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Piper betle and Some Indian Plant for Antidepressant Activity: A Review.

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ABSTRACT

Piper betle Linn, is commonly known as Betel leaf or paan, belonging to the family Piperaceae. The leaves are pungent, bitter sweetish acrid in nature. It is commonly found in lowland tropical rainforests. Many species of piper have been used for treating different disease in many traditions examples P. cubeba as a cigarette flavoring. P. darienense is used to intoxicate fish. Black Pepper (P. nigrum) essential oil is used as herbalism.The leaf contain water, protein, carbohydrates, tannin, alkaloids, terpenoids (cineole, cadinene, camphene, euginol and chavibetol). The leaf has a significant antimicrobial activity against broad spectrum of micro-organisms (Streptococcus pyrogen, Staphylococcus aureus, E-coli, Pseudomonas aeruginosa etc.), gastro protective activity, antioxidant activity, antidiabetic activity, Radioactivity activity, it will also effect on the cardiovascular system/platelet, inhibition activity or as cardio tonic antifertility activity, immunomodulation activity cholinomimetic effect, Hepato-protective activity, as an oral care agent.

Keywords: Piper betle Linn, andidepressant, tropical.

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INTRODUCTION

Piper betle Linn blessed as evergreen and perennial plant, a member of the *Piperaceae* family is an edible plant and have the shape of heart.[1] It is about 10 genera, 2000 species of these, 30 species have been recorded in India 18 in Srilanka and 3 are endemic.[2] The parts of Piper betle utilized are leaves, root, stems, stalks and fruits. According to Unani system leaf has sharp burning taste, good smell, improves taste and appetite, tonic to brain, heart and liver. In various properties of betel leaf include antioxidant, antifungal, antiulcergenic, antiplatelets, antidiabetic, immunomodulatory, antiamoebic, antiinflamatory and antimicrobial, antifertility, antihyperglycemic and radioactive properties.[3] Betel leaf has been described from the ancient time as an aromatic stimulo carminative, astringent and aphrodisiac. The alkaloid arakene has properties resembling cocain in some respect Indian drugs containing P. betel dry extract was found to be an effective long lasting oral contraceptive.

Several solvent system have been used to extract from betel leaf. An ethanolic extract of Piper betel leaf decreased histamine production suggesting that it may be useful for relief of allergic symptoms caused by histamine in type I hypersensitivity disorder. Recently, the ointment of the Piper betel leaf extract has cured and improved ringworm skin lession.

Taxonomical classification:[3]

Kingdom	Plantae
Unranked	Angiospermae
Unranked	Magnoliidae
Order	Piperales
Family	Piperaceae
Species	P. betle
Genus	Piper
Class	Mangnolipsida
Binomial name	Piper betle L.

Vernacular name:[3]

Bengali	Paan
Hindi	Paan
Sanskrit	Tambula and Nagavalli
Persian	Tanbul
Telugu	Tamalapaku
Gujarati	Naagarvel na pan
Kannada	Veeleyada yele
Malayalam	Vettila
Malaysia	Sirih, Sirih melayu,Sirih cina
Tamil	Vetrilai

Chemical studies carried out on Brazilian Piperaceae species have revealed the occurance of pyrones, lignoids and chromenes beside various amides bearing isobutyl, pyrrolidine,dihydropyridone and piperidine moieties.These amide have generated interest as a result of their potent insecticidal and antifungal properties.[4]

Geographical source- It is widely grown in central and eastern Malaysia. In India, it is widely cultivated in Tamil Nadu, Madhya Pradesh, West Bengal, Orissa, Maharashtra and Uttar Pradesh. It reached Madagascar and East Africa much later and was introduction into the West Indies. With known ethanol medicinal properties, this plant is widely use in India, Indonesia and other countries of the Indochina region.[5]

Morphology:

Macroscopy character:[6]

Colour	Yellowish green to dark green in color with smooth surface
Odour	Pleasant
Taste	Aromatic with varied taste, ranging from sweet to pungent taste.
Shape and size	The leaf is heart shaped with different size from 7-15 cm in length and 5-14 cm in width.

Leaves are alternatively arranged and slightly cordate. About 5-7 veins are arising from the base to the tip.[7]

Microscopic characters :

T.S. of leaf through midrib shows 4 layered upper and 2 layered lower epidermis.The leaf is semicircular in shape with even outline .The adaxial side is flat with circular secretary canal and small secretory cells, while the adaxial side is hemispherical and has small secretory cells with dark contents.The narrow epidermis of midrib is thin and has spindle shaped cells with smooth surface vascular bundles are single ovate collateral with cluster of xylem elements and think are of phloem. The palisade layer are well distinguished they are double layered short wide compact cells and mesophyll cells are 3-4 layered and small lobed. Thick walled irregular secretory cells are seen with dense content of probable an essential oil. The trichomes are glandular which have unicellular optical cell and a short pedicel. The pedicel has thicker wall, surrounded by 5 or 6 epidermal cell arrange in rosette disk like manner. The influrocence is an axillaries spike which is 5.5cm long.

Chemical Constituents: The fresh Piper betel leaves ether extract have piperol –A piprol-P, methyl piper betel. Phytochemical analysis on leaves revealed the presence of Alkaloids, Tannins, Carbohydrates, Amino acids and steroidal component. It also contains vitamins like Vit C , Nicotinic acid vitamin A Thiamine, Riboflavin and some minerals such as calcium (0.2-o.5%) iron (0.005-0.007), iodine, phosphorus(0.05-0.6%) potassium(1.1-4.6%) . It contain phenol betle phenol (chavibetol and chavicol) codeine has also been found.

Chavibetol is natural chemical compound of phenylpropranol class. It is the most important component of the essential oil form the lives of p betle plant.

Eugenol is one of the principal constituent of betel leaf, its effect on CNS encompassing seizure are control, Parkinsons disease, antidepressant effect etc.

Other phenolic constituent of betel leaves are Hydroxychevicol(HC) Allylprocatechol, Quercetin, Beta Caryophyllene.[8]

Biological activity:

Antifertility activity- As the structural and functional integrity of reproductive organ depend on circulating level of estrogen, any small change in estrogen level may lead to altered structural and functional activity of reproductive organs.[9]

Antimicrobial activity- The leaf extract also poses the bacterial activity against the urinary tract pathogenic bacterial such as Enterococcus faecalis, C. koseri, C. fruendi etc.[10,11] The chloroform extract of Piper betel shows the much efficacy than the methanol fraction against dermatophytes because of presence of non- polar component in the fraction.

Gastro protective activity- The hot water extract significantly increased the mucus content adhering to the wall of gastric mucosa. It is generally believed that enhanced acid secretion is the most important factor for the induction of gastric lesions. The higher dose of hot water extract does not causes significant inhibition in

acidity or pH of gastric fluid. Ulceration progression is caused by free radical- induced chain process. Consequently, its arrest by radical scavengers helps in the faster healing. [12, 13]

Immunomodulatory activity- The methanolic extract has lymphocytes proliferation, interferon C receptors and the production of nitric oxide were measured in vitro. Further, the extract at different dose levels was studied in vivo for the humoral and cellular immune responses on mice immunized with sheep red blood cells. The same could be further evaluated for its anticancer activity or as a potential candidate in a treatment of autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematous or emphysema.

Hepato protective activity- The antitoxic effect of betel leaf extract was evaluated on ethanol and carbon tetrachloride (CCl_4) induced in the liver injury in a rat model. Fibrosis and hepatic damage, as revealed by histology and the activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were induced in rats by CCl_4.

Cholinomimetic effect- Betel leaf rise in body temperature due to cholinergic responses. Aqueous and ethyl acetate extract were evaluated for their cholinergic responses using isolated guinea pig ileum.

Antioxidant activity- Oxidative effect is an important effect of ionizing radiation on biological membranes. It is chain reaction[14]. The extract reduce most of the Fe^{3+} ions and possess strong reductive ability [15].

Antidiabetic activity- The aqueous extract of betel leaves possess marked hypoglycaemic activity when tested in fasted normoglycaemic rat. In glucose tolerance test, both extracts markedly reducedthe external glucose load. The ability of lowering blood glucose level of Streptazocine (STZ) induced diabetic rat gives a suggestion that the extract have the insulinomimetic activity[16].

Radio protective activity- The ethanolic extract of betel leaf shows the radio protective activity and it has been studied using rat liver mitochondria and $p^{BR}322$ plasmid DNA as two model in vitro systems. The radical scaverging capacity of betel leaf was primarily due to its constituent phenolics, which were isolated and identified as chavibetol and allylpyrocatechol[17].

Some Piper betle extract &activity found in them-

S no.	Plant part / Extract	Activity/Animal model	Result
1	Aqueous extract of fresh piper betle extract	Antimicrobial activity/Various microorganism/disc diffusion method	Aqueous extract showed effective inhibition action against the microorganisms
2	Piper betle leaves/ hot water extract/cold ethanolic extract	Antioxidant activity/Initial antioxidant activity, Antioxidant activity with time and at elevated temperature(200^{o}C)	The extract obtained from the leaves of piper betle had profound antioxidant activity
3	Piper betle spray dried powder	Antidiabetic activity/ diabetic mellitus patient	Piper betle as a nutriceuticals result as a potential treatment for type2 diabetes patients
4	Aqueous extract of fresh Piper betle leaves	Antioxidative and antihemolytic activity/ microorganisms (Streptococcus pyrogens, Staphylococcus aureus, Pseudomonas aerugenosa and Escherichia coli	The antioxidant and antihemolytic activity were attributed to the high concentration and combined activity of flavonoids and polyphenols
5	Crude ethanolic extract of Piper betle leaves	Antidermatophytic activity/zoonotic dermatophytes and yeast like Candida albicans	Testing showed Piper betle cream formulation with potential therapeutic value for the treatment of dermatophytosis
6	Aqueous and ethanolic extract of Piper betle leaves	Antibacterial activity/ Gram positive and gram negative bacteria/ Agar diffusion method	The study reveals that both the aqueous and alcoholic extract be active beside the strains of bacteria which are the common cause of infections
7	The hot water Piper betle	Gastro protective activity	The study showed that it can protect against indomethacin induced gastric

	leaves extract		ulceration due to ita antioxidant and mucin protecting properties
8	The petroleum ether extract and 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 Ostriniasalentialis
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	The dose produced a significant increase in plin threshold in hot plate method whereas significantly reduced the writhing caused by acetic acid and caused significantly inhibition of carrageenan induced paw edema
10	Piper betle extract	Antifertility activity/femal rats	The data suggests that betle extract brought about antifertility and antiestrogenic effect in female rats
11	The Piper betle extract	Antihepatotoxic effect/ ethanol/ ethanol and carbon tetrachloride (CCl_4) induced liver injury in a rat model	The histological examination shows that Piper betle leaves extract secluded liver from the damage induced by CCl_4 by declining alpha smooth muscle actin (alpha-sma) expression)
12	The Piper betle leaf infusion	Skin antiseptic/ pre- surgery cataract patient	Result showed that 20% Piper betle leaf infusion to have an antiseptic
13	The methanolic extract of Piper betle leaves	Immunomodulatory activity/Mice	The study revels that it significantly suppressed hemagglutinin stimulated peripheral blood lymphocytes proliferation in a dose- dependent manner
14	The ethanolic Extract of Piper betle leaves	Antidepressant Activity/ Mice	The study showed that it has significant antidepressant activity greater than Imipramine and has the potential to be used as an antidepressant

Some other plant that have antidepressant activity

S no.	Plant name	Common name	Family	Part used
1	Areca catechu[18,19]	Betel nut	Arecaceae	Areca nut
2	Apocynuuvenetum Linn[21]	European dogbane	Apocynacea	Leaves
3	Albizzia julibrissin[20]	Persian silk tree	Fabaceae	Bark
4	Albizzia lebbeck[22]	Siris tree	Mimosaceae	Bark
5	Aniba riparia[23]	St. John's wort	Lauraceae	Unripe fruit
6	Aloysia polystachya[24]	Tede burro	Verbenceae	Aerial part
7	Allium cepa[25]	Bulb onion	Liliaceae	Bulb powder
8	Asparagus racemosus[26]	Shatavari	Liliaceae	Root
9	Bacopa monneria[27]	Brahmi	Scrophulariaceae	Aerial part
10	Boophone distica[28]	Tumbleweed	Amaryllidaceae	Whole plant
11	Bupleurum falcatum[29]	Chinese thoroughwax	Apiaceae	Fruit
12	Clitoria ternatea[30]	Butterfly-pea	Fabaceae	Plant

				powder
13	Canavalia brasiliensis[31]	Brazilian jackbean	Fabaceae	Seed
14	Curcuma longa[32]	Turmeric	Zingiberaceae	Root (rhizome)
15	Cecropia glazioui[33]	Embauba	Cecropiaceae	Leave
16	Cimicifuga racemosa[34]	Black snakeroot	Ranunculaceae	Root (rhizome)
17	Crocus sativus L[35]	Saffron	Iridaceae	Petais
18	Emblica Officinalis[36]	Amla	Euphorbiaceae	Fruit
19	Galphimia glauca[37]	Rain of gold	Malpighiaceae	Whole plant
20	Gentiana kochiana[38]	Trumpet gentian	Gentanaceae	Aerial plant
21	Gastrodia elata[39]	Tian ma	Orchidaceae	Rhizome
22	Glycyrrhza uralmsis[40]	Liquorice	Leguminaceae	Root
23	Glycyrhiza glabra[41]	Liquorice	Leguminaceae	Root
24	Hypericumperforatum[(42]	Goat weet	Hypericaceae	Aerial part
25	Hypericumreflexum[(43)]	Hypercom	Hypericaceae	Aerial part
26	Kaemferiaparviflora	Peacock ginger	Gingerbiraceae	Whole plant
27	Lepidiummeyenii	Maca	Brasscaceae	Hypocotyls
28	Marceliamenuta Linn	Dwafwaterclover	Marsileaceae	Whole plant
29	Momoridicapudicacharantia	Karela	Cucurbitaceae	Seed
30	Magnolia officinalis	Beaver tree	Magnolicaceae	Bark
31	Morindaofficinalis FC How	Mulberry	Rubiaceae	Root
32	Mimosa pubic Linn	Humble plant	Mimocaceae	Leaves
33	Nardostachysjatamansi	Nard	Balerianaceae	Root (rhizome)
34	Ocoteaduckei	Sweetweet	Lauraceeae	Whole plant
35	Piper methysiticumForst	Kava	Piperaceae	Root
36	Piper laetispicum	Xiao Chang feng	Piperaceae	Stem root
37	Paeonialactiflora	Garden peony	Paeoniaceae	Root
38	Ptychopetalumolacoides	Marapama	Olacaceae	Bark root
39	Rhazyastricta	Senhwar	Apacynoceae	Leaves
40	Radix puerariae	Kudzo root	Leguminaceae	Whole plant
41	Rosmarinusofficinalis	Rosmarry	Lamiaceae	Leaves
42	Siphocamphylusverticillatus	Mufunbo	Campanulacae	Aerial part
43	Salvia elegans	Pineapple sage	Lamiaceae	Aerial part
44	Schniusmolle L	Brazillianpeper tree	Anacardiaceae	Leaves
45	Tinosporacordiofolia	Giloea	Menispermaceae	Whole plant
46	Thymus pubescences	Firflyphwine	Lamiaceae	Root
47	Tabebuiaavellanedae	Moreton bay chestnut	Bignoniaceae	Bark leaves
48	Zingiberoffcinale	Ginger	Zingiberaceae	Rihzome

CONCLUSION

The medicinal important of the herb as discussed above evidently prove that betel leaf is one of the most promising commercial botanical which possess a lot of therapeutic values. The leaf has a greater potency to act as natural antioxidant. The antioxidant property is correlated with the different biological activities like hepatoprotective, antidiabetic, antiarthritis anti-stroke and anticancer properties, since free radicals are

involved in all these diseases. Considering the above properties, it comes to conclusion that betel leaf place its position in nature same as our heart in our body and role the same with lots of biological activities and has tremendous strength to come out as a *future green medicine*, hence Piper betle L. leaf regard as "Golden heart of Nature".

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