



### RESEARCH ARTICLE

#### A COMPREHENSIVE REVIEW ON THE MAGICAL INDIAN FOLK MEDICINE: *PIPER BETLE* LINN

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#### Abstract

India has rich resources of medicinal plants and their uses in Ayurveda, Unani, and Siddha traditional medicine is quite popular around the world. There are over 2000 medicinal plant species, amongst them, *Piper betle* Linn. (Paan) is one of the most used ones. It is cultivated mainly in South-East Asia like Vietnam, Srilanka, Pakistan, China and India. Some phytochemical studies have found that betel leaf contains a wide variety of biologically active compounds such as Eugenol, Allylpyrocatechol, Methyl Eugenol, Chavibetol, Hydroxychavicol, Triterpenes and  $\beta$ -Caryophyllene. These help in treating many diseases like diabetes, stomach ulcer, cancer, obesity, swelling of gum, malaria, rheumatism, cuts and injuries, etc. This review article is a compilation of traditional, phytochemistry, therapeutic as well as nutraceutical properties of betel leaf based on scientific evidence.

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#### Introduction:-

Medicinal plants have been using for healing and curing purposes in local communities around the world for thousands of years. Some studies have found that in developing countries, up to 80% of people are dependent on herbal drugs for their primary healthcare. And over 25% of prescribed medicines are derived from wild plant species<sup>[1]</sup>. In the Indian traditional medicinal system, *Piper betle* L. (Paan) is one of the most popular medicinal plants that has been using for therapeutic as well as traditional purposes. In Ayurveda, betel leaf is known by its Vedic name **Saptasira** and **Nagavallari**. This plant belongs to the Piperaceae family. It is a dioecious, annual creeper, climbing by many small adventitious rootless, grows to a height of about one meter in hotter and damper parts of the country. The leaf is heart-shaped with different sizes from 7-15 cm in length and 5-14 cm in width. It is Yellowish green to dark green with a smooth surface, Aromatic, sweet to pungent in taste. Commonly, it is found in South-East Asia, such as Vietnam and China and India. Here, it is grown mainly in Uttar Pradesh, Bihar, Bengal, Orissa, Tamil Nadu, Andhra Pradesh and Karnataka. Betel leaf has many vernacular names in India such as **Taambula** (in Ayurveda), **Paan** (in Unani/Hindi, Bengal), **Phodi Paan** (in Konkani) and **Tamalapaka** (in Telugu)<sup>[5]</sup>.

#### Classification<sup>[2]</sup>

Kingdom	Plantae
Class	Magnoliopsida
Order	Piperales
Family	Piperaceae
Genus	Piper L.
Species	Piper betle L.

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**Figure 1:-** Betel leaf <sup>[3]</sup>



**Figure 2:-** Cultivation of betel leaf <sup>[4]</sup>

The *Piper betle* L. is enriched with nutrients, those are as follows- Water 85-90%, Carbohydrate 0.5-6.1%, Protein 3-3.5 %, Fat 0.4-1%, Fiber 2.3%, Vitamin A 1.9-2.9 mg/100g, Thiamine 10-70 ug/100g, Riboflavin 1.9-30 ug/100g, Nitrogen 2-7%, Potassium 1.1-4.6%, Calcium 0.2-0.5%, Iodine 3.4 ug/100g <sup>[6]</sup>. Many phytochemical investigation of bio active compounds has been reported that betel leaf has chavibetol 53.1%, chavibetol acetate 15.5%, allylpyrocatechol diacetate 0.71%, camphene 0.48%, eugenol 0.32%, alpha-pinene 0.21%, safrol 0.11% and 1,8-cineole 0.04% <sup>[7]</sup>.

**Table 1:-** Some major phytochemical constituents of betel leaf.

Name of the Phytochemicals	Uses & Pharmaceutical properties
Chavibetol	<ul style="list-style-type: none"> <li>➤ It is an aromatic compound with a spicy odor and one of the major constituents of betel leaf.</li> <li>➤ It has antioxidant and cancer-preventing properties <sup>[8]</sup>.</li> </ul>
Eugenol	<ul style="list-style-type: none"> <li>➤ It is used to relieve toothache.</li> <li>➤ It has anti-microbial, analgesic, anti-oxidant, antiviral and anticancer activity, especially its effect on the central nervous system (CNS) encompassing seizure control, Parkinson's disease, antidepressant effect <sup>[8]</sup>.</li> </ul>
Hydroxychavicol	<ul style="list-style-type: none"> <li>➤ It has hypoglycemic and hypolipidemic properties.</li> <li>➤ It could be a potential therapeutic agent for the prevention and treatment of atherosclerosis and other cardiovascular diseases through its anti-inflammatory and antiplatelet effects <sup>[9]</sup>.</li> </ul>
Allylprocatechol	<ul style="list-style-type: none"> <li>➤ It is widely used as a mouth freshener.</li> <li>➤ It also has antioxidant and healing properties <sup>[9]</sup>.</li> </ul>
Beta - caryophyllene	<ul style="list-style-type: none"> <li>➤ It has anti-inflammatory, antimicrobial and cancer preventive activities.</li> <li>➤ It also can improve mood and pain-relieving properties.</li> <li>➤ Due to its unique aroma it can be used as a food additives, toothpaste and cosmetics <sup>[10]</sup>.</li> </ul>

### Traditional Uses <sup>[11,12]</sup>

1. For curing obesity, one *Piper betle* leaf mix with *Piper nigrum* is prescribed for two months.
2. A mixture of *Piper betle* juice with honey is using to treat coughs, dyspnoea, and indigestion amongst children.
3. Betel leaves are smeared with oil and applied to the breasts of a lactating woman. It is supposed to promote milk secretion
4. A local application of betel leaf is recommended for inflammatory swelling such as orchitis, arthritis and mastitis
5. Leaves are used for recovery from bad breath, body odor and prevent tooth decay.
6. It also prevents and treats vaginal ejection, and reduces itching of the vagina.
7. Leaves are also used for curing eczema, lymphangitis, asthma and rheumatism.
8. Leaf oil is used for irritation in the throat, larynx, bronchi.
9. Juice of leaves is used as stomachic and febrifuge.
10. The paste of leaves is also applied to cuts and wounds.

Chewing a paan after a meal is an ancient food tradition in India. But this heart-shaped leaf is much more than just a mouth freshener that is less known among people.

Therefore, the main objective of this paper to showcase many scientific pieces of evidence that prove the phytochemical constituents of betel leaf have medicinal and therapeutic properties that could help in combating many health-related problems and may keep diseases at bay.

### Review Of Literature:-

#### Antioxidant activity

Dasgupta *et al.* studied the antioxidant activity of the aqueous extract of three local varieties of *betel* leaf (Kauri, Ghanagete, Bagerhati) by DPPH radical scavenging activity, superoxide radical scavenging activity and found that all three varieties of **betel leaf** having a different level of antioxidant activity, as well as, the leaf has more potential to prevent lipid peroxidation than does tea <sup>[13]</sup>. Jaiswal *et al.* found that six varieties of betel leaves from different locations of India have a promising source of natural antioxidants that can be used in the food and pharmaceutical industries <sup>[13]</sup>. A report has also suggested that Allylpyrocatechol, a phytochemical constituent of betel leaf has more scavenging capacity than Chavibetol <sup>[15]</sup>.

#### Antimicrobial activity

Both the aqueous and ethanolic extract of *Piper betle* L. has antibacterial activity against Gram-positive and Gram-negative bacteria. But among them, the ethanolic extract is considerably more effective than the aqueous extract to inhibit the microbial strains <sup>[16]</sup>. Hydroxychavicol, a major constituent of betel leaf has the potential to inhibit and reduce the formation of **Candida albicans** biofilms that can cause oral infection *by disrupting the membrane* <sup>[17]</sup>. Garg *et al.* reported that the essential oil of betel leaf is highly active against the growth of bacterial organisms like *B. subtilis*, *B. pumilus*, *S. aureus*, *S. typhi* and *V. cholera* and also against tapeworms (*Taeniasolium*) and hookworms (*Bunostomumtrigonocephalum*), by comparing the synthetic anthelmintics **Piperazine phosphate** and **Hexylresorcinol** <sup>[18]</sup>.

#### Gastroprotective activity

Allylpyrocatechol is one of the major phytochemical constituents that can protect the stomach from ulceration due to its antioxidant and mucin protecting properties <sup>[19]</sup>. Hazal *et al.* confirmed that the ethanolic extract of piper betel leaf can reduce the growth of *Helicobacter pylori* with the best minimal inhibitory concentration (MIC) value against the bacterial strain. Hence, it can be considered as a useful source for the treatment of *Helicobacter pylori* infection <sup>[20]</sup>. Recently, it has also been reported that hydroalcoholic extract *Piper betle* L. has great anti-ulcer activity when compared with the standard drug, **Ranitidine** <sup>[21]</sup>.

#### Anti-fertility activity

Alcoholic extract of the betel leaf has a contraceptive effect mainly on the maturation process of spermatozoa in epididymides but without influencing systemic hormonal profiles, reported by Sarkar *et al.* <sup>[22]</sup>. Adhikary *et al.* found that stalk extract of betel leaf could produce a significant decrease in the weights of estrogen and androgen-dependent target organ along with prolonged dioestrus in the vaginal smear, as well as, decreasing number, motility

of sperm in treated female and male albino rats respectively <sup>[23]</sup>. A study also confirms that both aqueous and methanolic extracts of the leaf can develop infertility in female albino rats <sup>[24]</sup>.

#### **Anti-diabetic activity**

Khatun *et al.* found that the juice of betel leaf can significantly decrease the blood glucose level without any adverse health effects <sup>[25]</sup>. It has also been reported that both hot water extract (HWE) and cold ethanolic extract (CEE) of betel leaf can significantly lower blood glucose levels in streptozotocin-induced diabetic rats. Hence, it can be considered as a safe and strong anti-diabetic agent <sup>[26]</sup>.

#### **Anticancer activity**

It has been found that acetone extract of *Piper betle* L. has significant anticancer activity on lung cancer cell line (A549) due to the presence of its phytochemicals and their free radical scavenging properties <sup>[27]</sup>. Abraham *et al.* stated that ethyl acetate extract of betel leaf shows the highest inhibitory effect against the proliferation of breast cancer cell line MCF -7, due to its natural source of antioxidants. Hence, medicine from betel leaf could be developed for cancer treatment <sup>[28]</sup>. It has also been reported that silver nano- bio conjugates synthesized from *Piper betle* have shown significant anti-cancer potential than unconjugated forms <sup>[29]</sup>.

#### **Stimulatory influence on intestinal digestive enzyme**

Prabhu *et al.* studied two varieties of betel leaf such as pungent Mysore and non-pungent Ambadi on digestive enzymes of the pancreas, intestinal mucosa and bile secretion. The results indicated that these leaves don't influence bile secretion and composition but they have a significant stimulatory effect on pancreatic lipase activity. The Ambadi variety of leaves has a positive stimulatory influence on intestinal digestive enzymes, especially lipase and amylase, while slightly lower activity is found in the Mysore variety. Furthermore, both the leaf varieties have shown a decreasing influence on pancreatic trypsin and chymotrypsin activities <sup>[30]</sup>.

#### **Effect of betel leaf on the thyroid function**

The effect of betel leaf on thyroid function in male swiss mice was investigated. The findings suggest that the leaf extract has a dual role depending on different doses. While the lowest dose can decrease thyroxine (T4) and increase serum triiodothyronine (T3) concentrations as well as the reverse effects are also observed at higher doses. So, it can be concluded that betel leaf may have both stimulatory and inhibitory activity of thyroid function <sup>[31]</sup>. Panda *et al.* have also been reported the antithyroid property of ethyl acetate extract of betel leaf in T4 induced hyperthyroidism mainly due to the presence of flavonoid ( quercetin, rutin, kaempferol and luteolin), without any hepatotoxicity <sup>[32]</sup>.

#### **Anti-inflammatory activity**

Allyprocatechol, a phytoconstituent of betel leaf has potent anti-inflammatory activity and it could be used to treat inflammation-associated disorders like Rheumatoid Arthritis, reported by Kundu *et al.* <sup>[33]</sup>.

#### **Antimalarial Activity**

Al-Adhroey *et al.* state that crude methanol extract of *Piper betle* L. contains some vital anti-plasmodial chemical constituents that could fight against Plasmodium berghei (NK65) during early and established infections <sup>[34]</sup>.

#### **Lipid-lowering activity**

**Eugenol**, an active constituent of betel leaf has an anti hypercholesterolemic property. It can lower mean blood/serum levels of glucose, total cholesterol, triglycerides, LDL, VLDL and its effectiveness is the same as the standard lipid-lowering drug, **Lovastatin** <sup>[35]</sup>.

#### **Antiplatelet activity**

Lei *et al.* reported that Hydroxychavicol from the aqueous extract of betel leaf has an inhibitory effect on platelet aggregation. So, it could be used as a potential therapeutic agent for the prevention and treatment of atherosclerosis and other cardiovascular diseases through its anti-inflammatory and anti-platelet effects <sup>[36]</sup>.

#### **Radioprotective activity**

Bhattacharya *et al.* examined the radioprotective activity of ethanolic extract of betel leaf by using rat liver mitochondria and pBR322 plasmid DNA as two models in vitro systems. And results show that the extract can effectively prevent gamma-ray-induced lipid peroxidation as well as radiation-induced DNA strand breaks in a

concentration-dependent manner. So, this radioprotective activity of the betel leaf may due to its hydroxyl, superoxide radicals scavenging properties along with its lymphoproliferative activity<sup>[37]</sup>.

### Anti- filarial activity

Antifilarial activity of *Piper betle* L. has investigated and found the crude methanolic extract of betel leaf and its n-hexane, chloroform fractions could trigger different arms of immune responses in BALB/c mice and exhibit anti filarial activity against human lymphatic filaria *Brugia malayi*<sup>[38]</sup>.

### Oral hygiene

It has been observed that a mouthwash prepared by betel leaf can give oral protection from inhibiting the growth of *P.aeruginosa*, *E.coli*, *S.aureus*, *B.cereus*, *A.niger*, *S. mutans*, mainly the presence of hydroxychavicol in it<sup>[39]</sup>. In another study, it is also found that crude aqueous extract *Piper betle* and its bioactive compounds ( hydroxybenzoic acid, chavibetol, hydroxychavicol) has potent fungistatic activity on candida species by suppressing the cell growth, alteration in morphology and can reduce colonization in oral tissues<sup>[40]</sup>.

### Conclusion:-

1. In Ayurveda & Unani, *Piper betle* L. has been using for its curative and healing properties from ancient times.
2. Many studies have been reported that betel leaf has many active phytochemical compounds like Allyprocatechol, Eugenol, Chavebetol, Hydroxychavicol, Beta-Caryophyllene. Those are responsible for its therapeutic activities.
3. Eugenol, an active constituent of piper betle leaf was found to be a better hypercholesterolemic compound than that of the standard lipid-lowering drug, **Lovastatin**.
4. Allypyrocatechol, one of the major phytochemical compounds has potent scavenging activity and could be considered as the treatment of inflammation-associated disorders like Rheumatoid Arthritis.
5. Hydroxychavicol of betel leaf has the potential to inhibit and reduce the formation of *Candida albicans* biofilms that can cause oral infection by disrupting the membrane.
6. Hydroalcoholic extract of betel leaf has great gastroprotective activity than that of the standard drug, **Ranitidine**.

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