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Review study on potential activity of *Piper betle*

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Abstract

Piper betle is glorified as evergreen and perennial plant that God designed and have given the shape of his own heart. The heart shaped of *Piper betle* leaves are initiate in ancient Sanskrit texts, include Charaka, Sushruta Samhita and Astanga Hridayam. *Piper betle* L. has been use in Chinese, Indian traditional medicine for centuries. The purpose of it is to reveal the possible effect of this plant in the development of therapeutically active herbal drugs.

Keywords: *Piper betle* L., Chavicol, Chavibetol, Medicinal properties, Green heart.

1. Introduction**2. Plant Profile:** [1, 2]**Taxonomical classification**

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnolipsida
Order: Piperales
Family: Piperaceae
Genus: Piper
Species: betle

Vernacular name

Sanskrit: Tambool, Mukhbhushan, Varnalata
Hindi: Paan
English: Betle, Betle pepper, Betle-vine
Telugu: Nagballi, Tamalapaku
Tamil: Vetrilai
Gujarati: Nagarbael



Fig 1: *Piper betle* Plant

Piper betle Linn. (Local name 'Paan') Piperaceae, a dioecious, annual creeper, climbing by many small adventitious rootless, grows to a height of about one metre, generally grown in hotter and damper parts of the country [3, 4]. It is extensively found in damp forests and is propagated in India and other countries in South-East Asia, such as Vietnam and China. In India it is found in Uttar Pradesh, Bihar, Bengal, Orissa, Tamilnadu, Andhra Pradesh and Karnataka. In Tamilnadu, three varieties of *Piper betle* leaves, Sirugamani, Karpoori and Vellaikodi are accessible mostly [5].

It is used in variety of decoction, in curing wounds, burns, impetigo, furunculosis, eczema, lymphangitis and juice is beneficial stomatic. Kammaru (a variety of *Piper betle*) leaf has a good level of juice that heals pharyngitis, abdominal pain and swelling. Generally betle leaf cures urticaria and as per ayurvedic medicine, it recovers the loss of equilibrium between the three 'humours,' namely, Vatha, Pitha and Kapha. The roots and fruits are well-known for treatment of malaria, asthma [6, 7].

The chief Ayurvedic preparations of *Piper betle* plant are Lokantha Rasa, Puspadhava Rasa, Brhat sarwajwarahara, lanha, laghu sutaseknara Rasa, Brhat visamaj warantaka Rasa. In Ayurveda, betle leaf juice is commonly utilized as an adjuvant & combined with different other medicines most likely for better effects beside its separate use as medicine. In Susrta-Samhita, tambool leaves have been described as aromatic, sharp, hot, acrid and valuable for voice, laxative, appetizer, beside this they soothe vata and aggravate pitta [8].

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3. Chemical constituents

The *Piper betle* leaf has been described to have Piperol-A, Piperol-B, methyl piper betlol and they also have been isolated [9]. The betle leaves have starch, sugars, diastases and an essential oil composing of terpinen-4-ol, safrole, allyl pyrocatechol monoacetate, eugenol, eugenyl acetate, hydroxyl chavicol, eugenol, piper betol and the betle oil contains cadinene carvacrol, allyl catechol, chavicol, p-cymene, caryophyllene, chavibetol, cineole, estragol, etc. as the key components [10].

Phytochemical analysis on leaves revealed the presence of Alkaloids, Tannins, Carbohydrate, Amino acids and Steroidal components. The chief component of the leaves is a volatile oil in the leaves from different countries, called Betle oil and contains 2 phenols, betle phenol (Chavibetol and Chavicol). Codinene has also been found [11].

4. Volatile Chemical Composition and Chemotypes

The different chemotypes have been recorded from various parts of the world and these are-

1. Chavicol chemotype: Indian 'Sagar Bangla' cultivar [12].
2. Germacrene D chemotype: Indian *Piper betle* var. sirungamani [12].
3. Isoeugenol chemotype: Indian *Piper betle* 'Meetha' cultivar and Vietnamese betel sample [13].
4. Chavibetol chemotype: Philippine sample, Malaysian sample and our sample from Nepal [13].
5. Eugenol chemotype: 'Kapoori' cultivar and 'Kapoori' and 'Bangla' cultivars from India [14].
6. Anethole chemotype: 'Meetha' *Piper betle* cultivar from India [14].
7. Safrole chemotype: Sri Lankan *Piper betle* leaf essential oil, South Indian sample, Indian 'Desawari' betel, and 'Sanchi' cultivar of India [15].
8. The major component of Taiwanese betel floral essential oil is safrole (28%). The major component of the Vietnamese betel rhizome is α -cadinol [16].

5. Description of chemical constituents

Chavibetol

Chavibetol is a natural chemical compound of the phenylpropanoid class. It is the most important component of the essential oil from the leaves of the *Piper betle* plant. It is an aromatic compound with a spicy odor and is an isomer of eugenol [17, 18].

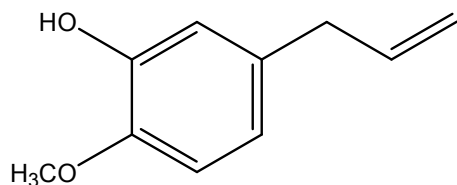


Fig 2: Chavibetol

Eugenol

Eugenol, one of the principal constituent of betle leaf, has also been shown to possess anti-inflammatory property in a variety of animal models of studies with various inflamogens [19]. Antimicrobial, analgesic, anti-oxidant, antiviral and anticancer activity, other identified activities such as its anti-ulcerogenic potential and effect on osteoporosis and especially its effect on the central nervous system (CNS) encompassing seizure

control, Parkinson's disease, antidepressant effects etc [20].

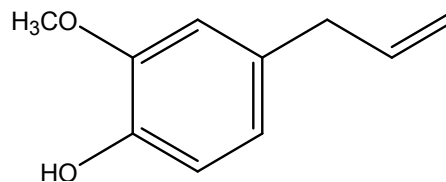


Fig 3: Eugenol

6. Hydroxychavicol (HC)

The new, immature leaves contains various beneficial bioactive compounds, among which Hydroxychavicol is most important phenolic compound which reported to possess anticarcinogenic, antinitrosation, antimutagenic effects [19] beside this, it has a considerable potency to act as an anti-inflammatory, antioxidant, antibacterial, anti-platelet and anti-thrombotic effects without impairing haemostatic function. In the aqueous extract of betle leaf it is reported to exhibit useful bioactivities – antimutagenic and anticarcinogenic activities, whereas isolated from the chloroform withdrawal from aqueous extract of *Piper betle* leaves show inhibitory action alongside oral cavity pathogens [20]. 0.5% Hydroxychavicol inhibited the biofilm produced by anaerobes and biofilm produced in pooled saliva the use of Hydroxychavicol as an oral care agent. Hydroxychavicol show compelling anti-inflammatory action by considerably inhibits the phrase of the proinflammatory cytokine TNF- α . Methyl chavicol, a biogenic oxygenated aromatic compound, reported to have antioxidant activity [21].

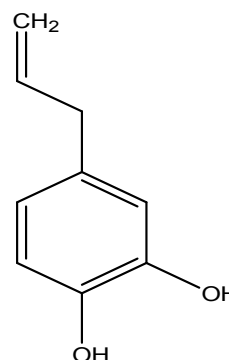


Fig 4: Hydroxychavicol

7. Allylpyrocatechol

The phenolic constituent allylpyrocatechol obtained from the leaves, show action against obligate oral anaerobes responsible for halitosis. The leaf extract also has a stimulatory outcome on pancreatic lipase and antioxidant activity [21]. Oral administration of APC at different doses accelerates the rate of remedial of gastric lesion induced by indomethacin due to its antioxidative and mucin defensive properties [22].

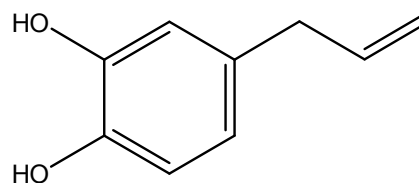


Fig 5: Allylpyrocatechol

8. Quercetin

Quercetin is one of the most important dietary flavonoids belong to a group of flavonols. It occurs chiefly as glycosides, but other derivatives of quercetin have been recognized as well. Joined substituent's changing the biochemical activity and bioavailability of molecules when compare to the aglycone [23]. Quercetin has also been verified to exhibit the antiviral, antibacterial, anticarcinogenic and anti-inflammatory properties. The anticarcinogenic property of quercetin result from its important impact on an increase in the apoptosis of mutated cells, inhibition of DNA synthesis, [24] inhibition of cancerous cell growth, decrease and alteration of cellular signal transduction pathways. Animal evidence suggest Quercetin's antioxidant effects provides protection of the brain, heart, and other tissues adjacent to ischemia-reperfusion injury, toxic compounds, and other factors that can persuade oxidative stress [25].

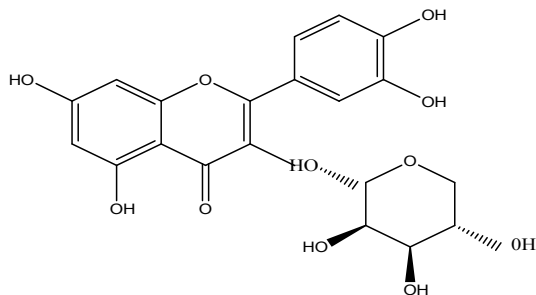


Fig 6: Quercetin

9. β -Caryophyllene

β -Caryophyllene is a chief volatile compound establish in huge amounts in different spice and food plants. β -caryophyllene has shown to posses potent anti-inflammatory properties. β -caryophyllene is an FDA- approved food additive and it is apparently a non-toxic compound with no genotoxic or cytotoxic effect *in vivo*. Clinical studies prove its efficiency in treating endometriosis. β -caryophyllene exerts anti-inflammatory activity by acting as a potent, selective and non-psychoactive full agonist for CB2 receptor *in vivo* [26].

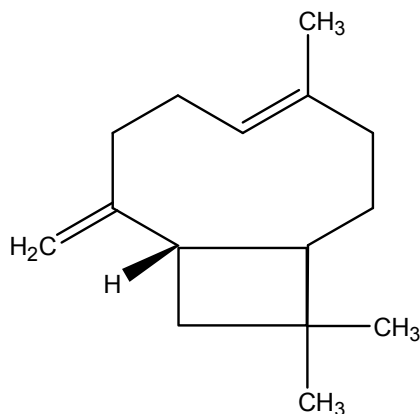


Fig 7: β - Caryophyllene

The *Piper betle* used as anti-depressant, CNS stimulant, Immunomodulator, antioxidant, antibacterial, antiulcer, cardiovascular, anti-diabetic, anti-infective. *Piper betle*, found to be safe in terms of hepatotoxicity, renotoxicity, hematotoxicity [27].

10. Traditional uses [28-30]

1. The paste of *Piper betle* leaves assorted with salt and hot water able to be administering for filariasis.
2. For curing obesity, one *Piper betle* leaf mix with *Piper nigrum* is prescribed for two months.
3. Juice of *Piper betle* with honey is accommodating to treat coughs, dyspnoea, and in indigestion, amongst children.
4. Leaves of *Piper betle* smeared with oil are useful on the breasts of lactating women; it is supposed to promote milk secretion.
5. A local application is recommended for inflammatory swelling such as orchitis, arthritis and mastitis.
6. For childhood and old people, leaves are mixed with mustard oil, warmed and are apply to the chest for treatment to reduce cough and dyspnoea.
7. Recovers bad breath, body odor and prevent tooth decay.
8. Prevents and treats vaginal ejection, and reduce itching of the vagina.
9. Stop bleeding in the nose.
10. It contains vitamins such as thiamine, niacin, riboflavin and carotene.
11. In India, leaves used for curing eczema, lymphangitis, asthma and rheumatism.
12. Paste of leaves is applied on cuts and wounds.
13. Roots with black pepper used to generate sterility in women.
14. Oil used for irritation in throat, larynx, bronchi, gargle and inhalation in diphtheria.
15. Juice of leaves is used as stomachic and febrifuge.

11. Modern medicinal use [30, 31, 32, 33, 34]

1. Betle leaves are advantageous in pulmonary infection in childhood and old age. The leaves, mixed in mustard oil warmed and applied to the chest to relive cough and intricacy in breathing.
2. Limited application of the leaves is efficient in procuring sore throat. The flattened fruit or berry should be mixed with honey and used to reduce irritating cough.
3. Betle leaves are helpful for the treatment of nervous pain, nervous exhaustion and debility. The extract of few betle leaves, with honey serve up as a good tonic.
4. On applied locally, betle leaves are valuable in the treatment of swelling such as arthritis and orchitis i.e. inflammation of the testes.
5. Betle leaves also shows analgesic and cooling properties.
6. It is also a priceless remedy for boils. A leaf is lightly warmed till it gets soft, and then coated with a layer of castor oil. The oiled leaf is placed over the inflammation.
7. A hot poultice of the leaves or their extract mixed with some bland oil as refined coconut oil which can be applied to the loins with beneficial results in lumbago.
8. The leaves can also be used to heal wounds. The juice of the leaves should be extracted and applied locally to the wounds.
9. The application of leaves coating with oil and said to encourage secretion of milk when applied over the breast during lactation.
10. According to Unani system, these leaves has a sharp taste and good smell which helps to improve appetite.
11. It also used as a tonic for brain, heart and liver.
12. It also helps to promote healthy teeth and skin.
13. It helps in procurement of Disorders in physiological function of body, Skin diseases, and several Eye diseases.

14. Betle leaf also contains diuretic property. Juice of leaves given with milk or honey helps in easing urination.
15. Betle leaf is used in aphrodisiac i.e. an agent that stimulates sexual desire.
16. The essential oils which contains in the leaves are antibacterial, antiprotozoal and antifungal properties. Therefore, the oil kills or inhibits expansion of outrageous bacteria causing typhoid, cholera, tuberculosis etc and helps in proper evaluation and exploitation.
17. The leaves are nutritive and hold considerable quantity of vitamins and minerals and therefore, six leaves with a small bit of slaked lime are said to be equivalent about 300 ml of cow milk mainly for the vitamin and mineral nutrition.
18. The leaves also hold the enzymes like diastase and catalase as well as major amount of all the essential amino acids except lysine, histidine and arginine, which are found only in traces.

Table 1: Different therapeutic activities reported in *Piper betle* plant [35-47]

S.no.	Plant part/ Extract	Activity/Animal/ Model	Result	Reference
1.	Aqueous extract of the fresh <i>Piper betle</i> leaves.	Antimicrobial activity/Various microorganisms /disc diffusion method.	Aqueous extracts showed effective inhibitory action against the microorganisms	Shameem Pasha MD; <i>et al</i> , (2013)
2.	<i>Piper betle</i> leaves/hot water extract/cold ethanolic extract.	Antioxidant activity/Initial antioxidant activity, Antioxidant activity with time & at elevated temperature (200 °C).	The extracts obtained from the leaves of <i>Piper betle</i> had profound antioxidant activity.	Arambewela Lakshmi; <i>et al</i> , (2006)
3.	<i>Piper betle</i> spray dried powder.	Antidiabetic activity/diabetes mellitus patients.	<i>Piper betle</i> as a nutraceutical resulted as a potential treatment for type 2 diabetes patients.	HewageeganaSujatha; <i>et al</i> , (2011)
4.	Aqueous extract of the fresh <i>Piper betle</i> leaves.	Antioxidative & antihemolytic activity/Microorganisms (<i>Streptococcus pyogenes</i> , <i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> & <i>Escherichia coli</i>).	The antioxidative & antihemolytic activities were attributed to the high concentration & combined activity of flavonoids & polyphenols.	Chakraborty Devjani; <i>et al</i> , (2011)
5.	Crude ethanolic extracts of <i>Piper betle</i> leaves.	Antidermatophytic activity/ zoonotic dermatophytes (<i>M. canis</i> , <i>M. gypseum</i> , and <i>T. mentagrophytes</i>) and yeast-like <i>Candida albicans</i> .	Testing showed <i>Piper betle</i> cream formulation with potential therapeutic values for treatment of dermatophytosis.	Trakranrungsiea N.; <i>et al</i> , (2008)
6.	Aqueous and ethanol extract of the <i>Piper betle</i> leaves.	Antibacterial Activity/ Gram positive (<i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> & <i>Micrococcus luteus</i>) & Gram negative (<i>Escherichia coli</i> & <i>Pseudomonas aeruginosa</i>) bacterial/ Agar diffusion method.	The study reveals that both the aqueous and alcoholic extracts be active beside the strains of bacteria which are common cause of infections.	Kaveti Balaji; <i>et al</i> , (2011).
7.	The hot water <i>Piper betle</i> leaves extract.	Gastroprotective activity.	The study showed that it can protect against indomethacin-induced gastric ulceration due to its antioxidant and mucin protecting properties.	Pradhan D.; <i>et al</i> , (2013).
8.	The petroleum ether extract & methanol extract of the <i>Piper betle</i> leaves.	Insect Attractant Property /Field tests in a cornfield.	Field tests in a cornfield using trap contain the extracts, which does not detect adult moths of <i>Ostrinia salentialis</i> .	Yusoff Z.; <i>et al</i> , (2005)
9.	The methanolic extract of the <i>Piper betle</i> leaves.	Analgesic and anti-inflammatory activity/ Carrageenan induced hind paw edema model, hot plate, writhing and formalin tests/ Swiss albino mice and Wistar Rats.	The dose produced a significant increase in pain threshold in hot plate method whereas significantly reduced the writhing caused by acetic acid & caused significant inhibition of carrageenan induced paw edema.	Akter Fahima; <i>et al</i> , (2012)
10.	The <i>Piper betle</i> plant extract.	Antifertility activity/ female rats.	The data suggests that betle extract brought about antifertility and antiestrogenic effects in female rats.	Pradhan Manas Ranjan.; <i>et al</i> , (2013)
11.	The <i>Piper betle</i> leaf extract.	Antihepatotoxic effect/ ethanol & carbon tetrachloride (CCl4) induced liver injury in a rat model.	The histological examination shows that <i>Piper betle</i> leaf extract secluded liver from the damage induce by CCl4 by declining alpha smooth muscle actin (alpha-sma) expression.	Young S.C.; <i>et al</i> ,(2007)
12.	The <i>Piper betle</i> leaf infusion.	Skin Antiseptic/ pre-surgery cataract patients.	Results showed that 20% <i>Piper betle</i> leaf infusion to have an antiseptic	Husnun Amallia.; <i>et al</i> , (2009)

			potential.	
13.	The ethanolic extract of <i>Piper betle</i> leaf.	Radioprotective activity/ Rat liver mitochondria and pBR 322plasmid DNA.	The extract of <i>Piper betle</i> effectively prevented γ -ray induced lipid Peroxidation.	Bhattacharya S.; <i>et al</i> , (2005)
14.	The methanolic extract of the <i>Piper betle</i> .	Immunomodulatory activity / Mice.	The study reveals that it significantly suppressed hemagglutinin stimulated peripheral blood lymphocyte proliferation in a dose-dependent manner.	Kanjwani, D. G; <i>et al</i> , (2006)
15.	The ethanolic Extract of <i>Piper betle</i> leaves.	Antidepressant Activity/ Mice.	The study showed that it has significant antidepressant activity greater than Imipramine and has the potential to be used as an antidepressant.	Meti Vinayak <i>et al</i> ; (2012)

12. Conclusion

The medicinal importance of the herb as discussed above evidently prove that betle leaf is one of the most promising commercial botanical with earlier reported to possess a lot of therapeutic values. The leaf has the great potency to act as natural antioxidant. The anti-oxidant property is correlated with different biological activities like hepatoprotective, antidiabetic and anticancer properties, since free radicals are involved in all these diseases. The leaf poses the broad spectrum antimicrobial activity against various bacterial strains including *Bacillus cereus*, *Pseudomonas Aeruginosa*, *Escherichia coli*, *Micrococcus luteus*, *Staphylococcus aureus*, *Aeromonas hydrophila*, etc. The leaf extract shows the Gastroprotective activity by enhancing the mucus rather than decrease the acid production. Considering the above properties, it comes to conclusion that betle leaf place its position in nature same as our heart in our body and role the same with lots of biological activities and has a tremendous strength to come out as a future green medicine, hence *Piper betle*. L. leaf regard as “Green heart”.

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