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Piper betle A herbal plant: A Review

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Abstract
Piper betle Linn., a significant member of the Piperaceae family, is a perennial and evergreen climbing plant characterized by its glossy, heart-shaped leaves, which serve as rich sources of phenolic compounds exhibiting antiproliferative, antimutagenic, antibacterial, and antioxidant effects. This species has been the subject of extensive research regarding its pharmacological attributes, including antimicrobial, anticancer, antioxidant, and antidiabetic properties. Various extraction methods have been employed for *Piper betle*, including soxhlet extraction, sonication extraction, maceration, ultrasound-assisted extraction (UAE), supercritical fluid extraction (SFE), and microwave-assisted extraction (MAE). *Piper betle* is extensively grown in Sri Lanka, India, Thailand, Taiwan, and various other Southeast Asian nations. The essential oil derived from this plant serves as a valuable industrial raw material for creating medicines, perfumes, mouth fresheners, tonics, and food products. The aim is to highlight the potential of this plant in developing therapeutically effective herbal medications to combat various microbial infections, particularly those affecting the oral cavity, skin, and digestive system. This also presents an opportunity for pharmaceutical companies to engage in the formulation and production of natural product-based drugs aimed at specific health issues.

Keywords: *Piper betle*, antimicrobial, herbal medication, chavibetol, wound healing, hydroxychavicol, indigestion

Introduction

Piper betle is a plant of significant global importance, particularly noted for its medicinal value and its role in traditional practices. In India, it enjoys widespread popularity, being integral to various aspects of life, including social, cultural, and religious activities. States such as Tamil Nadu, Kerala, Uttar Pradesh, Maharashtra, and Madhya Pradesh recognize it as a key commercial crop. *Piper betle* L. is a perennial, dioecious, tropical creeper that thrives in shaded environments and belongs to the Piperaceae family. This climbing plant is a vital asexually propagated cash crop. The name Piperaceae is derived from the Sanskrit term "pippali," which refers to long peppers like *Piper longum*. Several species within the genus Piper are commercially significant across diverse agro-climatic regions in numerous countries. Notable examples include P. betle, *P. nigrum*, *P. longum*, *P. aduncum*, and *P. cubeba*, all of which are traditional members of the Piperaceae family. Among these, P. betle is extensively researched and widely cultivated due to its valuable bioactive compounds and the therapeutic properties of its essential oil [5].

Fig 1: *Piper betle* L.

Traditional treatments utilizing medicinal plants and herbs are currently prevalent within the community. The therapeutic application of naturally occurring plants not only avoids side effects but also allows for prolonged use. Betel leaf extract is commonly employed as a mouthwash to alleviate swelling, combat bad breath, halt bleeding, and address various ailments such as vaginal discharge, cough, hoarseness, and skin injuries. [6] The phytochemical composition of the betel plant includes saponins, flavonoids, polyphenols, and triterpenoid essential oils, along with essential oils comprising chavicol, chavibetol, carvacrol, eugenol, and estragol, as well as sesquiterpenes, sugars, and starch. Piper species thrive in lowland tropical rainforests and are also cultivated at higher elevations, such as cloud forests. P. betle is believed to have originated in Malaysia and is widely distributed across the southern and southwestern regions of China. Its cultivation is commonly undertaken in various Asian countries, including India, Indonesia, Nepal, Sri Lanka, Bangladesh, Myanmar, Pakistan, Vietnam, Thailand, Laos, and Cambodia, primarily for its ethnomedicinal benefits [5].

Plant profile:

Taxanomic classification:

Table 1: Taxanomic Classification

Kingdom	Plantae
Division	Magnoliophyta
Sub-division	Angiosperms
Class	Magnoliopsida
Sub-class	Magnolilidae
Order	Piperales
Family	Piperaceae
Genus	Piper
Species	*Piper betle* L.
Synonyms	Chavica Beta, Artanthe Hixagona, Pepper vine

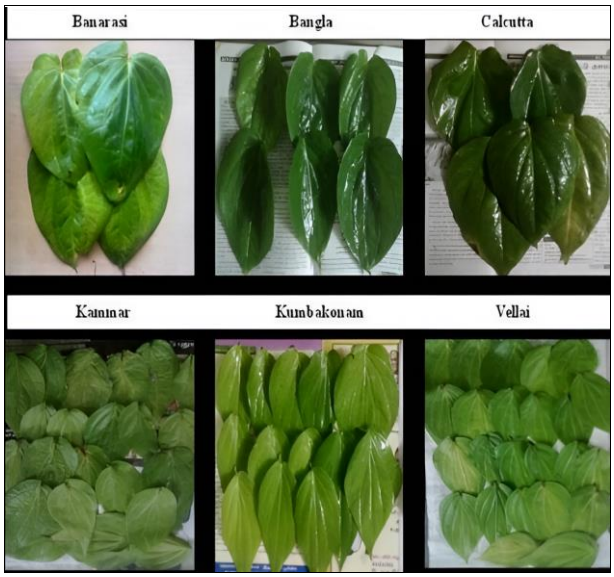

Fig 2: Types of betel leaves

Fig 3: Betel Leaf

Vernacular names:

Table 2: Vernacular Names

Sanskrit	Tambool, Mukhbhushan, Varnalata
Hindi	Paan
English	Betle, betle pepper, Betle-vine
Telugu	Nagballi, Tamalapaku
Tamil	Vetrilai
Gujarati	Nagarbael
Marathi	Vidyache paan
Malayalam	Vettila
Indonesia	Bakik serasa, Daun sirih, Serasa
Kannada	Eleballi, Panu, Vileyadele

Macroscopic characters:

Table 3: Macroscopic Characters

Stem	Semi-woody, cylindrical
Flower	Naked, unisexual, dioecious, fairly long
Fruit	Globose drupes
Shape	Heart shaped
Length	15-18 cm long
Width	10cm
Margin	Entire
Apex	Acute
Base	Symmetric

Organoleptic characters:

Table 4: Organoleptic Characters

Colour	Yellowish green to dark green in colour with glossy upper surface.
Odor	Characteristic to pungent
Taste	The betel leaves are aromatic with varied taste, ranging from sweet to pungent due to the presence of essential oils.

Microscopic characters

The transverse section of the leaf, taken through the midrib, reveals a structure characterized by a four-layered upper epidermis and a two-layered lower epidermis. The cuticle exhibits a pronounced thickness on the upper epidermis, while it is comparatively thinner on the lower epidermis. The outer epidermal cells on both surfaces of the leaf are diminutive and contain tannins and oils. In contrast, the subepidermal cells on the abaxial side are notably enlarged, serving the function of water storage. Both sides of the leaf also contain subepidermal cells that house crystalline and oil reserves. The palisade layer is distinctly identifiable, consisting of two layers of short, wide, and compact cells, whereas the mesophyll is composed of 3 to 4 layers of small lobed cells. Additionally, thick-walled, irregular secretory cells are present, filled with dense contents that likely include essential oils [10].

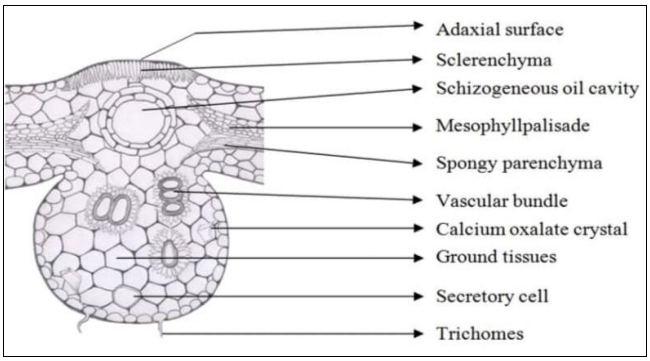

Fig 4: T.S of Betel leaf with midrib

The leaves exhibit hypostomatic characteristics, with tetra-cytic stomatal complexes being a prevalent feature typical of the Piperaceae family. Glandular trichomes are present, characterized by a unicellular apical cell and a short pedicel. The pedicel possesses a thicker wall and is encircled by five or six epidermal cells arranged in a rosette-like formation. The apical cell of the trichome is slightly pointed or clavate in shape. Vascular bundles are situated at the center of the midrib, consisting of single ovate collateral cells, with distinct xylem elements and a robust phloem observed. The stems are dichotomous, articulate, swollen, and exhibit rooting at the nodes, measuring 3 mm in diameter, and are woody with internodes ranging from 2.5 to 4 cm in length. The stem is stout, featuring a pinkish stripe along the nodes, which are dilated and capable of rooting. The inflorescence takes the form of an axillary spike, measuring 5.5 cm in length. The fruits are drupaceous, orange in color, and approximately 3 mm in diameter [11].

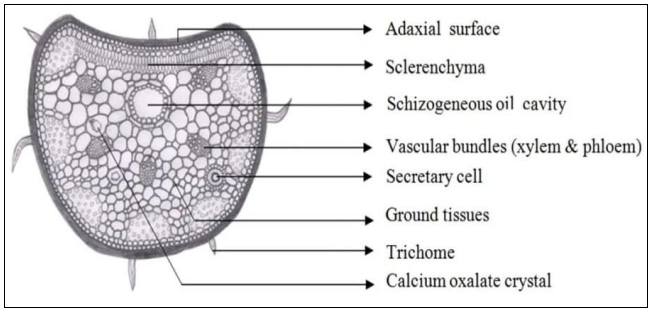

Fig 5: T.S of petiole of Betel leaf

Cultivation and propagation

Cultivation

The plant is grown in black, friable clay loam soil that resembles tank earth and is rich in organic matter. However, the finest specimens are cultivated in Bengal, where the soil is a light, reddish loam. This plant can thrive at elevations from sea level up to 1,000 meters, requiring a minimum rainfall of 179 cm. It flourishes best in tropical forest environments that provide ample shade, high humidity, and abundant soil moisture. There are primarily two cultivation systems: one under natural conditions and the other under controlled conditions. The open cultivation system is utilized in areas where high humidity and moderate sunlight are consistent throughout the year. This plant is a climber that needs support from trees such as areca nut (Areca catechu) and coconut (Cocos nucifera), typically reaching heights of 10 to 15 meters with extensive branching and foliage. Close planting of the vines aids in moisture retention and creates a microclimate that is favorable for growth. In contrast to practices in the northeast, where vines are allowed to grow to the height of their supporting trees, here they are kept to just 1 to 2 meters. This adjustment in growth habit is achieved by limiting vertical growth and encouraging branching. In partially controlled cultivation, the plant is adapted to fit the existing environmental conditions. However, weather conditions that provide sufficient sunlight (with photosynthetically active radiation of 1200-1800 µmol m²/s) are not ideal for optimal growth. With advancements in greenhouse and glasshouse technology, it has become increasingly feasible to relocate plants from their natural environments and cultivate them under controlled conditions, allowing for precise regulation of humidity, light exposure, and temperature [12, 13].

Propagation

Propagation can be easily achieved through root division or cuttings, ideally during the spring or summer months. Betel leaf thrives in nutrient-rich soil and favors a semi-shaded environment. Consistent feeding and watering will promote vigorous growth.

Geographical distriburtion

Piper betle originates from central and eastern Malaysia and has been cultivated for over 2500 years across Malaysia and tropical Asia. Its introduction to Madagascar and East Africa occurred at a later date, and it was also brought to the West Indies.

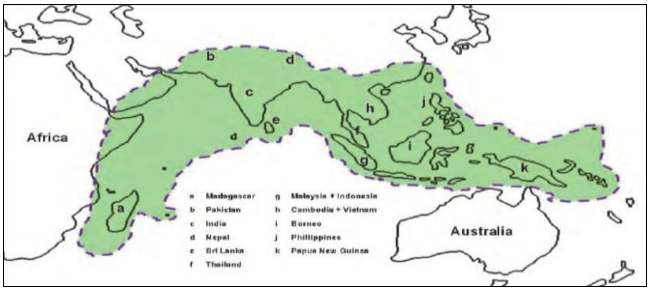

Fig 6: Geographical Distribution

Phytoconstituents:

1. Chavibetol:

Chavibetol is a naturally occurring chemical compound belonging to the phenylpropanoid class. It serves as the

primary constituent of the essential oil extracted from the leaves of the *Piper betle* plant. This aromatic compound is characterized by its spicy fragrance and is an isomer of eugenol.

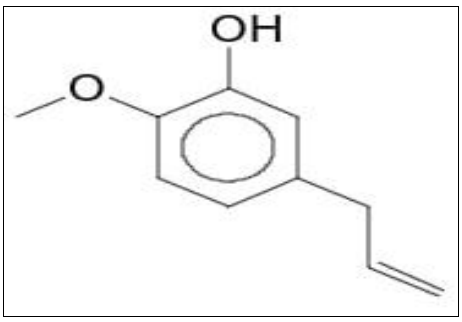

Fig 7

2. Eugenol

One of the key components of betel leaf has demonstrated anti-inflammatory properties in several animal studies involving various inflammatory agents. Additionally, it exhibits antimicrobial, analgesic, antioxidant, antiviral, and anticancer activities. Other notable effects include its potential to prevent ulcers, influence osteoporosis, and impact the central nervous system (CNS), particularly in relation to seizure management, Parkinson's disease, and antidepressant effects.

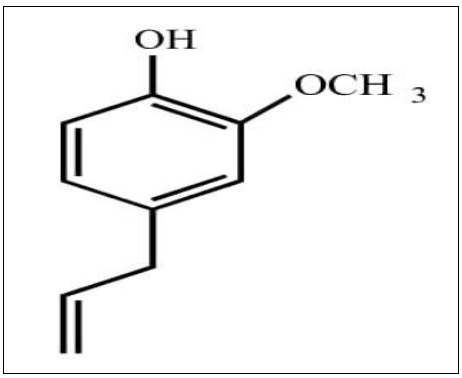

Fig 8

3. Allylpyrocatechol

Phenolic compounds derived from the leaves exhibit inhibitory effects on obligate oral anaerobes that contribute to halitosis. Additionally, the leaf extract demonstrates a stimulating effect on pancreatic lipase and possesses antioxidant properties. The oral administration of APC at varying doses enhances the healing process of gastric lesions induced by indomethacin, attributed to its antioxidative and mucin-protective characteristics.

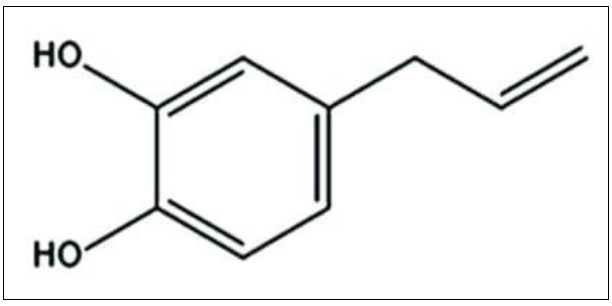

Fig 9

4. Hydroxychavicol

Hydroxychavicol is a significant phenolic compound recognized for its anticarcinogenic, antinitrosation, and antimutagenic properties. Additionally, it demonstrates substantial efficacy as an anti-inflammatory, antioxidant, antibacterial, anti-platelet, and anti-thrombotic agent, all while maintaining normal haemostatic function. The aqueous extract of betel leaf has been shown to possess beneficial bioactivities, particularly in terms of its antimutagenic and anticarcinogenic effects. Furthermore, the chloroform extract derived from the aqueous extract of *Piper betle* leaves exhibits notable inhibitory activity.

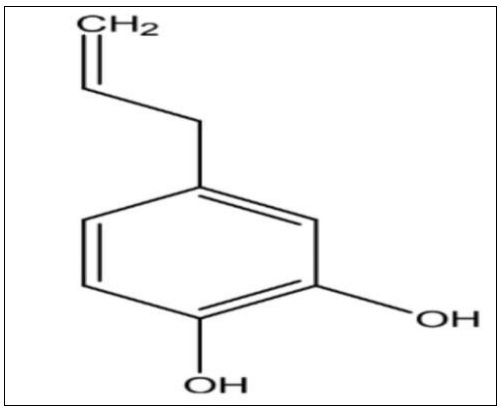

Fig 10

5. Quercetin

Quercetin is recognized as a significant dietary flavonoid that belongs to the flavanol category. It primarily exists in the form of glycosides, although various derivatives of quercetin have also been identified. The presence of different substituents can modify the biochemical activity and bioavailability of these compounds in comparison to the aglycone form. Research has demonstrated that quercetin possesses antiviral, antibacterial, anticarcinogenic, and anti-inflammatory properties. Its anticarcinogenic effects are attributed to its crucial role in promoting apoptosis in mutated cells, inhibiting DNA synthesis, suppressing the proliferation of cancerous cells, and modulating cellular signal transduction pathways. Evidence from animal studies indicates that the antioxidant properties of quercetin may offer protective benefits to the brain, heart, and other tissues affected by ischemia-reperfusion injury, as well as by toxic substances and other factors that contribute to oxidative stress [25].

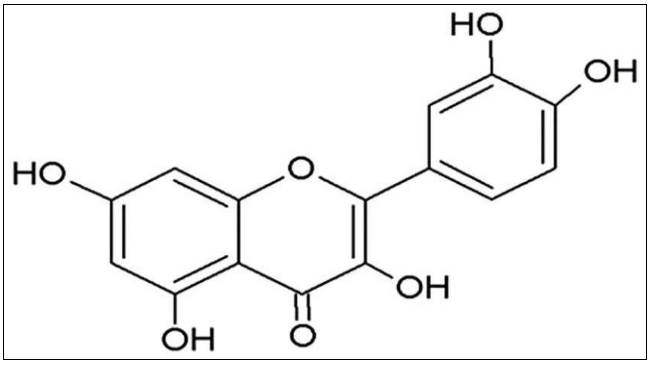

Fig 11

6. β-Caryophyllene

B-Caryophyllene is a prominent volatile compound found in significant quantities in various spices and food plants. This

compound has demonstrated strong anti-inflammatory effects. Additionally, β-caryophyllene is recognized as an FDA-approved food additive and is considered non-toxic, exhibiting neither genotoxic nor cytotoxic effects *in vivo*. Clinical research has validated its effectiveness in the treatment of endometriosis. The anti-inflammatory action of B-caryophyllene is mediated through its role as a potent, selective, and non-psychoactive full agonist of the CB2 receptor *in vivo*. [26]

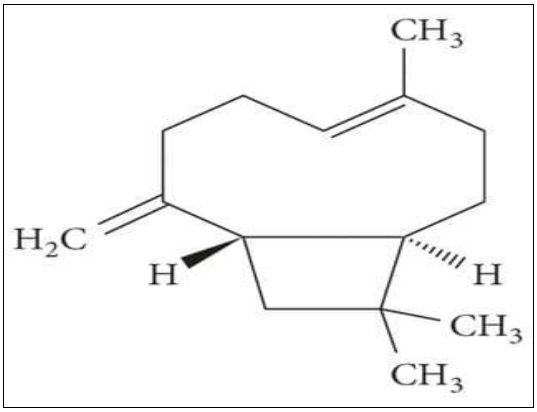

Fig 12

Traditional uses:

1. A paste made from *Piper betle* leaves combined with salt and hot water can be used to treat filariasis.
2. To address obesity, a combination of one *Piper betle* leaf and *Piper nigrum* is recommended for a duration of two months.
3. The juice of *Piper betle* mixed with honey is beneficial for treating coughs, shortness of breath, and indigestion in children.
4. Oil-coated *Piper betle* leaves are beneficial when applied to the breasts of nursing mothers, as they are believed to enhance milk production.
5. A topical application is advised for managing inflammatory conditions such as orchitis, arthritis, and mastitis.
6. For children and the elderly, warmed leaves mixed with mustard oil can be applied to the chest to alleviate cough and shortness of breath.
7. It helps to eliminate bad breath, body odor, and prevent dental decay.
8. It aids in preventing and treating vaginal discharge and alleviating vaginal itching.
9. It can help stop nasal bleeding.
10. The leaves are rich in vitamins, including thiamine, niacin, riboflavin, and carotene.
11. In India, the leaves are utilized for treating conditions such as eczema, lymphangitis, asthma, and rheumatism.
12. A paste made from the leaves is applied to cuts and wounds for healing.
13. The roots combined with black pepper are used to induce sterility in women.
14. The oil is effective for throat irritation, laryngeal issues, bronchial discomfort, and can be used for gargling and inhalation in cases of diphtheria.
15. The juice extracted from the leaves serves as a stomachic and febrifuge.

Modern medicinal uses:

1. Betel leaves are beneficial for treating pulmonary infections in both children and the elderly. When mixed with warmed mustard oil and applied to the chest, they can alleviate cough and ease breathing difficulties.
2. The limited use of betel leaves is effective in soothing sore throats. When the flattened fruit or berry is combined with honey, it can help reduce persistent coughs.
3. Betel leaves are advantageous for addressing nerve pain, fatigue, and weakness. An extract made from a few leaves mixed with honey serves as an excellent tonic.
4. When applied topically, betel leaves are effective in treating swellings, including arthritis and orchitis, which is the inflammation of the testes.
5. Betel leaves also exhibit analgesic and cooling effects.
6. They are a valuable remedy for boils; a leaf can be gently warmed until soft, then coated with castor oil and placed over the affected area.
7. A hot poultice made from the leaves or their extract, combined with a mild oil like refined coconut oil, can be applied to the lower back for relief from lumbago.
8. The leaves can aid in wound healing; the juice should be extracted and applied directly to the wounds.
9. Coating the leaves with oil and applying them to the breast during lactation is said to promote milk secretion.
10. According to the Unani system, these leaves possess a sharp taste and pleasant aroma, which can enhance appetite.
11. They are also utilized as a tonic for the brain, heart, and liver.
12. Additionally, betel leaves contribute to the maintenance of healthy teeth and skin.
13. They assist in addressing disorders related to physiological functions, skin diseases, and various eye conditions.
14. Betel leaves have diuretic properties; their juice, when mixed with milk or honey, can aid in promoting urination.
15. Betel leaves are recognized as an aphrodisiac, stimulating sexual desire.
16. The essential oils found in the leaves possess antibacterial, antiprotozoal, and antifungal properties, effectively inhibiting the growth of harmful bacteria.

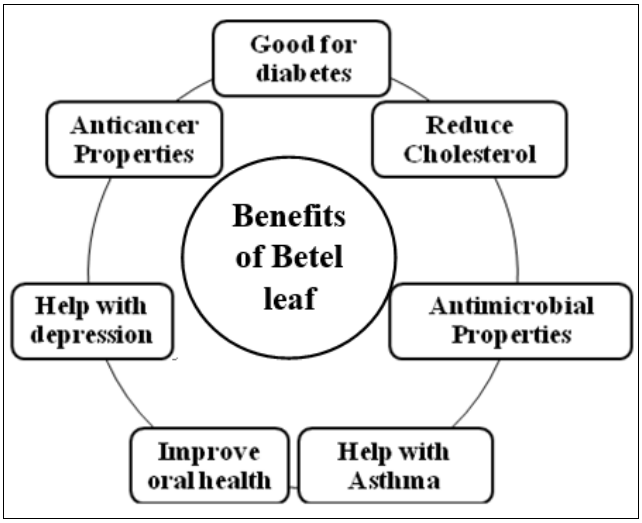

Fig 13: Benefits of Betel Leaf

Pharmacological activity:

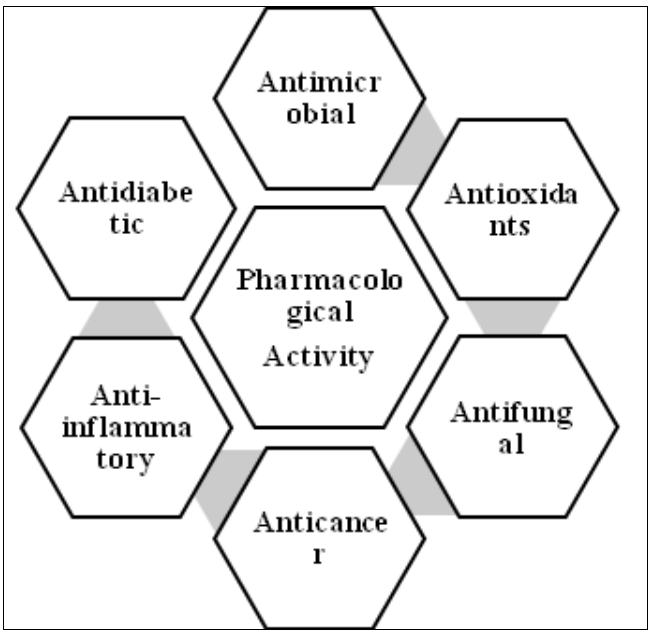

Fig 14: Pharmacological Activities

1. Antimicrobial Activity

The leaf exhibits notable antimicrobial properties against a wide range of microorganisms, including Streptococcus pyogenes, Staphylococcus aureus, Proteus vulgaris, Escherichia coli, and Pseudomonas aeruginosa. Additionally, the leaf extract demonstrates bactericidal effects against urinary tract pathogens such as Enterococcus faecalis, Citrobacter koseri, Citrobacter freundii, and Klebsiella pneumoniae. The bioactive compound believed to contribute to this antibacterial activity is sterol, which is present in significant amounts in betel leaf extracts. The mechanism of action is thought to involve the interaction of the sterol molecules with the bacterial cell wall and membrane, resulting in alterations to the cell wall's primary structure, ultimately leading to pore formation and degradation of bacterial components [30].

2. Antioxidant Activity

Ionizing radiation significantly impacts biological membranes through oxidative damage, which occurs as a chain reaction. Free radicals produced from the radiolytic breakdown of water can target the fatty acid chains within membrane lipids. A free radical with enough energy to remove an allylic hydrogen from the methylene carbon of polyunsaturated fatty acids can trigger the peroxidation process. In this context, polyphenolic compounds found in betel leaf extract, such as catechol and allylpyrocatechol, effectively inhibit the lipid peroxidation induced by radiation. This effectiveness is likely due to their capacity to scavenge free radicals involved in both the initiation and propagation phases. The extracts demonstrated a strong ability to reduce most Fe ions and exhibited significant reductive properties. Additionally, the extract displayed robust scavenging activity against hydroxyl radicals and superoxide anion radicals when compared to standards like ascorbic acid and BHT [33, 34].

3. Antifungal Activity

The bioactive compound hydroxychavicol, a polyphenol present in betel leaves, has demonstrated the ability to inhibit fungal growth and may serve as a treatment for fungal infections. Betel leaves can be applied topically as an antifungal agent or used as a mouthwash to address oral fungal infections. Nevertheless, further studies are required to explore the antifungal effects of betel leaves in human subjects, particularly in cases of suspected fungal infections [35, 36].

4. Anticancer Activity

Betel leaves may offer protective benefits against cancer due to their potential anti-cancer properties. Research indicates that extracts from betel leaves contain phenolic compounds that could inhibit the development of cancerous cells. While the combination of betel leaves with tobacco and betel nuts is associated with a heightened risk of oral cancer, it is important to recognize that betel leaves themselves are abundant in beneficial phenolic compounds that exhibit antioxidant, mutagenic, and anti-proliferative effects. Additionally, betel leaves are rich in phytochemicals known for their anti-cancer capabilities [40, 41].

5. Anti-inflammatory Activity

Betel leaves are rich in anti-inflammatory compounds that can greatly alleviate joint pain, a common symptom of various chronic conditions like rheumatoid arthritis and osteoporosis. When fresh betel leaves are heated and applied tightly to affected areas, they can notably diminish pain and inflammation, providing relief from arthritis symptoms. Research indicates that paan leaves possess natural anti-inflammatory effects, which can help mitigate inflammatory issues such as arthritis and asthma, often exacerbated by histamine [42, 43].

6. Anti-diabetic Activity

The aqueous extract of betel leaves demonstrates significant hypoglycaemic effects when evaluated in fasted normoglycaemic rats. In glucose tolerance tests, both extracts notably diminished the external glucose load. The leaf suspension significantly lowered blood glucose levels, glycosylated hemoglobin, and reduced the activities of liver glucose-6-phosphatase and fructose-1,6-bisphosphatase. In contrast, liver hexokinase levels increased in Streptozocin (STZ) diabetic rats compared to untreated diabetic rats. The extract's ability to reduce blood glucose levels in STZ-induced diabetic rats suggests that it may possess insulinomimetic properties [45, 46].

Home remedies of betel leaves:

Table 5: Home Remedies of betel leaves

Sr No.	Part Used	Name of Recipe	Photo	Use
1	Leaf	Betel leaf flavour cham cham		Digestive [13]
2	Leaf	Coconut gulkand ladoo		Anti-inflammatory [14]
3	Leaf	Paan leaf dosa		Food beverages [15]
4	Leaf	Betel leaf Sharbat		Soft drink variety [16]
5	Leaf	Betel leaf fried rice		Food beverages [17]
6	Leaf	Paan modak		Food beverages [18]
7	Leaf	Paan shots		Soft drink variety [19]

References

1. Rekha VPB, Kollipara M, Gupta BRS, Bharath Y, Pulicherla KK. A review on *Piper betle* L.: nature's promising medicinal reservoir. Am J Ethnomed,2014:7(5):276-289.
2. Azahar NI, Mokhtar NM, Arifin MA. *Piper betle*: a review on its bioactive compounds, pharmacological properties, and extraction process. In: IOP Conference Series: Materials Science and Engineering,2020 Dec:9(1):012044.
3. Pradhan D, Suri KA, Pradhan DK, Biswasroy P. Golden heart of the nature: *Piper betle* L. J Pharm Phytochem,2013:1(6):147-167.
4. Rekha VP, Kollipara M, Gupta BR, Bharath Y, Pulicherla KK. A review on *Piper betle* L.: nature's

promising medicinal reservoir. Am J Ethnomed,2014:1(5):276-289.
5. Verma N, Gautam BS. *Piper betle*: Deep insights into the pharmacognostic and pharmacological perspectives. Int J Med Pharm Sci,2023:13(2):4.
6. Depi S. Review of traditional use, phytochemical and pharmacological activity of *Piper betle* L. Galore Int J Health Sci Res,2020:5(3):59-66.
7. Rawat AKS, Tripathi RD, Khan AJ, Balasubrahmanyam VR. Essential oil components as markers for identification of *Piper betle* L. cultivars. Biochem Syst Ecol,1989:17:38-55.
8. Bhalerao S, Verma D. Phytochemistry, pharmacological profile and therapeutic uses of *Piper betle* Linn, an overview. RRJPP, 2013, 1(2).
9. Tripathi S, Verma NK, Singh DP, Chaudhary SK. *Piper betle*: Phytochemistry, traditional use & pharmacological activity– A review. IJPRD,2011:4(4):216-223.
10. Kamatou GP, Vermaak I, Viljoen AM. Eugenol – From the remote Maluku islands to the international market place: A review of a remarkable and versatile molecule. Molecules,2012:17:6953-6981.
11. Periyanayagam K, Jagadeesan M, Kavimani S, Vetriselvan TS, "Pharmacognostical and phyto-physicochemical profile of the leaves of *Piper betle* L. var Pachaikodi (Piperaceae)-valuable assessment of its quality." Asian Pac J Trop Biomed,2012:2(2):S506-S10.
12. Vasuki K, Senthamarai R, Kirubha TSV, Balasubramanian P, Selvadurai S. Pharmacognostical studies on leaf of *Piper betle*. Der Pharmacia Lett,2011:3(5):232-235.
13. Available from: http://muktisahay.blogspot.in.
14. Available from: https://cookpad.com/in/recipes/10841917-paan-leaf-dosa-betel-leaf-dosa.
15. Available from: https://cookpad.com/in/recipes/8254859-betel-leaf-sarhat.
16. Available from: https://cookpad.com/in/recipes/6648546-betel-leaf-fried-rice.
17. Available from: https://cookpad.com/in/recipes/10477041-betel-leaf-modak-paan-modak.
18. Available from: https://hebbarskitchen.com/refreshing-paan-shots-recipe.
19. Bhalerao S, Verma D. Phytochemistry, pharmacological profile and therapeutic uses of *Piper betle* Linn, an overview. RRJPP, 2013, 1(2).
20. Tripathi S, Verma NK, Singh DP, Chaudhary SK. *Piper betle*: Phytochemistry, traditional use & pharmacological activity– A review. IJPRD,2011:4(4):216-223.
21. Kamatou GP, Vermaak I, Viljoen AM. Eugenol – From the remote Maluku islands to the international market place: A review of a remarkable and versatile molecule. Molecules,2012:17:6953-6981.
22. Pradhan D, Biswasroy P, Suri KA. Various factors influencing the percentage content of hydroxychavicol in different extracts of *Piper betle* L. by altering the extraction parameters. IJATR, 2014, 4(2).
23. Sharma S, Khan IA. Evaluation of the antimicrobial, antioxidant, and anti-inflammatory activities of hydroxychavicol for its potential use as an oral care agent. Antimicrob Agents Chemother,2009:53(1):216-222.
24. Bhattacharya S, Banerjee D. Healing property of the *Piper betle* phenol, allylpyrocatechol against indomethacin-induced stomach ulceration and mechanism of action. World J Gastroenterol,2007:13(27):3705-3713.
25. Deshpande SM, Upadhyay RR, Singh RP. Chemical study of *Piper betle* leaves. Curr Sci,1970:39:372.
26. Gregory S, Kelly ND. Quercetin. Altern Med Rev,2011:16(2):172-194.
27. Małgorzata M. Quercetin and its derivatives: Chemical structure and bioactivity – A review. Pol J Food Nutr Sci,2008:58(4):407-413.
28. Harborne JB, Williams CA. Advances in flavonoid research since 1992. Phytochemistry,2000:55:481-504.
29. Abbas MA, Taha MO, Zihlif MA, Disi AM. β-Caryophyllene causes regression of endometrial implants in a rat model of endometriosis without affecting fertility. Eur J Pharmacol,2013:702:12-9. Gertsch J, Leonti M, Randuner J, Jian-Zhong C, Xie XQ, Karl-Heinz A, Meliha K, Zimmer A. Beta-caryophyllene is a dietary cannabinoid. Proc Natl Acad Sci,2008:105(26):9099-9104.
30. Pradhan D, Suri KA, Pradhan DK, Biswasroy P. Golden heart of the nature: *Piper betle* L. J Pharm Phytochem,2013:1(6):147-167.
31. Health Benefits. Available from: http://healthtips-sastha.blogspot.in/2013/01/health-benefits-of-betel-leaves.html. Accessed 22 Oct 2014.
32. Santhanam G, Nagarajan S. Wound healing activity of Curcuma aromatica and *Piper betle*. Fitoterapia,1990:61:458-459.
33. Santhanam G, Nagarajan S. Wound healing activity of Curcuma aromatica and *Piper betle*. Fitoterapia,1990:61:458-459.
34. Antonio AM, Brito ARMS. Oral anti-inflammatory activity of a hydro alcoholic extract and partitioned reactions of *Turnera ulmifolia* (Turneraceae). J Ethnopharmacol,1998:61:215-228.
35. Guha P. Betel leaf: The neglected green gold of India. J Hum Ecol,2006:19(2):87-93.
36. Sharma RN. Contribution of Ayurveda towards management of bronchial asthma. Sachitra Ayurveda,1991:44:349-352.
37. Hasan SMR, Jamila M, Muntazar MM. Analgesic and anti-inflammatory activity of hydromethanolic extract of Mikania scandens wild leaves. Am J Pharmacol Toxicol,2009:4:1-7.
38. Guha P. Paan theke kutir silpa sambhabana (in Bengali). Exploring betel leaves for cottage industry. In: Krishi, Khadya-o-Gramin Bikash Mela. A booklet published by the Agriculture and Food Engineering Department, IIT, Kharagpur, India, 1997, 15-19.
39. Satyavati GV, Raina MK, Sharma M. Medicinal plants of India. New Delhi: India Council of Medical Research, 1987, 1.
40. Patra AP, Mukherjee AK, Acharya L. Comparative study of RAPD and ISSR markers to assess the genetic diversity of betelvine (*Piper betle* L.) in Orissa. Am J Biochem Mol Biol,2011:1(2):200-211.

41. Kirtikar KR, Basu BD. Indian medicinal plants. Vol. III, 2nd ed. Latin Mohan BUSA Prakashan, Allahabad, 1993, 2131.
42. Patra AP, Mukherjee AK, Acharya L. Comparative study of RAPD and ISSR markers to assess the genetic diversity of betelvine (*Piper betle* L.) in Orissa. Am J Biochem Mol Biol,2011:1(2):200-211.
43. Gundala SR, Yang C, Mukkavilli R, Paranjpe R, Brahmbhatt M, Pannu V, *et al*. Hydroxychavicol, a betel leaf component, inhibits prostate cancer through ROS-driven DNA damage and apoptosis. Toxicol Appl Pharmacol,2014:280(1):86-96.
44. Gundala SR, Yang C, Mukkavilli R, Paranjpe R, Brahmbhatt M, Pannu V, *et al*. Hydroxychavicol, a betel leaf component, inhibits prostate cancer through ROS-driven DNA damage and apoptosis. Toxicol Appl Pharmacol,2014:280(1):86-96.
45. Yusoff Z, Mahmud Z, Saleh SH, Mohd Esa Y. Study on the chemical constituents of *Piper betle* L. in relation to their possible insect attractant property. Malays J Sci,2005:24(1):1-2.
46. Badrul AM, Fahima A, Nahida P, Rashna SP, Akter S, Chowdhury J, *et al*. Antioxidant, analgesic and anti-inflammatory activities of the methanolic extract of *Piper betle* leaves. Avicenna J Phytomed,2012:1-14.
47. Pradhan MR, Mohanty M, Mohapatra S, Sahoo S. Antifertility effect of alcoholic stalk extract of Piper betel Linn on female albino rats. IRJP, 2013, 4(1).
48. Young SC, Wang CJ, Lin JJ, Peng PL, Hsu JL, Chou FP. Protection effect of Piper betel leaf extract against carbon tetrachloride-induced liver fibrosis in rats. Arch Toxicol,2007:81(1):45-55.
49. Bhattacharya S, Subramanian M, Bauri A, Kamat JP. Radioprotecting property of the ethanolic extract of the Piper betel leaf. J Radiat Res,2005:46:165-171.
50. Kanjwani DG, Marathe TP, Chiplunkar SV, Sathaye SS. Evaluation of immunomodulatory activity of methanolic extract of Piper betel. Scand J Immunol,2008:67:589-593.
51. Vinayak M, Ruckmani A, Chandrashekar K, Gopala RK, Madhavi E, Swati B, *et al*. Antidepressant activity of ethanolic extract of *Piper betle* leaves in mice. Curr Res Neurosci,2012:2:11-6.