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Review Article

Therapeutic Potential and Multifaceted Benefits of *Piper Betle* Linn: A Comprehensive Review

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ABSTRACT

A plant in the Piperaceae family, the piper betle has heart-shaped leaves that are deep green in color. Paan, or "Green Gold," is another name for piper betle leaves in India. It contains a lot of vitamins, minerals, nutrients, antioxidants, and phytochemicals. It is a valuable herb with numerous health benefits. It is herbal drug described by ancient charayas, nighantus and Rajnighantu. It is widely used in community for their non side effects and long-lasting benefits. Its extract used for mouthwash breath cleansing and treating various diseases. Its phytochemical includes phenolic, alkaloids, terpenoids, flavonoids, tannins, saponins, and sugar etc. Its antimicrobial, antioxidant, anti-cancer, and anti-inflammatory pharmacological qualities have all been investigated. This review article focuses on phytochemical of active constituents, pharmacological properties and anti-microbial effect of Piper betle Linn.

INTRODUCTION

A plant in the Piperaceae family, the *piper betle*, has over 700 species found worldwide (Rabiatal Umar *et al*, 2018). The plant leaves are basic long stalked, and have an acuminate crown (Depi Sakinah *et al*, 2020). *Piper betle* is a deep green in Color and heart shaped plant native to India (Depi Sakinah *et al*, 2020). The *Piper betle* Linn is known as Paan leaves and is consumed by 15-20 million people in India (Aishwarya *et al*, 2016). The plant prefers a warm and humid climate and has dense male spikes and pendulums. The plant has various

names in different language including paan, Tanbol, Bulung Samat, Vettila, Vettillakkoti, Plu, Maluu, Plue, Vetrilai, burg-e-tanbol, Daun sirih, Papulu and trau (Saikat Mazumder *et al*, 2016). They are found in hot and moist climates and are produced in various regions, including Bihar, South India. It is best grown in moderate moist soil, with light irrigation and proper drainage. They are classified into odorous and non-pungent type based on their form, length and flavour. Venmony, Mysore, Salem, Calcutta, Banarsi, Kauri, Ghanagete, Bagerhati, and Magadhi are

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some of the well-known Indian types (Sunil Shah *et al*,2016). The best betle leaf is the ‘Magadhi’ variety grown near Patna in Bihar (Sunil Shah *et al*,2016). They contain bioactive compounds including minerals, vitamins, enzymes, proteins and essential oil. It is utilized in many facets of human existence, such as social, cultural, and religious facets. Other foods include fruit pulp, clove cardamom, coriander, anise, areca nut, slaked lime, and fruit (Maira Afridi *et al*, 2021). The leaves of *Piper betle* Linn are regarded auspicious in ancient times and have been utilized for ages in Indian traditional medicine.

In the Indian subcontinent, medicinal plants are a valuable resource, providing primary medicine for rural communities in emerging nations. Due to their use as intermediates for synthetic medications or as model compounds for lengthy drug manufacturing, substances produced from plants have attracted a lot of attention. These leaves are also useful for treating brain, liver, and cardiac disorders. It is used for Various producing products. Egenol, hydroxychavicol, and chavibetol have various pharmacological properties (N I Azahar *et al*,2020). The plant is subjected to various extraction processes including Soxhlet, Sonication. etc. Its leaf extraction has potential for treating toxoplasmosis, treating wounds and cuts, aiding, lucorrhea (Anjali Soni *et al*,2013). Plant-based medications are defined by the World Health Organization as herbal preparations made through extraction, fractionation, purification, concentration, and other physical or biological procedures (Nagy Morsy *et al*, 2014).



Image no 1: *Piper betle* Linn Plant

Chemical composition:

Piper betle linn is a highly researched plant with a variety of biologically active compounds (Rabiatul Umar *et al*,2018). The leaves contain water, protein, fat, carbohydrates, fibres, essential oil and tannins. In addition, they include minerals and vitamins such as calcium, potassium, phosphorus, iron iodine, carotene, thiamine, nicotinic acid, riboflavin, vitamin C, and amino acids (Rabiatul Umar *et al*, 2018). Together with additional substances including allypyrocatechol diacetate, camphene, eugenol, α -pinene, β -pinene, α -limonene, 1,8-cineole, and allypyrocatechol monoacetate, the essential oil extracted from the leaves contains chavibetal (53.1%) and chavibetal acetate (15.5%) (Sunil Shah *et al*, 2016). *Piper betle*'s hexane fraction contains four pure aliphatic chemicals, such as alipyrocathechol and chromanol. It also contains important antioxidants and can prevent gastrointestinal ulcers caused by using indomethacin. The primary component of betle leaf that has anti-inflammatory and anti-fungal properties is eugenol (V.P.B. Rekha *et al*, 2014).

Table no.1: Chemical components of *piper betle* Linn (V.P.B. Rekha *et al*,2014) :(Sunil Shah *et al*,2016).

Components	% Of components
Chavibetol	53.1

Chavibetol acetate	15.5
Caryophyllene	3.71
Allylpyrocatechol Diacetate	0.71
Camphene	0.48
Chavibetol methyl ether	0.48
Eugenol	0.32
A-Pinene	0.21

f-Pinene	0.21
U-Limonene	0.14
Saprobe	0.11
1,8-Cineol	0.04
Allylpyrocatechol Monoacetate	0.23

Nutritional components:

The macro and micro nutrients are listed in table were found in the proximate analysis of *Piper betle* leaves (P. Guha,2006)

Table no 2: Nutritional composition of fresh betle leaves

Sr. No.	Components	Approximate
1.	Water	85-90%
2.	Protein	3-3.5%
3.	Fat	0.4-10%
4.	Mineral	2.3-3.3%
5.	Fibre	2.3%
6.	Chlorophyll	0.01-0.25%
7.	Carbohydrate	0.5-6.10%
8.	Iron	0.005-0.007%
9.	Nicotinic acid	0.63-0.89mg/100g
10.	Vitamin-c	0.005-0.01%
11.	Vitamin-A	1.9-2.9 mg/100g
12.	Thiamine	10-70 µg /100 g
13.	Riboflavin	1.9-30µg/100g
14.	Tannin	0.1-1.3%
15.	Nitrogen	2.0-7.0%
16.	Phosphorus	0.05-0.6%
17.	Potassium	1.1-4.6%
18.	Calcium	0.2-0.5%
19.	Iodine	3.4µg/100g
20.	Essential oil	0.08-0.2%
21.	Energy	44 kcal/100 g

Phytochemical analysis:

Piper betle contain various biologically active compounds with concentration varying based on variety of Plants, season and climate (Aishwarya

et al, 2016). The alcoholic extract of betle vine was analyzed for phytochemicals, revealing various pharmacological activities (Sahu *et al*, 2022) The extracts, prepared using various solvents,



contained flavonoids, tannins, alkaloids, quinones, glycosides and reducing sugars (Depi terpenoids, saponins, cardiac glucosides anthraquinone sakinah *et al*, 2020)

Table no.3: The Phytochemical analysis of various Solvents reported in betle plants

Phytochemical constituents	Aqueous Extracts	Reference
Flavanoids	+	Bhide <i>et al</i> , 2020, Sonalkar <i>et al</i> , 2018 Chakraborty <i>et al</i> , 2011
Steroids	- / +	Chakraborty <i>et al</i> , 2011 Bhide <i>et al</i> , 2020
Saponins	+	Sonalkar <i>et al</i> , 2018
Carbohydrates	-/+	Bhide <i>et al</i> , 2020, Sonalkar <i>et al</i> , 2018
Proteins	+	Chakraborty <i>et al</i> , 2011
Glycosides	+	Bhide <i>et al</i> , 2020, Sonalkar <i>et al</i> , 2018
Alkaloids	-/+	Bhide <i>et al</i> , 2020, Sonalkar <i>et al</i> , 2018 Chakraborty <i>et al</i> , 2011
Terpenoids	-	Sonalkar <i>et al</i> , 2018
Tannins	+	Bhide <i>et al</i> , 2020, Sonalkar <i>et al</i> , 2018 Chakraborty <i>et al</i> , 2011
Phenol	+	Chakraborty <i>et al</i> , 2011

Phytochemical constituents	Ethyl acetate	Reference
Flavanoids	+	Perumal and Saravanabhavam, 2018 Sonalkar <i>et al</i> , 2018 Chakraborty <i>et al</i> , 2011
Steroids	-/ +	Chakraborty <i>et al</i> , 2011
Saponins	-/+	Sonalkar <i>et al</i> , 2018 Perumal and Saravanabhavam, 2018, Manisha <i>et al</i> , 2019
Carbohydrates	+	Sonalkar <i>et al</i> , 2018 Manisha <i>et al</i> , 2019
Proteins	+	Manisha <i>et al</i> , 2018
Glycosides	-/+	Sonalkar <i>et al</i> , 2018 Manisha <i>et al</i> , 2019
Alkaloids	-/+	Perumal and Saravanabhavam ,2018, Sonalkar <i>et al</i> , 2018 Chakraborty <i>et al</i> , 2011
Terpenoids	-	Perumal and Saravanabhavam, 2018,
Tannins	+	Manisha <i>et al</i> , 2019, Sonalkar <i>et al</i> , 2018 Chakraborty <i>et al</i> , 2011
Phenol	+	Chakraborty <i>et al</i> , 2011, Perumal and Saravanabhavam, 2018

Phytochemical constituents	Methanol	Reference
Flavanoids	+	Amrutesh <i>et al</i> , 2015, Chakraborty <i>et al</i> , 2011
Steroids	+	Chakraborty <i>et al</i> , 2011 Amrutesh <i>et al</i> , 2015
Saponins	-	Amrutesh <i>et al</i> , 2015
Carbohydrates	+	Amrutesh <i>et al</i> , 2015

Proteins	+	Amrutesh <i>et al</i> ,2015
Glycocides	+	Amrutesh <i>et al</i> ,2015
Alkaloids	-	Amrutesh <i>et al</i> ,2015, Chakraborty <i>et al</i> , 2011
Terpenoids	-	Amrutesh <i>et al</i> ,2015
Tannins	+	Amrutesh <i>et al</i> ,2015, Chakraborty <i>et al</i> , 2011
Phenol	+	Chakraborty <i>et al</i> , 2011

Phytochemical constituents	Petroleum ether	Reference
Flavanoids	+	Amrutesh <i>et al</i> ,2015, Chakraborty <i>et al</i> , 2011
Steroids	-/ +	Chakraborty <i>et al</i> , 2011 Amrutesh <i>et al</i> ,2015
Saponins	-/+	Amrutesh <i>et al</i> ,2015
Carbohydrates	+	Amrutesh <i>et al</i> ,2015
Proteins	+	Amrutesh <i>et al</i> ,2015
Glycocides	-/+	Amrutesh <i>et al</i> ,2015
Alkaloids	-/+	Amrutesh <i>et al</i> ,2015, Chakraborty <i>et al</i> , 2011
Terpenoids	-	Amrutesh <i>et al</i> ,2015
Tannins	+	Amrutesh <i>et al</i> ,2015, Chakraborty <i>et al</i> , 2011
Phenol	+	Chakraborty <i>et al</i> , 2011

Pharmacological properties:

Insecticidal activity

The roots of *Piper betle* were liable to methanolis solvent extraction for the separation of various bioactive constituents. (Sindhu S Nair *et al*,2017). In this activity Extract was studied against *Tribolium castaneum*, adult *Brunches pisorum*, *Sitophilus oryzae* by direct contact application method (Sindhu S Nair *et al*, 2017). The piper essential oil Exhibits insecticidal properties against storage insect pests like bean weevil, corn weevil and lesser grain borer, suppressing progenie production and egg developmentand potentially acting as a grain protectant (AK Sahu *et al*,2022).It has been discovered that betle vine essential oil can be used as an alternative bioinsecticide (AK Sahu *et al*,2022)

Anti-oxidant activity

Substances known as antioxidants have the ability to counteract free radicals, which are unstable chemicals that harm cells. Oxidants cause various health issues like cancer (Chandra Risdian *et al*, 2011). the ethanolic leaf extract of *Piper betle*

Linn's capacity to scavenge free radicals (Chandra Risdian *et al*, 2011). Solution in stock DPPH and 1 milliliter of plant extract (different concentrations, such as 200, 400, 600, 800, and 1000 ug/ml) are present. Ascorbic Acid Used in positive Control or standard (Devjani Chakraborty *et al*, 2011). Allow the reaction mixture to incubate for 30 minutes at 37°C under dark conditions. After the incubation period, absorbance at 530 nm. The DPPH free radical scavenging activity percentage can be determined using the subsequent equation (KY pin *et al*, 2010).

Anti-inflammatory effects assessed via Protein Denaturation Assay

Inflammation is the response seen after cellular damage leading to the development of an exudate rich in proteins. Innate immunity is a component of this process, which manifests as discomfort, heat, redness, swelling, and reduced function (Rintup D *et al*, 2015). protein denaturation is the process of causing a protein's secondary and tertiary structures to unfurl and be disrupted without causing peptide bonds to break or

hydrolyze (Pushal De *et al.* (2017). the reaction mixture contains 0.4ml of egg albumin and 5.6ml of 6.9 PH PBS (phosphate buffer saline). further add 1ml of various concentration of plant extract and standard Diclofenac Sodium. Allow the reaction mixture to sit for 5 minutes at room temperature, then heat it to 70°C for 15 minutes. Once the incubation is complete, let the mixture cool down and determine its absorbance at 530 nm.

Antibiofilm assay

It Involves The ability to inhibit the formation and stability of Bacterial Biofilm. this is typically Done by Exposing biofilm structure, biofilm viability, Common methods Include crystal violet staining, Microscopy and Quantification of biofilm Associated factors. The experimental setup consists of combining 2ml of nutrient broth, 10 µl of bacterial suspension, and 50 µl of varying concentrations of plant extract and Standard Streptomycin in sterile conditions. This mixture is subsequently incubated for 24 hours at 37°C. The following day, remove the reaction mixture and add 1ml of 0.1% Crystal violet Stain. Allow the mixture to incubate at room temperature for 10 minutes. Subsequently, discard the stain and introduce 70% ethanol. Measure the absorbance at 560 nm.

Antifungal assay

The widespread use of broad-spectrum antibiotics and immunosuppressive treatments has led to a significant clinical problem: fungal infections. *Candida* stands out as the most prevalent among all fungal species (Rattiporn *et al.*, 2018). To prepare Sabouraud dextrose agar media, combine the necessary components and sterilize in a 121°C autoclave for 15 minutes. Subsequently, pour the media into petri plates according to the required well sizes. Spread 100 µl of bacterial suspension evenly across the growth medium. Create 6 mm diameter wells using a cork borer. Add the standard to the designated well. For 24 hours,

place the plates in an incubator set at 37°C. Following successful incubation, examine and measure the zone of inhibition.

Antibacterial assay

Antibacterial is a suppresses their bacterial growth using the well diffusion Method involves introducing antibacterial Substances into wells on an agar plate (K. Kabesh *et al.*, 2015). Prepare the nutrient agar media by using media Components. Sterilize the prepared growth media in an autoclave at 121°C for 15 minutes. Distribute the media into petri dishes according to the required well sizes. Spread 100 µl of bacterial suspension evenly across the growth medium. Use a cork borer to drill wells that are 6 mm in diameter. Introduce the standard streptomycin and test sample into their respective wells. For 24 hours, place the plate in an incubator set to 37°C. After the successful incubation Observe and Measured the zone of Inhibition.

Antihelminthic assay

Parasitic worms & infect crops, domestic pets and livestock and affecting food production with an economic impact (sonalkar *et al.*, 2017). Antihelminthic assay involves evaluating Substances with for their ability to inhibit or kill parasitic helminths. This is typically done by exposing helminths to the test Substance and assessing parameters such of motility, viability or Structural integrity, aiming to identify Compounds with Antihelminthic properties for the treatment of parasitic worm infections. Take two petri dishes with lids and label it has Standard and test. Wash the earthworms with the help of Distilled water takes Earthworm each plate. Pour the 20 ml of Standard and sample in respective petri plate. Using a stopwatch, record the duration of paralysis and the time of death for each earthworm.

Anti-fertility activity

Female albino rats administered 100 mg/kg of Piper betle Petiole's ethanolic extract shown antiestrogenic properties. Serum glucose

concentration, fertility, litter number, estrogen levels, reproductive organ weights, and enzyme activity were all decreased, although ascorbic acid and cholesterol levels were raised (Sunil Shah *et al*, 2016). A study on male contraceptive agents using *Piper betle* leaf stalk extract in mice showed no toxicity and reversible fertility after treatment withdrawal (Aishwarya *et al*, 2016).

Anticancer activity

According to the study, the aqueous extract of *piper betle* leaves demonstrated strong cytotoxicity and possible anticancer effects, with a

CTC50 of 96.25 ug/ml (Sunil Shah *et al*, 2016; Aishwarya *et al*, 2016).

Antiulcerogenic activity

Rats given an ethanolic extract of *Piper betle* Linn leaf orally had a strong protective effect against indomethacin-induced stomach lesions. Additionally, the extract demonstrated scavenging activity against superoxide and hydroxyl free radicals. Its antioxidant component, allyl pyrocatechol, also protected against indomethacin-induced stomach ulceration (Aishwarya *et al*, 2016).

Table no.4: Various therapeutic effects of *piper betle* Linn

S. No	Extract	Effects	Result	Reference
1.	Essential Oil of <i>piper betle</i> Linn	Insecticidal activity	<i>Piper betle</i> Linn essential oil has the potential to combat <i>Aedes aegypti</i> L. alternatives of new bioinsecticide	Wahyuni <i>et al</i> ,2012
2.	Ethanol-Based <i>Piper betle</i> Linn Extract	Anti-ulcerogenic activity	Ethanol-Based <i>Piper betle</i> Linn Extract was potential	Majumdar <i>et al</i> ,2002
3.	<i>piper betle</i> Linn leaf Extract	Anticancer activity	Extract from <i>piper betle</i> linn leaves on KB cell lines has strong	Veettil <i>et al</i> ,2022
4.	Extract of <i>Piper betle</i> Linn's Steam	Anthelmintic assay	Potent properties of <i>piper betle</i> linn steam extract	Adate <i>et al</i> ,2012
5.	Ethanol-Based <i>Piper betle</i> Linn Extract	Antibacterial assay	The Study of ethanol extracts be active the Strain of <i>Staphylococcus aureus</i>	Ryan Christopher <i>et al</i> ,2023
6.	Solvents extraction of <i>piper betle</i> Linn	Antifungal assay	The <i>piper betle</i> linn extract had the potential to have antifungal properties.	Sarika Pawar <i>et al</i> ,2017
7.	<i>Piper betle</i> Linn's alcoholic and aqueous extract	Anti-inflammatory effects assessed via Protein Denaturation Assay	The alcoholic and aqueous extracts made from <i>piper betle</i> leaves exhibited strong anti-inflammatory properties.	KY Pin <i>et al</i> , 2010; Puspall De <i>et al</i> ,2017
8.	<i>Piper betle</i> Linn's alcoholic and aqueous extract	Anti-oxidant activity	The alcoholic and aqueous extracts made from <i>piper betle</i> leaves exhibited strong antioxidant properties.	KY Pin <i>et al</i> , 2010
9.	Ethanol-Based <i>Piper betle</i> Linn Extract	Anti-fertility activity	The evidence indicates that betle extract had antifertility effects on female rats.	J.D. Sharma <i>et al</i> ,2007

10.	Ethanol-Based <i>Piper betle</i> Linn Extract	Antibiofilm assay	The Study of ethanol extracts be active potential the Strain.	Ryan Christopher et al,2023
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CONCLUSION

The herb *Piper betle* Linn exhibits significant potential of a source of pharmacological components that combat a range of infections. *piper belle* Linn is known to offer numerous Health benefits Including aiding in proper digestion, preventing diseases, and controlling. the harmful oxidants. The conclusion we reached was that *piper betle linn* has therapeutic qualities and can be used to cure and prevent a number of infections. To thoroughly examine the possible therapeutic uses of *piper betle* Linn, more research is also required.

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