubeba}. 
Microscopic features of the fruit

The pericarp consists of an epidermis beneath which is an interrupted row of small thick wall cells. Within this, the parenchyma is composed of cells containing starch and oil, in the latter, bundles of needle shaped crystals of Cubebin may be observed, lastly the innermost layer of pericarp is formed by several rows of tangentially extended cells containing essential oil. The nut is yellow and brittle. The seed when present is seen to contain crystals of Cubebin. Transverse section of the fruit show an outer layer of epidermis, externally covered with thick cuticle, arrow of 2-5 small, crushed, brown and thick walled cells below, mesocarp composed of large thin- walled parenchymatous cells, oil cell and vascular bundle, endocarp of multi layered sclerieds heavily lignified with narrow lumen, testa and genman composed of elongated cells, tegmen cells, hyaline and kernel cells grayish in colour.\textsuperscript{[8,23,24]}

Description of Tissue from powdered: Cubeb (Piper cubeba).\textsuperscript{[23,27]}

1. Lignified fiber  
2. Perisperm  
3. Thin wall perisperm  
4. Starch grains  
5. Spermoderm in surface view  
6. Small calcium oxlate prisms  
7. Spermoderm in section view  
8. Yellowish brown wall.
Phytochemical studies

The dried cubeb berries contain essential oil consisting monoterpenes (sabinene 50%, -thujene, carene, 1,4-cineol and 1,8-cineol) and sesquiterpenes (caryophyllene, copaene, - and -cubebene, "-cadinene, cubebol, germacrene). About 15% of a volatile oil is obtained by distilling cubebes with water. Cubebene, the liquid portion, has the formula C15H24. It is a pale green or blue-yellow viscous liquid with a warm woody, slightly camphoraceous odour. After rectification with water, or on keeping, this deposits rhombic crystals of camphor of cubebes (C15 H60). Rao, Sudborough and Watson (1925) have studied the oil distilled from the cubebes experimentally grown there. They were able to obtain 11.85% of the oil with the following constant; specific gravity 0.9167, optical rotation-29.9dig, refractive index 1.4894, saponification value after acetylation.

Cubebin is a crystalline substance existing in cubebes, discovered by Eugène Soubeiran and Capitaine in 1839. It may be prepared from cubebene, or from the pulp left after the distillation of the oil. The drug, along with gum, fatty oils, and malates of magnesium and calcium, contains also about 1% of cubebic acid, and about 6% of a resin. A lignan-cubebin, mp. 133 – isolated from fruits. Two new sesquiterpene hydrocarbons-bicyclosesquiphellandrene and 1epibicyclosesqui-phellandrene-isolated from essential oil. Hexane extract of Piper cubeba seeds contained palmitic, linoleic, oleic, linolenic, stearic, arachidic and behenic acids. (-)Clusin, (-) Cubebin, (-) dihydrocubebin, (-)hinokinin and (2R, 3R)2-(3”, 4”, 5”-trimethoxybenzyl)-3-(3’, 4’-methylenedioybenzyl)-1,4-butanediol isolated from fruit alpha-ethoxycubebin, beta-ethoxycubebin, dihydrocubebin monoacetate, hetrotrapan, magnosalin, 5”-methoxyhinokinin and 2,4,5-trimethoxybenzaldehyde isolated. The lignan profiles of aerial part of Piper cubeba, was determined using GC, MS and HPLC. The number of lignans found in the leaves was 15, followed by berries and the stalks with respectively 13 and 5 lignans. Cubebin, hinokinin, yatein, isoyatein are common lignans in the genus Piper and appeared as major components in all part of Piper cubeba investigated. Piperine is an abundant alkaloid in the berries of this species. Twenty four lignans have so far been reported from P. cubeba.

Lignans are an important group of secondary metabolites that are also assumed to contribute to the biological activity. Some of these lignans showed inhibitory activity against cytochrome P450 enzymes that are involved in the metabolism of all currently used drugs. Yatein, hinokinin, cubebin, dihydrocubebin have been reported to have
antifeedant activity against a number of stored product insects. This activity is comparable to podophyllotoxin.\textsuperscript{[43]} Hinokinin has been reported to have anti-inflammatory and analgesic effect. Because of the structural relationship, hinokinin can be synthesized using cubebin as Precursor.\textsuperscript{[44]} Cubebin has been shown to possess anti-inflammatory, analgesic and trypanocidal activities.\textsuperscript{[44,45,46]} Yatein is also an interesting lignan due to its biological activity and its function as a biosynthetic precursor of deoxypodophyllotoxin and podophyllotoxin that are well known for their anticancer properties.

**Pharmacological Studies**

**Antioxidant effect**
Gayatri N et al, Had studied and examined the pyridine class alkaloid i.e. piperine is available in rich amount in *Piper nigrum* and *Piper cubeba* having family of Piperaceae. It is commonly used in preparation of various herbal cough syrups and used as anti malarial, anti inflammatory and anti leukemia. Ethanol extract of *Piper cubeba* having high antioxidant activity.\textsuperscript{[47]} Aboul-Enein HY et al, Had studied and examined *Piper cubeba* isolates for antioxidant action viz. magnitude of *Piper cubeba* capabilities to search free radicals, DPPH, hydroxyl radical (HO) and superoxide anion radical in different type of systems.\textsuperscript{[48]}

**Antimicrobial effect**
The essential oil of *Piper cubeba* showed anti bacterial activity against *B. subtilis, Vib. cholere, C. diphtheria, Sal. typhi, Strep. pyogenes, B. pumilus and Ps. solanaceous.* Being most active against *Ps. solanaceous.* A combination of *piper cubeba* with *Litsea glutinosa,* of the various combinations was found to be the most active. The essential oil of *Piper cubeba* also showed anti bacterial effect against *B. subtilis, Esch. coli, Staph. aureus, Sal. typhi, Sal. paratyphi and pestalotia sp.* but not against *Sh. niger.* The activities of the crude ethanol extract from *Piper cubeba* seeds, (-)-cubebin and its semi-synthetic derivatives were evaluated against oral pathogens. The crude ethanol extract was more active against *Streptococcus salivarius* (MIC value of 80μg/mL). (-)-Cubebin displayed MIC values ranging from 0.20 mm for *Streptococcus mitis* to 0.35 mm for *Enterococcus faecalis.* The natural product (-)-cubebin and its semi-synthetic derivative (-)-hinokinin displayed bacteriostatic activity at all evaluated concentrations, as well as fungicidal activity against *Candida albicans* at 0.28 mm. The O-benzyl cubebin derivative showed fungistatic and fungicidal effects against *C. albicans* at 0.28 mm and 0.35 mm, respectively. Also, the other dibenzylbutyrolactone derivatives [(-)-6,6 –dinitrohinokinin and (-)-O-
(N,Ndimethylaminoethyl)- cubebin] displayed bacteriostatic and fungistatic effects at the evaluated concentrations. Moreover, the semi-synthetic derivative (-)-6, 6 - dinitrohinokininin was the most active compound against all the evaluated micro organisms. Therefore, it may be suggested that the presence of the carbonyl group at C-9 plus the introduction of polar groups in the aromatic rings improve the antimicrobial activity of dibenzylbutyrolactone compounds.

The oils and oil combinations (1:1) were screened against fifteen pathogenic and non-pathogenic bacteriae. The essential oil of laciniata showed maximum activity against C. diphtheriae, V. cholerae, B. subtilis and S. aureus and Piper cubeba against S. faecalis, B. pumilus and P. solanacearum. The combinations of L. chinensis with P. cubeba and C. asiatica displayed the maximum inhibitory response and the rest failed to show any synergistic or potentiating effect.

Twenty eight extracts prepared from the fruits of four species, viz. Piper cubeba, P. retrofractum Vahl syn. P. chaba Hunter non Blume, P. longum and P. nigrum, were evaluated against bacterial pathogens, such as Staphylococcus albus, Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli and Bacillus megaterium and one fungus, Aspergillus niger. Compared to Streptomycin all the extracts exhibited a good antibacterial activity. Some of the extracts showed antifungal activity as well.

**Anthelmintic effect**

The oil of the Piper cubeba also showed significant antifungal activity against Aspergillus flavus, A. fumigatus. Trichodermavird. Curvulari alunata, Alternariatenuis penicillium funiculosum, P. javanicum, P. striatum and Fusarium solani. The essential oil from fruits revealed anthelmintic activity against earthworm and tapeworm in vitro. Anti-inflammatory activities of Piper cubeba (fruit), Physalis angulata (flower) and Rosa hybrida (flower) clearly exhibited inhibitory effects against acute and subacute inflammation by oral administration (200 mg/kg) and it also showed significant inhibition of type IV allergic reaction in mice.

**Antileishmanial Activity**

The n-hexane, ethyl acetate, methanol, and acetone extracts of Piper cubeba and P. retrofractum, Vahl. (Piperaceae) were evaluated in vitro against promastigotes of Leishmania donovani, and all exhibited significant in vitro activity at 100 μg/ml. Two lignans, cubebin...
and hinokinin, were isolated from the hexane extract of *P. cubeba*; and one bis-epoxy lignan, \((-\)-sesamin, and two amides, pellitorine and piplartine, were isolated from the hexane and methanol extracts of *P. retrofractum*. Cubebin and piplartine showed significant antileishmanial activity *in vitro* at 100 μM and were further tested *in vivo* in a hamster model of visceral leishmaniasis. Piplartine showed activity at 30 mg/kg dose. This is the first report of antileishmanial activity of these two plants and their isolated constituents.\(^{[53]}\)

**Hepatoprotective activity**

Methanol and water extract of *P. cubeba* berries have been shown to display an inhibitory effect against the hepatitis C virus.\(^{[54]}\) Piper cubeba ethanolic extract has been found effective in prevention of CCl4-induced hepatic damage in rats. Findings demonstrated that the treatment with PCEE significantly and dose dependently prevented drug induced increase in serum levels of hepatic enzymes. Furthermore Piper cubeba ethanolic extract significantly reduced the lipid peroxidation in the liver tissue and restored activities of defense antioxidant enzymes NP-SHandCAT towards normal levels. The hepatoprotective effect of PCEE is attributed to downregulation of proinflammatory cytokines, for example, TNF-α and IL-6 mRNA expression as well as mRNA expression of iNOS and HO-1 gene, and upregulation of the IL-10. Histopathological studies have also shown that the PCEE and silymarin could prevent CCl4-induced hepatic damage in the liver.\(^{[55]}\) The fruits of the *Piper cubeba* plant were studied for antioxidant and hepatoprotective activity. The antioxidant potential of the ethanol extract was examined using a 1, 1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging activity, reducing power, hydroxyl radical scavenging activity, nitric oxide radical scavenging activity and hydrogen peroxide radical scavenging activity. The extract had significant dose-dependent antioxidant activity in all in vitro experiments. Hepatoprotective activity of the extract was evaluated in rat model of carbon tetrachloride (CCl4) induced liver damage. CCl4 significantly altered serum marker enzymes and total protein. The ethanol extract of *Piper cubeba* attenuated CCl4 induced serum marker enzymes and total protein. Histology of liver sections of the animals treated with the extracts showed the presence of normal hepatic cords, absence of necrosis and fatty infiltration which further evidence the hepatoprotective activity.\(^{[56]}\) In this study extracts of *Piper cubeba* fruit were prepared using mechanical method. These extracts include alcoholic, acetonic, chloroformic and water extract. The chemical composition of each extracts were analyzed also. After that the antibacterial activity of these extracts were tested against gram negative (G-) *Escherichia coli*, *Pseudomonas aeruginosa* and gram positive (G+) *Staphylococcus aureus*. All extracts
show antibacterial activity on these bacteria, but ethanol and acetone extracts were show the best antibacterial activity \textit{S. aureus}, followed by chloroform extract and then water extract, on the other hand water extract showed inhibition activity against \textit{E.coli} and \textit{P. aeruginosae} followed by ethanol, acetone and chloroform extract.\cite{57}

**Anti inflammatory, Analgesic and Antiarthritic activity**

Anti inflammatory, anti oxidant, anti-allergic and analgesic activities of \textit{Piper cubeba} has been studied using chemically-induced edema and arthritis \textit{in vivo}.\cite{52} Hinokinin has been reported to have anti-inflammatory and analgesic effect. Because of the structural relationship, hinokinin can be synthesized using cubebin as precursor.\cite{44} Cubebin has been shown to possess anti-inflammatory, analgesic and trypanocidal activities.\cite{58}

**Anticancerous activity**

Yatein is also an interesting lignan due to its biological activity and its function as a biosynthetic precursor of deoxypodophyllotoxin and podophyllotoxin that are well known for their anticancer properties. It was found that P9605 significantly inhibited growth induced by beta-estradiol in MCF-7, a human breast cancer cell line. It inhibited aromatase activity, which is responsible for transforming androgens into estrogens. Competitive binding assays also indicated P9605 binding to both human apoptosis. This anti growth effect was less pronounced in androgen-independent PC-3 prostate cancer cell lines. P9605 potently inhibited 5 alpha-reductase II activity, which is responsible for converting testosterone to its active form, dihydrotestosterone (DHT), in the prostate. It also acted as an antagonist at recombinant wild-type androgen receptors (AR). P9605 suppressed cell growth and prostate-specific antigen (PSA) secretion stimulated by physiological concentrations of DHT in LNCaP cells. Interestingly, it down-regulated AR levels. In conclusion, the findings suggest that P9605 may potentially retard the growth of androgen-dependent PC via several mechanisms.\cite{59,60}

**Diuretic and nephroprotective activity**

The curative and protective effect of \textit{Piper cubeba} was studied in gentamicin and cisplatin induced nephrotoxicity in albino rats. The experimental study demonstrated a significant protective as well as curative effect of \textit{Piper cubeba} in both the histological and biochemical parameter.\cite{61,62}
CONCLUSION
Kabab Chini (*Piper cubeba*) is commonly used in different traditional medicine viz Ayurveda, Unani and Chinese medicine for various disorders and equally acclaimed by Unani physicians for successful treatment of urogenital disorder and other ailments. Some experimental researches in recent years also demonstrated its bacteriostatic, anti-viral and ant cancerous effect. In view of above a comprehensive series of clinical trial should be carried out to develop it as a drug to combat the different disorders as acclaimed by traditional medicine.

REFERENCES
2. Chirstopher Wiart. Medicinal plant of Asia and pacific C R C Tylor & Francis Boca raton Publisher London, 2006; 23.
38. Medicinal plants of India vol. 2, ICMR Cambridge printing work, Naraina Phase II, New Delhi, 1987; 433.


