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Review Article

A SCIENTIFIC REVIEW ON COMMON CHEWING PLANT OF ASIANS: *PIPER BETLE LINN.*

Rahul Shukla[1]*, Sandeep Sachan[2], Ashutosh Mishra[2], Sankul Kumar[3]

[1]Amity Institute of Pharmacy, AUUP, Noida, India
[2]A.N.D. College of Pharmacy, Babhnan, Gonda, India
[3]Sant Gadge Baba Amravati University, Amravati, Maharastra, India

Abstract: Pan consists of leaf of *Piper betle* Linn. (Family; Piperaceae); a dioecious, perinnial creeper, climbing by many short adventitious rootlets, widely cultivated in hotter and damper parts of the country. The plant is prescribed in the ancient Ayurvedic literature as a general tonic and voice, laxative, appetizer, beside this they pacify vata and aggravate pitta. In addition to these, the aphrodisiac effect of betel chewing has been indicated in ancient texts. The scrutiny of present overview revealed pharmacognostical, phytochemical and some notable pharmacological activities of the plant.

Keyword: Creeper, laxative, appetizer and aphrodisiac.

Introduction

Piper betle is heart shaped leaf belonging to the Piperaceae family. It is consumed both as a mild stimulant and for its medicinal properties. Betel leaf is mostly consumed in Asian countries, some Asian emigrants, as paan, with or without tobacco, in an habit-forming psycho-stimulating and euphoria-inducing formation with a dangerous clinical effects. The betel plant is an evergreen and perennial creeper. The betel plant is indigenous to South and South East Asia[1-2].

In Ayurveda betel leaf extract is frequently used as an adjuvant & mixed with different medicines possibly for better effects beside its independent use as medicine. In Susrta Samhita (Ch 28-46,279-280) tambool leaves have been described as aromatic or stimulant, sharp, hot, acrid in taste and advantageous for voice, laxative, appetizer. In addition to these, the aphrodisiac effect of betel chewing has been indicated in ancient texts. Pan also believed to provide strength to heart and regulate blood. Its utility as anti-inflammatory and anti-microbial is emphasized at several place. In ayurveda it acts as vata and kapha suppressant. It also helps in expel out the mucus or cough from respiratory organs because of its hot strength [3].

For Correspondence:
shuklarhl@gmail.com
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According to Unani system the leaf has a sharp taste and good smell improves taste and appetite, tonic to brain, heart and liver, lessens the thirst, clear the throat and purify the blood[4-5].

Plant profile:

Pan consists of leaf of Piper betle Linn. (Piperaceae); a dioecious, perennial creeper, climbing by many short adventitious rootlets, widely cultivated in hotter and damper parts of the country. The betel leaf is a heart shaped with different size. The size of the leaf varies with different cultivar from 7- 15cm in length and 5-14cm in width. Betel leaves are simple alternate stipulate petiolate with 0.75 to 3.8cm, ovate oblong broadly ovate cordate or obliquely elliptic entire glabrous coriaceous 10 to 18 cm long and 5 to 10 cm broad acuminate oblique and rounded base [6-8].

Fig.1: piper betle stem and leaf

Taxonomy of piper betle[9]

Kingdom: Plantae
Subkingdom: Tracheobionta
Super division: spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: magnoloidae
Order: piperales
Family: piperaceae
Genus: piper
Species: piper betle linn.

Vernacular names[10]

Sanskrit : Tambuli
Assame : Pan
Bengali : Pan
English : Betel leaf
Gujarati : Pan, nagarbael
Marathi : Nagbael
Hindi : Pan
Kanada : Veelyadele Ele
Malayali : Pan, Nagvel, Vidyachepan
Punjabi : Pan
Tamil : Vettilai
Telgu : Tamalapaka, Tamulapaku
Urdu : Pan
Malaysia : Sirih,

Varieties: Ambadi, Bhubna, Chennur, Desavari, Gangeri, Kaker, Kali, Kammar, Kanriballi, Kootakodi, Kulajedu, Kunalaballi.

Parts Used: leaf and root

Distribution: India, Malaysia, Bangladesh, Burma, Nepal and Sri Lanka; particularly in hot parts.

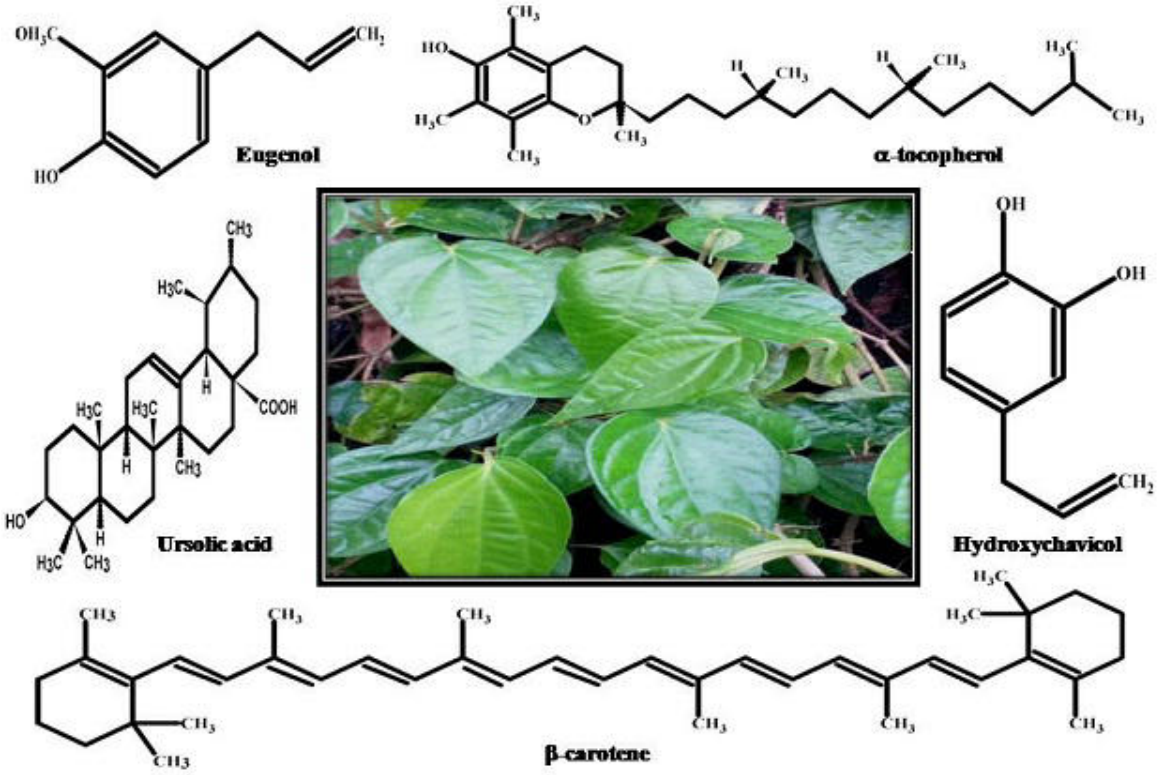
Chemical composition:

Composition (for 100g of betel leaves)

- Moisture 85.4g ; Proteins 3.1g ; Fats 0.8g ; Minerals 2.3g ; Fiber 2.3g ; Carbohydrates 6.1g

Special compounds present

Minerals, Vitamins (calcium, carotene, thiamine, riboflavin, niacin and vitamin C), Tannins, Sugar, Diastases. Essential oil, Phenol (chavicol), Alkaloid



Action and Uses:

The plant is bitter, sweet, sour , thermogenic, laxative, anthelmintic, carminative, digestive, stomachic, depurative, homeostatic, aphrodisiac, anodyne, ophthalmic and union promoting. It is useful in helminthiasis, anorexia, dyspepsia, colic, flatulence, skin diseases, leprosy, haemorrhages, haemoptysis, ophthalmopathy, otorrhoea, chronic ulcers, tumours, haemorrhoids, epilepsy, convulsions, scanty menstruation, fractures, and swellings. The shoots are useful in colonopathy, scurvy, otorrhoea, asthma, burns, and wounds. Powdered roots as well as the stem paste are very specific for bone fractures. The stem is bitter and it is given internally and applied topically for broken bones, used in complaints of the back and spine, removes pus .Leaves and young shoots are powerful alteratives for bowel affections, juice of stem is useful in irregular menstruation.

Ayurvedic properties[9]

Guna (Quality): Laghu, Ruksha, Tikshan
Rasa (Taste): Tikta
Vipak (Metabolism): Katu
Virya (Potency): Ushan
Prabhav (Impact): Hridya

Pharmacognostical review

Pharmacognosy although closely related to botany and photochemistry, many other field have a natural association with this like pharmacology, analytical chemistry, microbiology, plant tissue culture biotechnology, genetic engineering etc and all other rapid developments in many other areas have expended the horizon of Pharmacognosy.

Description[4]

a) Macroscopic:

Leaf varies greatly in size, 7.5-20.0cm, ovate cordate, entire, glabrous, apex acuminate to acute, lamina membranous, upper surface deep green and lower surface lighter in colour, primary or sub-primary nerves usually 7, some times 5-9: odour: aromatic, taste: slightly pungent.

b) Microscopic:

1) Leaf-

a)Petiole:- Single layered epidermis composed of cubical to slightly tangentially elongated cells covered with thick, striated cuticle; epidermal cells elongate to form uni to bicellular, occasionally multicellular hairs;

epidermis followed by a discontinuous collenchymatous zone in the form of arcs, and a multilayered parenchymatous zone; vascular bundle arranged in the arcs, phloem surrounds xylem; vascular bundle usually of vascular bundle usually of two sizes larger ones 7 in number and smaller one 2 in number.

b) Midrib: - Epidermis single layered, composed of colorless cubical cells, covered with wavy cuticle; epidermis followed by 2-3 layers of irregular colorless cells of hypodermis and a few layers of collenchyma, towards lower side collenchyma multilayered; vascular bundle shows phloem surrounding xylem; lower epidermis single layered and covered with wavy cuticle; some epidermal cells elongate to form uni to bicellular, occasionally multicellular hairs.

c)Lamina:- Shows dorsiventral structure; epidermis single layered, tangentially elongated, tangentially elongated, covered with thick striated cuticle on both sides; hypodermis 2-3 layered, having chloroplasts. Occasionally with secretorey cells; mesophyll differtiated in to palisade and spongy parenchyma; palisade single layered; spongy parenchyma 3-4 layered composed of irregular round cells, a few secretory cells also present in this region; hairs a few uni to bi cellular, occasionally multicellular, all being uniseraite present on both surfaces.

2)Powder:- Grayish-green; shows polygonal epidermal cells in surface view, simple pitted vessels and a few uni to tricellular hairs, anisocytic type of stomata, palisade and spongy parenchyma cells and simple pitted vessel.

Phytochemical review

- Dixit BS, Banerji R, Aminuddin, Johri JK (1995) have isolated Diosgenin in the petroleum ether layer of dried root of *Piper betle*. Dried roots was hydrolyzed by 2.5N HCl then extracted with petroleum ether in soxhlet (8hr) & it was treated with methylene chloride. An aliquot was subjected to GC analysis[8].
- Thanh L, Dung NX, Luu HV, Leclercq PA have showed chemical composition of the leaf oil from *Piper betle* L. cultivated in Vietnam (2002). The volatile oil of *Piper betle* cultivated in Vietnam was obtained by steam distillation of the fresh leaves. More than 27 components have been identified by GC-MS, the major ones being isoeugenol (72.0 %) and isoeugenyl acetatae (12.2%)[9].
- Balasubramanyam VR, Rawat AKS (1990) have reported that the *Piper betle* have α thujene, trans β-ocimene, terpinolene, allo-ocimene, Δ cadinene, terpene-1-ol, α-costol, Δ cadinol, methyl-2-hexadecane-1-ol-geraniol, hexa-decanoic acid, methyl benzoate etc[10].
- Saeed SA, Farnaz S, Simjee RU, Malik A. (1993) have isolated Triterpenes & β-Sitosterol from *Piper betle* & reported as antiplatelet & anti-inflammatory agent[11].
- Wang CK, Peng CH. (1996) have searched arecoline a alkaloids from a combination of *Piper betle* slaked lime and areca nut. N-nitrosoguvaline (NG), one of the N-nitrosation products of arecoline, is the only one N-nitrosamine found in Taiwanese betle quid chewing saliva[12].
- Evans PH, Bowers WS, Funk EJ (1984) have isolated 5 propenylphenols with significant fungicidal & nematocidal activity from the chloroform extract of leafs of *Piper betle*. The compounds are identified as chavicol, chavibetol, allyl pyrocatechol, chavibetol acetate and allyl pyrocatechol diacetate[13].
- Zeng HW, Jiang YY, Cai DG, Bian J, Long K, Chen ZL (1997) have isolated Piper betol, methyl piper betol, piperol A & B. These compounds showed selectively inhibition of the washed rabbit platelet aggregation induce by platelet activating factor (PAF) in a concentration dependent manner[14].
- Kar S, Misra PK (1997) have extracted ketoacids from leaves of pan by using 2,4-dinitrophnyl hydrazine. The ketoacids identified were: Pyruvic acid, ascorbic acid and beta-keto-butyric acid (in dark grown leaves). Levulinic acid, pyruvic acid, phenyl pyruvic acid, alpha-keto-glutaric acid and glyoxalic acid were found in light grown leaves[15].

Pharmacology review

Preclinical toxicity studies:

Sengupta A, Adhikary P, Basak BK, Chakrabarti K, Gangopadhyay P, *et al* (2000) have studied on preclinical toxicity to determine the haematological and biochemical changes after administration of alcoholic extract of leaf stalk of *Piper betle* in rats and mice. Haematological, biochemical profiles and enzymatic studies (transaminases and phosphatases) indicated that the plant extractives were devoid of toxicity[16].

Anticancer activity

Murakami A, Ali AM, Mat- Salleh K, Koshimizu K, Ohigashi H (2000) have carried out the in vitro anti-tumor promoting activities of edible plants of *Piper betle* from Malaysia. A total 114 methanolic extracts from 42 plant families of edible Malaysian plants were taken for their inhibitory activities toward tumour promotor 12-o- hexadecanoylphorbol-13-acetate (HPA)-induced Epstein Barr Virus (EBV) activation in Rajin cells. By testing at a concentration of 200 micro g/ ml, 74 % of the 114 extracts inhibited EBV activation by 30 percent or more. Further dilution by 30 percent or more. Further dilution experiments indicated that an extract from the leaves of *Piper betle* Family Piperaceae to be one the most promising species[17].

Antiulcer activity

Majumdar B, Ray chaudhuri SG. Ray A, Bandyopadhyay SK (2003) have showed by treatment with ethanolic extract of leaf of *Piper betel* at a calculated dose of 150 mg/kg body weight for 10 days, after induction of peptic ulcer by NSAID in albino rats, produced significant healing effect[18].

Ramji N, Iyer R, Chandrasekaran S (2003) have showed that *Piper betle* leaves have preventive action of oral molodor. It was examined by bioassay guided fraction to yield allylpyrocatechol (APC) as the main active constituent oral anaerobes responsible for halitosis[19].

Local anesthetic activity

Kaushik N, Geeth VS, Alice K (2004) have showed that the betel leaf extract have local anesthetic activity in the in situ gas trocnemiussciatic nerve preparation of a pithed frog[20].

Effect on glucose and lipid profiles

Saravanan R, Pugalendi KV (2005) have showed the effect of *Piper betle* on blood glucose and lipid profiles in experimental rats after continual ethanol administration. Administration of ethanol (7.9g/kg bodyweight) for 60 days resulted in a significant reduction in blood glucose levels and an elevation of serum & tissue lipids, as compared to normal control[21].

Antifertility effect

Sarkar M, Gangopadhyay P, Baskar B, Chakrabarty K, Banerji J, Adhikary P (2000) have explored the antifertility outcome of an extract (alcoholic) of the leaf trail of *Piper betle* Linn, Oneset of experiments with two different doses in Swiss male albino mice were evaluated. Results suggest that the contraceptive effect of the extract of leaf –stalk of *Piper betle* Linn. is mainly on the maturation process of spermatozoa in epididymides without influencing hystemic hormonal profiles. Withdrawal of the extract restored all altered parameters including organ weights and fertility after 60 days[22].

Anti diabetic activity

Arambewela LS, Arawwawala LD, Ratnasooriya WD, (2005) have reported that leaves of *Piper betle* (Piperaceae) possess safe and strong anti diabetic activity. This was tested in normologlycaemic and strepozotocin (STZ) induced diabetic rats using oral administration of hot water extract (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[23].

Radio protective activity

Bhattacharya S et .al (2005) have studied radio protective activity of *Piper betel* ethanolic extract using rat liver mitochondrion and BR322 plasmid DNA as two different model in vitro systems, The extract effectively prohibited gamma-ray induced lipid peroxide and conjugated diene. Likewise, it prevented radiation-induced DNA strand break in a concentration dependent manner[24].

Antioxidant activity

Lei D et.al., (2003) have shown aqueous inflorescence of *Piper betel*, as a scavenger of H_2O_2 , superoxide radical, and hydroxyl radical induced PUC 18 Plasmid DNA breaks at Concentrations (IC 50) of about 80, 28 & 73 micro g/ml, respectively. Inflorescence *Piper betle* extract also prohibited the hydroxyl radical induced PUC 18 Plasmid DNA breaks at concentrations higher than that IPB extract also inhibited the arachidonic acid (AA) induced and collagen-induced platelet aggregation, with a IC (50) of 207 and 335 µg/ml, respectively[25].

Rao AR, Sinha A, Selvan RS, (1985) have showed when an aqueous extract of the leaves of *Piper betel*, a medicinal plant, was given orally at different dose levels during the initiation phase of 7, 12 dimethylbenz[A] anthracene (DMBA) induced mammary carcinogenesis in rats, higher doses of the extract inhibited the emergence of tumors[26].

Spasmogenic effect

Gilani AH, *et al*., (2000) have studied that crude aqueous extract (Pb.Cr) of *Piper betle* leaves for the possible presence of cholinominetic & calcium channel antagonist constituents. Pb.Cr at doses of 1-10mg/ml caused a moderate spasmogenic effect in isolated guinea-pig ileum and this activity was concentrated in the aqueous fraction, which was found to be 5 times more potent[27].

Anti adhesive effect

Razak FA, Othman RY, Rahim ZH(2006), have studied the effect of aqueous extract of plants *Psidium guajava* and *Piper betel* on the cell surface hydro-phobicity of early settlers of dental plaque in vitro. It was also observed that the anti adhesive effect of the two extracts on the binding of the early plaque settlers to hexadecane is concentration dependent[28].

Antihepatotoxic effect

Young SC, Wang CJ, Lin JJ, Peng PL, Hsu JL, Chou FP have evaluated the antihepatotoxic effect of *Piper betel* leaf extract on carbon tetrachloride induced liver injury in a rat model. Fibrisis and hepatic break, that was reveled by histology and the activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were induced in rats by an administration of CCl_4 (8%, 1ml/kg body weight), thrice a week for 4 weeks. *Piper betel* leaf extract significantly inhibited the elevated AST and ALT activities cause by CCl_4 intoxication[29].

Steroidogenic activity

Yang NY, Kaphle K, Wang PH, Jong DS, Wul S, Lin JH(2004) have explored the potential Steroidogenic activity of hot water extract from betel quid and its constituents arecoline on testosterone producing ability in an experiment conducted in vitro. Enzyme dissociate interstitial cells which was taken from adult mouse testes (ICR strain) were cultured with/without different doses of the extracts and the level of testosterone produced was estimated by an enzyme immunoassay technique. It was found that of lower doses of arecoline, areca catechu linn and *Piper betel* linn. extract have significantly stimulated testosterone production over the basal level[30].

Antihypertensive activity

Runnie I, Sallah M, Head RJ, Abeyawardena MY (2004) have studied the vasodilatory actions of 9 edible tropical plant extracts. *Piper betle* showed vasorelaxation on isolated perfused mesenteric artery preparation[31].

Pancreatic lipase activity

Prabhu MS, *et al*., (1995) have studied the effect of orally administered betel leaf on digestive enzyme of pancreas and intestinal mucosa and on bile production in rats. The outcome indicated that betel leaves do not influence bile secretion and composition, they have a considerable stimulatory influence on pancreatic lipase activity[32].

Effect on central and autonomic nervous system

Chu NS.(2001) has studied effect of betel chewing on the CNS and ANS. It has been claimed that Betel chewing produces a sense of well being, alertness, euphoria, sweating heightened, salivation a hot sensation in the body and increasing capacity to work. It also leads to habituation, addiction & extraction. Betel chewing may affect sympathetic, GABAnergic and parasympathetic functions. Betel chewing produces an increase in blood pressure and heart rate. In autonomic function tests, both the sympathetic skin response and

RR interval plasma concentrations of nor epinephrine and epinephrine[33].

Hypotensive and Tachycardiac effects

Chen SJ, Wu BN, Yen JL, Lo YC, Chen IS, Chen IJ(1995) have revealed that intravenous injections of water extracts of *Piper betle* inflorescence (PBE), eugenol and safrole in rats induced hypotensive and bradycardiac effects, where as both intraarterial and intrathecal injections of PBE, eugenol and safrole resulted in hypotensive and tachycardiac effects. This report suggests that acute administration of betel inflorescence extracts by different routs may activate C-fiber-evoked parasympathetic & sympathetic cardiovascular reflexes in rats[34].

Interceptive effect

Choudhuri D, P Adhikary (1991) have revealed that *Piper betle* have pregnancy interceptive effect[35].

Wound healing activity

Santhanam G, S Nagarajan (1990) have reported wound healing activity of curcuma aromatic & *Piper betle*[36,37].

Antimicrobial activity

Shitut S, Pandit V, Mehta BK (1999) have studied the antimicrobial activity of different varieties of *Piper betel* linn, leaf stalk extracts against human pathogenic bacteria & phytopathogenic fungi in vitro by comparing the results with standards microbial susceptibility testing biodiscs. The ethanolic and ethyl acetate extracts of all the four varieties have shown significant activity against bacteria vibrio cholerea ogawa, staphylococcus aureus, diplococcus pheumoniae and Klebsiella aerogens. Ethanolic and ethyl acetate extracts of all the varieties have showed moderate to considerable activity[38].

Anti-Asthmatic Effect

In asthma histamine also plays an important role. So here ethanolic extract of *Piper betel* Linn. at a calculated dose of 100mg/kg body weight and 200mg/kg body weight is studied in Gunea Pigs for its effect in asthma. It is compared with a standard drug that is Chlorpheniramine, which is an antihistaminic drug. The Preconvulsive time of all the drugs were compared. Here asthma is induced by 0.2% histamine aerosol. The results obtained from this study show that *Piper betel* Linn. at a calculated dose of 100 mg/kg body weight and 200 mg/kg body weight has significant antiasmatic property[39].

Discussion

Since synthetic medicines get resistance day by day for the many microorganisms. Therefore, it is needed to move towards herbal medicines and their combinations. Some diseases don't have any proper treatment. Hence the only option remains folk medicines like *Coccolus hirsutus*[40], *Muraya coignii*[41], *Anogiessus latifolia*[42]. Now a day more emphasis is on having better health instead of taking medicine, hence the use of nutraceuticals is also on the rise. Some herbal drugs which can be used as nutraceuticlas are *Typha angustifolia*[43] and *Typha latifolia*[44, 45], *wheat grass*[46, 47], *Piper betle*[48], *Bamboo.*[49, 50]

Herbal medicines have good scope in the field of new drug therapy as well as nutraceuticals. This review article on *Piper betle* will provide help to know the potency of the medicine for different diseases.

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