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A REVIEW ON BETEL LEAF (PAN)

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ABSTRACT: The World Health Organization adopted a major policy change in accepting that most developing nations would have to make use of more traditional medical practices for primary health care. *Piper betel* L. belongs to family *Piperaceae* commonly known as *Pan*. It is extensively grown in Sri Lanka, India, Thailand, Taiwan and other Southeast Asian countries. This oil may be used as an industrial raw material for manufacturing medicines, perfumes, mouth fresheners, tonics, food additives etc. The leaves are nutritive and contain anti carcinogens showing promise for manufacturing of a blood cancer drug. The present review aims to compile medicinal values of *Piper betel* generated through the research activity using modern scientific approaches and innovative scientific tools.

INTRODUCTION: The scientific name of betel vine is *Piper betel* L. belongs to the family Piperaceae, i.e. the Black Pepper family.

In spite of its alienness, the plant is much more popular in India than in any other country of the world since the antiquity. This would be evident from the numerous citations laid down in the ancient literature, particularly the Indian scriptures.

In these citations, significance of the leaves has been explained in relation to every sphere of human life including social, cultural, religious and even day-to-day life, which is very much relevant even these days.

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It is also used as a special item offered to the guests in order to show respect and for such traditional use of betel leaf in the Indian society, the leaf really stands alone without any parallel even today [1]. The Essential oil isolated from the leaves is supposed to be useful in treating respiratory catarrhs and as an anti-septic [2]. Piper betel is claimed to be useful to improve learning and memory, in Indian traditional system of medicine yet not documented scientifically in this regard [3].

Vernacular Names:

Sanskrit: Tamboolavalli, Tamboola, Tamboola vallika

English: Betel leaf plant.

Hindi: Pan

Malayalam: Vetta, Vettila

Bengali: Pan

Plant description: A perennial dioecious creeper. Stems semi woody, climbing by means of short adventitious roots. Leaves 10-20 cm long, broadly ovate, slightly cordate and often unequal at the base, shortly acuminate, glabrous, glaucous on both sides, bright green or yellowish, petiole stout 2.0-2.5 cm long. Male spikes cylindrical dense. Female spikes 2.5-5.0cm long, pendulous. Fruits rarely produced, often sunk in the fleshy spike, forming nodule-like structures [4]. Betel leaf is the most valuable home remedy for common illness.

The Betel (*Piper betel*) is a spice whose leaves have medicinal properties. The branches of the plant are swollen at the nodes. The plant has alternate, heart-shaped, smooth, shining and long-stalked leaves, with pointed apex. It has five to seven ribs arising from the base; minute flowers. Betel is a native of central and eastern Malaysia. It spread at a very early date throughout tropical Asia and later to Madagascar and East Africa. In India, it is widely cultivated in Tamil Nadu, Madhya Pradesh, West Bengal, Orissa, Maharashtra and Uttar Pradesh. Offering betel morsel (pan-supari) to guests in Indian subcontinent is a common courtesy.

Chemical Constituents: Plant contains a terpinine, P-cymene, carvacrol, chavicol and its derivatives, allyl catechol, eugenol, estragol, oxalic acid, malic acid and amino acids. Leaves contain good amounts of vitamins particularly nicotinic acid, ascorbic acid and carotin. They also contain significant amounts of all essential amino acids except lycine, histidine and arginine. Large concentrations of asparagines are present while glycine and proline occur in good amount. Essential oil of leaf gives it the aromatic flavour. β-sitosterol is present in the root [5].

Contents of Betel leaves: Betel leaves contain tannins, sugar and diastases and an essential oil. The essential oil is a light yellow liquid of aromatic odor and sharp burning in taste. It contains a phenol called chavicol which has powerful antiseptic properties. The alkaloid arakene in it has properties resembling cocaine in some respects .An analysis of the betel leaf shows it to consist of moisture 85.4 per cent, protein 3.1 per cent, fat 0.8 per cent, minerals 2.3 per cent, fiber 2.3 per cent and carbohydrates 6.1 per cent per 100 grams. Its minerals and vitamin contents are calcium, carotene, thiamine, riboflavin, niacin and vitamin C. Its calorific value is 44 [6].

Traditional uses of Betel leaves: The use of betel leaf can be traced as far back as two thousand years. Betel leaves help to heal the following illnesses. Such as

- **Headache:** Betel leaf is a popular home remedy for headache. The betel leaf has analgesic and cooling properties. It can be applied with beneficial results over the painful area to relieve intense headache.
- **Scanty or Obstructed Urination:** Betel leaf juice is credited with diuretic properties. Its juice, mixed with dilute milk and sweetened slightly, helps in easing urination.
- **Weakness of Nerves:** Betel leaves play a vital role in the treatment of nervous pains, nervous exhaustion and debility. The juice of a few betel leaves, with a teaspoon of honey, will serve as a good tonic. A teaspoon of this can be taken twice a day.
- **Sore Throat:** Betel leaf is an excellent household remedy in the treatment of cough and sore throat. Local application of the leaves is effective in treating sore throat. The crushed fruit or berry should be mixed with honey and taken to relieve irritating cough.
- **Respiratory Disorders:** Betel leaves are useful in pulmonary affection in childhood and old age. The leaves, soaked in mustard oil and warmed, may be applied to the chest to relieve cough and difficulty in breathing.
- **Constipation:** In the case of constipation in children, a suppository made of the stalk of betel leaf dipped in castor oil can be introduced in the rectum. This instantly relieves constipation.
- **Problem of Breast milk secretion:** The application of leaves smeared with oil is said to promote secretion of milk when applied on the breasts during lactation [7].

- **Inflammation:** Applied locally, betel leaves are beneficial in the treatment of inflammation such as arthritis and orchitis that is inflammation of the testes.

- **Wounds:** Betel leaves can be used to heal wounds. The juice of a few leaves should be extracted and applied on the wound. Then a betel leaf should be wrapped over and bandaged. The wound will heal up with a single application within 2 days.

- **Boils:** Betel leaf is also an effective remedy for boils. A leaf is gently warmed till it gets softened, and is then coated with a layer of castor oil. The oiled leaf is spread over the inflamed part. This leaf has to be replaced, every few hours. After a few applications, the boil will rupture draining all the purulent matter. The application can be made at night and removed in the morning [8].

Various proved therapeutic values of *Piper betel*:

Antimicrobial Activity: Nair and Chanda (2008), were studied the Aqueous and methanol extract of the leaves of *Terminalia catappa* L., *Manilkara zapota* L. and *Piper betel* L., for antibacterial activity against 10 Gram positive, 12 Gram negative bacteria and one fungal strain, *Candida tropicalis*. Piperacillin and gentamicin were used as standards for antibacterial assay, while fluconazole was used as standard for antifungal assay. The three plants showed different degree of activity against the microorganisms investigated. The methanolic extract was considerably more effective than aqueous extract in inhibiting the investigated microbial strains. The most active antimicrobial plant was *Piper betel* [9].

Antihistaminic activity: Hajare *et al*., (2011), were evaluated Piper betel Linn. leaves for its antihistaminic activity. In the study, the pharmacological evaluation of ethanolic extract and essential oil extract of leaves of *P. betel* Linn. has been done for their antihistaminic activity on guinea pig. In isolated guinea pig tracheal chain preparation, there was a right side shift of dose response curve (DRC) of histamine. Chlor-pheniramine maleate was used as a standard drug. Moreover extracts of *P. betel* disturbed histamine aerosol induce bronchoconstriction in whole guinea pig, where essential oil was more effective comparatively to ethanolic extract. Thus, they concluded that ethanolic extract and essential oil of P. betel Linn possess antihistaminic activity [10].

Anti-inflammatory effects: The betel leaf is used as a common household remedy for inflammation in the oral cavity [11]. Dohi *et al*., (1989), has shown that the ethanolic extract of betel leaf has been reported to possess anti-inflammatory activities at non-toxic concentrations in the complete Freund's adjuvant-induced model of arthritis in rats. Eugenol, one of the principal constituent of betel leaf has also been shown to possess anti-inflammatory effects in various animal models of studies with various inflamogens [12].

Antioxidant effects: Azuine *et al*., (1991) and Bhide *et al*., (1991) described that the betel leaf constituent's eugenol, hydroxychavicol and alpha-tocopherol were also shown to enhance the levels of GSH in mouse skin and liver [13, 14]. Together all these observations clearly indicated that the betel leaf extracts and some of its constituents increased the cellular antioxidants and mediate the chemopreventive effects at least in part.

Lei *et al*., (2003) have shown that the aqueous extract of the inflorescence of Piper betel extract was effective in scavenging H_2O_2, superoxide radical and hydroxyl radical. The extract also prevented the hydroxyl. Radical-induced DNA strand breaks in the PUC18 plasmid [15]. Rathee *et al*., (2006) have shown that the ethanol extracts of Bangla, sweet, and Mysore varieties of betel leaf were effective in scavenging DPPH radicals in vitro, with best effects being observed with the Bangla variety.

Recently, Manigauha *et al*., (2009) observed that the methanolic extracts of the betel leaves possess reducing power, DPPH radical, superoxide anion scavenging and deoxyribose degradation activities [16]. Studies have also shown that the hydroalcoholic extract of the betel leaf possess nitrogen oxide scavenging effect *in vitro* [17].

Antimutagenic effects: Multiple studies have shown that the betel leaf is devoid of mutagenic activities in both prokaryotic and eukaryotic assay

system [18, 19, 20] and also to possess antimutagenic (Shirname *et al*., 1983) and anticlastogenic effects (Bhattacharya *et al*., 2005). In vitro studies with cultured cells have shown that betel leaves did not cause any morphological transformation of the hamster embryo cells or induce sister chromatid exchanges in both virally transformed cells and PHA-stimulated human lymphocytes [16]. Additionally, the ethanolic extract of betel leaf is also reported to possess γ-ray induced clastogenesis in plasmids [20].

Anti - haemolytic activity: Anti-haemolytic activity was studied by Chakraborty *et al*., (2011), using erythrocytes model piper betel leaf extracts and the extent of lipid peroxidation of the same was also determined [21]. The erythrocyte membranes are susceptible to peroxidation because they are rich in polyunsaturated fatty acids. They contain haemoglobin, which may catalyze the oxidation as they are continuously exposed to high concentration of oxygen. The oxidation of erythrocytes serves as good models for the oxidative damage of biological membranes. It has been found that certain chemicals, having ability to generate radicals attack the erythrocyte membrane, inducing the chain oxidations of lipids and proteins and eventually causing membrane damage leading to haemolysis. When red blood cells were treated with betel leaf extract along with H_2O_2 marked reduction in haemolysis was found [22, 23].

Antiulcer Activity: Vyawahare *et al.*, (2010), evaluated the antiulcer activity of hydroalcoholic extract of *Piper betel* (HEPB) leaves, in rats employing the HCl-ethanol, acute stress and pylorusligation models to induce the experimental gastric ulcers. Pre-treatment with *Piper betel* extract provided significant ulcer protective effect in all the experimental models along with significant increase in gastric pH and decrease in gastric fluid volume. The hydroalcoholic extract of *Piper betel* leaves possesses antiulcer activity which can be attributed to its putative mechanism of action [24].

Antibacterial activity: The four varieties of *Piper betel*; namely Desawari, Desi, Bangladeshi and Jaleswar, cultivated in India. Agarwal *et al*., (2012) evaluated that the cold aqueous, methanolic, ethanolic, and ethyl acetate extracts of dried leaves of all the four varieties of *Piper betel* at a final concentration of 500 mg/ml were tested against pathogenic microorganisms such as *Pseudomonas aeruginosa, Staphylococcus aureus* and *Escherichia coli* using agar well diffusion method [25].

Antifungal activity: Ali *et al*., (2010) have shown that the Hydroxychavicol, isolated from the chloroform extraction of the aqueous leaf extract of *Piper betel* L., (Piperaceae) was investigated for its antifungal activity against 124 strains of selected fungi. Hydroxychavicol exhibited inhibitory effect on fungal species of clinical significance, with the MICs ranging from 15.62 to 500 μg/ml for yeasts, 125 to 500 μg/ml for Aspergillus species, and 7.81 to 62.5 μg/ml for dermatophytes whereas the MFCs were found to be similar or two fold greater than the MICs. There was concentration-dependent killing of *Candida albicans* and *Candida glabrata* up to 8 × MIC. Hydroxychavicol also exhibited an extended post antifungal effect of 6.25 to 8.70 h at 4 × MIC for Candida species and suppressed the emergence of mutants of the fungal species tested at 2 × to 8 × MIC concentration. Their conclusion was that antifungal activity exhibited by this compound can be used as an antifungal agent particularly for treating topical infections, as well as gargle mouthwash against oral Candida infections [26].

Anti-diabetic activities: Arambewela *et al*., (2005) investigated the antidiabetic activity of *Piper betel* leaves, tested in normoglycaemic and strepozotocin (STZ)-induced diabetic rats using oral administration of hot water extract (HWE) and cold ethanolic extract (CEE). In normoglycaemic rats, both HWE and CEE significantly lowered the blood glucose level in a dose-dependent manner. In glucose tolerance test, both extracts markedly reduced the external glucose load. The antidiabetic activity of HWE is comparable to that of CEE. Both extracts were found to be non-toxic and well tolerated after following chronic oral administration (no overt signs of toxicity, hepatotoxicity or renotoxicity). However, the weight of the spleen had increased in treated groups possibly indicating lympho-proliferative activity [27].

Palpebral skin antiseptic: The antiseptic effectiveness was measured by Amalia *et al*., (2009), counting the microbial colonies before and after administration of the antiseptic solutions.

This study demonstrates that the mean colony counts after application of 20% *Piper betel* leaf infusion showed a significant reduction of 27-100% compared with those before administration (p=0.001). Mean colony counts after 10% povidone-iodine administration showed a significant reduction of 88-100% compared with the mean counts before the solution was applied (p=0.000). The 20% *Piper betel* infusion has an antiseptic potential [28].

Local anaesthetics action: Krishnakumar *et al*., (2001), have shown that, extracts of plain betel leaf with betel nut, with and without autoclaving, were tested for surface and infiltration anesthetic activities using rabbits and Guianese pigs. The results were compared with normal saline control and xylocaine drug control. Betel leaf showed dose-dependent infiltration anesthetic activity comparable with xylocaine. As a surface anesthetic, the onset was as quick as xylocaine and the duration was shorter than xylocaine. Betel nut significantly reduced the infiltration activity and abolished the surface anesthetic activity of betel leaf. Autoclaving did not result in any loss of activity. Betel leaf has potent local anesthetic action both by surface and infiltration techniques. This effect is reduced by the addition of betel nut but not lost on autoclaving [29].

Role of betel leaf extract on thyroid function: Panda and Kar (1998) demonstrated that the effects of betel leaf extract (0.10, 0.40, 0.80 and 2.0 g kg−1day−1for 15 days) on the alterations in thyroid hormone concentrations, lipid peroxidation (LPO) and on the activities of superoxide dismutase (SOD) and catalase (CAT) were investigated in male Swiss mice. Administration of betel leaf extract exhibited a dual role, depending on the different doses. While the lowest dose decreased thyroxine (T4) and increased serum triiodothyronine (T3) concentrations, reverse effects were observed at two higher doses.

Higher doses also increased LPO with a concomitant decrease in SOD and CAT activities. However, with the lowest dose most of these effects were reversed. Their findings suggested that betel leaf can be both stimulatory and inhibitory to thyroid function, particularly for T3generation and lipid peroxidation in male mice, depending on the amount consumed [30].

Anti-nociceptive Activities: Arambewela *et al*., (2005), examined the antinociceptive activity of hot water extract (HWE) and cold ethanol extract (GEE) of *P. betel* leaves using rats and three models of nociception (tail flick, hot plate, and fonnalin tests). Different concentrations of H WE (125, 200, 300, 500mg/kg) and CEE (125, 200, 300, 500mg/kg) were made and orally administrated to rats, and the reaction times were determined. Their results showed that the extracts have marked antinociceptive activity when evaluated in the hot plate and the formalin tests but not in the tail-flick test. The overall antinociceptive effect of CEE was higher than that of HWE [31].

As contraceptive: Singh *et al*., (2011), studied the mitochondrial activity of sperm, after treating semen with different concentrations of *Piper betel*. The mitochondrial activity was also evaluated after subjecting the semen samples for different incubation time periods. Test was done on more than 75% motile normozoospermic semen sample and was found that as the concentration of extracts increases the mitochondrial activity decreases significantly ($p < 0.001$), similar results were observed when constant concentration of extracts with increasing time intervals.

The mitochondrial activity decreases significantly ($p < 0.001$) in 5 minutes to 20 minutes incubation time. They concluded that Piper betel has properties to decrease mitochondrial activity in human sperm and ability to work as contraceptive [32].

CONCLUSION: It is quite evident from this review that betel leaf contains a number of phytoconstituents which reveals its uses for various therapeutic purposes. The Plant or its individual parts can be used for the treatment of various disorders in human being such as, diabetes, fungal infection, microbial infection, inflammation, antihistaminic, antiulcer, local anaesthetic etc.

The betel leaves really as a cheap, natural and easily available appetizer, digestive, mild stimulant, aphrodisiac and refreshing mastication .Still, so much work is required with the betel leaf to investigate the mechanism of actions with other therapeutic activities. This adequately justifies its nomenclature as the “Green Gold of India”.

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