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Pān (*Piper betle* L.): An assessment on medicinal profitability in outlook of Unani medicine

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Abstract

The betel (*Piper betle* L.) constitutes the foliage of a vine that falls under the Piperaceae family. This plant is cultivated in regions of India characterized by warmer and moister climates. Displaying evergreen characteristics, it is a perennial plant with leaves shaped like heart. The leaves, roots, and fruits of the betel plant possess medicinal properties and find application for both internal and local treatments in various diseases. Its pharmacological effects encompass roles as a carminative, stomachic, antihelminthic, aphrodisiac, laxative, ozene remedy, and treatment for conditions like bronchitis and elephantiasis of the leg. For night blindness, the juice from the leaves is applied to the eyes. Numerous scientific studies like antimicrobial, antihistaminic, antiulcer, antibacterial and anti-haemolytic activities has been done to explore the pharmacological actions of this herb. This chapter delves into the modern and Unani perspectives on the pharmacological properties of *Piper betle* L., providing insights into its Phytochemistry and the results of pharmacological studies.

Keywords: *Piper betle* L, Pān, betel, Piperaceae, Unani medicine

Introduction

Unani medicine, one of the oldest traditional systems, is widely practiced in the Indian subcontinent and Arab countries. It has served humanity for centuries by treating ailments with natural resources, primarily using plant-derived drugs. Among these, medicinal climbers hold a significant place. Some of the useful climbers are *Piper nigrum* (Filfil Siyāh), *Piper cubeba* (Kabābchīnī), *Piper betle* (Pān) [1, 2] *Cuscuta reflexa* (Aftimūn), *Gymnema sylvester* (*Gurmār Būtī*) etc. are used for centuries, these plants have shown effective results, especially in managing chronic and life-threatening diseases [3]. The *Pān* or *Tambol* known as betel leaf in English, is commonly used remedy in Unani medicine and is recognized for its deep green, heart-shaped leaves, referred to as *Pān* in India. Scientifically named *Piper betle* L., it belongs to the Piperaceae family, also known as the Black Pepper family. This dioecious vine, meaning it has separate male and female plants, is a perennial root climber that thrives in shaded environments. Worldwide, there are approximately 100 varieties of betel vine, with around 40 found in India, and 30 of those specifically in West Bengal. Believed to have originated in Malaysia, the betel vine has gained immense popularity in India since ancient times, as reflected in numerous references in Indian scriptures and literature. The leaves of the betel vine have been highlighted in ancient texts for their significance in various aspects of human life, encompassing social, cultural, religious, and daily routines. This relevance persists today, where a well-prepared betel quid remains valued as an excellent mouth freshener and mild vitalizer. It continues to be a customary offering during social, cultural, and religious events such as weddings, religious festivals (*Puja*), and post-cremation ceremonies (*Sraddha*). Additionally, it is presented as a sign of respect to guests, making the traditional use of betel leaf in Indian society unique and unparalleled in contemporary times [4]. Possessing a sharp taste and a pleasant aroma, it not only enhances taste and appetite but also serves various therapeutic purposes. The betel leaf holds significant value as a home remedy for common illnesses [5]. It is employed as a carminative, stomachic, Antihelminthic, cardi tonic, neurotonic, liver tonic, aphrodisiac, and laxative. Its application extends to conditions such as ozene, bronchitis, elephantiasis of the leg, leprosy, poisoning, alcoholism, and asthma. Furthermore, the betel leaf is known for its abilities to strengthen teeth, alleviate thirst, clear the throat, and act as a

vulnerary and styptic agent [6]. The *Pān* contains a variety of bioactive compounds, including β - and γ -sitosterol, hentriacontane, pentatriacontane, n-triacontanol, stearic acid, and chavicol. The essential oil extracted from its leaves consists of carvacrol, eugenol, chavicol, allyl catechol, cineole, estragol, caryophyllene, cardinene, p-cymene, and eugenol methyl ether. These diverse bioactive compounds play a crucial role in the plant's pharmacological actions [7].



Fig 1: Showing climber of *Piper betle* a. fresh leaves available on shop b., anterior c., and posterior image d. of the leaf

Distribution:

This spice, native to Central and Madagascar, as well as East Africa [5], also found in Sri Lanka, Vietnam, Nepal, and Singapore. In India, it is specifically grown in states such as Assam, Bengal, Bihar, Uttar Pradesh, Maharashtra, Karnataka, and Kerala [7].

Botanical Description

The betel (*Piper betle* L.) is a perennial, dioecious creeper characterized by semi-woody stems that climb using short adventitious roots. Its leaves, measuring 10-20 cm in length, are broadly ovate, slightly cordate, often uneven at the base, and shortly acuminate. The leaves are glabrous, glaucous on the sides, and display a bright green or yellowish color. The petiole is stout, measuring 2.0-2.5 cm in length. Male spikes are cylindrical and dense, while female spikes range from 2.5-5.0 cm in length, appearing pendulous. Fruits are rarely produced, often sunken in the fleshy spike, forming nodule-like structures [5].

Taxonomical classification

Kingdom: Plantae
Phylum: Tracheophytes
Class: Angiosperms
Order: Magnolids
Family: Piperales
Genus: *Piper*
Species: *P. betle*

Description in Unani literature

Tambool is a leaf similar to the leaves of *Lobia* and grapes. The *Pān* leaf is smooth, green pointed at apex with broad base. On back of the leaf prominent veins are present. People in the Arab region around Oman cultivate it, and in India, there are various types of *Pān*.

1. **Sikri Pān:** This type of has soft and small leaves that turn white with repeated chewing type, and is cultivated in the specific village "Sikri" of the Bihar province. So it is named as "Sikri Pān" due to its origin. This *Pān* is beautiful, has an excellent taste, is low in sweetness, and is moderate in heat and dryness.
2. **Gangiri Pān:** This type of *Pān* is found in Delhi, Agra, and the surrounding areas. Its leaf is larger than the *Sikri Pān*, and it possesses various properties and flavors that are somewhat similar to *Sikri Pān*.
3. **Kapūrī Pān:** This type of *Pān* has large, green, very delicate, and soft leaves. This variety is produced in the "Sitaraganj" region of Bengal. It gives off a strong fragrance and has a sharp taste like cloves.
4. **Sānchī Pān:** This type of *Pān* has large, medium green and soft leaves, and with a specific process, they turn white. This is often produced in India and Bangladesh. It is also delightful and aromatic, but its fragrance delicacy is not like all three types. It is warm and dry, in the first degree.
5. **Bangla Pān:** The leaves of this type of *Pān* are large and green, its leaf has a sharp taste and is fragrant. It is specifically produced in Bengal that is why it is named as *Bangla Pān*. It is hot and dry in the second degree. Based on the region and location, there are various types of *Sanchi* and *Bangla Pān*
6. **Malkapuri Pān:** It is considered as the best type of *Bangla Pān*. It consists of soft, small, and moderately wide leaves. Its name *Malkapuri Pān*, is attributed to the Malkapur village in Murshidabad as it is abundantly produced there [8].

Mutarādifāt (Vernacular Names)

The plant is used by different vernacular names in Unani Medicine as:

Arabic: Fān [9], Tambūl
Bengali: Pān [10]
English: Betel leaf Vine [6]
Gujrati: Nagurvel [10], Pān [6]
Hindi: Pān [10]
Kannad: Veelyadale Ele [10]
Marathi: Pān, Nagvel, Vidyachepan [10]
Panjabi: Pān [10]
Persian: Tambol [9]
Sanskrit: Tambuli [10] Tambol [9]
Tamil: Vettilai [10], Sambol [9]
Telugu: Tamalapaku, Tamulapa [10]
Parts Used: Leaves and fruit [11]

Mizāj (Temperament)

Hot and dry in 2nd degree [9, 12]

Most Greek physicians have classified the temperament of *Pān* as *Har* (hot) in the 1st degree and *Yabis* (dry) in the 2nd degree. Some individuals have mentioned it as *Hār* (hot) and *Yābis* (dry) in the 2nd degree. Ibn Sina, however, wrote that it is *Bārid* (cold) in the 1st degree and *Yābis* (dry) in the 2nd degree [8].

Af'āl (Action)

The betel leaves have *Kāsir-i-Riyāh* (carminative), *Muḥarrrik* (stimulant), *Muqawwi-i-Qalb* (cardiac tonic), *Muqawwi-i-Dimāgh* (brain tonic), *Mufriz-i-Lu'āb-i-Dahan* (sialagogue), *Qābiḍ* (astringent), *Mulayyin* (laxative), *Māni'-i-Nazla* (anti-catarrh), *Dāfi-i-Ta'affun* (antiseptic), *Muḥallil-i-Warm* (anti-inflammatory), *Dāfi'-i-Tashannuj* (antispasmodic), *Mukhrij-i-Balgham* (expectorant), *Munaffith-i-Balgham* (expectorant), *Musakkīn* (analgesic), *Mulattif* (deobstruent), *Muqawwi-i-Jigar* (liver tonic), *Muwallid-i-Lu'āb-i-Dahn* (sialagogue), *Muqawwi-i-Dandān* (gum and tooth strengthener), *Matīb-i-Nikhat*, *Nāfi' Saylān-i-Ruṭūbat*, *Mudir-i-Bawl* (diuretic), *Mulayyin* (emollient),^[3, 8, 9, 12, 13] antispasmodic, anti-catarrh etc^[7].

Iste'mālāt (therapeutic uses)

Leaves are used in *Su'āl* (cough), *Diq-al-Nafas* (asthma), *Waram-al-Liththa* (gingivitis), *Waja'-al-Asnan* (toothache), *Qulā'* (mouth ulcer), *Jarha* (wound), *Waram* (swelling)^[13] *Ḥumma* (fever), *Qīla Ma'iyya* (hydrocele) *Dīdān-i-Am'ā'* (helminthiasis), *Fasād al-Haḍm* (Dyspepsia), *Khafaqān* (palpitation)^[8]. *Buḥḥa al-Ṣawt* (Hoarseness of voice) *Aṭash Mufrīṭ* (Polydipsia)^[9].

Tarkīb-i-Iste'māl (method of administration) in Unani Medicine

1. Drinking doses of cough syrup mixed into the juice of Pan Plant, and making pills from it, helps relieve cough^[7].
2. Applying oil on the stem of the betel leaf and inserting it into the baby's rectum helps to alleviate constipation. It is also used to treat abdominal disorders in children. To relieve swelling and pain, applying oil, heating it, and then binding it on an affected area can be beneficial^[7].
3. Applying it to the breasts can stop milk flow^[7].
4. Eating it with honey helps to alleviate cough^[7].
5. To stop a miscarriage, the soft roots of this plant should be ground with black pepper and then used^[7].
6. Make an extract from 3.75 grams of pan, and use it two to three times a day to help relieve fever^[7].
7. Applying it to the temples can also relieve headaches^[7].
8. To treat conditions such as spirits and supernatural afflictions in women, betel leaf extract should be mixed with milk and given to them^[7].
9. Applying betel leaves to the stomach can relieve flatulence-related pain. Conditions caused by adverse environmental factors are kept at bay by consuming betel leaves^[7].
10. A drop of betel leaf extract in the eye can alleviate inflammation^[7].
11. Applying the extract on head can help to dissolve the blood clots in the brain^[7].
12. For relieving stomach heat and thirst, betel leaves are effective. Betel leaf juice stimulates appetite and applying it to the eyes can help with dryness and irritation^[7].
13. For children's ailments, such common cold and chest pain, betel leaves should be smeared with oil, heated over a fire, and then placed on the chest. On top of this, five to seven betel leaves should be placed, and a bandage should be applied. Using this method helps to relieve children's cough and difficulty in breathing^[7].

14. To alleviate indigestion in children's, it is advisable to administer betel leaf extract^[7].
15. Wrapping warm *Bangla Pān* leaves around the scrotum benefits in hydrocele. Initially, placing two or three leaves above and below provides significant relief, and within two to three days, the swelling resolves. If the heat is intense and unbearable, then just wrap one or two leaves or apply them at intervals of one or two days, the swelling will gradually reduce^[8].

Method of administration according to various region and folklores

16. In the Konkan region, the fruit is combined with honey to serve as a remedy for cough, while in Orissa the root is believed to be utilized for birth control^[7].
17. In the Philippines, the leaves are highly regarded as remedies for various childhood ailments such as indigestion, colic, diarrhoea, pulmonary catarrh, and laryngitis. When applied hot to the chest, they are believed to promote lactation^[7].
18. In Cambodia, freshly pounded Pan Leaves are utilized in creating lotions and baths for individuals enduring prolonged fever, smallpox, enlarged glands, and lymphangitis^[7].
19. The juice extracted from the leaves is applied to the eyes to alleviate discomfort in eye-related conditions^[7].
20. Additionally, it is employed to alleviate cerebral congestion, satyriasis, and to quench thirst^[7].
21. The juice from the leaves is also used in the treatment of night-blindness^[7].
22. The essential oil derived from the leaves has proven effective in treating catarrhal disorders and serves as an antiseptic^[7].
23. The juice of a few betel leaves, with a teaspoon of honey, will serve as a good tonic. A teaspoon of this can be taken twice a day^[7].
24. In the case of constipation in children, a suppository made of the stalk of betel leaf dipped in castor oil can be introduced in the rectum. This instantly relieves constipation^[7].
25. Betel leaves play a vital role in the treatment of nervous pains, nervous exhaustion and debility^[7].
26. The application of Pan Leaves smeared with oil is said to promote secretion of milk when applied on the breasts during lactation^[7].

Maḍarrat (Toxicity, side effect and adverse effect)

Understanding that the Pān might serve various traditional medicinal purposes, it is crucial to be aware that excessive consumption can be detrimental, particularly for individuals with a hot temperament. Eating pan on an empty stomach is harmful particularly in individuals with hot temperament^[8].

Musleh (Corrective)

Ila'ichī Safed (*Elettaria cardamomum*), *Sikanjabīn* (a syrup of honey and vinegar) and *Imlī* (Tamarind) are the correctives of Pān, they are recommended to use along with Pān to prevent from side effects^[8].

Badal (Substitute or alternative)

The following drugs are mentioned in the Unani text as substitutes for Pān. They are *Lawng*, *Sāzaj Hindī*, and *Qarnful*^[8].

Compound formulations*Habb-i-Pān*^[14] *Habb-i-Kattha*, *Habb-i-Nishat*, *Arq-i-Juzam*,*Jawarish-i-Utraj* (see detail in Table 1)^[15].**Table 1;** Compound formulations having *Piper betle* L. leaves as one of the main ingredients, with their dose, method of administration, action and uses:

S.N.	Name of the compound	Dose and method of administration	Action and uses
1	<i>Habb-i-Pān</i>	15-25 mg	It is Useful in <i>Ātashak</i> (syphilis), <i>Fasād-i-Dam</i> (impairment of Sanguine)
2	<i>Habb-i-Kattha</i>	250-500 mg	<i>Mubarrid</i> (Astringent), <i>Daf-i-Taffun</i> (Antiseptic) <i>Muṣaffi-i-Dam</i> (Blood purifier), It is useful in <i>Ātashak</i> (syphilis).
3	<i>Habb-i-Nishāt</i>	250-500 mg	<i>Muqawwi-i-Bah</i> , <i>Muharrrik</i> , It is useful in <i>Du'f-i-Bah</i> , <i>Sur'at-i-Inzal</i> (premature ejaculation), <i>Izmihlāl</i> (weakness)
4	<i>Arq-i-Juzam</i>	50-100 ml	<i>Muṣaffi-i-Dam</i> (blood purifier), it is useful in <i>Juzām</i> (leprosy), <i>Baras</i> (leukoderma), <i>Jarab</i> (Scabies), <i>Qurooh</i> (ulcer)
5	<i>Jawarish-i-Utraj</i>	5-10 g	<i>Muqawwai-i-Meda</i> (Stomachic), <i>Daf-i-Safra</i> (Ant bilious), It is useful in <i>Du'f-i-Mi'da</i> (Weakness of stomach), <i>Du'f-i-Kabid</i> (weakness of liver)

Bioactive Compounds

The leaf has been reported to contain water, proteins, carbohydrates, minerals, fat, fibre, essential oil, tannin and alkaloid (arakene). The leaves afforded β and δ sitosterol, hentriacontane, pentatriacontane, *n*-triacontanol, stearic acid and chavicol. The essential oil from leaves contained carvacrol, eugenol, chavicol, allyl catechol, cineole, estragole, caryophyllene, cardinene, *p*-cymene and eugenol methyl ether^[7].

Pharmacological studies**Antimicrobial Activity**

Nair and Chanda (2008) conducted a study on the antibacterial activity of the aqueous and methanol extracts from the leaves *Piper betle* L. The investigation included 10 Gram-positive bacteria, 12 Gram-negative bacteria, and one fungal strain, *Candida tropicalis*. Piperacillin and gentamicin served as standards for the antibacterial assay, while fluconazole was the standard for the antifungal assay. The results indicated varying degrees of activity among the three plants against the tested microorganisms. The methanolic extract demonstrated significantly higher effectiveness compared to the aqueous extract in inhibiting the microbial strains under investigation^[16].

Antihistaminic activity

Hajare *et al.* (2011) conducted an assessment of the antihistaminic activity of the ethanolic extract and essential oil extract of *Piper betle* L. leaves on guinea pigs model. In the isolated guinea pig tracheal chain preparation, a right-sided shift in the dose-response curve (DRC) of histamine was observed. Chlorpheniramine maleate served as the standard drug in this evaluation. Additionally, the extracts of *P. betle* were found to disrupt histamine aerosol-induced bronchoconstriction in the entire guinea pig, with the essential oil exhibiting greater effectiveness compared to the ethanolic extract^[17].

Antiulcer Activity:

Vyawaharre *et al.* (2010) conducted an assessment of the antiulcer activity of the hydroalcoholic extract of *Piper betle* leaves in rats, utilizing experimental gastric ulcer induction models such as HCl-ethanol, acute stress, and pylorus ligation. The pre-treatment with *Piper betle* extract demonstrated a notable protective effect against ulcers in all experimental models, accompanied by a significant increase in gastric pH and a decrease in gastric fluid volume. The

antiulcer activity of the hydroalcoholic extract of *Piper betle* L. leaves is suggested to be linked to its potential mechanism of action^[18].

Antibacterial activity

The study conducted by Agarwal *et al.* (2012) investigated four varieties of *Piper betle*, namely *Desawari*, *Desi*, *Bangladeshi*, and *Jaleswar*, all cultivated in India. The researchers evaluated the antimicrobial properties of cold aqueous, methanolic, ethanolic, and ethyl acetate extracts derived from the dried leaves of these four *Piper betle* varieties. The testing was performed at a final concentration of 500 mg/ml against pathogenic microorganisms, including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Escherichia coli*, using the agar well diffusion method^[19].

Palpebral skin antiseptic

Amalia *et al.* (2009) assessed the antiseptic effectiveness by quantifying microbial colonies before and after the application of antiseptic solutions. The study revealed that the mean colony counts significantly decreased by 27-100% after the administration of 20% *Piper betle* leaf infusion compared to counts before application ($p < 0.001$). Similarly, the mean colony counts after administering 10% povidone-iodine exhibited a significant reduction of 88-100% compared to the counts before solution application ($p < 0.000$). This suggests that the 20% *Piper betle* infusion possesses antiseptic potential^[20].

Anti-haemolytic activity

Anti-haemolytic activity was studied by Chakraborty *et al.* (2011), using erythrocytes model *Piper betle* leaf extracts and the extent of lipid peroxidation of the same was also determined^[21]. The erythrocyte membranes are susceptible to peroxidation because they are rich in polyunsaturated fatty acids. They contain haemoglobin, which may catalyze the oxidation as they are continuously exposed to high concentration of oxygen. The oxidation of erythrocytes serves as good models for the oxidative damage of biological membranes. It has been found that certain chemicals, having ability to generate radicals attack the erythrocyte membrane, inducing the chain oxidations of lipids and proteins and eventually causing membrane damage leading to haemolysis. When red blood cells were treated with betel leaf extract along with H₂O₂ marked reduction in haemolysis was found^[22, 23].

As contraceptive

Singh *et al.* (2011) conducted a study on the impact of various concentrations of *Piper betel* on the mitochondrial activity of sperm. They also examined the mitochondrial activity at different incubation time intervals using semen samples. The investigation involved more than 75% motile normozoospermic semen samples. The findings revealed a significant decrease in mitochondrial activity with an increase in extract concentration ($p < 0.001$). Similar results were observed when the extracts were maintained at a constant concentration but subjected to varying time intervals. Notably, there was a significant reduction in mitochondrial activity ($p < 0.001$) between 5 to 20 minutes of incubation time. The researchers concluded that *Piper betel* possesses properties that can diminish mitochondrial activity in human sperm, suggesting its potential as a contraceptive agent [24].

Conclusion

This review highlights the various medicinal properties inherent in the *Pān*, or betel leaf. With its sharp taste and pleasant aroma, the leaf not only enhances flavour and appetite but also serves multiple therapeutic functions. It is utilized as a carminative, stomachic, Antihelminthic, cardiogenic, neurotonic, liver tonic, aphrodisiac, and laxative. Its applications extend to addressing conditions such as ozene, bronchitis, elephantiasis of the leg, leprosy, poisoning, alcoholism, and asthma. Additionally, the betel leaf is recognized for its capacity to strengthen teeth, alleviate thirst, clear the throat, and act as a vulnerary and styptic agent. It is suggested that the betel leaf could serve as a potent traditional Unani drug, and further research in terms of Phytochemistry, clinical studies, and advanced exploration is recommended for the benefit of humanity.

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Conflict of interest

The authors declare no any conflict of interest.

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