

A Comprehensive Review on Piper Betel Linn.

Vaibhavi K. Nerkar, Poonam I. Lal ., Pankaj H. Chaudhary,, Dipti B. Ruikar,
*Research Scholar, P.R. Pote Patil College Of Pharmacy, Kathora road, Amravati - 444604,
Maharashtra, INDIA.*

*M.Pharm, Assistant Professor, Department of Pharmacognosy, Kathora road, Amravati – 444604,
Maharashtra, INDIA.*

*M.Pharm Assistant Professor, Department of Pharmacognosy, P. R. Pote Patil College of
Pharmacy, Kathora road, Amravati - 444604, Maharashtra, INDIA.*

*M.Pharm., PhD. , Principal, P. R. Pote Patil College of Pharmacy, Kathora road, Amravati - 444604,
Maharashtra, INDIA.*

Submitted: 15-04-2023

Accepted: 25-04-2023

ABSTRACT :-

Betel leaf (*Piper betle* L.) is a business crop, which is historically ate up with inside the uncooked kingdom as a mouth freshener and stimulant in Southeast Asia due to the fact antiquity. It possesses various practical and medical properties, together with antimicrobial, antioxidant, antidiabetic, anticarcinogenic, etc. The leaf carries essential oil, which has a completely unique aroma contributing flavour and fragrances. This essential oil is an aggregate of focused phytochemicals, amongst which the main additives are estragole, chavicol, chavibetol, s-cubebene, and caryophyllene.

*Piper betle*L. belongs to own circle of relatives Piperaceae normally recognized as Paan. It is considerably grown in Sri Lanka, India, Thailand, Taiwan and other SoutheastAsian countries. Betelvine (*Piper betle* L.) is cultivated for its deep inexperienced coronary heart formed leaf for 15-20 million Indian and a couple of billion foreign customers annually. The leaves are not most effectively used without delay for chewing purposes however additionally possesses anti-oxidant, anti-inflammatory, anti-apoptotic, anti-microbial properties. The phenolic constituent allylpyrocatechol from the leaves confirmed hobby towards obligate oral anaerobes chargeable for halitosis and eugenol has been proven to possess anti-inflammatory activity. In terms of toxicity Betel leaf is not considered safe enough when taken orally for longer periods or in high doses.

Keywords : Piper betle, Essential oil, Pharmacological action, Chemical constituent, Antimicrobial, Anti-oxidant, Anti-halitosis, Toxicity.

I. INTRODUCTION :-

Since the antiquity, betel leaf (*Piper betle* L.) is getting used for ceremonial, nonsecular and medicinal values in Southeast Asia. Different forms of betel leaf are usually discovered in this region. It is broadly fed on in India with inside the shape of 'Paan' or betel quid. A quid is ready with inexperienced or decolorized betel leaf incorporating many other ingredients, together with slaked lime, areca nut chips, catechu, aniseed, clove, sweeteners, and tobacco etc.[1]



Figure 1. Piper betel fruit[2]

It is extensively utilized by the network as decorative plants, vegetables, spices, medical herbs, or as device in conventional ceremonies. In the sector there are round sevenhundred species of piper, a thousand types. There are among 1400-2000 styles of pipers from numerous countries. On the Island of Java, there are approximately 23 species of piper. Piper grows at an altitude of 2500 m, and only some species develop at an altitude above 3000 m.[3] In conventional medicinal drug practices, betel leaves are used for vaginal douching in Indonesia as a gargle mouthwash in India and Thailand and as a remedy for dental

problems, headaches, arthritis, and joint ache in Malaysia . In Srilanka, the betel leaf juice is used to deal with pores and skin ailments. Additionally, its boiled leaves might be used as cough medicinal drug, tonic, or astringent.[4]There are numerous styles of leaves, the maximum popular being: Calcutta, Banarasi, Magahi, etc. In Bangladesh, Dinajpur, Rangpur, Chittagong, Faridpur, Jessore, Narayanganj, Barisal and Sylhet are the areas generating the maximum betel[5].

Taxonomical position

For the motive of uniformity and universality with inside the know-how of flowers, a device of class and designation of flowers has been evolved with inside the technological know-how of botany referred to as Taxonomy. Naagavalli may be designated beneath

Neath the subsequent Taxonomic position :

Table no.1:- Taxonomical Position[5,6]

Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Magnoliidae
Order	Piperales
Family	Piperaceae
Genus	Piper
Species	betel

Table no.2 :- Vernacular Names[5,6]

Sanskrit	Tambool, Mukhbhushan, Varnalata.
Hindi	Paan leaf.
English	Betle, Betle pepper, Betle-vine.
Telugu	Nagballi, Tamalapaku.
Tamil	Vettilai.
Bengali	Paan, Pane, Tambulaballi (plant), Parnakari (leaf).

Assamese	Paan, Paana.
Kannada	Eleballi, Panu, Vileyadele.
Gujarti	Paan, Tanbolaa.
Malayalam	Fetial.
Nepalese	Naagavallii (plant), Paan (leaf).
Indonesia	Bakikserasa, Daunsirih.
Semang	Serasa, Cabe.

ETHNOBOTANICAL USES :- [7]

Leaf: The Leaf extract is used as an antifungal, antimalarial, and antioxidant. It is also used to treat coughs and indigestion, especially in children. It is also antimalarial, antibacterial, insecticidal, antidiabetic, gastric protective and cytotoxic.

Stem: It has been shown to be effective in treating cough, asthma, indigestion and bronchitis.

Whole plant:Piper Betel is used as a food and as a spice. Due to its pungent taste, it also finds notable uses in perfumes, oils, hallucinogens and anti-infectives. Recent research has also shown its use against worms. Some other uses include normalizing the digestive tract and maintaining the digestive system. This is due to its light properties.

CULTIVATION AND COLLECTION :-[8]

Propagation

Propagation is straightforward with the aid of using root department or cuttings. Betel requires well-tired fertile soil semi-color position. Waterlogged, saline and alkali soils are flawed for its cultivation.

Cultivation

First of all put together a lawn referred to as a barouj where in to grow betel. The barouj is fenced with bamboo sticks and coconut leaves.

The soil is plowed into furrows of 10 to15 meter length, 75 cm in width and 75 cm in depth. Oil cakes, manure and leaves are very well integrated with the topsoil of the furrows and wooden ash. The cuttings are planted on the beginning of the monsoon season. Proper coloration and irrigation are critical for a success cultivation of this crop. Betel desires continuously wet soil, but there must not be any immoderate moisture. Irrigation is common and mild status water must now no longer continue to be extra than ½ of an hour.

Collection

In three to six months vine attain a 150 - 180 cm in top and they will branch. Harvest begins,

with the farmer plucking the leaf and its petiole together along with his proper thumb. The harvest lasts for 15 days to at least 1 month.



Figure no.2 :- Cultivation of Piper betel[9]

MORPHOLOGY :-[10]

The plant is a dioecious root climber, and the shoots attain any peak from 3 to 10 m in line with available centers for climbing. The plant bears lateral branches alongside its entire duration that develop multiple ft from the ground. The stems are swollen and articulate, with dichotomous branching and rooting on the nodes. The stems are stout, nearly terete, barely flattened; while young, they may be light inexperienced and marked via way of means of short, raised, whitish streaks and with pinkish stripes alongside the node. The internodes generally gain a duration of approximately 12 cm. and a diameter of 1.2cm. Leaves are characterized as simple blade, alternate, spiral and ex-stipulate; petioles are 2-5 mm long pubescent and channeled. Leaf blades are glabrous, coriaceous, fleshy, greenish to yellowish, shining, broadly ovate, width 78.5cm, duration 9–11cm; base cordate; apex acuminate; margin is entire, narrowly recurved; venation reticulate, 7–9veins in or 3 pairs coming from the midrib, one pair elevating from base.

The inflorescence is an axillary spike as much as five cm long. The male inflorescence a cylindrical pendulous catkin of 10 cm in duration and a couple of cm in diameter. Female spikes also are cylindrical, pendulous; duration 2.5–4cm and diameter 0.5 cm. Individual vegetation are very minute and unisexual, reduced, along with a couple of stamens and stigmas inserted into the axil of every bract. The bracts are orbicular, peltate, organized in a thickly crowded spiral series. The mature inflorescence is strongly aromatic. Fruiting spikes are 3-5 cm in duration, orange and

drugging, entrenched at the rachis of the mature inflorescence.

CHEMICAL CONSTITUENT :-

Betel vines are one of the exceedingly investigated vegetation and their phytochemical studies display that Piper betel carries a huge kind of biologically active compounds whose awareness relies upon the kind of the plant, season and climate. Chemical composition of important oil represent safrole gift in the leaf, stalk, stem, root and β -phellandrene gift with inside the fruit. The aroma of betle leaf is because of the presence of important oils, including phenols and terpenes[11]. Younger leaves stated to yield extra essential oil. The leader constituent of the leaves is a risky oil whose chemical composition is depending on the location it's far observed. It is likewise referred to as betle oil. Leaf and different plant elements have yielded lively compounds like hydroxychavicol acetate, allylpyrocatechol, chavibetol, piperbetol, methylpiperbetol, piperol A and piperol B. Leaves of Piper betel stated to yield an alkaloid: arakene, with residences just like cocaine[11].

The lively factor of piper betle oil that is received from the leaves are number one a category of allyl benzene compounds, chavibetol (butylphenol; 3-hydroxy-methoxyallylbenzene), Chavicol (p-allylphenol; 4-allylphenol), Estragole (p-allylanisole; 4-methoxyallylbenzene), Eugenol (allylguaiacol; 4-hydroxy-3-methoxy allyl benzene; 2-methoxy-4-allyl-phenol), methyl eugenol (Eugenol methyl ether; 3,-dimethoxyallylbenzene) and hydroxy catechol (2,4-dihydroxy-allylbenzene)[12]. Hexane fraction of leaf stalks yielded 4 aliphatic compounds in natural shape i.e. pentadecyl 6-hydroxytridecanoate, pentatriacontanol, methyl hexacos-7-enoate and 6,9heptacosadiene. The extract of betle leaves possesses antimutagenic, anticarcinogenic, antidiabetic, anti-inflammatory and antibacterial activities. Hydroxychavicol (HC) and eugenol (EU) are vital phytochemicals observed in betle leaves. They are stated to make a contribution to many bioactivities in betle leaves. HC and EU are phenolic compounds which encompass a monocyclic fragrant ring with an alcoholic, aldehydic or carboxylic group[13].

Table No. 3 :- Chemical Constituents of Piper betel Leaf[13]

SR NO.	CHEMICAL CONSTITUENTS	% OF CHEMICAL CONSTITUENTS
1.	Chavibetol	53.1
2.	Chavibetol acetate	15.5
3.	Caryophyllene	3.71
4.	Allyl pyrocatechol diacetate	0.71
5.	Chavibetol methyl ether	0.48
6.	Eugene	0.32
7.	a-Pinene	0.21
8.	f-Pinene	0.21
9.	Safrole	48.7
10.	1, 8-Cineole	0.04

Chavibetol

Chavibetol is a natural chemical compound of the phenylpropanoid class. It is one in all the number one component of the crucial oil from the leaves of the betle plant (Piper betle). It is a fragrant compound with a highly spiced odor[14].

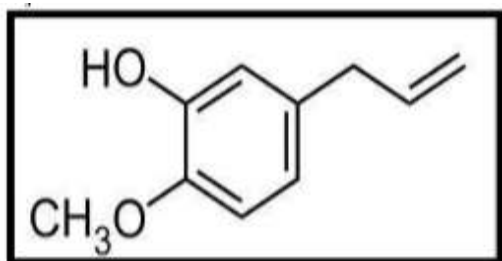


Figure no.6 :- Structure of Chavibetol[14]

Allylpyrocatechol

The phenolic constituent allylpyrocatechol from the leaves confirmed hobby towards obligate oral anaerobes chargeable for halitosis. The leaf extract additionally has a stimulatory impact on pancreatic lipase and antioxidant property[15].

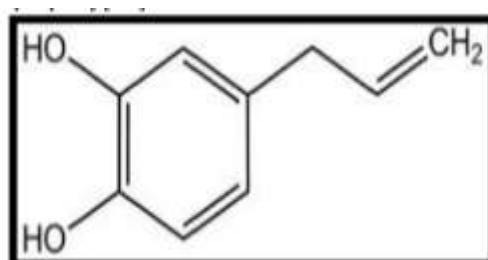


Figure no.7 :- Structure of Allylpyrocatechol[15]

Eugenol

Eugenol, one of the most important constituent of betel leaf has additionally been proven to possess anti-inflammatory result in diverse animal fashions of research with diversity in flamogens. Mechanistic research with in vitro structures confirmed that eugenol blocked the discharge of the bone resorbing mediators, which include IL-1 β , TNF- α and PGE2 from of LPS-inspired human macrophages through suppressing the messenger RNA expression of LPS-brought on IL-1 β , TNF- α , and COX-2 in macrophages. Eugenol suppressed the COX-2 gene expression in LPS-inspired mouse macrophages cells[16].

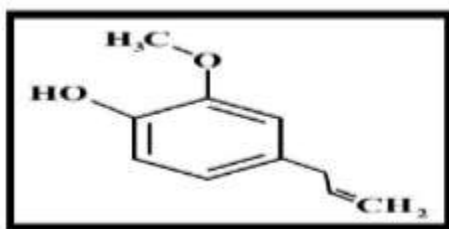


Figure no.8 :- Structure of Eugenol[16]

Hydroxychavicol

The phenolic compound, Hydroxychavicol, determined with inside the aqueous extract of betle leaf is said to showcase beneficial bioactivities anticarcinogenic and antimutagenicactivities[16].

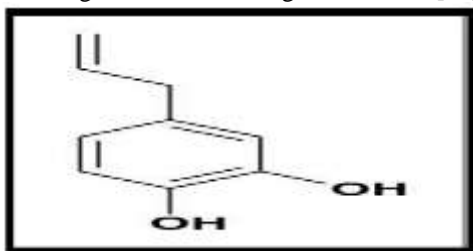
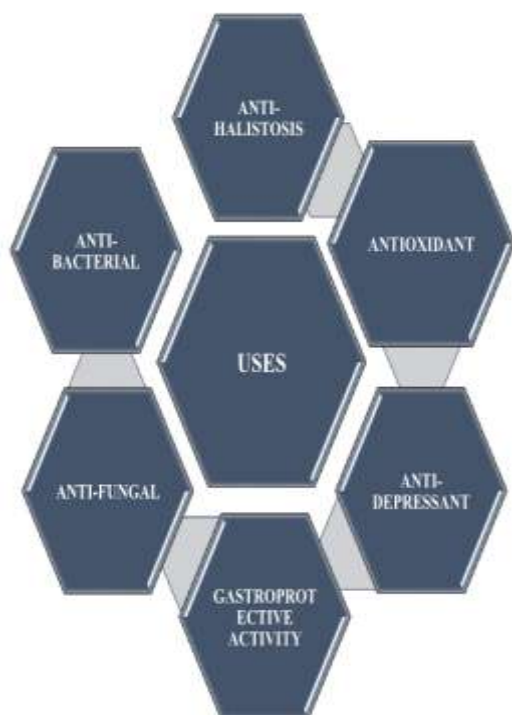


Figure no.9 :- Structure of Hydroxychavicol[16]

PHARMACOLOGICAL ACTION :-



Different activities are shown by Piper betel by using different models (Rabbit, Mice, Rat, Guinea pig).

Antioxidant

Prasanna SV. et al., (2021) studied that the Betel leaf ethanol extract is an antioxidant with a mean IC50 ($\mu\text{g/mL}$) for the ascorbic acid radical DPPH of 3.128. The mean IC50 ($\mu\text{g/ml}$) of the ethanol extract was found to be 9,362. The ethanolic extract of Piper betle L. leaves showed a moderate effect on the DPPH radical. The ethanolic extract of betel leaves (Piper betle) has shown in various concentrations (5%, 10% and 15%) an antioxidant effect by animal experiments or experiments used in rabbits. The rabbits were shaved, then hot metal was attached to the rabbit's back, down to the dermis and underlying tissues, causing blistering of the skin. The treatment was carried out for seven days, watering the treatment evenly once a day. He then performed macroscopic observations of the development of wound healing on the rabbit's back. Bioplacenton was used as a positive control. Ethanol extract of betel leaves in concentrations of 5%, 10% and 15% for healing burns on the skin of the back of rabbits (*Oryctolagus cuniculus*). The healing process is faster because betel leaves contain bioactive molecules such as saponins, tannins, essential oils, flavonoids and phenols.¹⁰ Eugenol, hydroxychavicol, and alpha-tocopherol from the betel leaf component have been reported to increase GSH levels in the skin and liver of mice[17].

Anti-depressant Activity

Prasanna SV. et al., (2021) tested the antidepressant capacity of Piper betle leaf extract in animal models of depression which showed remarkable antidepressant effects in the most commonly used behavioral samples. It has antidepressant effects and works by blocking the uptake pathways of Dopamine, Norepinephrine, and Serotonin through their respective transporters. However, further studies are needed to analyze its mechanism of action in depth[17].

Anti-allergic Activity

Afridi M. et al., (2021) had studied the inhibitory effects of Piper betel on the production of allergic mediators by bone marrow-derived mast cells and lung epithelial cells. The effects of ethanolic extract of Piper betel on histamine and granulocyte-macrophage colony-stimulating factor (GM-CSF) production by murine bone marrow mast cells (BMMC) and on exotoxin and IL-8 secretion by the human lung epithelial cell line. BEAS2B, were studied in vitro. The extracts significantly

reduced histamine and GM-CSF produced by an IgE-mediated hypersensitivity response and inhibited exotoxin and IL-8 secretion in a TNF- α and IL-4-induced allergic response. The results suggest that Piper betel can control allergic diseases by inhibiting the production of allergic mediators[18].

Anticancer Activity

Studies show that various plants possess mixtures of bioactive compounds to act as anticancer agents and anti-proliferative against cancer cells for anti-cancer drug development. The antioxidant activities in the plant also contributed to the positive correlation with inhibition of cancer cell growth.

Azahar et al., (2020) studied human breast cancer cells used MCF-7 for the antiproliferation study. Cells were grown in 96-well culture plates and left for 24 hours to allow cells to adhere to the plates prior to treatment with Piper Betle extracts obtained using four different solvents; ethyl acetate, hexane, methanol and water. Based on the assessment, ethyl acetate possesses the highest antioxidant and antiproliferative effects, followed by hexane extract, which exhibits dose-dependent inhibitory effects on MCF-7 cells with IC₅₀ values of 56.00 ± 0.00 $\mu\text{g/mL}$ and 163.30 ± 2.89 $\mu\text{g/mL}$. Evaluation of the cytotoxicity and cell migratory effect of Piper betle extract against human MCF-7 breast cancer cells by incorporation of the plant extract into transdermal patches. Based on the experiment, the researcher found that Piper Betle extract has both cytotoxic and anti-migratory properties. The cytotoxic activity of MCF-7 shows that increasing the dose of Piper Betle extract decreases the viability of MCF-7 cells. While the cell migration of MCF-7 was suppressed with a remarkable result at a dose of 25 $\mu\text{g/mL}$, in which the cell migration was suppressed 30% more than in the control group[19].

Antidiabetic Activity

Hossain tested the antidiabetic effect of Piper Betle extract on model rats. Model rats were divided into three groups and fed different concentrations of Piper Betle extract, starting at 50 mg/kg body weight for Group A, 100 mg/kg body weight for Group B, and 200 mg/kg body weight for Group B.C. The study found that the plasma glucose levels of the administered rats were significantly reduced; 36.1% for Group A, 16.6% for Group B, followed by 23.76% for group C.

Azahar et al., (2020) induced diabetic rats by destroying beta cells with streptozotocin, which were then maintained with piper betle extract. According to general studies, both Piper Betle extract (hot water extract and cold ethanolic extract) possess marked hypoglycemic activity (tested on fasting normoglycemic rats) and antihyperglycemic activity (by improving glucose tolerance test and reducing blood sugar level in diabetic rats induced by streptozotocin). The results therefore indicated the ability of Piper Betle to exert insulin-mimetic activity. Regardless of the beneficial claim, the researchers faced some difficulties where they had to repeatedly feed the tested rats Piper Betle extract to keep the extract effective[19].

Antifungal Activity

Piper Betle has antifungal activity against *Candida albicans*. The antifungal activity of hydroxychavicol from Piper Betle extract showed fungicidal effects against all fungal species tested, including *Candida* species, *Aspergillus* species and dermatophytes including *Trichophyton rubrum*. According to **Umar et al. (2018)** the fungi *Candida albicans*, *Candida parapsilosis* and *Candida tropicalis* showed low adhesion production when treated with the crude aqueous extract of Betel. These adhesins are crucial as they allow fungi to colonize various substrates and bind to host tissues.

The crude essential oil demonstrated a broad spectrum of antimicrobial activity against the organisms tested, specifically *Candida albicans*, followed by *Staphylococcus aureus* and *Malassezia pachydermatis*. Research has identified phenols (carvacrol) and phenylpropane (eugenol and chavicol) from Piper betel that exhibit antifungal activity by increasing the permeability of fungal membranes[20].

Oral care Agent

Aishwarya J. et al., (2016) concluded that dental caries is a chronic endogenous infection caused by the normal oral commensal flora. The carious lesion is the result of the demineralization of the enamel and later the dentin by the acids produced by the plaque microorganisms when they metabolize dietary carbohydrates. The bacterium mainly responsible for dental caries in humans is *Streptococcus mutans*. Particular importance is attributed to this enzyme in the establishment of dental plaque. Therefore, it is the top natural substance and its rating as the second most popular

daily consumer item in Asia that contributes to the best oral hygiene of the oral cavity[21].

Gastro protective Activity

Betel shows antimicrobial activity against *Streptococcus pyrogens*, *Staphylococcus aureus*, *Proteus vulgaris*, *Escherichia coli* and *Pseudomonas aeruginosa*. In addition, the leaf extract also has a bactericidal effect against pathogenic bacteria from of the urinary tract such as *Enterococcus faecalis*, *Citrobacter koseri*, *Citrobacter freundii* and *Klebsiella pneumoniae*. Dermatophytosis is a curable disease of the keratinized parts of the body (skin, hair and nails) caused by three genera of highly specialized fungi called dermatophyte.

Aishwarya J. et.al., (2016) conducted a study to evaluate the protective and curative effects of allylpyrocatechol against indomethacin-induced gastric ulcer in a rat model[21].

Platelet Inhibition Activity

Hydroxychavicol (HC), a component of the leaves of *P. betle*, was tested for its inhibitory effect on platelet aggregation. The results showed that HC has the ability to regulate COX1/COX-2 cyclooxygenase activity, platelet calcium signaling, thromboxane B production and aggregation and remove reactive oxygen. **ChanEW. et al., (2014)** study concluded that HC could be a potential therapeutic agent for the prevention and treatment of atherosclerosis and other cardiovascular diseases due to its anti-inflammatory and anticoagulant effects[22].

Antimicrobial Activity

Betel shows antimicrobial activity against *Streptococcus pyrogens*, *Staphylococcus aureus*, *Proteus vulgaris*, *Escherichia coli* and *Pseudomonas aeruginosa*. In addition, the leaf extract also has a bactericidal effect against pathogenic bacteria of the urinary tract such as *Enterococcus faecalis*, *Citrobacter koseri*, *Citrobacter freundii* and *Klebsiella pneumoniae*. Dermatophytosis is a disease of the keratinized parts of the body (skin, hair and nails) caused and curable by three genera of highly specialized fungi called dermatophytes.

Protective and Curative Activity Recently, **Rekha VP. et al., (2014)** conducted study to evaluate the protective and curative effects of allylpyrocatechol against indomethacin-induced gastric ulcer in a rat model[23].

Anti-halitosis Activity

The anti-halitosis activity of Piper Betle was performed by **Rekha VP. et al., (2014)**. The leaves of Piper betle L. (Piperaceae), traditionally used in India and China to prevent bad breath, were analyzed by bioassay guided fractionation to yield allylpyrocatechol (APC) as main active ingredient, showing promising activity against the obligatory oral anaerobes responsible for bad breath. Biological studies with allylpyrocatechol showed that the potential to reduce methyl mercaptan and hydrogen sulfide is mainly due to the antimicrobial activity detected by dynamic in vitro models[23].

Local anesthetic Action

Senagupta et al., (2013) showed that simple betel leaf extracts with betel nut were tested for surface and infiltration anesthetic effects with and without autoclaving in rabbits and Guinea pigs. The results were compared to the normal saline control and the xylocaine drug control. Betel leaves showed dose-dependent infiltration anesthetic activity comparable to that of xylocaine. As a topical anesthetic, the onset of action was as rapid as xylocaine and the duration shorter than xylocaine. Betel nut significantly reduced the infiltration activity and eliminated the surface anesthetic activity of betel leaves. Autoclaving resulted in no loss of activity. Betel leaf has a strong local anesthetic effect by both surface and infiltration techniques. This effect is reduced by the addition of betel nut but is not lost by autoclaving[24].

TOXICITY:-

Not Enough is known about the short-term safety of oral betel nut. However, betel nut is not considered safe when taken orally for long periods or in high doses. Some chemicals in betel nut have been linked to cancer. Some chemicals are toxic.

Eating 8 to 30 grams of betel nut can cause death. Chewing betel nut can cause redness of the mouth, lips, and stool. It can cause side effects like caffeine and tobacco use. It can also cause serious side effects, including vomiting, diarrhea, gum disease, drooling, chest pain, irregular heartbeat and low blood pressure, shortness of breath and shortness of breath, heart attack, thirst, and death[25].

II. CONCLUSION :-

Piper betel is thought to International and ate up often as mouth freshener and also used as mighty supply for novel therapeutically effect. This

effect well-known shows it to be match for its destiny utilization as a promising supply for treating numerous conditions. There is a developing recognition amongst clients to apply herbal materials over artificial preservatives with inside the meals and beverage industries. Essential oils are potential options to artificial chemical compounds for meals preservation. From this study, it may be concluded that betel leaf is a vast supply of vital oil. This vital oil consists of a widespread quantity of bioactive compounds, such as phenols, flavonoids, alkaloids etc. These bioactive compounds are mainly accountable for numerous useful properties like, antimicrobial, antioxidant, antidiabetic, anti-inflammatory, anti-carcinogenic, etc. The phenolic constituent allylpyrocatechol from the leaves confirmed hobby towards obligate oral anaerobes chargeable for halitosis. Chavibetol is the number one component of the crucial oil from the leaves of Betle plant has highly spiced odour. Hydroxychavicol shows beneficial bioactivities anticarcinogenic and antimutagenic activities. Therefore, with inside the close to destiny the standardization and stabilization research at the leaf extract may be accomplished that may assist in enhancing its utilization for varied medical usage.

ACKNOWLEDGEMENT :-

I would like to express my sincere gratitude to my supervisors and I would also like to thank P. R. Pote Patil College Of Pharmacy, Amravati for providing facilities and for providing platform to enhance my knowledge.

REFERENCES :-

- [1]. Roy A, Guha P. Traditional and functional uses of betel leaf (*Piper betle* L.) pertaining to food sector: a review. *Journal of Postharvest Technology*. 2021;9(1):72-85.
- [2]. [.https://www.britannica.com/plant/Piperaceae](https://www.britannica.com/plant/Piperaceae). Accessed 8 December 2022. **Referred on :- 04/09/2022.**
- [3]. Suri MA, Azizah Z, Asra R. A Review: Traditional Use, Phytochemical and Pharmacological Review of Red Betel Leaves (*Piper Crocatum* Ruiz & Pav). *Asian Journal of Pharmaceutical Research and Development*. 2021;9(1):159-163.
- [4]. 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;26(8):2321.
- [5]. 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;38(2):181-189.
- [6]. Ratna BR, Kasaudhan R. A Review on *Tambula* (*Piper Betel* Linn.) from ayurvedic and modern perspective. *World J Pharm Res*. 2021;10(5):1652-1663.
- [7]. Pawar S, Bhane P, Jha U. Review on Betel Pepper Leaf for Anti-inflammatory Activity. *World Journal of Pharmaceutical Research*. 2022; 11(2), 1196-1208.
- [8]. Patel NM, Jain DD, Suryawanshi HP, Pawar SP. *Phytopharmacological Study of Piper betle Leaf*. *Saudi Journal of Medical and Pharmaceutical Sciences*. 2019; 5(11):964-971.
- [9]. [.https://www.agrifarming.in/wp-content/uploads/2015/03/Betel-Leaf-farming2.jpg](https://www.agrifarming.in/wp-content/uploads/2015/03/Betel-Leaf-farming2.jpg). Referred on :- 18/10/2022.
- [10]. Biswas P, Anand U, Saha SC, Kant N, Mishra T, Masih H, Bar A, Pandey DK, Jha NK, Majumder M, Das N. *Betelvine* (*Piper betle* L.): A Comprehensive insight into its ethnopharmacology, phytochemistry, and pharmacological, biomedical and therapeutic attributes. *Journal of Cellular and Molecular Medicine*. 2022;(26): 3083–3119.
- [11]. 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;24(12):1283-1286.
- [12]. 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. *J PharmacognPhytochem*. 2013;1(2):10-19.
- [13]. Rimando AM, Han BH, Park JH, Cantoria MC. Studies on the constituents of Philippine *Piper betle* leaves. *Archives of Pharmacal Research*. 1986;9(2):93-97.
- [14]. Dwivedi BK, Mehta BK. Chemical investigation of aliphatic compounds of *Piper betle* (leaf stalk). *J Nat Prod Plant Resour*. 2011;1(2):18-24.
- [15]. Amonkar AJ, Nagabhushan M, D'souza AV, Bhide SV. *Hydroxychavicol*: A new

- phenolic antimutagen from betel leaf. Food and chemical toxicology. 1986 1;24(12):1321-1324.
- [16]. Vikash C, Shalini T, Verma NK, Singh DP, Chaudhary SK, Asha R. Piper betel Phytochemistry, traditional use & pharmacological activity a review. International Journal of Pharmaceutical Research and Development (IJPRD). 2012;4(4):216-223.
- [17]. Prasanna SV, Ramya D, Haritha C, Pandey V, Nadendla RR. A Comprehensive review on the therapeutic potential of Piper betel leaf for the treatment of neurological diseases. 2021;6(4): 611-619.
- [18]. Afridi M, Muhammad Ishaque M.R., Ahmad T, Hussain A, Akram M, Ghotekar S, Oza R, Marasini BP. Ethno-Medicinal Uses of Piper betel— A Review. Advanced Journal of Chemistry, Section B, 2021;3(3), 199-208.
- [19]. Azahar NI, Mokhtar NM, Arifin MA. Piper betel: a review on its bioactive compounds, pharmacological properties, and extraction process. In IOP Conference Series: Materials Science and Engineering 2020 (Vol. 991, No. 1, p. 012044). IOP Publishing.
- [20]. Umar RA, Zahary MN, Rohin MA, Ismail S. Chemical composition and the potential biological activities of Piper betel—a Review. Malaysian Journal of Applied Sciences. 2018;3(1):1-8.
- [21]. Aishwarya J, Chauhan ES, Singh A, Tiwari AA. Review: Nutraceuticals Properties of Piper betel (Paan). American Journal of Phytomedicine and Clinical Therapeutics. 2016;4(2):28-41.
- [22]. Chan EW, Wong SK. Phytochemistry and pharmacology of three Piper species: An update. International Journal of Pharmacognosy. 2014;1(9):534-44.
- [23]. Rekha VP, Kollipara M, Gupta BR, Bharath Y, Pulicherla KK. A review on Piper betel L.: nature's promising medicinal reservoir. American Journal of Ethnomedicine. 2014;1(5):276-89.
- [24]. Sengupta R, Banik JK. A review on betel leaf (pan). International Journal of Pharmaceutical Sciences and Research. 2013;4(12):4519.
- [25]. Pradhan D, Suri KA, Pradhan DK, Biswasroy P. Golden heart of the nature: Piper betel L. Journal of Pharmacognosy and Phytochemistry. 2013;1(6): 147-167.