IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Invitro Study Of Anti -Oxidant, Anti- Inflammatory, Anti-Microbial Activities Of Piper Betel (Betel Vine)

Yasaswini Yedlapalli [1] , Vinay sai Vella[2] , Bhaskararaju Vatchavai [3] ,Dhabal Satapathy [4], Srinivasu Matta [5]

***Students,B.pharmacy*[1,2],Principal[3],Associate professor[4],Professor[5]**

Department of pharmacology[1]

Sri Vasavi Institute of Pharmaceutical sciences, Pedatadepalli,Tadepalligudem,Andhra Pradesh ,India

Abstract: Piper betel is the scientific name for betel leaf, normally called as paan leaf. It belongs to the genus Piper. Piper betle L., a member of the Piperaceae family, is utilized in Asian nations as an age-old herbal treatment over a number of illnesses.The leaves contain a variety of compounds that contribute to their flavor and aroma, including alkaloids, flavonoids, tannins, and saponins. A number of investigations indicate significantchemical constituents in Piper betel, including chavibetol, the chemical chavibetol acetate, caryophyllene, allylpyrocatechol diacetate, campene, chavibetol methyl ether, eugenol, a-Pinene, f-Pinene, uLimonene, safrole, 1-8-cineol, and allylpyrocatecholmonoacetate. Paan, a concoction of betel leaf, slaked lime, and areca nut, is a common culinary usage for betel leaves. Because of its large level of phenolic compounds and other natural compounds like flavonoids, tannins, and catechols, piper betel (betel leaf) has tremendous antioxidant capacity and considerable DPPH radical-fighting action. The alcohol extract of the betel plant was screened for antibacterial capacity using the disc diffusion process. Betel leaf juice and essential oil (EO) Being demonstrated to include a variety of bioactive components, particularly terpenes and polyphenols. Numerous medicinal properties, such as antibacterial, antioxidant, anti-inflammatory, analgesic, anti-diabetic, anticancer, and gastroprotective qualities, are displayed by piper betel.

Index terms: Betel leaf , Medicinal properties, anti microbial, anti oxidant, anti inflammatory, Traditional use.

I. INTRODUCTION

The betel brace is an immutable, everlasting creeper with a shiny, heart-shaped, white catkin. The majority of the world's tropical climates are home to the Piper rubric (Piperaceae). India, Sri Lanka, Malaysia, Indonesia, the Philippines, islands, and East Africa are all places where piper betel is grown. It has a crisp flavor with a light, unassuming, delicious essential oil painting. There are more than 90 varieties of betel vines worldwide, with roughly 45 of them found in India and 30 in West Bengal. It is produced in tropical and subtropical regions for its perpetual branches, which are used as a gnawing tool and in pooja and prayers of

faith.[1]Betel vine is the common name for betel splint.In the harshest nations, such as India, it is commonly utilized for chewing activities to prevent foul breath, improve adhesives, and stimulate the digestive fire. Betel leaves are used as clang mouthwash in India and to cure vaginal douching in Indonesia. In Sri Lanka, cutaneous problems cured with betel splint juice. Because of their tart flavor, betel leaves are often cooked to be utilized as a coughing remedy .[2] According to a 2019 study on the usage of betel splint in colored ailments, betel splint (Piper betle) has numerous advantages in the medical area because to its healing properties. It is the most intriguing botanic that can be sold.

Significant chemical components such as safrole, 1-8-cineol were also identified. Its anti-fungal, anti-itching, cancer-fighting, immunity-modulating, anti-halitosis, anti-diabetic, gastro-defensive, anti-allergic, anti-ovulation, antibacterial, anti-larval, repairs cracks, and anti-cutaneous properties are triggered by these factors .[3] People typically utilize green betel leaves (Piper betle L.) to aid with various ailments including itching, coughing, and toothaches.[4] The natural substances such as phenols, chavicol, flavonoids, alkaloids, saponins, tannins, and steroids found in green betel leaves (Piper betle L.) have implicit antibacterial abilities .[5]

Archaeological evidence suggests that betel leaves and areca nuts have been consumed since very old times. When these two distinct goad compounds were initially combined is unknown. While areca nut was thought to be an aphrodisiac, betel leaves are used as a goad, an antibiotic, and a breath freshener .[6] Piper betel is an imperishable evergreen vine that prefers tropical shade. It might reach a height of 10 to 15 feet. A warm, humid atmosphere is ideal for the Piper betel splint. The leaves are brilliant green, simple, alternating, ovate, cordate, acuminate, or acute.

The male harpoons in this facility are thick and cylindrical, whereas the female harpoons are swinging pendulums. The roots produced by each knot aid in securing the factory to the host tree. The color of pepper betel varies from ordinary green to dark green with a glossy upper face, and it has a unique and pleasant aroma. The betel leaves contain a range of flavors, from sweet to spicy, because of the existence of fundamental chemicals. [7,8]

Figure 1 :Betel plant

II. TRADITIONAL SIGNIFICANCE:

Betel leaves, also known as Piper betle, have been an integral part of traditional drug and artistic rituals for centuries. deified in Ayurveda and other ancient mending systems, these heart- shaped leaves offer multitudinous health benefits that ultramodern wisdom is beginning to validate.The betel splint, or paan, holds deep traditional significance in India and Southeast Asia, emblematizing hospitality, respect, fellowship, and substance. It's used in religious observances and artistic rituals like marriages and offered to guests as a gesture of welcome and goodwill. In Hinduism, the splint is considered sacred, a seat for the goddess Lakshmi, and a symbol of chastity, newness, and new onset.[9]

III. BOTANICAL CLASSIFICATION:

- Kingdom:Plantae
- Division:Spermatophyta
- Sub-division:Angiosperms
- Class: Magnoliopsida
- Sub-class: Magnolilidae
- Order: Piperales
- Family: Piperaceae
- Genus: piper

- Species: betel
-

IV. PLANT DESCRIPTION:

The climbing geste of betel splint(Piper betle L.) is exceptional under ideal growing conditions, it can reach noteworthy heights of over to 4 measures. In order to grease its upward growth, the factory is generally supported by structures like casinos or rustic poles. A identifying specific of the betel vine are its leaves, which are easily identifiable due to their unique heart shape and deep green colour.Piper betel or the betel vine, is a imperishable, evergreen, woody climbing factory belongs to Asia, called for its lustrous, heart- shaped leaves with a pungent, sweet, and kindly bitter taste. The factory features stout stems with accidental roots for climbing, and it produces small, invisible white catkin- suchlike flowers and fleshy, round fruits. The lustrous leaves are its primary point, cultivated extensively for traditional chewing practices and for their colorful medicinal uses in Asian societies.[10] Small, greenish-white flowers arranged in harpoons make up the betel vine's rather invisible blossoming. The flowers contribute to the factory's reproductive cycle indeed though they've little aesthetic value. The bitsy, spherical berries that the betel vine produces are pivotal to the factory's life cycle indeed though they are n't generally used in traditional styles. Betel splint husbandry is a technical agrarian system. It grows stylish on rich, well- drained soil that has a pH between 6.0 and 6.5. For optimum growth, enough watering and shade from violent sun are essential. slices are generally used to propagate shops; they're first planted in a nursery and also moved to the field.[11] Culturally, the betel splint holds deep emblematic value. It's used in Hindu rituals, marriages, and carnivals, frequently as an immolation to divinities or as a commemorative of respect and hospitality. In social traditions, biting betel splint with areca nut, lime, and occasionally tobacco(known as paan) is a common practice believed to prop digestion and refreshen the breath.

Figure 2 :Betel creeper

Figure 3:Betel leaf

V. AYURVEDIC SIGNIFICANCE:

Piper betle, sometimes referred to as "Tambool" in Ayurvedic cultures, is a prominent herbal remedy that is used for huge number of health benefits, including the treatment of skin problems, constipation, coughing, obesity, and parasite infections. Its caloric worth, which is high in vitamins and minerals, is also acknowledged; some customs even liken the nutritious value of a few leaves to that of milk. To increase their effectiveness in treating a variety of illnesses, betel leaf medicines are joined with other medicinal herbs. Piper betel, also called as Tambool, Nagvelleri, and Nagani in Sanskrit, is a Vedic plant that was utilized to cure a variety of illnesses. Its Vedic title is Saptasira. From Vatsyayana's Kamasutra and Panchatantra to Kalhan's Rajatarngni—possibly the final known ancient Sanskrit work of significant significance—there are references to Tambool. [12]

Guna (Quality): Laghu, Ruksha, Tikshan

Rasa (Taste): Tikt

Vipak(Metabolism):Katu

Virya(Potency):Ushan

Prabhav(Impact):Hridy

VI. CHEMICAL CONSTITUENTS:

The splint contains Water(85- 90), Proteins(3- 3.5), Carbohydrates(0.5- 6.1), Minerals(2.3- 3.3), Fat(0.4- 1), Fibre(2.3), Essential oil painting(0.08- 0.2), Tannin(0.1- 1.3), Alkaloid. Additionally, it's full of many vitamins, such as nicotinic acid (0.63–0.89 mg) and the antioxidant vitamin C (0.005–0.01), Vitamin-A(1.9- 2.9 mg/ 100gms), Thiamine(10- 70µg/ 100gms), Riboflavin(1.9- 30µg/ 100gms) along with also consists of minerals similar as Calcium(0.2- 0.5), Iron(0.005- 0.007), Iodine(3.4 µg/ 100gms), Phosphorus(0.05- 0.6), Potassium(1.1- 4.6. Leaves contain bitter composites that are about(0.7- 2.6). The leaves contain specific strong pungent sweet flavour is due to phenol and terpene likebodies.[13] Numerous physiologically active composites found in piper betel leaf vary depending on the factory, season, and climate. Safrole found in the splint, stalk, stem, root, and ß-phellandrene found in the berries make up the chemical compositions of essential oil paintings.The presence of hydroxychavicol acetate, allylpyrocatechol piperbetol composites are also set up in Piper betel.[14] Betel splint(Piper betle L.) is famed for its complex chemical profile, which contributes to its different natural conditioning. The splint contains a variety of bioactive composites, including essential canvases, alkaloids, flavonoids, and phenolic composites.

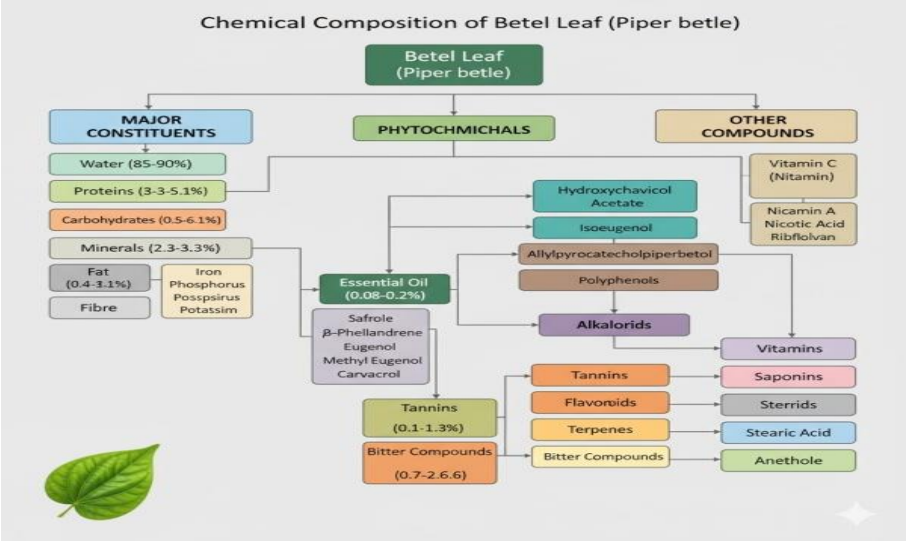


Figure 4:Chemical constituents

Essential Oils:

The essential oil composition of betel leaf represents a complex mixture of compounds

•Eugenol and chavibetol derivatives constitute 30-55% of the total oil content

•Safrole appears predominantly in certain chemotypes

•Terpenes including caryophyllene and germacene D form significant components

•Hydroxychavicol and allylpyrocatechol contribute to antimicrobial properties [15, 16]

Alkaloids:

Numerous alkaloids, including piperine, which has energizing and intestinal qualities, are found in betel leaf. In addition to giving the leaf its strong flavor, piperine also looked at with regard to itscapacity to enhance the bioavailability of other substances. [17]

Flavonoids:

The flavonoid content in betel leaf includes compounds like quercetin and kaempferol. The leaf's curative value is enhanced by these flavonoids' well-known anti-inflammatory and protective effects .[18]

Phenolic compounds:

Phenolic constituents in betel leaf demonstrate significant antioxidant properties:

•Polyphenols including catechins and tannins

•Flavonoids such as quercetin derivatives

•Phenylpropanoids and their derivatives

•Hydroxychavicol acetate and related compounds [19, 20]

Table-1 : Phytoconstituents in piper betel

Category	Major Constituents	Pharmacological Relevance
Phenols	Chavicol, Eugenol, Hydroxy-chavicol	Antioxidant, antimicrobial, anti-inflammatory
Terpenes	Caryophyllene, β-pinene	Anti-inflammatory, analgesic
Alkaloids	Arakene, Piperine	CNS activity, antimicrobial
Others	Tannins, flavonoids, saponins	Antioxidant, anti-ulcer

Other compounds:

Saponins and tannins elements are looked into astheir astringent and antibacterial qualities ,are other substances present in betel leaf.These substances contribute to the therapeutic applications such as the treatment of wounds and infections.[21]

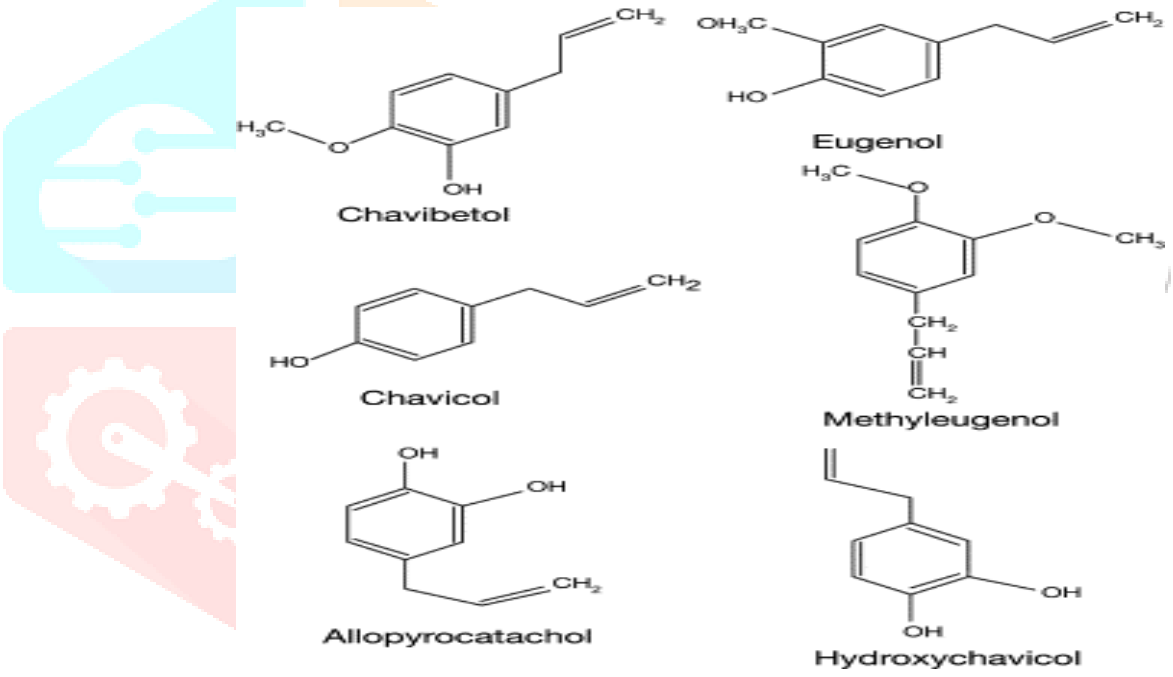


Figure 5:Structures of chemical constituents

VII. CULTIVATION

Certain climate variables are necessary for the best growth of betel vine civilization. Tropical areas with degrees between 15 and 40 °C and sporadic precipitation of 1500 to 2500 mm are ideal for the facility's growth .[22]Optimal soil conditions include well- draining, rich soil with pH situations between 5.6 and 8.2. Shade plays a pivotal part in civilization, with shops generally taking 40- 60 shade for proper development.[23]

Since the betel factory is a creeper, it needs a compatible tree or a long pole for support. Paan civilization is a specialised type of husbandry. High ground and especially rich soil are stylish for betel. doused, saline and alkali soils are infelicitous for its civilization. A typical ranch will be fended with bamboo sticks and coconut leaves, with the cocoon of paddy laid over it. The soil is dug well and laid out into furrows of 10-15m length, 75 cm range and 75 cm depth. oil painting galettes, cow soil, rotten cropland ordure and leaves are completely incorporated with the clod of the furrows along with wood ash. The slices of the betel creeper are planted after proper dressing in the month of June and July — at the morning of the thun-

derstorm season. The shops are neatly arranged in resemblant rows about half a metre piecemeal, and the saplings entwined around upright sticks of split bamboo and doormats.

Proper shade and water facility are important for successful civilization of this crop. The shops are regularly doused in the hot months. The leaves of the factory come ready for plucking after one time of planting and the creeper remains productive for several times from the date of planting. Betel needs constantly wettish soil, but there should n't be inordinate humidity. Hence frequent light irrigation is needed, but only to the extent that the standing water does n't remain for further than half an hour in the bed.However, drainage should be arranged incontinently, If water logging due to heavy rains or redundant irrigation occurs. The stylish time for irrigation is in the morning or evening. Dried leaves and wood ash are applied to the furrows at fortnightly intervals and cow soil slurry sprinkled. operation of different kinds of leaves at yearly intervals has been set up to be profitable for the growth of the betel.[24]

Harvesting starts 6 – 8 months after planting, and healthy mature leaves are plucked precisely without injuring the vines. To preserve freshness during storage and transportation, leaves are sorted, whisked, and placed in containers wrapped using banana fibers.Each factory continues to produce leaves for 3 – 5 times under good operation, yielding around 50,000 – 70,000 leaves per 1,000 vines annually. Major betel splint kinds similar as Desawari, Bangla, Sanchi, and Kapoori are cultivated in countries like West Bengal, Odisha, Tamil Nadu, Andhra Pradesh, and Karnataka. The betel splint not only has significant marketable value but also holds artistic andmedicinalsignificance, being used as a digestive aid, antiseptic, and symbol of hospita ltraditions.

Figure 7:Betel cultivation

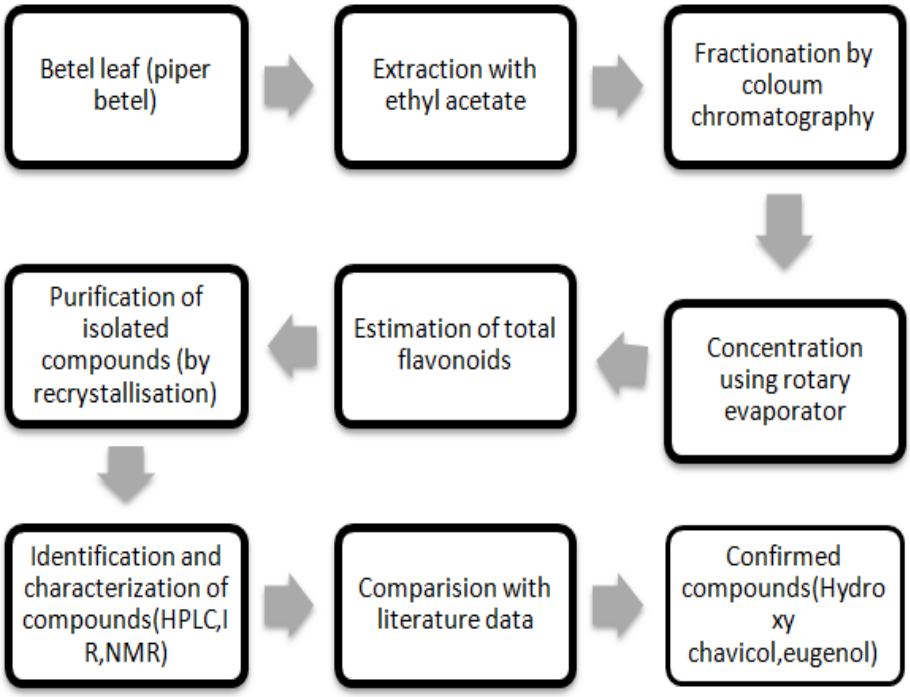
VIII. EXTRACTION OF PHYTOCHEMICALS:

The betel splint was created using a variety of detergents, videlicet ether (40–60 oC), chloroform, ethanol, and water as the solvent to obtain phytosterol. All extracts, with the except the water extract, are the outcome of this process. Alkaloids were not established by hydrocarbon ether extracts, however carbohydrates, liquid tannins, and phenols were established by ethanol and water extracts.Only the water excerpt contained essential oil painting, while the ethanol excerpt contained flavonoids. The extract from Piper betle splint is found to contain phytosterols, alkaloids, water, tannins, phenols, flavonoids, and essential canvases. Carvacrol, eugenol, chavicol, allylkatekol, cineol, estragol, caryophyllene, cardinene, pcymenedan, and eugenol methylether are among the essential canvases found in the leaves. [25]

Finding the essential canvases from the fresh varieties of Piper betle and Bangla desi. For three hours, traditional Clevenger-style water distillation was used to insulate deswari leaves. Independently, the essential canvases were attained at 0.12 and 0.15 (v/w). The oil painting is kept in a sterile tube at 4 °C in the refrigerator when Unsaturated sodium is used to dry them. sulfate. The Perkin-Elmer GC 8500, which has a honey ionization sensor, was used to anatomize the essential canvases using BP-1 (polydimethylsiloxane, 50 mx 0.25 mm). The findings of GC and GC-MS's analysis of the key canvases connected 25 and 35 factors, respectively. [26]

Column chromatography was used to fractionate an ethylacetate extract from betel splint (Piper betle). Additionally, a rotary evaporator is used to concentrate the collected bit. The colorimetric system of aluminum chloride is utilized to measure the total flavonoids, and a UV-Visible Spectrophotometer is found at absorbance at 420 nm. Recrystallization further purifies the insulated element. HPTLC, 1 H-NMR and IR, and the composites' diapason were used to link and validate the composites. Based on spectroscopic analysis, the composites were described and contrasted with data from the literature. The presence of

Hydroxy Chavicol, Chavibetol, and Eugenol as composites in the splint excerpts of various betel splint excerpts was discovered by spectral detection of the insulated bit. [27]



IX. PHARMACOLOGICAL ACTIVITIES:

Betel leaf contains many compounds with potent anti-inflammatory, antioxidant, antibacterial, and anti-cancer properties.

➢ *ANTIOXIDANT*

The ethanol excerpt of betel splint is antioxidant with a mean IC50(µg/ ml) for DPPH ascorbic acid revolutionary was set up to be 3.128. The mean IC50(µg/ ml) of the ethanol excerpt was set up to be 9,362. The ethanolic excerpt of betel vine L. leaves showed a moderate effect on DPPH radical.[28]

The free revolutionary- scavenging assay of different excerpts was measured in terms of hydrogen giving or radical- scavenging capability using the stable radical DPPH described by Blois system.Stock results of excerpts(0.001 g/ ml) were prepared in DMSO. Various concentrations of test findings (20, 40, 60, 80, and 100 µg) were prepared from stock and built up to 2 ml with methanol. One milliliter of the DPPH (0.1 mmol) in methanol result has been included to each of the test results listed below. The absorbance of each test result was measured at 517 nm after the admixture was thoroughly agitated and incubated for 30 minutes. Each test was performed in triplicate and reported as average ± standard deviation (SD). DMSO served as the antagonistic control, and ascorbic acid (AA) served as the standard or positive control. The following formula was used to determine the DPPH revolutionary's scavenging capacity.

% inhibition=Absorbance(control) --Absorbance (sample) 100÷ Absorbance(control).[29]

➢ *ANTI-INFLAMMATORY*

Soxhlet apparatus was used to extrude the betel leaf hydroalcoholic extract (HEPBL), and phytochemical analysis is performed. Swiss albino mice measuring 22–25 g of both sexes and Wistar rats weighing 150–220 grams (aged 8–12 weeks) were used as test subjects. The analgesic efficacy was investigated using tail-flick and acetic acid induction techniques, while the anti-inflammatory action was investigated using cotton pellet granuloma models and carrageenan-induced paw edema. At dosages of 50 mg/kg, 100 mg/kg, and 200 mg/kg, HEPBL had strong analgesic and anti-inflammatory effects. Additionally, the subtherapeutic impact of the usual analgesic dose is strengthened by the subtherapeutic dose of HEPBL at 50 mg/kg. The analgesic and anti-inflammatory qualities of P. betle are caused by phytochemicals like flavonoids, tannins, phenols, and glycosides. [30]

➢ *ANTI-MICROBIAL*

The research found that the ethanol derivative of betel leaves was more efficient than water-based preparation with reduced inhibition zones. The extract of ethanol at 50–100 µg/mL had the largest inhibition zones (8.9–11.0 mm) on E. coli, but P. aeruginosa displayed modest inhibition (<7.2 mm). On the other hand, the water extract at 50 µg/mL did not significantly reduce the proliferation of bacteria. [31] A different study using the agar well thickening system found that an alcohol infusion of betel leaves had narrower inhibitory zones on Gram-negative than Gram-positive bacteria. [32] A study demonstrated the antibacterial qualities of five distinct types of BLE with differing levels of wiping efficacy. Of the six bacteria examined, S. aureus was the most susceptible, and the acetone and ethyl acetate extracts shown the most remarkable effort. Furthermore, BLEs' antimicrobial abilities were associated with their phenol and flavonoid content. [33]

X. OTHER ACTIVITIES

➢ *ANTI-CANCER*

Numerous human disorders, including cancer and tumors, have been linked to chronic inflammation, according to laboratory and scientific studies. [34, 35, 36] Oral carcinoma comprised one of the top 10 most common malignancies, with almost 90% of cases originating from South East Asia, where tobacco chewing and smoking are common. In one of the earliest investigations, Rao (1984) discovered that topical application of betel leaf extract inhibited B(a) P-induced oral carcinogenesis in hamsters. [37] In breast tumor cell lines, Widowati et al. (2013) investigated the chemotherapeutic and free oxygen radical detoxifying capabilities of extracts from vinca rosea, dandelion pentandra, Piper betle, and Curcuma long mangga. [38, 39]

➢ WOUND HEALING

Nilugal et al. (2014) evaluated the crack-mending ability of betle vine leaves and stem extract in experimental wistar rats. Damage was described as a disruption of normal anatomical structure and function. A number of biological and biochemical processes were involved in the incredibly intricate, multifactor chain of events that led to crack repair. The usage of an ointment expression containing Piper betle leaves and stem excerpt, which was emphasized by the entire consistency content of the crack region by a systematized epidermis, expedited crack mending and formation, based on the findings. The male albino rats incorporated with ointment expression including ten betle vine leaves and stems showed notable results in relation to the affected group and control group. [40]

➢ *RADIOPROTECTIVE*

Human systems may be negatively impacted by radon exposure, such as premature cell death and an increased risk of chronic illnesses. The curative properties of Piper betel Leaf leaves' alcoholic extract have recently been studied as an affordable replacement for artificial radio shields, which are thought to be toxic. The capacity of the preparation in reducing lipid damage caused by g-rays DNA damage and cancer stress in the liver of rats Mitochondria were evaluate and available to ascertain its radio defense action's methodology. It suggests that the herbs are a cheap, promising, and easily accessible natural radioprotectant for the general public.[41]

➢ *ANTIHYPERGLYCEMIC*

Because P. betle is eaten as a snack post meals, this research assessed its impact on the utilization of glucose. The findings indicated that P. betle use has a positive impact on the utilization of glucose. Oxidizing in STZ Insulin Rats: Research revealed that P betle leaf slurry has notable oxidizing benefits in STZ obese rats.[42]

➢ *ANTIDEPRESSANT*

The research evaluated the antidepressant effects of P. betle leaf extracts containing ethanol using Swiss albino mice. The duration of rigidity decreased, suggesting a significant depressive impact. The 100 mg plant extract concentration had a greater effect than imipramine. [43]

XI. ADVERSE EFFECTS

- *CARCINOGENICITY*

The use of betel leaves and the possibility for malignancy have complicated ties, according to study results. There is little chance of cancer when betel leaf is used on its own. But when combined with nicotine and the almond nut, it greatly raises the chances of tumors in the mouth. Personal vulnerability to negative consequences may be influenced by family history and surrounding circumstances.[44,45]

- *REPRODUCTIVE PROBLEMS*

Consequences on fertility have not been thoroughly studied. Owing to the lack of protective information, pregnant women ought to be cautious. Research on rats indicates possible effects on the growth of the baby, therefore both gestation and breastfeeding should be carefully considered.[46]

- *ACUTE EFFECTS*

When unprocessed betel leaf is consumed directly, those with allergies may react right away. Typical symptoms are discomfort and inflammation of the oral cavity and throat. The amount ingested determines the severity, which fluctuates from person to person. Although constant pain can require therapeutic measures, such symptoms usually go away on their own.[47]

CONCLUSION

The review claims that betel leaf has a number of beneficial benefits on human health. The leaves also have antibacterial qualities and can prevent the growth of food-borne pathogens. The sensory profile of both stored leaves and food products may be analyzed to ascertain consumer acceptability with the goal to extend the shelf life of betel leaves and create food products produced from them. Drying has a negative effect on color, chlorophyll concentration, etc., as the analysis has shown. But the leaves also have a great mineral and vitamin profile. As a result, the dried leaves can be added to food items to increase their vitamin and mineral value. [48]

ACKNOWLEDGEMENT

I want to express my gratitude to everyone who assisted me in completing my investigation on the phytocostituents and pharmacological activities of piper betel. Their knowledge and help are invaluable.I am appreciative of the resources provided by the library and my instructors , also the databases and research articles that improved my understanding of piper betel medical uses.Finally I would like to thank my friends for their encouragement.

REFERENCES

1. Ullah F, Ali S, Siraj M, Akhtar MS, Zaman W. Plant Microbiomes Alleviate Abiotic Stress-Associated Damage in Crops and Enhance Climate-Resilient Agriculture. Plants. 2025 Jun 19;14(12):1890.
2. Nayaka NM, Sasadara MM, Sanjaya DA, Yuda PE, Dewi NL, Cahyaningsih E, Hartati R. Piper betle (L): Recent review of antibacterial and antifungal properties, safety profiles, and commercial applications. Molecules. 2021 Apr 16;26(8):2321.
3. Shah SK, Garg G, Jhade D, Patel N. Piper betle: phytochemical, pharmacological and nutritional value in health management. Int J Pharm Sci Rev Res. 2016 May;38(2):181-9..
4. Hulu LC, Fau A, Sarumaha M. Pemanfaatan daun sirih hijau (Piper Betle L) sebagai obat tradisional di Kecamatan Lahusa. TUNAS: Jurnal Pendidikan Biologi. 2022 Dec 24;3(1):46-57.
5. Sadiah HH, Cahyadi AI, Windria S. Kajian Daun Sirih Hijau (Piper betle L) Sebagai Antibakteri. Jurnal Sain Veteriner. 2022;40(2):128-38.
6. Bhide SV, Shivapurkar NM, Gothoskar SV, Ranadive KJ. Carcinogenicity of betel quid ingredients: feeding mice with aqueous extract and the polyphenol fraction of betel nut. British journal of cancer. 1979 Dec;40(6):922-6.

7. Bhalerao SA, Verma DR, Gavankar RV, Teli NC, Rane YY, Didwana VS, Trikannad A. Phytochemistry, pharmacological profile and therapeutic uses of Piper betle linn.–an overview. Journal of Pharmacognosy and Phytochemistry. 2013 Oct;1(2):10-9.

8. Lakshmi B.S. and Naidu K.C. Comparative morphoanatomy of Piper betel L. cultivars in India. Annals of Biological Research. 2010; 1(2): 128-134.

9. Ahuja SC, Ahuja U. Betel leaf and betel nut in India: History and uses. Asian Agrihist. 2011 Jan 1;15(1):13-35.

10. Rekha VP, Pulicherla KK. A review on Piper betle L.: nature's promising medicinal reservoir. American Journal of Ethnomedicine. 2014.

11. Nouri L, Nafchi AM, Karim AA. Mechanical and sensory evaluation of noodles incorporated with betel leaf extract. International Journal of Food Engineering. 2015 Apr 1;11(2):221-7.

12. Bissa S, Songara D, Bohra A. Traditions in oral hygiene: chewing of betel (Piper betle L.) leaves. Current Science. 2007 Jan 10;92(1):26-8.

13. Bajpai V, Sharma D, Kumar B, Madhusudanan KP. Profiling of Piper betle Linn. cultivars by direct analysis in real time mass spectrometric technique. Biomedical Chromatography. 2010 Dec;24(12):1283-6.

14. Periyanayagam K, Jagadeesan M., Kavimani S and Vetriselvan T. Pharmacognostical and phytophysicochemical profile of the leaves of Piper betel L. var pachaikodi (Piperaceae) valuable assessment of its quality. Asian Pacific Journal of Tropical Biomedicine. 2012; 2(2): S506- S510.

15. Tarmale VA, Wankhede S, Sen AK, Uppalwar SV. Pharmacological Properties, and Traditional Applications of Betel Leaf (Piper betle L.). Journal of Pharma Insights and Research. 2024 Dec 5;2(6):131-41

16. . Rahman MM, Uddin MJ, Reza AS, Tareq AM, Emran TB, Simal-Gandara J. Ethnomedicinal value of antidiabetic plants in Bangladesh: A comprehensive review. Plants 2021, 10, 729. s Note: MDPI stays neutral with regard to jurisdictional claims in published. 2021.

17. Tiwari P, Kumar B, Kaur G, Kaur H. Phytochemical screening and extraction. Int Pharm Sci. 2011;1:98-106.

18. Savithramma N, Rao ML, Suhrulatha D. Screening of medicinal plants for secondary metabolites. Middle East J Sci Res. 2011;8:579-584.

19. Lakshmi B, Naidu KC. Comparative morphoanatomy of Piper betle L. cultivars in India. Mol Biol Rep. 2020;47(2):1519-1526.

20. Syahidah A, Saad CR, Hassan MD. Therapeutic potential of Piper betle in human health: A comprehensive review. Molecules. 2017;22(10):1706.

21. Al-Adhroey AH, Nor ZM, Al-Mekhlafi HM, Amran AA, Mahmud R. Antimalarial activity of methanolic leaf extract of Piper betle L. Molecules. 2010 Dec 28;16(1):107-18.

22. Kumar N, Misra P, Dube A, Bhattacharya S, Dikshit M, Ranade S. Piper betle Linn. a maligned Pan-Asiatic plant with an array of pharmacological activities and prospects for drug discovery. Current science. 2010 Oct 10:922-32.

23. Salehi B, Zakaria ZA, Gyawali R, Ibrahim SA, Rajkovic J, Shinwari ZK, Khan T, Sharifi-Rad J, Ozleyen A, Turkdonmez E, Valussi M. Piper species: A comprehensive review on their phytochemistry, biological activities and applications. Molecules. 2019 Apr 7;24(7):1364.

24. Palaniappan G, Sengottiyan A, Saravanan T. Betel leaf: the green gold of India. *Facts For You*. 2012 Apr;21-24.

25. Saini SA, Dhiman AN, Nanda SA. Pharmacognostical and phytochemical studies of Piper betle Linn. leaf. Int J Pharm Pharm Sci. 2016 Jan;8(5):222-6.

26. Saxena M, Khare NK, Saxena P, Syamsundar KV, Srivastava SK. Antimicrobial activity and chemical composition of leaf oil in two varieties of Piper betle from northern plains of India. Journal of Scientific and Industrial Research. 2014 Feb 1;73(2):95-9.

27. Patel N, Mohan JS. Isolation and characterization of potential bioactive compounds from Piper betle varieties Banarasi and Bengali leaf extract. Int J Herb Med. 2017;5(5):182-91.

28. Perumal PA, Saravanabhavan KA. Antidiabetic and antioxidant activities of ethanolic extract of Piper betle L. leaves in catfish, Clarias gariepinus. Asian J Pharm Clin Res. 2018;11(3):194-8.

29. Blois MS. Antioxidant determinations by the use of a stable free radical. Nature. 1958 Apr 26;181(4617):1199-200..

30. Reddy PS, Gupta RK, Reddy SM. Analgesic and anti-inflammatory activity of hydroalcoholic extract of Piper betle leaves in experimental animals. Int. J. Basic Clin. Pharmacol. 2016 May;5(3):979-85..

31. Kaveti, B.; Tan, L.; Sarnnia; Kuan, T.S.; Baig, M. Antibacterial Activity Of Piper Betel Leaves. *Int. J. Pharm. Teach. Pract.* **2011**, *2*, 129–132. [Google Scholar]

32. Teanpaisan R, Kawsud P, Pahumunto N, Puripattanavong J. Screening for antibacterial and antibiofilm activity in Thai medicinal plant extracts against oral microorganisms. Journal of traditional and complementary medicine. 2017 Apr 1;7(2):172-7.

33. Taukoorah U, Lall N, Mahomoodally F. Piper betle L.(betel quid) shows bacteriostatic, additive, and synergistic antimicrobial action when combined with conventional antibiotics. South African Journal of Botany. 2016 Jul 1;105:133-40.

34. Chen CL, Chi CW, Chang KW, Liu TY. Safrole-like DNA adducts in oral tissue from oral cancer patients with a betel quid chewing history. Carcinogenesis. 1999 Dec 1;20(12):2331-4.

35. Halliwell B. Biochemistry of oxidative stress. Biochemical society transactions. 2007 Nov 1;35(Pt 5):1147-50.

36. Kangralkar VA, Kulkarni AR. In vitro antitumor activity of alcoholic extract of Piper betel leaf. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2013; 4(4):1558-1561.

37. Rao AR. Modifying influences of betel quid ingredients on B (a) P-induced carcinogenesis in the buccal pouch of hamster. International journal of cancer. 1984 May 15;33(5):581-6.

38. Widowati W, Mozef T, Risdian C, Yellianty Y. Anticancer and free radical scavenging potency of Catharanthus roseus, Dendrophthoe petandra, Piper betle and Curcuma mangga extracts in breast cancer cell lines. Oxid Antioxid Med Sci. 2013 Apr;2(2):137-42.

39. Rekha VPB, Kollipara M, Gupta BRSSS, Bharath Y, Pulicherla KK. A review on Piper betle L.: Nature's promising medicinal reservoir. American Journal of Ethnomedicine. 2014; 1(5):276-289.

40. Nilugal KC, Perumal K, Ugander RE, Chittor AI. Evaluation of wound healing activity of Piper betle leaves and stem extract in experimental Wistar rats. Am. J. PharmTech Res. 2014;4(3):276-89.

41. Chauhan ES, Aishwarya J, Singh A, Tiwari A. A review: Nutraceuticals properties of Piper betel (Paan). Am J Phytomed Clin Ther. 2016;4(2):28-41.

42. Arambewela LS, Arawwawala LD, Ratnasooriya WD. Gastroprotective activities of Sri Lankan Piper betle leaf extracts in rats. SLAAS. 60th Annual Session. 2004;117.

43. Ramji N, Ramji N, Iyer R, Chandrasekaran S. Phenolic antibacterials from Piper betle in the prevention of halitosis. Journal of ethnopharmacology. 2002 Nov 1;83(1-2):149-52.

44. Alam B, Majumder R, Akter S, Lee SH. Piper betle extracts exhibit antitumor activity by augmenting antioxidant potential. Oncology letters. 2015 Feb 1;9(2):863-8.

45. Pin KY, Chuah AL, Rashih AA, Mazura MP, Fadzureena J, Vimala S, Rasadah MA. Antioxidant and anti-inflammatory activities of extracts of betel leaves (Piper betle) from solvents with different polarities. Journal of Tropical Forest Science. 2010 Oct 1:448-55.

46. Fazal F, Mane PP, Rai MP, Thilakchand KR, Bhat HP, Kamble PS, Palatty PL, Baliga MS. The phytochemistry, traditional uses and pharmacology of Piper Betel. linn (Betel Leaf): A pan-asiatic medicinal plant. Chinese journal of integrative medicine. 2014 Aug 26:1-1.

47. Shahrajabian MH, Marmitt DJ, Cheng Q, Sun W. Natural antioxidants of the underutilized and neglected plant species of Asia and South America. Letters in Drug Design & Discovery. 2023 Oct 1;20(10):1512-37.

48. Nayaka NMDMW, Nayaka AS, Kaveri K, Hebbar S. *Piper betle (L): Recent Review of Antibacterial and Antioxidant Activities.* Int J Phytomed. 2021;13(2):149-63.

Type equation here.