Review Article

Piper Betle: Phytochemical, Pharmacological and Nutritional Value in Health Management

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ABSTRACT

Many of the health benefits bonded with Piper betel (locally known as Paan) belongs to the Piperaceae or pepper family. It has been an important herb distributed throughout of world. Betle leaves are the most valued part of the plant, in the past were routinely used as a chewing agent to restrict offensive breath and they contain tannins, chavicol, phenyl, propane, sesquiterpene, cyneole, alkaloid, sugar and some essential oil and found various medicinal value, digestive, appetizer, aromatic, expectorant, stimulant, anti-bacterial, euphoria-inducing, antiprotozoan, carminative, anti-fungal and aphrodisiac etc. The leaves are also supposed to harden the gum, conserve the teeth and to prevent indigestion, bronchitis, constipation, congestion. This review for the first time provides information on therapeutically effects and also addresses the various mechanisms which might be involved.

Keywords: Piper betel-leaf, Nutrients, Phytochemical, Pharmacological.

INTRODUCTION

The leaves of *Piper betle* Linn have long been use in the Indian local system of medicine. In ancient India, Betel leaves are considered auspicious and are still extensively used during religious functions in Asia. It is generally found in hot and moist climatic condition. In India it is found in Bihar, Bengal, Orrisa, south India and Karnataka. The betel plant is an evergreen and perennial creeper, with glossy heart-shaped leaves and white catkin.[1]

There are various types of leaves, the most popular being: Calcutta, Banarasi, Magahi, etc. In Bangladesh Dinajpur, Rangpur, Chittagong, Faridpur, Jessore, Narayanganj, Barisal and Sylhet are the areas producing the most betel. The harvested leaves are used both for domestic consumption and for export to Middle East, to European countries, USA, UK, Pakistan, and Myanmar. Paan is one of the major economic sources of rural Bangladesh. The best Betel leaf is the "Magadhi" variety (literally from the Magadha region) grown near Patna in Bihar, India. In Kerala, the famous variety of betel leaf is from Venmony near Chengannur and it is called "Venmony Vettila". Betel leaf cultivated in Tirur in Kerala, Hinjilicut in Odisha are of fine quality. Betel leaves exported from Tirur are famous in Pakistan as "Tirur Pan". *Piper betle* is one of the invaluable medicinal plants where its leaves have been used for many medicinal purposes. Piper betel, a member of the Piperaceae, which is a large plant family, is also known Paan in India and Sirih in Malaysia and Indonesia, show in figure 1. The fresh leaves of betel leaves have been wrapped together with the areca nut, mineral slaked lime, catechu, flavoring substances and spices are chewed since the ancient time[2]. The whole betel plant had some very bad press due to reports associating the usage of the herb with mouth cancer. It also helps in reducing difficulty in breathing for people suffering from asthma. Some apply mustard oil to the leaves of the betel plant, warm it and then keep it on the chest to bring relief from asthma.[3]

A preliminary study has reported *Piper betle* leaves extract contains large numbers of bioactive molecules (Devjani Chakraborty*). *Piper betle* contains a wide variety of biologically active compounds whose concentration depends on the variety of the plant, season and climate. Pharmacological Profile has shown antiplatelet, anti-inflammatory effects as well as immuno modulatory, gastro protective and antidiabetic activity (Satish A Bhalerao1*). Paan has been referred to in Sakta-tantra as one of the means of achieving siddhi. It was believed that without betel chewing and offering pan to Guru no siddhi can be gained.

Tambool has also been referred to as facilitating the sadhak in chewing dharma, yasha aisvarya, Srivairagya and mukti (D. Pradhan1*). It was reported that fresh leaves contains: moisture 85.4, protein 3.1, fat 0.8, carbohydrate 6.1, fibre 2.3, calcium 230mg, phosphorous 40mg, iron 7mg, ionisable iron 3.5mg, iodine 3.4 µ.

They have a high content of potassium nitrate (0.26-0.42%). The sugars identified in betel leaves include glucose, fructose, maltose and sucrose.

The average content of free reducing sugars in different types of betel leaves varies from 0.38-1.46%. It also contains the enzyme like diastase and catalase. (K.Periyanayagam1). *Piper betle* leaves are earlier reported to possess anticancer potential.

Hence, the aqueous extract of the leaves was subjected to cytotoxicity studies on Hep-2 cell line using Micro culture Tetrazolium and Sulphorhodamine B assays (Chaurasia, Sundeep *et al*). *Piper betle* leaf oil can be used as an industrial raw material for manufacturing

medicines, perfumes, food additives etc. The leaves are nutritive and contain anti carcinogens showing promise for manufacturing of a blood cancer drug (Sengupta).

Figure 1: P. Betle Pant

Scientific Classification

Synonyms: Chavica Beta. Artanthe Hixagona

Fingdom: Plantae

Order: Piperales

Family: Piperaceae

Genus: Piper

Species: P.Petle

Test: Pungent tasting and warming.

Division: Magnoliphyta

Vernacular Names

Sanskrit: Tambool, Mukhbhushan, Varnalata

Hindi: Paan leaf, English: Betle, Betle pepper, Betle-vine

Telugu: Nagballi, Tamalapaku

Tamil: Vetrilai Gujarati: Nagarbael

Bengali: Paan, Paana, Tambulaballi (plant), Parnakari (leaf).

Assamese: Paan, Paana.

Kannada: Eleballi, Panu, Vileyadele

Gujarti: Paan, Tanbolaa

Malayalam: Vettila

Nepalese: Naagavallii (plant), Paan (leaf).

Indonesia: Bakik serasa, Daun sirih, Sirih, Serasa, Séwéh, Seureuh.

German : Betelpfeffer, Betel-Pfeffer

Chinese : Ju jiang, Tu bi ba, Tu wei teng, Wei zi, Wei ye, Da geng teng, Ch'ing Chu.

Physical Characters

A green leafy vine growing as a ground cover or small climber, very similar in growth habits to pepper. The betel leaf plant is a branching vine that may climb as high as 10-15ft, although it often grows as an understory ground cover. It is generally too tender to grow outside of the tropics[6]. The plant growing environment prefers warm, humid conditions, but can tolerate some drought. The betel leaf is used in a number of traditional remedies for the treatment of stomach ailments, infections, and as a general tonic. It is often chewed in combination with the betel nut (*Areca catechu*), as a stimulatory. Some evidence suggests that betel leaves have immune boosting properties as well as anti-cancer properties.[7]

Nutritional Composition

The proximate analysis of the leaves of *Piper betle* showed that it contained macro and micro nutrients as well as phytochemical shown in table 1.[8]

Table 1: Elemental Composition of *Piper betle* Linn

S. No.	Constituents	Approximate	Composition
1	Water	85-90%	
2	Protein	3-3.5%	
3	Fat	0.4-1.0%	
4	Minerals	2.3-3.3%	
5	Fiber	2.30%	
6	Chlorophyll	0.01-0.25%	
7	Carbohydrate	0.5-6.10%	
8	Energy	44	kcal/100g
9	Essential Oil	0.08 - 0.2%	
10	Iodine	3.4	µg/100g
11	Iron	0.005-0.007%	
12	Calcium	0.2-0.5%	
13	Potassium	1.1-4.6%	
14	Nicotinic acid	0.63-0.89	mg/100g
15	Vitamin C	0.005-0.01%	
16	Vitamin A	1.9-2.9	mg/100g
17	Thiamine	13-70	µg/100g
18	Riboflavin	1.9-30	1.9-30
19	Tannin	0.1-1.3%	
20	Nitrogen	2.0-7.0%	
21	Phosphorus	0.05-0.6%	

Chemical Constituents

Chief constituent of the leaves is the volatile oil, Betel oil, Contains two phenols, betelphenol (chavibetol) and chavicol. Leaves reported to yield an alkaloid: arakene, with properties similar to cocaine. Volatile oil, 0.8 - 1.8% - chavicol, betelphenol, eugenol, allyl pyrocatechin,

terpene, cineol, caryophyllene, cadinene, menthone. Chemical compositions of essential oil differ: safrole in the leaf, stalk, stem and root, ß-phellandrene in the fruit. Younger leaves reported to yield more essential oil[6]. Leaf and other plant parts have yielded active compounds: hydroxychavicol, hydroxychavicol acetate, allypyrocatechol, chavibetol, piperbetol, methylpiperbetol, piperol A and piperol B. Study of essential oil and ether soluble fraction of leaves yielded fourteen components including eight allypyrocatechol analogs. Major constituents show in table 2 was chavibetol (53.1%) and chavibetol acetate (15.5%). Other constituents were allypyrocatechol diacetate (0.71%), campene (0.48%), chavibetol methyl ester (methyl eugenol 0.48%), eugenol (0.32%), a-pinene (0.21%), ß-pinene (0.21%), a-limonene (0.14%), safrole (0.11%), 1,8-cineole (0.04%) and allypyrocatechol monoacetate[8]. Hexane fraction of leaf stalks yielded four alipathic compounds in pure form i.e. pentadecyl 6-hydroxytridecanoate, pentatriacontanol, methyl hexacos-7-enoate and 6, 9-heptacosa diene. Sri Lankan study on essential oil yielded saffrole as the major compound from the leaf, stem, stalk, and root and ß-phellandrene from the fruit. The composition of some contents changed with maturity of the leaf.[9]

Table 2: Chemical constituents of *Piper betle L.*[10]

Component	Percentage of Components
Chavibetol	53.1
Caryophyllene	3.71
Chavibetol acetate	15.5
Allylpyrocatechol Diacetate	0.71
Chavibetol methyl ether	0.48
Campene	0.48
f-Pinene	0.21
Eugenol	0.32
u-Limonene	0.14
a-Pinene	0.21
1,8-Cineol	0.04
Saprobe	0.11
Allylpyrocatechol Monoacetate	0.23

Components % of components

Pharmacology Profile

Antioxidant/Antiproliferative

An ethyl acetate extract showed the highest ferric reducing activity and radical scavenging activities against DPPH, superoxide anion and NO radicals, which was attributed to its high phenolic content. Analyses yielded catechin, morin, and quercetin in the leaves. The plant extract also showed highest inhibitory effect against proliferation of MCF-7 cells, with increased activities of catalase and superoxide dismutase.[11]

Antifertility effect

Ethanolic extract of *Piper betle* Petiole given to female albino rats at a dose level of 100 mg/kg caused antiestrogenic effects Phytochemical analysis showed the presence of carbohydrates, alkaloids, gums, oils, steroids, glycosides, tannins, phenols, vitamins, organic acids and inorganic constituents. Extract treatment caused reduction in reproductive organ weights, circulating level of estrogen, fertility, number of litters, serum glucose concentration, enzyme activity of acid phosphatase, SGOT and SGPT Whereas, the concentration of cholesterol and ascorbic acid increased. This is needed to be investigated whether cholesterol is increased due to non-utilization of it or by de novo synthesis.[12]

Cytotoxicity/Anticancer Potential

Study evaluated an aqueous extract of leaves to cytotoxicity studies on Hep-2 cell line. The mean CTC50 was 96.25 ug/ml suggesting potent cytotoxicity and probable anticancer property. *Piper betle* leaf extract showed significant LC50 values of >100 µg/mL towards A. salina. The presence of cytotoxic compounds also suggests potential antitumor or anticancer property.[13]

Potential Anti-Diabetic/Leaves

Study evaluated the possibility of P. betle as a neutraceutical for diabetes mellitus patients. Patients were treated with either P. betle or triphal (an herbal antidiabetic drug). Results demonstrated the ability of P. betle capsules made from spray dried powder of betel hot water extract as a potential treatment for type 2 diabetes patients.[14]

Antimalarial/Antioxidant

Study evaluated the phytochemical and antioxidant potentials of a crude extract for possible antimalarial effects. Phytochemical screening yielded antiplasmodial chemical constituents. The extract exhibited potent ability to scavenge free radicals and demonstrated significant schizonticidal activity in all three antimalarial evaluation models.[15]

Antigenotoxic/Gamma Irradiation and Cyclophsphamide Treatment

Study evaluated the antigenotoxic effect of P. betle leaves in gamma irradiation and cyclophosphamide treated animals. Results showed not drug toxicity at tested doses. A methanol extract 1/2 hour prior to irradiation protected the animals against gamma irradiation and cyclophosphamide treatment[16]

Anti-Ulcer/Wound Healing/Antioxidant

Study showed a significant healing effect on NSAID-induced peptic ulcer in albino rats. The healing action was attributed to the free radical scavenging activity of the plant extract. APC, one of the phenol constituents showed significant protection against indomethacin induced ulcers in Sprague-Dawley rats. The protection

was correlated with antioxidative and mucin protecting properties.[17]

Antifungal/Hydroxychavicol

Hydroxychavicol, isolated from the chloroform extraction of the aqueous extract of P. betle, was investigated for antifungal activity against 124 strains of selected fungi. Hydroxychavicol exhibited inhibitory effects on fungal species of clinical significance. It also exhibited an extended post antifungal effect for Candida species and suppression of mutant emergence. Results suggest a potential antifungal agent for topical applications, as well as a gargle for oral candida infections.[18]

Antimicrobial/Antioxidative/Anti-Hemolytic Activities

A study of leaf extract showed antibacterial, antioxidative, and anti-hemolytic activities. The bioactive molecule for antibacterial activity was presumed to be sterol, which was obtained in large quantities. The antioxidative and antihemolytic activities were attributed to the high concentration and combined activity of flavonoids and polyphenols.[19]

Antihistaminic Activity/Essential Oil/Leaves

Study evaluated the antihistaminic activity of P. betle. Results showed antihistamine activity, with a right shift of dose response curve of histamine and disturbed histamine induced bronchoconstriction in whole guinea pig. Chlorpheniramine was used as reference.[20]

Mosquito Repellent/Topical Mixture Leaves with Patchouli Oil/Ae Aegypti

Study evaluated the repellency, potency and safety of *Piper betle* (leaves) and patchouli oil modified gel against Aedes aegypti mosquitoes. Irritation test showed no safety concerns. The modified gel showed the same protective percentage as DEET. Results suggest betel vine oil withmodified formulation has a potential as Aedes aegypti mosquito repellent.[21]

Glucose Lowering/Analgesic

Antihyperglycemic activity evaluation of methanol extract of leaves in glucose-loaded Swiss albino mice showed dose-dependent and significant lowering of blood sugar. Antinociceptive evaluation in gastric pain models in mice showed significant and dose-dependent reduction in the number of gastric writhing in gastric pain-induced mice.[22]

Anticariogenic Effect/Action on Salivary pH

Study on the anticariogenic efficacy of *Piper betle* showed efficacy in resisting salivary pH change comparable to 0.05% sodium fluoride. *Piper betle* showed an anticariogenic effect through effective inhibition of acid production by salivary bacteria.[23]

Antitumor/Antioxidant

Study evaluated a methanolic extract of *Piper betle* leaves and fractions for antitumor activity against Ehrlich ascites carcinoma in Swiss albino mice. Results showed significant antitumor activity, which may be attributed to augmentation of endogenousantioxidant potential.

Stabilizing/Antioxidant

Study examined the effect of P. betle leaf extract on lipid peroxidation, antioxidant enzymes, and membrane-bound ATPases in mice. Results showed the leaf extract provided better dose-dependent antioxidant potential and membrane stabilizing action in Swiss mice over controls.[24]

Antimicrobial/Essential Oil

Antimicrobial screening of essential oil showed antibacterial activity against E. coli, Streptococcus pyogenes, and S. aureus and antifungal activity against Colletotrichum sp., Fusarium oxysporium sp., Corynospora cassicola, and Rigidoporous sp.49.

Larvicidal on Screwworm Fly (Chrysomya bezziana)/Essential Oil/Leaves: Study of essential oil of *Piper betle* showed effective larvicidal activity for first and second instar larvae *in vitro*, suggesting a potential for a natural and novel larvicide.[25]

Study evaluated the radioprotective activity of *Piper betle* ethanolic extract using rat liver mitochondria and pBR 322 plasmid DNA as two model in vitro systems. Results showed prevention of g-ray induced lipid peroxidation and radiation-induced DNA strand breaks in a concentration dependent manner.[25] The radioprotective effect was attributed to its hydroxyl and superoxide radical scavenging property along with its lymphoproliferative activity. The radical scavenging activity was attributed to constituent phenolics chevibetol and allyl pyrocatechol.

Anti-Cholinesterase Inhibitory Activity/Leaves

Study evaluated three leaf varieties Kaliganga, Meetha, and Haldi—for acetylcholinesterase inhibitory properties. Aqueous extracts of both fresh and dry leaves of all varieties inhibited acetylcholinesterase activity in a dose dependent manner. The AChE inhibitory property of P. betle may have a beneficial effect on memory function.[26]

Gastroprotective/Allylpyrocatechol/Antioxidative and Mucin Protecting

Study evaluated the gastroprotective activity of allylpyrocatechol (APC), the major antioxidant constituent of *Piper betle*, against indomethacin-induced stomach ulceration in a rat model. Results showed both APC and misoprostol effectively healed stomach ulceration. The protective activity was attributed to antioxidant activity and the enhancement of mucin content of gastric tissues.[27]

Anti-Adipogenic/Weight Reducing Potential

Out of 480 herbal extracts, *Piper betle* and Dolichos biflorus were chosen and evaluated for synergistic anti-adipogenic effects. The herbal formulation LOWAT was

significantly better than the individual extracts in terms of adipogenic inhibition. *In vitro* studies showed inhibition of pre-adipocyte differentiation and potentiation of lipid breakdown in mature adipocytes. *In vivo* studies showed reduced weight gain with increased serum adiponectin levels in rats on a high fat diet. Results suggest the formulation has potential as a weight management agent.[28]

Analgesic/Leaves

Study evaluated the analgesic activity of piper betel leaf using eddy's hot plate and heat conduction method. Results showed a dose-dependent response. The aqueous extract of leaf was safe up to 1000 mg/kbw p.o. dose.

Antidepressant/Leaves

Study evaluated the antidepressant activity of ethanolic extract of P. betle leaves in Swiss albino mice. Results showed significant antidepressant effect as indicated by reduction in duration of immobility. The 100 mg extract dose effect was greater than that of imipramine.[29]

Anticholesterolemic/Eugenol

Study evaluated the antihypercholesterolemic and antioxidative properties of an ethanolic extract of *Piper betle* and its active constituent, eugenol, in experimental hypercholesterolemia in Wistar rats. Results showed that eugenol possesses antihyper-cholesterolemic properties.

Anti-Adherence Effect of Dental Plaque on Saliva-Coated Glass Surfaces

Study evaluated aqueous extracts of P. betle and P. guajava for anti-adherence effect on adhesions of early plaque settlers (Strep. mitis, Strep sanguinis and Actinomyces sp.) using saliva-coated glass surface to simulate the pellicle coated enamel surface of the oral cavity. Results showed adherence of early plaque settlers was inhibited to a certain extent by *Piper betle* and Psidium guajava extracts. The mechanism may involve the modification of hydrophobic bonding between bacteria and buccal salivary components.[30]

Skin Antiseptic

Study evaluated the effectiveness of a 20% *Piper betle* leaf infusion as an antiseptic solution in pre-surgery cataract patients. Results showed the infusion to have an antiseptic potential. However, the 10% povidone-iodine solution was more effective antiseptic capability.

Antimicrobial/Leaves

Study evaluated an aqueous extract of fresh leaves for antimicrobial activity. Results showed effective inhibitory action against the tested organisms (E. coli, Vibrio cholera, S. typhi, and S. parathyphi A and B).[31]

Antidermatophytic

An ethnoveterinary study evaluated crude ethanolic extracts of P. betle leaves, A. galanga rhizomes, and A. escalonicum bulbs against selected zoonotic dermatophytes (M. canis, M. gypseum, and T. mentagrophytes) and yeast-like Candida albicans. All the extracts caused concentration dependent suppression of fungi growth. Testing showed Pb cream formulation with potential therapeutic values for treatment of dermatophytosis.[32]

Potential Natural Antioxidant

Study was carried out on CEE (cold ethanolic extract), HWE (hot water extract) and EO (essential oil) of the leaves of P betle grown in Sri Lanka. The initial free radical scavenging activity was higher in CEE. There were no deviations in the antioxidant activity of the 3 extracts up to 12 months. CEE extended the shelf-life of potato chips and increased the stability of Aloe gel.[30]

Bacteriostatic/Dental Plaque

A study investigating the bacteriostatic effect of *Piper betle* and P guajava showed both extracts have bacteriostatic effect on the plaque bacteria through suppression of growth and propagation of cells. Results suggest the decoction of plants would be a suitable if used in the control of dental plaque. Results of study showed the crude extract of P betle leaves may exert anticariogenic activities related to a decrease in acid production and changes to the ultrastructure of S mutans.

Anti-Platelet Aggravating Factory

Evaluation of *Piper betle* on Platelet Activating Factor (PAF) Receptor Binding Activities: Results showed antagonistic activity towards the PAF (platelet activating factor) in rabbit platelet receptor binding studies.

Antihyperglycemic

Study evaluated the effect of P.betle on glucose metabolism since it is consumed as betel-quid after meals. Results showed that P. betle intake influences glucose metabolism \beneficially. Antioxidant in STZ-Diabetic Rats: Study showed the leaf suspension of P betle showed significant antioxidant effects in STZ diabetic rats.[33]

Antibacterial

Study showed PB had a broad spectrum of antibacterial activity against all test pathogens, including Rastonia, Xanthomonas and Erwinia. Test also showed that PB solvent extract had an action superior to streptomycin. Study of crude aqueous extract of P. betle showed activity against most of the test bacteria, with the greatest zone of inhibition by the ethanol extract against Gram negative and Gram positive bacteria, with maximum bactericidal activity against E. coli, P. aeruginosa, and S. aureus.

Antioxidant

Study showed a leaf extract to inhibit the radiation-induced lipid peroxidation process effectively, attributed to its ability to scavenge free radicals involved in initiation and propagation steps with elevation of the antioxidant status in the study animals.

Antibacterial/Antifungal/Essential Oil

Essential oil from common betel was against against E coli, Pseudomonas aeruginosa, Staph aureus and Strep pyogenes. The major compound in the oil from the leaf, stem, stalk and root was saffrole; from the fruit, ß-phellandrene. Antifungal activity against Clodosporium sp. indicate the essential oil possesses at least one fungicidal compound.[34]

Antihistaminic/Essential Oil

Study was done of P. betel ethanolic extract and essential oil on its effects on histamine aerosol-induced bronchoconstriction in whole guinea pig. Results conclude the ethanolic extract and essential oil possess antihistaminic activity.

Antidiabetic/Leaves

Study of *Piper betle* leaves in STZ-induced diabetic rats showed both hot water extract and cold methanolic extract to have strong antidiabetic activity. The extracts were devoid of unacceptable side effects on chronic administration.[31]

Immunomodulatory/Leaves

Study evaluated the immunomodulatory effect of an ethanol extract of leaf of *Piper betle*. Results showed immunomodulatory activity with dose dependent increased in antibody production and enhanced the production of RBC, WBC, and Hb.

Antioxidant/HbE-beta Thalassemia

The frequent blood transfusions in HbE-beta thalassemia cause an iron overload that triggers an enhanced generation of free radicals. The study showed the ethanolic extract of *Piper betle* has promising antioxidant activity against erythrocytes from patients with HbE-beta thalassemia.

Tumor Inhibitory Effect/Melanoma

Study of hydroalcoholic extracts of leaves showed a tumor inhibitory effect on transplanted mouse melanoma, by delaying tumor growth and prolonging mean survival time. *Piper betle*-Mediated Green Synthesis of Gold Nanoparticles: Study reported the novel use of ethanolic leaf extract of P. betle for gold nanoparticle (AuNPs) synthesis. The AuNPs were nontoxic and presents a potential for an effective drug delivery tool and other biomedical applications.[34]

Biologic Activities of Extractives/ Antibacterial/ Antitermite

Study isolated and evaluated the biologic activities of extracts of leaves. Fractionation isolated a pure compound, amorphene. In antitermite toxicity test, a crude extract was found to be most toxic with 100% mortality.

Antibacterial testing showed growth inhibition at 10.0% concentration.

Carcinogenicity

Study of rats on rats fed a dry powder of betel nuts, leaves and lime showed epidermal thickening in the upper digestive tracts in rats fed the betel nut mixed with lime and the betel leaves diet. A forestomach papilloma was seen in one rat on betel leaves diet. The epidermal changes were scarcely seen in rats on either betel nut or normal diet alone.[35]

Allypyrocatechol/Gastroprotective/Anti-Ulcer

The piper betel phenol, allypyrocatechol, its major antioxidant constituent, showed it can protect against indomethacin-induced gastric ulceration due to its antioxidant and mucin protecting properties.

Neuroprotective in Brain Alcohol Toxicity

The brain of ethanol-treated rats exhibited increased levels of lipids, lipid peroxidation and disturbances in antioxidant defenses. Study showed neuroprotective effects of P betle in experimentally induced alcohol toxicity.[32]

Phenolics/Anti-Photosensitizer

Inhibitory property of the Piper betel phenolic against photosensitization-induced biological damages: PB phenolics, allylpyrocatechol (APC) may play a role in protecting biological systems against damage by eliminating O2 generated from certain endogenous photosensitizers.[33]

Antioxidant/Hepatoprotective

Influence of *Piper betle* on Hepatic Marker Enzymes and Tissue Antioxidant Status in Ethanol-Treated Wistar Rats: Results indicate P. betle provide a significant hepatoprotective and antioxidant effect.

Hepatoprotective/Chemopreventive/Anti-Liver Fibrosis

Protection effect of piper betel leaf extract against carbon tetrachloride-induced liver fibrosis in rats: Study supports a chemopreventive potential of PB leaves against liver fibrosis.

Chemical Constituents/Insect Attractant Property

Study yielded chavibetol and B-sitosterol from the petroleum ether extract and allylpyrocatechol from the methanol extract. Field tests in a cornfield using traps containing the extracts did not detect adult moths of Ostrinia salentialis.

Pro-apoptotic Effect/Anti-Leishmaniasis

In a comparative *in vitro* anti-leishmanial activity of methanolic extracts from two landraces of *Piper betle*. The PB-BM (P betle landrace Bangla Mahoba) selectively inhibited both stages of Leishmania parasites without macrophage cytotoxicity. The efficacy mediated through apoptosis is probably due to higher content of eugenol.[34] Different therapeutic activities reported in *Piper betle* plant show in table 3.

Table 3: Different therapeutic activities reported in *Piper betle* plant[36]

S. No.	Plant part/Extract	Activity/Animal/Model	Result	Reference
1.	Aqueous extract of the fresh *Piper betle* leaves.	Antimicrobial activity/Various microorganisms /disc diffusion method.	Aqueous extracts showed effective inhibitory action against the microorganisms	Shameem Pasha MD (2013)
2.	*Piper betle* leaves/hot water extract/cold ethanoic extract.	Antioxidant activity/Initial antioxidant activity, Antioxidant activity with time & at elevated temperature (200 °C).	The extracts obtained from the leaves of *Piper betle* had profound antioxidant activity.	Arambewela Lakshmi; (2006)
3.	*Piper betle* spray dried powder.	Antidiabetic activity/diabetes mellitus patients.	*Piper betle* as a nutraceutical resulted as a potential treatment for type 2 diabetes patients.	HewageeganaSujatha; (2011)
4.	Aqueous extract of the fresh *Piper betle* leaves.	Antioxidative & antihemolytic activity/Microorganisms (*Streptococcus pyogenes, Staphylococcus aureus, Pseudomonas aeruginosa* & *Escherichia coli*).	The antioxidative & antihemolytic activities were attributed to the high concentration & combined activity of flavonoids & polyphenols.	Chakraborty Devjani; (2011)
5.	Crude ethanolic extracts of *Piper betle* leaves.	Antidermatophytic activity/ zoonotic dermatophytes (*M. canis*, *M. gypseum*, and *T. mentagrophytes*) and yeast-like *Candida albicans*.	Testing showed *Piper betle* cream formulation with potential therapeutic values for treatment of dermatophytosis.	Trakranrungsiea N.; (2008)
6.	Aqueous and ethanol extract of the *Piper betle* leaves.	Antibacterial Activity/ Gram positive (*Bacillus subtilis, Staphylococcus aureus* & *Micrococcus luteus*) & Gram negative (*Escherichia coli* & *Pseudomonas aeruginosa*) bacteria/	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; (2011).
7.	The hot water *Piper betle* 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.; (2013).
8.	The petroleum ether extract & methanol extract of the *Piper betle* 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 *Ostrinia salentialis*.	Yusoff Z.; (2005)
9.	The methanolic extract of the *Piper betle* 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; (2012)
10.	The *Piper betle* plant extract.	Antifertility activity/female rats.	The data suggests that betle extract brought about antifertility and antiestrogonic effects in female rats.	Pradhan Manas Ranjan.; (2013)
11.	The *Piper betle* leaf extract.	Antihepatotoxic effect/ ethanol & carbon tetrachloride (CCl4) induced liver injury in a rat model.	The histological examination shows that *Piper betle* leaf extract secluded liver from the damage induce by CCl4 by declining alpha smooth muscle actin (alpha-sma) expression.	Young S.C.; (2007)
12.	The *Piper betle* leaf infusion.	Skin Antiseptic/pre-surgery cataract patients.	Results showed that 20% *Piper betle* leaf infusion to have an antiseptic.	Husnun Amallia.; (2009)

CONCLUSION

This review is submitting to great potential of medicinal and Nutrients value. Piper betel is known to worldwide and consumed frequently as mouth freshener and also used as potent source for novel therapeutically value. This value le reveals it to be fit for its future usage as a promising source for treating various conditions. Therefore, the same with lots of biological activities and has a tremendous strength to come out as a future herb medicinal and nutrients uses.

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