Original Article

Phytochemistry & Pharmacological Studies Of Betel Piper

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Abstract

The Betle (Linn's Piper betle) is the leaf of a vine in the family Piperaceae. Malaysia is most likely where the betle vine originated, but it is also grown in India, Sri Lanka, Bangladesh, Burma, and Nepal. The betle plant is an evergreen, perennial creeper with white catkins and glossy, heart-shaped leaves. The concentration of a wide range of biologically active compounds in the Piper betle is determined by the variety of the plant, season, and climate, according to phytochemical research. It is valued for both its stimulant and medicinal properties. Diosgenin, eugenol, allylpyrocatechol, methyl eugenol, chavibetol, hydroxychavicol, triterpenes, and β-sitosterol are all found in piper betle. Antiplatelet, anti-inflammatory, immunomodulatory, gastroprotective, and anti-diabetic effects have been observed in the pharmacological profile. The areca nut—also known as the betle nut—and mineral slaked lime—also known as calcium hydroxide—are chewed together in a wrapped package in India. Arecoline, an alkaloid found in the areca nut, is a stimulant and makes people salivate. The research on Piper betle Linn's therapeutic properties, phytochemistry, and pharmacological profile are the primary focus of this review. The Piperaceae, or pepper family, is responsible for many of the health benefits associated with Piper betel, also known as Paan in the region. It was a significant herb that was distributed all over the world. Betle leaves are the most valuable part of the plant. In the past, they were used to control bad breath by chewing on them. Betle leaves contain tannins, chavicol, phenyl, propane, sesquiterpene, cyneole, alkaloid, sugar, and some essential oil. They have been found to have a variety of medicinal uses, including digestive, appetizer, aromatic, expectorant, stimulant, antibacterial, euphoric, antiprotozo. Additionally, the leaves are said to prevent indigestion, bronchitis, constipation, and congestion as well as to harden the gums and preserve the teeth. For the first time, this review discusses the various potential mechanisms and provides information on therapeutic effects.

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

INTRODUCTION

Piper betle Linn., ordinarily known as the betle plant is a significant restorative and sporting plant in Southeast Asia. There are numerous varieties of betle leaf based on color, size, flavor, and scent. The Magadhi, Venmony, Mysore, Salem, Calcutta, Banarasi, Kauri, Ghanagete, and Bagerhati are among the most widely consumed varieties in India.

A tropical shade-loving perennial evergreen vine known as betle (*Piper betle*) It could reach heights of 10 to 15 feet. The plant has a similar growth pattern to the pepper plant and can occasionally grow as a ground cover. The leaf of the Piper betle thrives in moist, warm environments. The leaves are bright green, simple, alternate, ovate, cordate, acuminate or acute, or entire. Female spikes on this plant are pendulus, while male spikes are dense and cylindrical. Each node produces roots that aid in the plant's attachment to the host tree. The leaves are utilized in various customary cures, for example, for treatment of stomach sicknesses, diseases and as an overall tonic. The immune system may be boosted by betle leaves, according to some research. In the Indian subcontinent, a little heap of betle, known as a 'pan-supari' is proposed to visitors as politeness. There are a huge number of Asians who consume everyday the betle leaf, generally in mix with betle nut, kava and kolanut. There are around 125 to 150 cultivars of betle plant in India. Betle is normally spread agamically from stem cuttings instead of from seeds.

The Indian traditional medical system has long utilized the leaves of *Piper betle* Linn. Betel leaves were used in religious ceremonies in ancient India because they were thought to bring good luck. It is for the most part tracked down in hot and clammy climatic condition. It is found in the states of Bihar, Bengal, Orrisa, south India, and Karnataka in India. The betel plant is an evergreen and enduring creeper, with reflexive heart-formed leaves and white catkin. There are different sorts of leaves, the most famous being: Calcutta, Banarasi, Magahi, and so forth. The most betel-producing regions in Bangladesh are Sylhet, Dinajpur, Rangpur, Chittagong, Faridpur, Jessore, Narayanganj, Barisal, and Sylhet. The leaves that have been harvested are used for both domestic consumption and export to the Middle East, Europe, the United States, the United Kingdom, Pakistan, and Myanmar. Rural Bangladesh's primary source of income is paan. The

"Magadhi" variety, which comes from the Magadha region and is grown close to Patna in Bihar, India, is the best Betel leaf. The well-known variety of betel leaf in Kerala is known as "Venmony Vettila," and it comes from Venmony, which is close to Chengannur. The betel leaf grown in Tirur, Kerala, and Hinjilicut, Odisha, is of high quality. In Pakistan, betel leaves exported from Tirur are referred to as "Tirur Pan." Flute player betle is one of the significant restorative plants where its leaves have been utilized for the majority restorative purposes. Figure 1 depicts Piper betel, a member of the large Piperaceae plant family that is also known as Paan in India and Sirih in Malaysia and Indonesia. Since ancient times, the fresh betel leaves have been wrapped with the areca nut, mineral-slaked lime, catechu, flavorings, and spices and chewed. Due to reports claiming that using the herb could cause mouth cancer, the entire betel plant received a lot of negative press. Additionally, it aids in easing asthmatics' breathing difficulties. Some apply mustard oil to the leaves of the betel plant, warm it and afterward keep it on the chest to bring help from asthma. A primer report has detailed Flautist betle leaves separate contains huge quantities of bioactive particles (Devjani Chakraborty*). Flautist betle contains a wide assortment of naturally dynamic mixtures whose fixation relies upon the assortment of the plant, season furthermore, environment. According to Satish A Bhalerao, the pharmacological profile exhibited antiplatelet, anti-inflammatory, immunomodulatory, gastroprotective, and antidiabetic effects. Paan has been alluded to in Saktatantra as one of the method for accomplishing siddhi. It was believed that no siddhi could be obtained without chewing betel and offering pan to Guru. According to D. Pradhan, tamboul also aids the sadhak in chewing the dharma, yasha aisvarya, Srivairagya, and mukti. It was accounted for that new leaves contains: dampness 85.4, protein 3.1, fat 0.8, sugar 6.1, fiber 2.3, calcium 230mg, phosphorous 40mg, iron 7mg, ionisable iron 3.5mg, iodine 3.4 µ. They contain a lot of potassium nitrate (0.26-2.42 percent). The sugars recognized in betel leaves incorporate glucose, fructose, maltose and sucrose. In various varieties of betel leaves, the average amount of free reducing sugars ranges from 0.38 to 1.46 percent. It too contains the chemical like diastase and catalase. (K.Periyanayagam). Flautist betle leaves are prior answered to have anticancer potential. Thus, the watery concentrate of the leaves was oppressed to cytotoxicity concentrates on Hep-2 cell line utilizing Miniature culture Tetrazolium and Sulphorhodamine B measures (Chaurasia, Sundeep et al). Flute player betle leaf oil can be utilized as a modern unrefined substance for assembling pharmaceuticals, cosmetics, food additives, etc. The leaves are nutritive and contain enemies of cancer-causing agents showing guarantee for assembling of a blood malignant growth drug (Sengupta).

Figure 1: P. Betle Plant

PHYTOCHEMISTRY

Betle plants are one of the exceptionally examined plants and their phytochemical concentrates on show that Flute player betle contains a wide assortment of naturally dynamic mixtures whose focus relies upon the assortment of the plant, season and environment. Safrole, which can be found in the leaf, stalk, stem, and root, and ß-phellandrene, which can be found in the fruit, are the chemical components of essential oils. The presence of essential oils made up of phenols and terpenes in betle leaf is what gives it its flavor. It is said that younger leaves produce more essential oil. The central constituent of the leaves is an unpredictable oil whose compound structure is subject to the district it is found. It is otherwise called betle oil. Active compounds like hydroxychavicol, hydroxychavicol acetate, allypyrocatechol, chavibetol, piperbetol, methylpiperbetol, piperol A, and piperol B have been obtained from plant parts like the leaves of the Piper betle. arakene, with properties like cocaine. The dynamic element of flautist betle oil which is gotten from the leaves are essential a class of allyl benzene compounds, chavibetol (betlephenol; Chavicol (p-allyl-phenol), 3-hydroxy-4-methoxyallylbenzene 4-allyl-phenol), Estragole (p-allylanisole; Eugenol (allylguaiacol; 4-methoxy-allylbenzene); 4-hydroxy-3-methoxyallylbenzene; 2-methoxy-4-allyl-phenol), methyl Eugenol (Eugenol methyl ether; hydroxycatechol (2,4-dihydroxy-allylbenzene) and 3,-dimethoxy-allylbenzene). There were fourteen components found in the leaves' essential oil and ether-soluble fraction, including eight allypyrocatechol analogs. Significant constituents were chavibetol (53.1%) and chavibetol acetate (15.5%). 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 (0.71%) were the other constituents. Hexane part of leaf stalks yielded four alipathic intensifies in unadulterated structure for example pentadecyl 6-hydroxytridecanoate, pentatriacontanol, methyl hexacos-7-enoate and 6,9-heptacosa diene. The concentrate of betle leaves has antimutagenic, anticarcinogenic, antidiabetic,

calming and antibacterial exercises. Hydroxychavicol (HC) and eugenol (EU) are significant phytochemicals found in betle leaves. They are accounted for to contribute an excessive number of bioactivities in betle leaves. HC and EU are phenolic intensifies which comprise of a monocyclic sweet-smelling ring with a drunkard, aldehydic or carboxylic gathering.

PHARMACOLOGICAL PROFILE

Antioxidant/Antiproliferative

Due to its high phenolic content, an ethyl acetate extract had the highest ferric reducing and radical scavenging activities against DPPH, superoxide anion, and NO radicals. Investigations yielded catechin, morin, and quercetin in the leaves. The plant extricate additionally showed most elevated inhibitory impact against multiplication of MCF-7 cells, with expanded exercises of catalase and superoxide dismutase. Ionizing radiation has a significant impact on biological membranes through oxidative damage. It's a chain reaction. Fatty acid chains in membrane lipids can be attacked by free radicals produced by the radiolytic decomposition of water. The peroxidative process can be started by a free radical with enough energy to extract an allylic hydrogen from the methylene carbon of polyunsaturated fatty acids. The presence of polyphenolic compounds such as chatecol, allylpyrocatecol, and others here. effectively inhibited the radiation-induced lipid peroxidation process in betle leaf extract. This could be because it can scavenge free radicals that are involved in the steps of initiation and propagation. The extracts are highly reductive and reduced the majority of Fe3+ ions. When compared to various standards like ascorbic acid and BHT, the extract also demonstrated strong hydroxyl and superoxide anion radical scavenging properties.

Cytotoxicity/Anticancer Potential

The study compared the cytotoxicity of an aqueous extract of leaves to a Hep-2 cell line. The fact that the mean CTC50 was 96.25 ug/ml suggests that it may have anticancer properties and be highly cytotoxic. Flute player betle leaf remove showed huge LC50 upsides of >100 µg/mL towards A. salina. Potential antitumor or anticancer properties are also suggested by the presence of cytotoxic compounds.

Antifertility effect

The phytochemical analysis revealed the presence of carbohydrates, alkaloids, gums, oils, steroids, glycosides, tannins, phenols, vitamins, organic acids, and inorganic constituents when ethanolic extract of Piper betle Petiole was administered to female albino rats at a dose of 100 mg/kg. Separate treatment caused decrease in conceptive organ loads, flowing level of estrogen, fruitfulness, number of litters, serum glucose fixation, chemical action of corrosive phosphatase, SGOT furthermore, SGPT Though, the convergence of cholesterol and ascorbic corrosive expanded. This is required to have been examined whether cholesterol is expanded due to non-use of it or by all over again union. Various doses of Piper betle leaf stalk extract were used in extensive research to create an orally effective male contraceptive in male mice. Intriguingly, the contraceptive efficacy emphasized reversible fertility after treatment withdrawal. The results show that there is no toxicity in all metabolically active tissue of mice.

Antimicrobial activity

The betle has antimicrobial activity against Streptococcus pyrogenes, Staphylococcus aureus, Proteus vulgaris, Escherichia coli, Pseudomonas aeruginosa, and other microorganisms. The leaf has significant antimicrobial activity against a wide range of microorganisms. In addition, the leaf extract is bactericidal against pathogenic bacteria in the urinary tract, including Enterococococcus faecalis, C. koseri, C. fruendi, Klebsiella pneumonia, and others. Sterol, which can be found in large quantities in betle leaf extracts, is the bioactive molecule thought to be responsible for antibacterial activity. The sterol molecule in the extracts may interact with the bacterial cell wall and membrane on the surface, causing a change in the cell wall's primary structure that eventually results in the formation of pores and the breakdown of the bacteria's components. Sterols are said to act by removing the permeability barrier from microbial membrane structures. Gram-positive microorganisms were more powerless to the inhibitory impacts of the plant separate due to single layer and miss the mark on regular strainer impact against huge atoms, though gram negative microbes are diverse and complex cell wall structure. Additionally, the leaf exhibits antifungal activity against numerous fungal infections. One of them is dermatophytosis. Dermatophytosis is an infection of the keratinized pieces of the body (skin, hair, and nail) brought about by athree genera (Trichophyton, Microsporum, and Epidermophyton) of exceptionally concentrated growths called the Dermatophytes. Due to the presence of non-polar components in the fraction, the chloroform extract of Piper betle is significantly more effective against dermatophytes than the methanol fraction.

Potential Anti-Diabetic/Leaves

Concentrate on assessed the chance of P. betle as a neutraceutical for diabetes mellitus patients. Triphal, an herbal antidiabetic, or P. betle were used to treat the patients. The results showed that P. betle capsules made from spray-dried powder of betel hot water extract could be used as a treatment for people with type 2 diabetes. When tested in fasted normoglycemic rats, the aqueous and ethanolic extracts of P. betle leaves exhibit significant hypoglycemia. The extract had antihyperglycaemic activity in the external glucose level during the glucose tolerance test. The extracts' ability to lower blood glucose levels in diabetic rats induced by streptozotocin (STZ) suggests that they have insulinomimetic activity.

Antimalarial/Antioxidant

A crude extract's phytochemical and antioxidant potentials were examined for potential antimalarial effects in a study. Antiplasmodial chemical components were discovered through phytochemical screening. In all three antimalarial evaluation models, the extract demonstrated significant schizonticidal activity and a potent capacity to scavenge free radicals.

Gastroprotective activity

The amount of mucus adhering to the gastric mucosa wall significantly increased as a result of the hot water extract. The mucus layer is thought to play a crucial role in the mucosal defenses against external aggressors like acids and to aid in the repair process. It is by and large accepted that improved corrosive emission is the main variable for the enlistment of gastric sores. The acidity and pH of the gastric fluid are not significantly impacted by the higher dose of hot water extract. Therefore, rather than inhibiting acid secretion in the gastric mucosa, Piper betle's gastroprotective effect was mediated by increasing its mucus content. The gastroprotective exercises of the greater portion of high temp water separate altogether more noteworthy than Misoprostol. It has been demonstrated through extensive research that antioxidants may be an efficient mechanism not only for preventing injury to the gastric mucosa but also for preventing the progression of gastric ulceration. Ulceration movement is brought about by free revolutionary instigated chain process. As a result, it heals more quickly when radical scavengers stop it. In a variety of in-vitro models, allylpyrocatacol has demonstrated a potent anti-oxidant potential. The ulcer-healing process was significantly accelerated by treatment with Allylpyrocatacol, which typically speeds up the production of mucus and protects the ulcer crater from irritant stomach secretions (HCl and Pepsin), thereby speeding up the rate of local healing.

Oral care agent

Dental caries is an ongoing infection brought on by the normal oral bacteria. The carious injury is the aftereffect of demineralization of veneer and later of dentine by acids created by plaque microorganisms as they use dietary carbs. Streptococcus mutans is the bacterium that is primarily responsible for human dental decay. There are four main species groups of streptococci: mitis, anginosus, mutan, and salivarius Lactobacillus acidophilus bacteria probably play a minor role in the production of acid in the plaque as well as Streptococcis mutans. Streptococcus mutans ferments dietary sucrose to produce dextran, which is what gives the plaque its stickiness. At pHs below or above 5.5, the plaque bacteria, particularly Streptococcus mutans, produce lactic acid by reacting with fructose in the diet. This results in enamel decalcification. Enamel caries begins with plaque and carbohydrates in the diet. By using cell-surface and extracellular glucosyl transferase, certain cariogenic and highly acidogenic strains of streptococci, particularly S. mutans, can metabolize dietary sucrose and produce glucan. This compound is viewed as of unique significance in the foundation of S. mutans in the dental plaque. The watery concentrate repress the different corrosive creating oral microorganisms which changes in the ultra-construction of the veneer and its properties like Streptococci, Lactobacilli, Staphylococci, Corynebacteria, Porphyromonas gingivalis and Treponemadenticola. As a result, it is the best natural substance and the second most widely consumed daily item in Asia, contributing to optimal oral hygiene.

Hepato-protective activity

On a rat model of liver injury caused by ethanol and carbon tetrachloride (CCl4), the antihepatotoxic effect of betle leaf extract was examined. Fibrosis and hepatic harm, as uncovered by histology and the exercises of aspartate amino transferase (AST) and alanine amino transferase (ALT) were actuated in rodents by CCl4. Antioxidant enzymes like superoxide dismutase (SOD) and catalase (CAT) increased as a result of the extract's significant inhibition of the elevated activities of AST and ALT as well as attenuation of total glutathione S-transferase (GST). By decreasing alpha smooth muscle actin (alpha-sma) expression, inducing active matrix metalloproteinase-2 (MMP2) expression through the Ras/Erkpathway, and inhibiting TIMP2 level, the betle leaf extract protected the liver from the damage caused by CCl4. This resulted in less fibrosis in the liver. These results suggest that betle leaf may have chemopreventive properties against liver fibrosis.

Antimicrobial/Essential Oil

Antibacterial activity against E. coli, S. aureus, and Streptococcus pyogenes was found in essential oil antimicrobial testing, as was antifungal activity against Colletotrichum sp., Species of Fusarium oxysporium, Rigidoporous sp. 49 and Corynospora cassicola Larvicidal on Screwworm Fly (Chrysomya bezziana)/Rejuvenating balm/Leaves: A study evaluating the radioprotective activity of Piper betle ethanolic extract using rat liver mitochondria and pBR 322 plasmid DNA as two model in vitro systems showed effective larvicidal activity for first and second instar larvae in vitro, suggesting the potential for a natural and novel larvicide. The results showed that, depending on the concentration, it prevented g-ray-induced lipid peroxidation and radiation-induced DNA strand breaks. The radioprotective effect was attributed to its lymphoproliferative activity and hydroxyl and superoxide radical scavenging properties. Chevibetol and allyl pyrocatechol, two constituent phenolics, were cited as the source of the radical scavenging activity.

Radioprotective activity

Mammalian framework on the off chance that presented to radiation can cause harming impacts prompting cell demise and an expanded gamble of degenerative sicknesses. As a low-cost alternative to synthetic radioprotectants, which have

been reported to be toxic, the radioprotective property of ethanolic extract of P. betle leaves has recently been studied. The extract's ability to stop g-ray-induced lipid peroxidation and DNA damage in rat liver mitochondria was looked at to figure out how it protects against radiation. The presence of phenolic bioactives like chavibetol and allyl pyrocatechol may have contributed to the study's significant immunomodulatory and superior radical scavenging results. It suggests that the herb has a lot of potential because it is cheap and a natural radioprotectant that can be easily obtained by the general public.

THERAPEUTIC PROPERTIES AND ITS USES

Ethno botanical & medicinal use

Nature has been a wellspring of restorative specialists for millennia and a noteworthy number of current medications have been confined from regular sources, many in light of their utilization in conventional medication. All over the world, a variety of medicinal plants have been used to treat disease for years. One of the restorative plant for example Flautist betle is a wellspring of extraordinary monetary worth in the Indian subcontinent.

- Betle leaf has been used for centuries as an aphrodisiac, stimulant, astringent, and aromatic (katu).
- It has the ability to heal wounds.
- The passes on were bitten by artists to further develop their voice.
- Leaves considered being valuable in treating bronchitis and dyspnea, stomach illnesses, diseases and as an overall tonic.
- These leaves have been found to have digestive and pancreatic lipase stimulant properties by the Indian traditional system of medicine.
- Conjunctivitis, constipation, headache, itching, mastitis, mastoiditis, leucorrhoea, otorrhoea, gum swelling, rheumatism, cuts, and injuries are among the conditions for which it has been shown to be effective.
- The product of Flute player betle utilized with honey goes about as a solution for hack.
- Leaves are utilized in eye drops for eye injury/contamination as a child moisturizer for the new conceived, for hacks, asthma, clogging and to capture milk discharge.
- The leaves influences richness in male rodents and communicates against motility consequences for washed human spermatozoa.
- The clients accept that biting the 'paan' works on their productivity and endurance. Hypotensive, cardio tonic, and smooth and skeletal muscle relaxant actions were demonstrated by Piper betle.
- This plant's leaves have been used as an antiseptic and essential oil for respiratory catarrhs.
- The medicinal root is used as a long-lasting oral contraceptive for women in folk medicine.
- Betle leaves can help with pulmonary infections in children and the elderly. Warm, soaked leaves can be applied to the chest to alleviate coughing and breathing difficulties
- Nearby use of the leaves is compelling in treating sore throat. To alleviate a bothersome cough, mix the crushed fruit or berry with honey
- The treatment of nervous pain, nervous exhaustion, and weakness can all benefit from betel leaves. The juice of few betle leaves, with a teaspoon of honey, will act as a decent tonic
- When applied locally, betle leaves can help treat conditions like arthritis and orchitis, which is an inflammation of the testicles
- Betle leaves have pain relieving and cooling properties
- It is likewise a significant solution for bubbles. A leaf is delicately warmed till it gets delicate, and is then covered with a layer of castor oil. The inflammation is covered by the oiled leaf
- A hot poultice of the leaves or their juice blended in with some tasteless oil, for example, refined coconut oil can be applied to the flanks with helpful outcomes in lumbago
- The leaves can be utilized to recuperate wounds. Extract the juice from the leaves and apply it to the wounds
- When applied to the breast during lactation, oil-smeared leaves are said to encourage milk secretion
- As indicated by Unani framework the leaf has a sharp taste and great smell which further develops hunger. Additionally, it is a liver, heart, and brain tonic
- It aids in maintaining healthy skin and teeth
- Helps in Treatment of Problems in physiological capability, Skin sicknesses, and Eye illnesses
- Additionally, it acts as a diuretic. Drinking betel leaf juice with milk or honey can help you urinate more easily
- Betle leaf is regarded as an aphrodisiac, or a substance that induces sexual desire

CONCLUSION

The heart-shaped, glossy leaves of the Piper betle have a lot of potential as a potent source for new herbal medicines. It primarily consists of allylpyrocatechol, chavibetol, eugenol, and hydroxychavicol as active components; which supports folklore and has numerous therapeutic applications. The pharmacological profile uncovers it to be for its great antimicrobial movement, defensive and recuperating action, antidiabetic action, gastroprotective action, immunomodulatory action, platelet restraint action, Cancer prevention agent action, antifertility action, hepato-defensive

action, against photosensitizer, cytotoxicity/Anticancer Potential, radioprotective action and so on. In future the normalization and adjustment concentrates on betle leaves concentrate can be done which can help in demonstrating it to be a promising source in drug as well as neutraceutical industry.

This review points to a lot of potential for nutritional and medicinal use. Piper betel is well-known all over the world and is frequently used as a mouthwash and potent source of novel therapeutic value. This value indicates that it is suitable for use as a promising treatment source in the future. As a result, the same herb has a lot of biological activities and has a lot of potential to be used as a medicine and source of nutrients in the future.

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