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PIPER BETEL: PHYTOCHEMISTRY, TRADITIONAL USE & PHARMACOLOGICAL ACTIVITY-A REVIEW

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ABSTRACT

Piper betel Linn. Is one of the important plants in the different region belonging to the family piperaceae? The betel plant is an evergreen and perennial creeper with glossy heart shape leaves and white catkin. Piper betel leave extract contains large number of bioactive molecule like polyphenol, alkaloids, steroids, saponin and tannin. Piper betel has light yellow aromatic essential oil with sharp burning taste. The main constituents are Hydroxychavicol (HC)/Hydroxychavicol acetate (HCA), Allylpyrocatechol (APC), Chavibetol (CHV), Piperbetol etc. Other constituents are arecoline, carvacrol, caryophyllene, piperitol, piperbetol, eugenol, isoeugenol, allylpyrocatechol, chavicol, safrole, anethole, chavibetol, cadinene hydroxychavicol, β -sitosterol, β -sitosteryl palmitate, dotriacontanoic acid, tritriacontane, stearic acid, cepharadione, piperine, piperlonguminine, chavibetol acetate, allylpyrocatechol monoacetate, allyldiacetoxy benzene, estragole, methyl eugenol and hydroxycatechol, methylpiperbetol, piperol A and piperol B. cavacrol, eugenol acetate, and allyl pyrocatechol diacetate etc Leaf posses pharmacological activity like antibiotic, antiulcer, and platelets aggregation, anti- fertility, cardio-tonic, antitumor, anti-mutagenic, respiratory depressant and antihelminthetics. Piper betel is subjected to in vitro tests using plate and broth MIC assays bio-film assay, saliva chip model and a conductometric method. The result outcome suggests that the active constituent, allylpyrocatechol might be responsible for the antimicrobial activity against various obligate oral anaerobes. Piper betel is used to treat alcoholism, bronchitis asthma, leprosy and dyspepsia, nerve tonic hepatic marker, antidiabetic, allergic mediators, antiadherenceactivity, antiproliferative activity, antianxiety activity. This review is studied for the further development of the various formulations for their traditional use and pharmacological activities in the living individuals.

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INTRODUCTION

Piper betel Linn. A member of the piperaceae family is an edible plant with leaves that have been traditionally used in India, China, and Thailand. The betel plant is an evergreen and perennial, creeper, with glossy heart shaped and white catkin. The genus piper (piperaceae) is largely distributed in tropical and subtropical region of the world [1]. *Piper betel* is cultivated in India, Srilanka, Malaysia, Indonesia, Phillipine, Island and East Africa [2]. The part of *Piper betel* utilized are leaves, root, stem, stalks and fruits. *Piper betel* has light yellow aromatic essential oil, with sharp burning taste.

The chemical constituents and their pharmacological activities of the principle ingredients in the betel quid have been studied by many works [3, 4]. Betel leaves were reported to contain volatile oil such as betel phenol and chavicol (isomeric with euginol), tannin, sugar, vitamin-c, starch and diastase [5]. Betel phenols possess the property of reducing the central nervous stimulation, sialogogue and local anaesthesia. *Piper betel* leaves extract contains large number of bioactive molecule like polyphenol, alkaloids, steroids, saponin and tannin [6].

Betel leaves possess activity like antidiabetic, antiulcer, antiplatelet aggregation, antifertility, cardiogenic; antitumour, antimutagenic, respiratory depressant and antihelmenthetic [7-15] wound healing property. *Piper betel* is used to treat alcoholism, bronchitis, asthma, leprosy and dyspepsia, antihistaminic, antioxidant property [16, 17] antimicrobial activity [5] anti-inflammatory [18] radioprotective and immunomodulatory property [19-22].

The betel leaves is used by many people in Asia as a medicinal plant. Which can cure many diseases. The juice of betel leaves is credited with diuretic

properties. Its juice mixed with diluted milk and sweetend, slightly help in easing urination. Betel leaves are also beneficial in the treatment of nervous pain, nervous exhaustion and debility. The juice of a few betel leaves, with a teaspoon of honey will serve as a good tonic.

The betel leaf has analgesic and cooling properties. A mixture of onion and betel leaves juice can cure fungal infection. Betel leaves are used as a stimulant, an antiseptic and a breath freshener. Betel quid is also strongly carcinogenic [23, 24, 25,]. The betel leaf is predominantly consumed in the world as betel quid or cpan, which is a mixture of a substance. The pan almost always contain a betel leaf with two basic ingredients, either areca nut or tobacco or both with lime (calcium hydroxide, calcium carbonate) [26, 27]. Both tobacco and areca nut are considered as carcinogenic [28, 29]. In an extensive scientific research monograph, the world health organization expert group for research on cancer, reported 2004 [30] that the percentage of oral cancer among all cancers diagnosed in hospital in Asia, has always been much higher than that usually found in western countries. In India, the betel and areca nut play an important role in Indian culture, especially among hindus. Many traditional ceremonies governing the lives of Hindus use betel and areca. The betel and areca also play an important role in Vietnamese culture like wedding.

Scientific Classification:

Kingdom: Planate
(Unranked): Angiospermae
(Unranked): Magnoliidae
Order: Piperales
Family: Piperaceae
Genus: *Piper*
Species: *betel*
Bionomial name: *Piper betel* L.

Plant Profile

**Vernacular Names:**

Malaysia: Sirih, sirih melayu, sirih cina, sirih hudang, sirih carang, sirih kerakap

English: Betel, betel pepper, betel-vine

Tamil: Vetrilai

Hindi: Pan

Semang: Serasa, be, cabe

Jakun: Kerekap, kenayek

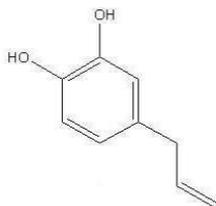
Sakai: Jerak

Javanese: Sirih, suruh, bodeh

Thai: Pelu

Chemical Constituents:

Hydroxychavicol (HC)/ Hydroxychavicol acetate(HCA):

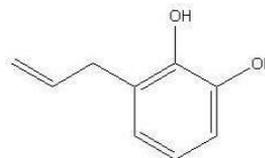


These constitute act as a hyperuremia (antidiabetic), immunomodulatory, inhibits platelet aggregation. The mode of action of these constitute is act via xanthine oxidase inhibition.[31] Suppressed T-bet expression, which is responsible for IL-2 suppression and IFN-gamma induction in Th-

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cell and inhibited T-bet-mediated Th1 cell differentiation[32]. Probably works through the disruption of the permeability barrier of microbial membrane structure [33,34]. A potent COX-1/COX-2-inhibitors, ROS scavenger and inhibits platelet calcium signalling, TXB [35] production and aggregation. Suppressed the mutagenic effect of tobacco specific [36, 37]

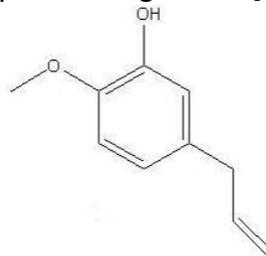
Allylpyrocatechol (APC):



The biological activity of APC is Gastric ulcer-healing action, anti-inflammatory effect. The mode of action is mediated by modulation of arginase metabolism and shift of cytokine balance [10]. Protect indomethacin-induced gastric ulceration due to its antioxidative and mucin-protecting properties [38]. Target the inflammatory response of macrophages via inhibition of iNOS, COX-2 and IL-12 p40 through down regulation of the NF-kappaB pathway, indicating that APC may have therapeutic potential in inflammation associated disorder [39]

Chavibetol (CHV):

The CHV act as Photoprotective/radioprotective these are protects photosensitization-mediated lipid peroxidation of rat liver mitochondria; prevents gamma-ray induced lipid peroxidation as assessed by measuring TBARS [40, 41, 21].



Piperbetol:

The biological activity of Piperbetol is platelet hyperactivity/cardiovascular diseases due to intravascular thrombosis. Selectively inhibited platelet aggregation factor (PAF) in a concentration-dependent manner [42].

Other constituents:

arecoline, carvacrol, caryophyllene, piperitol, piperbetol, eugenol, isoeugenol, allyl pyrocatechol, chavicol, safrole, anethole [43]. Chavibetol, cadinene [44]. Hydroxychavicol [45]. β -sitosterol, β -sitosteryl palmitate, dotriacontanoic acid, tritriacontane, stearic acid, cepharadione, piperine, piperlonguminine [46]. Chavibetol acetate, allylpyrocatechol monoacetate [47]. allyl diacetoxyl benzene [48]. estragole, methyl eugenol and hydroxycatechol [49]. methylpiperbetol, piperol A and piperol B [50]. cavacrol, eugenol acetate, and allyl pyrocatechol diacetate [43].

Traditional Use:

Betel pepper leaves, in which their lateral nerves make a complete loop rejoining the midrib, are believed to be more potent medicinally than the leaves in which these are not obvious. These leaves known as '*sirih bertemu urat*' are used in the treatment of ailments which are difficult to cure. The Ayurvedics claim that the leaves are anthelmintic, aphrodisiac, carminative and laxative. They are also known to be stomachic and tonic. The Yunani regard the leaves as a styptic and a vulnerary. They prescribe it to improve the appetite and taste, to strengthen teeth and as tonic for the brain, heart and liver. In Vietnam, the leaves in the form of a collutory made of the extract are claimed to have antibacterial properties. Malays find the betel quid useful for administering medicine but beyond that, the *sireh* leaf is apparently selected as a vehicle for its own stimulant value [21].

The chewing of betel acts as a gentle stimulant and beyond all other uses, it sweetens the breath. The Ayurvedics prescribe it to treat halitosis, bronchitis and elephantiasis. The Indians add the extract of the leaves to medications to treat the mucous membrane lining of the mouth, nose and stomach. The leaves are used in various ways to relieve constipation in children. In the Philippine Islands, the heated leaves are applied to the abdomen, while in India the stalks of the leaves with oil are used in place of an enema. Malays usually eat the leaf with '*gambir*' to treat diarrhoea. The extract is also prescribed in a mixture ingested to treat gonorrhoea. This plant is used for the treatment of

dysentery, fever, gastritis, rheumatism and leucorrhoea. It is also used to eliminate body odour [21].

The leaves are used externally as poultice in various ways. The lowest branches of the vines produce relatively juiceless, deformed leaves. There may be more rubefacient action in these leaves compared to the more juicy ones. These are used in lotions and paste which are applied to ulcers, swellings and wounds. A poultice of the leaves as well as a wash with the decoction are used in treating burns, impetigo, furunculosis, eczema and lymphangitis. The leaves are used as lotion to treat nose ulcer and are also applied to the body during confinement. The extract of the leaves is further used as ear-drops and eye-drops. Malays apply the heated leaves to chests to relieve cough and asthma. Malays and Indians apply the leaves to the breast to arrest lactation [21].

The oil obtained from the leaves is used as an external application for treating catarrh and breast abscesses. The oil is used in Indonesia as pessary during confinement. The leaf and root, mixed in oil, are believed to have been used as a salve or ointment to treat hard tumors and scirrhi [21].

Pharmacological activity

Platelet inhibition activity

Hydroxychavicol (HC) was tested for its inhibition effect on platelet aggregation. The results showed hydroxychavicol to be a potent inhibitor for cyclooxygenase activity, reactive oxygen scavenger and inhibits platelet calcium signalling, thromboxan B2 production and aggregation. HC could be a potential therapeutic agent for prevention and treatment of arteriosclerosis and other cardiovascular diseases through its anti-inflammatory and antiplatelet effects, without effects on haemostatic functions [45].

Antibacterial activity

In a search for major active principles from natural resources which can prevent halitosis or act as "breath fresheners", a methanol extract of fresh leaves of *Piper betle* was subjected to in vitro tests using plate and broth MIC assays bio-film assay, saliva chip model and a conductometric method. The result outcome suggests that the active

constituent, allylpyrocatechol might be responsible for the antimicrobial activity against various obligate oral anaerobes [47].

Antidiabetic activity

Both the aqueous and ethanolic extracts of *P. betle* leaves possess marked hypoglycaemic activity when tested in fasted normoglycaemic rats. In glucose tolerance test, the extracts showed antihyperglycaemic activity in the external glucose level. The ability of lowering blood glucose levels of streptozotocin (STZ)-induced diabetic rats gives a suggestion that the extracts have insulinomimetic activity [48].

Antioxidant activity

In a study, it was reported that aqueous extracts of three varieties of *P. betle* leaves showed antioxidant effects when evaluated by in vitro systems such as DPPH radical scavenging, superoxide radical scavenging, hydroxyl radical scavenging and prevention of lipid peroxidation [51].

Antifertility activity

A study to develop an orally effective male contraceptive agent was extensively carried out in male mice with various doses of the leaf-stalk extracts of *Piper betle*. The results show no toxicity in all metabolically active tissues of mice and interestingly, the contraceptive efficacy emphasised reversible fertility after withdrawal of treatment [52].

Radio protective activity

Mammalian systems if exposed to radiation can cause damaging effects leading to cell death and an increased risk of degenerative diseases. Recently the radioprotective property of ethanolic extract of *P. betle* leaves was studied as alternative low cost preventive medicine to synthetic radioprotectants which are reported to be toxic. The capacity of the extract in preventing g-ray induced lipid peroxidation and DNA damage in rat liver mitochondria were assessed and evaluated to establish the mechanism of its radioprotective action. The study revealed significant immunomodulatory and superior radical scavenging activities which may be due to the presence of phenolic bioactives such as chavibetol

and allyl pyrocatechol. It suggests that the herb has a great potential not only it is cheap but also easily accessible natural radioprotectant to the common people [43].

Protective and healing activity

Most recently, a study was undertaken to evaluate the protective and healing effects of allylpyrocatechol against the indomethacin-induced stomach ulceration in rat model. Results showed that allylpyrocatechol can protect indomethacin-induced gastric ulceration due to its antioxidative and mucin protecting properties [53]

CONCLUSION;

Piper betel is one of the most important plant in human life which has more significant medicinal value, advantages, various applications due to its various pharmacological activities. It is more valuable plant due to phytochemical constituent present in it, such as Hydroxychavicol (HC)/Hydroxychavicol acetate(HCA), Allylpyrocatechol (APC), Chavibetol (CHV), Piperbetol etc. Other constituents are arecoline, carvacrol, caryophyllene, piperitol, piperbetol, eugenol, isoeugenol, allyl pyrocatechol, chavicol, safrole, anethole, chavibetol, cadinene hydroxychavicol, β -sitosterol, β -sitosteryl palmitate, dotriacontanoic acid, tritriacontane, stearic acid, cepharadione, piperine, piperlonguminine, chavibetol acetate, allylpyrocatechol monoacetate, allyl diacetoxyl benzene, estragole, methyl eugenol and hydroxycatechol, methylpiperbetol, piperol A and piperol B, carvacrol, eugenol acetate, and allyl pyrocatechol diacetate etc. This review focused on the Phytochemical constituent, Traditional uses and The pharmacological activities of the Piper betel Linn and their advances in plant kingdom.

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