Socio, Economic and Cultural importance of Betel Vine (*piper betle* L.) Cultivation: Its present status and future perspectives

Comment [P1]: Should use one science name and indicate one time in the text.

Abstract

The present study aims to investigate the Socio, Economic and Cultural importance of Betel Vine (*piper betle* L.) Cultivation. Betel vine is the most important and useful asexually propagated cash crop having various cultivars. The betel leaf has many chemical constituents that have many important industrial applications. The leaves are found to contain a terpinene, P-cymene, carvacrol, chavicol and its derivatives, allyl catechol, eugenol, estragole, oxalic acid, malic acid and amino acids.The economic status of betel leaves in the worldwide market depends on the physical nature of the end products. Betel leaf and its products in different forms such as powder, liquid, capsules, etc., are highly remarkable due to its various medicinal applications.The properties like antimicrobial activity, antioxidant activity, antidiabetic, anticancer activity, etc. justify its bioprospecting for future green medicine.

Comment [P2]: delete

Keywords: Betel Vine, antimicrobial activity,green medicine, Cultivation

1. Introduction

Betel leaf (*Piper betle* L.) is a heart-shaped deep green leaf that grows on a climbing vine. Betel vine is the most important and useful asexually propagated cash crop having various cultivars. It belongs to Piperaceae family and is a shed loving plant. It is popularly known as "*Pan*" in the local vernaculars mostly in the north-east and eastern parts of India. Malaysia is known to be the place of origin of Pan (Chattapdayay and Maity, 1967). Inspite of its alienness, the plant is much more popular in India than in any other country of the world since the antiquity. It has been very intimately connected with

the ancient Indian history, religion and culture as is evident by many references in the early Sanskrit literature (3000 BC), like Vedas, Ramayana, Mahabharata etc. This crop is usually cultivated in India, Sri Lanka, Malaysia, Thailand, Taiwan and other Southeast Asian countries. In India, it is widely cultivated in Odisha, Tamil Nadu, Madhya Pradesh, West Bengal, Maharashtra and Uttar Pradesh. It is primarily consumed in South Asia and by certain Asian emigrants worldwide as betel quid or pan, in combination with areca nut or tobacco (Shah et al., 2021). Marcopolo (1295 AD) took notice of the pan chewing habit of the people in south India.

Piper betle is called by different names in India i.e.,"Pan" in Hindi, Odia, Bengali and Assamese; "Tambula" in Sanskrit; "Villayadela" in Kannada; "Vettilakkoti" in Malayalam; "Vettilai" in Tamil; "Tamalapaku" in Telugu; "Videch-pan" in Marathi, Nagarbel in Gujrati, also called Tanbol in Arabic and Burg-e-Tanbol in Persian (Das et al., 2016). This plant is economically, medicinally and traditionally important in the whole world. It is used as a traditional herbal medicine in Asian countries from time immemorial (Khan et al., 2012). It is also used as a special item offered to the guests in order to show respect and for such traditional use of betel leaf in the Indian society, the leaf really stands alone without any parallel even today. The betel vine is called as 'green gold of India' as about 20 million people derive their livelihood directly or indirectly from production, processing, handling, transportation and marketing of betel leaves in India (Guha, 2006).

Comment [P3]: *Piper betle or* Betel leaf, use one name whole the manuscript

2. Plant Description

Piper betle is a dicotyledonous creeper. Stems semi woody, climbing by means of short adventitious roots. The plant has alternate, heart-shaped, smooth, shining and long-stalked leaves, with pointed-apex. It has five to seven ribs arising from the base; flowers minute. Leaves 10-20cm long, broadly ovate, slightly cordate and often unequal at the base, shortly acuminate, glabrous, glaucous on both sides, bright green or yellowish, petiole stout 2.0-2.5 cm long. Male spikes cylindrical dense and female spikes 2.5-5.0cm long, pendulous (Sengupta and Banik, 2013). The female plants are found to rarely produce any flower or fruit in the Indian climate (Dassanayake and Fosberg, 1987). In the humid environment of East India, female plants often generate blooms or fruit (Rahman et al., 2020). The branches of the plant are swollen at the nodes (Arambewela et al., 2005). Based on shape, size, brittleness and taste of leaf blade, betel vine is divided into pungent and non-pungent varieties (Arambewela et al., 2005).

Fig 1: Piper betle

3. Chemical Constituents

The betel leaf has many chemical constituents that have many important industrial applications. The leaves are found to contain a terpinene, P-cymene, carvacrol, chavicol and its derivatives, allyl catechol, eugenol, estragole, oxalic acid, malic acid and amino acids. Good amounts of vitamins particularly nicotinic acid, ascorbic acid and carotene are also found in leaves. They also contain significant amounts of all essential amino acids except lysine, histidine and arginine. Large concentrations of asparagine are present while glycine and proline occur in good amounts. Essential oil of the leaf gives it the aromatic flavor. The essential oil is a light-yellow liquid of aromatic odor and sharp burning in taste. It contains a phenol called chavicol which has powerful antiseptic properties. The alkaloid arakene in it has properties resembling cocaine in some respects. Because of their antibacterial and antioxidant properties, these oils have a promising future in the novel food packaging industry (Nguyen et al., 2021), as well as being a prospective and appealing flavoring component for the food and beverage sectors (Sahu et al., 2022). β-sitosterol is present in the root (Joshi, 2009).

Betel leaves are high in minerals, vitamins, enzymes, proteins, and essential oil (EO),and they are very nutritious (Nayaka et al., 2021). Betel leaves also contain tannins, sugar and diastases.The Detail Components of a fresh betel leaf are presented in Table1.

Table 1:The Detail Components of Fresh Betel Leaf

Sl.No.	Component	Amount in Fresh Green Leaf
1	Water	85-90%
2	Protein	3-3.5%
3	Fat	0.4-1.0%
4	Minerals	2.3-3.3%
5	Fiber	2-2.3%
6	Chlorophyll	0.01-0.25%
7	Carbohydrate	0.5-6.10%
8	Nicotinic Acid	0.63-0.89mg/100g
9	VitaminC	0.005-0.01%
10	VitaminA	1.9-2.9mg/100g
11	Thiamine	10-70µg/100g

12	Riboflavin	1.9-30µg/100g
13	Tannin	0.1-1.3%
14	Nitrogen	2.0-7.0%
15	Phosphorus	0.05-0.6%
16	Potassium	1.1-4.6%
17	Calcium	0.2-0.5%
18	Iron	0.005-0.007%
19	Iodine	3.2-3.4µg/100g
20	Essential Oil	0.08-0.2%

Source: CSIR, 1969 and Gopalan et al.,1984

4. Agronomic Condition for Betel Vine Cultivation

4.1 Climate

Piper betle L. grows in the tropical as well as subtropical climatic regions (Rai et al.,2011) and requires high rainfall and a shady place for its vigorous growth. Conducive Environment for commercial betel vine cultivation comprises artificial shade, presence of considerable humidity and adequate supply of moisture in the soil, moderate and even temperature throughout the year. Thus, its cultivation is best done under controlled conditions or shade conditions. The ideal weather condition for the plant is mild temperature, i.e., about 10°C in winter and about 40°C in summer for good growth of this shade loving plant. About 170 cm rainfall and presence of high humidity (60 to 80%) throughout the year is ideal for this crop. Below 10°C and above 40°C temperatures cause wilting in the plant. The vines grow fast and their vegetative growth is good under high humidity.The amount of air movement affects the rate of evaporation and is therefore, one of the chief factors controlling the growth.

4.2 Soil

Betel vine requires loamy or sandy soil with good organic matter which is rich in humus and having best elements of soil with sufficient moisture-holding capacity. Sufficient drainage arrangements and laying on elevated sloppy lands formed an ideal soil for betel vine plantation (Dasgupta et al., 1993). Exceptionally well-drained soil is the best for betel vine cultivation. Red loamy soil, both light and heavy with good soil depth (fertile soil and

excellent drained) and pH (5.6–8.2) is most suitable for the growth of betel plants whereas saline,alkali soils and water logged areas are unsuitable (Pradhanetal.,2013). The clay soil is not good for the crop because it favors disease during the rainy season. However, this crop is very sensitive to saline and alkaline soils (Balasubrahamanyam, 1994). Soil with good water holding capacity and organic matter content is considered ideal. Loamy soil with a porous substratum below is also excellent.

Fig 2: 'Baraja':The artificial betel vineyard constructed for pan cultivation

Pan is cultivated in two different ways like under forest ecosystem and artificially created with shade conditions. Open and closed systems of cultivation of betel vine are practiced in India. The closed system of cultivation is called Baraja. 'Baraja' are generally rectangular in shape and its normal size is often 50 to 30 Sq. meter. Generally, Barajas are small because its maintenance ought to be easy and their cost of erection is within manageable limits. These structures are made up to a height of 2-2.5 m and covered with thatched coconut leaves or straw (Guha,2006). Baraja structure is made up of locally available materials such as bamboo, khar, straw, jute, sticks, arhar stalks, munj and a variety of grasses. 'Barajas' are normally made on slightly sloped nearer to a source of irrigation at a higher level than the adjoining area for quick drainage of excess water. The construction of 'Baraja' looks like a mandap. Its height is about 3-5 meters. This is surrounded by a thatched wall roof. The walls are strengthened with bamboo poles fixed at a distance of about 2.0 meter each. The top roof is covered with thick straw with longitudinally divided bamboo poles supported by bamboo posts inside the 'Baraja'. The

distance from one horizontal pole to another is about 2 meters to 2.5 meters. Criss cross supporting poles are used instead of erected poles. The wall and the top are covered with bamboo sticks and straw in order to protect the plants and soil surface from direct sun rays. Roof is thatched twice in a year, first at the time of construction of new 'Baraja',and second, after the rainy season. Structure of the 'Baraja' is built strongly, so as to withstand strong winds and storms. This shape carries sound logic in terms of humidity and temperature control. The expected economic life of a Baraja,on an average, is about five years from its erection (Changure,1960).

4.3 Features of 'Baraja'

Betel vine plants require high humidity and mild temperature for their growth. Thus, its cultivation is possible only by partially regulating the two critical factors. The design of 'Baraja' is such that it ensures suitable humidity levels within. Evaporation of water within the 'Baraja' not only raises the humidity,but also lowers the temperature. It is very crucial for plant survival during extreme summer, when low humidity coupled with high temperature can whither and damage the plants by photo inhibition. Blocking the intensity of light coming to the surface can effectively reduce the heating effect of solar radiation. The top of the 'Baraja' should be designed to block check light by spreading dry leaves or straw at the top. During summer the thatching is thick so that more than 75 percent of the incident of solar radiation is blocked. This reduces intensity of light falling on the tender leaves and soil, so that it can effectively check the increase in air and soil temperature inside the 'Baraja'. During the rainy season when climate is most suitable for the growth of vines, the thatching on the top is reduced so that about 50.00 per cent of the incident of solar radiation reaches the leaves and soil. With the onset of winter when temperature starts falling, the grass cover at the top is increased to some extent in order to avoid frost and cold injury. During this period, the incident of light in the 'Baraja' is more than in summer. The growth of plant during winter is very slow or even stopped (Changure, 1960).

4.4 Planting Method

Normally, the dibbling method is used for planting. Planting is done with the help of khurpi (a hand operated implement). For planting, a hole is made with khurpi, so that the internodes below the bud point are dipped in soil, but must be touching with surface soil.

The hole is completely packed with the help of thumb finger. After that, the planted material is covered with khar or straw. This planted betel vine plant needs to be watered twice a day with the help of watering cane or sprinkler. During irrigation special care is needed that after twenty days of continuous irrigation, cover on the plants needs to be removed. The newly planted Baraja is maintained very carefully. Over irrigation is avoided. A larger moist straw is spread on the planted vines to avoid evaporation (Balasubrahamanyam, 1994).

4.5 Irrigation

Betel vine is very fastidious in its water requirements. It needs a moist soil, but not too wet.That is to say, it requires frequent but light irrigation all-round the year. The plantation has to be located near the source of irrigation, which may be a pond or tank, a canal, or irrigation well. Frequencies of irrigation depend upon intensity of light and humidity of the atmosphere. During the summer season, irrigation is given almost every day in the new plant and weekly in the old plant. During the winter season, irrigation is reduced to a fortnight interval. During the rainy season, ordinarily no irrigation is done, unless the rare adverse climatic conditions. Excess irrigation causes decay of roots and dropping of leaves. Irrigation in betel vine crop was given through a sprinkler or pot. The pot method is very costly because of intensive labor use needed in it (Balasubramanyam ,1992).

4.6 Weeding/ Interculturing

Keeping the plantation free from weeds, its immediate removal is necessary. An Advantage of growing betel vine in closed conservatory or under shade is that it remains generally weed free. Only in a year during the month of November and in June, lowering of vines is done. The main aim of this practice is to give earthing to the vines lying on the soil surface. Thereafter, staking is done with the help of supporting materials. Each vine is supported with bamboo sticks or sharkanda (like wooden sticks). Each supporting material is tied to the roof and inserted into the soil. When the vine reaches to the roof of Baraja, it starts lowering. Auxiliary branches are removed from the main vine regularly in monsoon season. During monsoon all the leaves up to a height of 2 feet from the soil surface, are removed to reduce the infection of soil borne disease or pathogens. The ‘Baraja’ is always kept neat and clean (Balasubramanyam, 1992).

4.7 Insect Borne Disease Control Measures

The betel vine crop is attacked by a number of fungal and bacterial pathogens and they cause many types of diseases to the plant. Several unidentified infections and insects also harm betel vine cultivation, resulting in significant losses for growers (Vishwakarma and Purohit, 2020). The most common is marginal blight, anthracnose and leaf spot affecting both leaves and vines. Pathogens also affect root, stem and leaf to a large extent. The affected plant dies suddenly. Among the bacterial diseases, leaf spot is more common in newly planted crops and Baraja. Patra and Pradhan (2018) reported a leaf spot disease induced by *Fusarium semitectum*. The crop also suffers a lot with red spider mite. Causes turning of leaf lamina into brick red and it becomes unfit for consumption. *Sclerotium rolfsii* causes foot and root rot which is the most devastating disease that decreases the production of betel leaf (Rahman et al., 2021). For controlling pests, diseases and insects, different pesticides and insecticide are commonly used in the Baraja by the farmers. But some progressive farmers use integrated approaches for pest and diseases' management in their fields. For controlling disease, they use natural methods i.e In the Baraja adequate drainage facilities are provided,disease prone leaves and vines are removed and buried in the soil outside the Baraja. They also use Bordeaux mixture frequently for stem and leaf not infected. They also control the white flies through chemical pesticides. At the stage of harvesting, farmers often use pesticides, insecticides to make the soil germ-free. Only exposure of soil to sunlight is resorted under soil protection measures. This type of natural method is cheaper but less effective (Balasubramanyam, 1992).

4.8 Cultivation, Yield, Processing and Preservation

Its cultivation is highly labor-intensive and offers employment throughout the year to millions of people (Kaleeswari & Sridhar, 2013). Depending on the cultivation of betelvine, the planting season varies from state to state in India, but the onset of monsoon and October are the correct time of planting season for cultivation. The peak harvesting season extends from May to January. The usual productive life span of a betel vine is 12-15 years. Betel leaf can be plucked five times a year from a vine. The production yield of this crop is about 60-70leaves/ plant and 6-7 million leaves/ha in a year (Guha, 2006). Betel leaf involves a good deal of post-harvest processing, that is, storing the harvested leaves over some time (Caburian and Osi, 2010). Traditionally, harvested betel leaves

carried by farmers are kept on banana leaves for cotton material or on rice straw in bamboo baskets, and water is sprayed on the leaves to make them look fresh (Haider et al., 2013).

5. Economic Status

The economic status of betel leaves in the worldwide market depends on the physical nature of the end products. Betel leaf and its products in different forms such as powder, liquid, capsules, etc., are highly remarkable due to its various medicinal applications. Several types of value-added products are available in a wide range in the market as dietary supplements, food and beverage products, pharmaceuticals, oral care, and cosmetic products. The value-added products have been manufactured in industrial level namely betel leaf oil,betel toothpaste, and powders, pan masala, perfumes, mouthwash, betel ointment, shampoo, face cream, instant betel quid and pellets, antiseptic lotions, different medicinal and cosmetics products (Guha, 2000). The above-mentioned products have gained a good export potential and earned some foreign exchange through exports. India exports betel leaves to many countries like Bangladesh, Pakistan, Indonesia, Myanmar and Thailand. The marketing cost of betel leaves mostly depends on packing and transportation costs. The annual turnover of betel vine is estimated at Rs.10,000 million (Kumar,1999). The cost of cultivation of betel vine from Baraj varies, that is, about Rs 1-2 lakh/ha in the first year (Chattopadhyay,1981). More recently betel leaves are being exported fromIndia to UK, USA, Canada, Srilanka, Malaysia in addition to Pakistan, Bangladesh, Singapore, Myanmar and Thailand along with other Arabian countries with an annual earning of Rupees 198 lakh through foreign exchange. Its cultivation is highly labour intensive and offers employment to about 2.0 million families engaged in cultivation, trading and commerce in betel leaf throughout India (Jeng et al., 2002). This plant is grown as a cash crop in the Balasore, Jagatsinghpur, Puri, Khordha and Ganjam areas of coastal Odisha (Jena, 2021). However, the economic stability of the farmers decreased due to the fluctuation in the price of betel leaves. Another Issue is the damage of seedling during transportation (Sahu et al., 2022). The primary reasons for the low betel leaf output are conventionally handled operations, uneducated laborers, and inferior planting materials (Sahu et al., 2022). To overcome these problems, a well-regulated marketing system should be developed (Guha, 2006).

6. Traditional Uses of Betel Leaves

The medicinal properties of pan were recognized during 600 A D when the Ayurvedic System of medicine came into practice (Balasubramanyam, 1994). Betel leaf is one of the grandmother's remedies, prescribed by experienced,older members of the family. Betel leaves help to heal the following illnesses. Such as: -

6.1 Headache: Betel leaf is a popular home remedy for headache. The betel leaf has analgesic and cooling properties.It can be applied with beneficial results over the painful area to relieve intense headache (Guha, 2000).

6.2 Scanty or obstructed urination: Betel leaf juice is credited with diuretic properties. Its juice, mixed with dilute milk and sweetened slightly, helps in easing urination (Guha, 2006).

6.3 Weakness of nerves: Betel leaves play a vital role in the treatment of nervous pains, nervous exhaustion and debility. The juice of a few betel leaves, with a teaspoon of honey, will serve as a good tonic. A teaspoon of this can be takentwice a day (Chopra et al.,1982).

6.4 Sore throat: Betel leaf is an excellent household remedy in the treatment of cough and sore throat. Local application of the leaves is effective in treating sore throats. The crushed fruit or berry shouldbe mixed with honey and taken to relieve irritating cough (Rathee et al.,2006).

6.5 Respiratory disorders: Betel leaves are useful in pulmonary affection in childhood and old age. The leaves, soaked in mustard oil and warmed, may be applied to the chest to relieve cough and difficulty breathing (Madan et al.,2014).

6.6 Constipation: 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 (Rathee et al.,2006).

6.7 Problem of breast milk secretion: The application of leaves smeared with oil is said to promote secretion of milk when applied on the breasts during lactation (Chopra et al.,1982).

6.8 Inflammation: Applied locally, betel leaves are beneficial in the treatment of inflammation such as arthritis and orchitis that isinflammation ofthe testes (Azuine et al.,1991).

6.9 Wounds: Wounds are referred to as disruption of normal anatomic structure and function(Patra et al.,2016).Wound healing is a very complex, multi factor sequence of events involving several cellular and biochemical processes (Patra et al., 2016). Betel leaves can be used to heal wounds (Nilugal et al., 2014). The juice of a few leaves should be extracted and applied on the wound. Then a betel leaf should be wrapped over and bandaged. The wound will heal up with a single application within 2 days.

6.10 Boils: Betel leaf is also an effective remedy for boils. A leaf is gently warmed till it gets softened and is then coated with a layer of castor oil. The oiled leaf is spread over the inflamed part. This leaf has to be replaced every few hours. After a few applications, the boil willrupture, draining all the purulent matter. The application can be made at night and removed inthe morning (Dohi et al.,1989).

7. Other Therapeutic Values of *Piper betle L*

7.1 Antimicrobial Activity: Antimicrobial activity refers to the process of killing or inhibiting the disease-causing microbes. Antimicrobials may be anti-bacterial, antifungal or antiviral. The EO, extracted from betel leaves, possesses strong antimicrobial activities that reduce the adherence of early dental plaque bacteria (Punuri et al.,2012). Eugenol, an important compound extracted from *Piper betle, exhibited* strong antifungal activity against *Aspergillus flavus* (Parmar et al., 1998). The extracts of the betel vine parts (stalks and stems) and the EO extracted by leaves also exhibited strong anti-fungal activity and found to be effective at 450µg/ml concentration (Bandyopadhyay et al.,2006). Moreover, the aqueous and methanolic *Piperbetle* L. leaf extract were selected to analyse the antibacterial activity against some selected microorganisms (Antimicrobial activity using10 gram positive, 12-gram negative bacteria and one fungal strain, *Candida tropicalis*) and the methanolic extract was found to be more effective to inhibit the microbial strains (Nair & Chanda, 2008). Trakranrungsie et al. (2008) worked on the antimicrobial activity of crude ethanolic extracts of betel leaves against some zoonotic dermatophytes like *Microsporumcanis, Microsporumgypseum* and *Trichophyton mentagrophyte* and the yeast-like *Candida albicans*. The results of that anti-microbial

activity analysis revealed that betel leaves extract exhibited more effective antifungal properties having an antioxidant activity of average IC 50 values that ranged from 110.44 to 119.00 lg/ml. Row and Ho (2009) studied the antimicrobial activity of EO and solvent extract (methanolic and aqueous extracts) of *P.betle* against the selected yeasts like C. *chromatography-mass* and *M. pachydermatis* using disk diffusion method. The methanolic and aqueous extracts, along with lEO,exhibited strong activity against the yeasts. Four varieties of pan (Desawari, Desi, Bangladeshi and Jaleswar) were examined and reported by Agarwal et al.,2012. The results described that the cold aqueous, methanolic, ethanolic and ethyl acetate extracts of dried leaves of all the four varieties of *Piper betle* at concentration of 500mg/ml were tested against pathogenic microorganisms like *Pseudomonasaeruginosa, Staphylococcus Aureus and Escherichiacoli* using diffusion method and discussed the antimicrobial screening on leaves of *Piper betl*e. The results found that all the extracts exhibited a clear zone of inhibition against all the bacteria because of the high concentration of sterols. Also, the crude ethanol extract of Piper betel showed potent antimicrobial activity against *Pseudomonasaeruginosa*, *Klebsiellapneumonia*, *Proteus Vulgaris* and *Staphylococcus Aureus* (Datta et al.,2011). Khan and Kumar (2011) evaluated the antibacterial properties of *Piper betle* leaf extracts (ethanolic and methanolic) against pathogenic bacteria namely, *Escherichia coli*, *Pseudomonas aeruginosa andStaphylococcus aureus.* The methanolic extract was found to be more effective than ethanolic extract against the used pathogens. Besides this, three gram-positive bacteria (*Bacillus subtilis, Staphylococcus aureus, and Micrococcus luteus)*, and two gram-negative bacteria (*Escherichia coli and Pseudomonas aeruginosa)* were selected for the antibacterial activity of aqueous and ethanol betel leaf extracts. Ethanol extract showed more significant and effective antibacterial activity than aqueous ones due to the presence of alkaloids, tannins, phenolic substances,and glycosides,etc. (Kaveti et al.,2011). Moreover,the antibacterial activities of different varieties of dried betel leaves (Desawari, Desi, Bangladeshi and Jaleswar) extracts were tested against pathogenic bacteria like *Pseudomonasaeruginosa, Staphylococcus Aureus and Escherichiacoli* using agar well diffusion method. The dried leaf extracts were obtained by cold aqueous, methanol (80%), ethanol (70%), and ethyl acetate (80%) solvent extraction method.

The results revealed that Bangladeshi and Jaleswar varieties of betel leaf extract were an effective and good source of herbal drugs having strong antibacterial activity (Agarwal et al., 2012). Ali et al., (2010) have shown that the Hydroxychavicol, isolated from the

chloroform extraction of the aqueous leaf extract of *Piper betle* L., was investigated for its antifungal activity against 124 strains of selected fungi.

7.2 Antihistaminic Activity: Antihistamines are medicines often used to relieve symptoms of allergies, such as fever, hives, conjunctivitis and reactions to insect bites or stings. They are also sometimes used to prevent motion sickness and as a short-term treatment for insomnia. *Piper betle* L. leaves have been evaluated for its antihistaminic activity (Hajare et al., 2011). In that study, the pharmacological evaluation of ethanolic extract and essential oil extract of leaves of *P. betle* L. has been done for their antihistaminic activity on guinea pig. Extracts of *P. betle* disturbed histamine aerosol induces bronchoconstriction in the whole guinea pig, where essential oil was more effective comparatively to ethanolic extract. Thus, they concluded that ethanolic extract and essential of *P. betle* L. possess antihistaminic activity.

7.3 Anti-inflammatory effects: Inflammation is considered as a part of the complex biological response of vascular tissues to dangerous stimuli such as pathogens, damaged cells, etc. Anti-inflammatory is the activity that helps in the treatment of inflammation or swelling. Betel leaf has a great role in the anti-inflammatory activity which has been used as a household remedy for the inflammation of the oral cavity (Dohi et al.,1989). Eugenol, a principal compound of betel leaf, also possesses anti-inflammatory effects in different animal models of studies with different inflammations (Azuine et al.,1991).

7.4 Antioxidant effects: Antioxidants are molecules that fight free radicals in our body. Free Radicals are compounds that can cause harm if their levels become too high in our body. They are linked to multiple illnesses, including diabetes, heart disease and cancer. Free radical reactions occurring in the body are associated with neurological diseases and pulmonary diseases also. These free radicals play a major role in the aging process. It has been shown that the aqueous extract of the inflorescence of *Piper betle* extract was effective in scavenging H_2O_2, superoxide radical and hydroxyl radical (Lei et al., 2003). It has also been shown that the ethanol extracts of Bangla, sweet and Mysore varieties of betel leaf were effective in scavenging DPPH radicals in vitro, with best effects being observed with the Bangla variety (Rathee et al., 2006). Studies have also shown that the hydro alcoholic extract of the betel leaf possess nitrogen oxide scavenging effect *in* vitro (Jagetia et al., 2004). Moreover, it can help fight oxidative stress and eliminates free radicals by which it can prevent cancer (Rai et al., 2011). Ascorbic acid, as an excellent antioxidant, is very useful to reduce the free radicals in the body and thus prevents cancer.

Shah et al. (2016) also reported that betel leaf extracts exhibited free radical scavenging activity.

7.5 Antimutagenic effects: Mutagenicity refers to the induction of permanent changes in the DNA sequence of an organism, which may result in a heritable change in the characteristics of living systems. Antimutagenic agents are able to counteract the effects of mutagens. Identifying the antimutagenic compounds is among the most promising areas of research in recent years. Multiple studies have shown that the betel leaf is devoid of mutagenic activities in both prokaryotic and eukaryotic assay systems and also to possess antimutagenic effects (Shirname et al., 1983).

7.6 Antiulcer activity: Ulcer is a common gastrointestinal disorder which is seen among many people. Ulcers are an open sore of the skin or mucus membrane characterized by sloughing ofinflamed dead tissue. There are many types of ulcers such as mouth ulcer, esophagus ulcer, peptic ulcer and genital ulcer. Of these, peptic ulcer (gastric ulcer) is seen among many people. Betel leaf extracts can cure gastric ulcers and peptic ulcers (Chaurasia and Johri, 1990). Due to the presence of high flavonoid content of betel leaves, the anti-ulcerogenic activity has also been attributed. The antiulcer activity of *Piper betel* leaves has been evaluated (Vyawahare et al., 2010). Pre-treatment with *Piper betel* extract provided significant ulcer protective effect in all the experimental models along with significant increase in gastric pH and decrease in gastric fluid volume. Extracts of betel leaves have gastroprotective activity which helps in preventing gastric ulcers (Namburi et al, 2011). Polyphenols, especially tannins, present in betel leaves, are antioxidant phytochemicals and can protect against indomethacin-induced stomach ulcers (Ahmed et al., 2021).

7.7 Anti-diabetic activity: Nowadays, diabetes disorder is becoming common in human beings. It is a heterogeneous and metabolic disorder of carbohydrate, lipid and protein metabolism characterized by high blood glucose levels due to the absolute deficiency of insulin. Due to this deficiency, body cells do not respond properly to insulin. Therefore, some anti-diabetic drugs, as a medicine, are used to control the increased blood glucose level in the body. Some of the researchers reported that the oral administration of leaf suspension of betel leaf at 75 and 150 mg/kg of body weight for 30 consecutive days to streptozotocin-induced diabetic rats caused a significant decrease in blood glucose and glycosylated hemoglobin level. Administering betel leaf to diabetic animals is also

reported and, in this report, it was found that glucose 6-phosphatase and fructose-1, 6-bisphosphatase levels decrease in the liver with an increase of hexokinase levels (Madan et al., 2014). Arambewela et al., (2005) investigated the antidiabetic activity of *Piper betle* leaves.

7.8 Palpebral skin antiseptic: The antiseptic effectiveness of *Piper betle l*eaves has been measured by counting the microbial colonies before and after administration of the antiseptic solutions (Amalia et al.,2009).

7.9 Local anesthetics action: Extracts of plain betel leaf, with and without autoclaving, have been tested for surface and infiltration anesthetic activities using rabbits and Guinea pigs Krishnakumar et al., (2001). The results were compared with normal saline control and xylocaine drug control. Betel leaf showed dose-dependent infiltration anesthetic activity comparable with xylocaine. As a surface anesthetic, the onset was as quick as xylocaine and the duration was shorter than xylocaine. Autoclaving did not result in any loss of activity. Betel leaf has potent local anesthetic action, both surface and infiltration techniques.

7.10 Role of betel leaf extract on thyroid function: It has been suggested that betel leaf can be both stimulatory and inhibitory to thyroid function, particularly for T3 generation and lipid peroxidation in malemice, depending on the amount consumed (Panda and Kar, 1998).

7.11 As contraceptive: The mitochondrial activity of sperm, after treating semen with different concentrations of *Piper betle* has been studied (Singh et al., 2011). The mitochondrial activity was also evaluated after subjecting the semen samples for different incubation time periods.Test was done on more than 75% motile normozoospermic semen sample and was found that as the concentration of extracts increases the mitochondrial activity decreases significantly,similar results were observed when constant concentration of extracts with increasing time intervals. The mitochondrial activity decreases significantly in 5 minutes to 20 minutes incubation time. They concluded that *Piper betle* has properties to decrease mitochondrial activity in human sperm and ability to work as a contraceptive.

7.12 Anti-malaria activity: As compared to the well-known insect deterrent citronella oil,

EO provided greater resistance against mosquito bites from *Anopheles Stephensi* and *Culexfatigans* (Johirul et al., 2016). The oil provided greater than 4% of resistance from *Anopheles stephensi andCulex fatigans* when sprinkled at a rate of 20l/cm2, whereas citronella oil provided only 2.2 and 2.6h of protection, correspondingly. As a result, the power of a pan tores is mosquitoes has been established (Cang et al.,2020).

7.13 Anti-cancer activity: Betel vine has reported cancer preventative effects (Kudva et al., 2018; Shukla et al., 2018; Malkani et al., 2021; Chowdhury and Markus, 2022). An enriched source of calcium, vitamin C, niacin, thiamine, carotene and riboflavin (Yin et al.,2009), betel leaves are clearly associated with nutritive benefits. Other betel phytochemical sincludeallyl pyrocatechol (APC;2-hydroxy chavicol), 4-hydroxy catechol, b-caryophyllene, methyl eugenol, carotenes, starch, diastases, and an essential oil containing hydroxy chavicol (Singla et al., 2009). Hydroxy chavicol, aphenolic compound quantitatively present at approximately 26% in betel leaves, has been shown to exertanti proliferative activity in prostatecancer (Paranjpe et al., 2013). Hydroxy chavicol has also been shown to impedecell-cycleprogression of prostate cancer and oral KB carcinoma cells (Paranjpe et al., 2013). Other studies suggest that hydroxy chavicol also known as APC possesses anti ulcer ogenic activity and has been shown to alleviate indomethacin-induced stomach ulceration leading to gastric cancer (Bhattacharya et al., 2005). Chlorogenic acid (ChA), anotheractive ingredient isolated from betel leaves has been reported to eliminate cancerous cells without harming normal cells, unlike most conventional chemo therapeutics (Guha et al.,2006). Mouth cancer is among the ten most common cancers, with 90% of cases occurring in Southeast Asia, where cigarette and smoking behaviours are common (Jiang et al., 2019). One of the earliest studies (Toprani and Patel, 2013) discovered that topical treatment with leaf extracts inhibited pinene-induced oral cancer in hamsters. It was also discovered that combining leaf extracts and turmeric into the dietary supplements was beneficial. The leaf extracts contain anti-proliferative and preventative chemical potential and can thus be utilized to treat several conditions, including human lung cancer (Banerjee and Shah, 2014).

8. Betelvine And Cancer: Long lasting Controversy

Betel vine leaves are important because of their medicinal, religious and ceremonial (Rai et al. 2011). Despite its medicinal uses, for a long time betel vine has been a crucial point of argument that the consumption of betel vine leads to oral cancer. In many experiments, several scientists have proved that chewing of betel leaves along with areca nut, catechu, slaked lime and often tobacco induced cancer (Brunnemann et al. 1992). In contrast scientific studies have shown that betel leaf is itself devoid of mutagenic and carcinogenic effects. Along with curing different diseases betel leaf is found to be useful in preventing different other types of cancer. In the Indian subcontinent, where chewing tobacco with a pan is a common habit, cancer of the mouth is also very common. But the educated Indians are of the opinion that moderate use of betel leaf is not merely innocuous but that it may even be conducive to good health. According to Einsiedeln, Switzerland (1943) "**Everything Is Poisonous and nothing is not poisonous, only the dose makes things poisonous."**

9. Cultural Importance of Betel Leaf

Offering betel mersel (Pan-supari) or pan quid to guests in the Indian subcontinent is a common courtesy. A sheaf of betel leaves is typically presented in Odisha as a token of respect and auspicious beginnings in traditional culture (Sahu et al. 2022). Betel is linked symbolically to the Hindu trinity: the are canuto Brahma, the Creator; betel leaves to Vishnu, the Preserver; and lime to Shiva, the Destroyer (Pommaret, 2000). In India, betel nuts along with various fruits, such as dates, coconut etc., are placed in the lap of the bride or pregnant woman to scare the evil spirit, which is believed to cause barrenness (Piper, 1993). In India, a betel leaf is also used to sprinkle holy water at all the religious ceremonies. Hence, no religious ceremony or worship of Hindu culture is complete without "Pan"occupying an important place along with coconuts and flowers (Satyan, 1993). Even the various portions of a betel leaf are associated with different lords (Gods). The Goddess Laxmi (Hindu Goddess of wealth and prosperity) is believed to reside in the fore part, Parvati On the left, Vishnu resides inside, the moon outside, Shiva in all edges, Yama, the Lord of Death, resides in the stalk. Only the blade of betel leaf is consumed as masticatory; the stalk is associated with disease and the tip of the leaf with sin. Therefore, the leaf stalk and tip are discarded before use (Ahuja et al., 2011). In Hindu culture, betel

leaves along with mango leaves are tied around the neck of "kalasa" filled with water and it is an integral part of all religious ceremonies. In Hindu marriages also, "pan" plays an important part. "Pan" is an integral part of "dakshina" for the priests. Betel leaf is equally important in mourning ceremonies connected with death. It is the duty of those living on earth to honor and propitiate the spirits of their deceased ancestors. Betel quid and rice are typical offerings used for the rites associated with ancestors (Acharya, 2008).

10. Problems associated with betel vine cultivation and trade

The crop is usually cultivated by small farmer's generation after generation following traditional methods due to lack of research and development scientific method for its proper cultivation. Market price of betel vine frequently varies due to agro-climatic factors, transport facilities, farm location and demand supply ratio which discourage the cultivation thereby disturbing the economic condition of the plant growers. Major problems in marketing are transport, too many middle men, absence of grading, fluctuating practice and inadequacy of finance (Kaleeswari et al., 2013). Regularity in commercialization of betelvine with proper marketing system is needed to enhance the export potential and revenue generation. Revenue generated through betel vine export can easily be exceeded if agronomic practices are scientifically explored. Betel leaves are highly perishable in nature. Therefore, during storage and transportation periods, these can be easily spoiled due to microbial infections, pest attacks and discoloration. Harvested Betel leaves cannot be stored for a long period; as a result, sometimes a large portion of the leaves remain unsold. This post-harvest loss of betel leaves (35-70%) can be reduced if proper preservation methods are adopted like drying the leaves, extracting essential oil from the leaves, controlling senescence by different chemical treatments, bleaching, andcuring of the leaves, and adopting better packaging materials etc. (Guha, 2006).

The spoilage of betel leaves accounts for the post-harvest loss in the range of 35%–75% respectively (Rao et al.1997). Spoilage may be due to diseases, pest attacks, dehydration and discolouration of leaves. Besides,due to improper marketing, continuously changing price and unavailability of storage facility wastage of huge amounts of betel vine leaves occur. So, it is very important to maintain the quality of betel leaves under different seasons by applying different advanced techniques for storage and transport of betel leaves. Such wastages can be reduced by extracting essential oils from its leaves. This

essential oil has been reported as remarkably medicinal and aromatic which indicates a promising industry's future by development of its value-added products like talc, perfumes, beverages and food additives (Guha et al., 2006).

11. Betel vine cultivars

Betel vine cultivation has been facing lot of problems due to the existence of its synonyms. In some places the same betel plant is being cultivated with different names and at same region different betel plants are cultivated with the same names. Thus, landraces with prefix ‘Desi’ in their names invariably refer to the landraces ‘Bangla’ in West Bengal, landrace ‘Kapoori’ in Maharashtra and landrace ‘Desawari’ in Madhya Pradesh (Balasubrahmanyam et al. 1994). Reports on proper identification or its characterization are still scanty. As a result of which a lot of confusion is existing among the farmers. Cultivation is mainly through a traditional farming system and is controlled by families or communities.The betel vine growers invariably named the betel vine according to the region where it is cultivated, taste and shape of the leaves. Though the geographical distribution of the betel vines under cultivation is vast, the genetic variation may not be so well distributed (Ranade et al. 2002). Chemical or molecular fingerprinting in betel vine has not yet been reported in most of the cultivars. Therefore, it is always difficult to differentiate the cultivars which are named by the local farmers.

12. Conclusion

It is quite evident from the above discussion that betel vine is an important herbal cash crop from botanical, export potential, economic status, pharmacological, chemical and industrial point of view. Betel leaf is an abundant source of phenolic compounds that possess a lot of therapeutic values and responsible for many health benefits. Therefore, there is a growing interest to utilize betel leaf extract and essential oil in various industrial applications such as food supplements, cosmetic and pharmaceutical industries etc. The demand for thebioactivecompoundsidentifiedfrombetelleavesanditsderivedproductsisincreasingworldwide, which is highly effective. The properties like antimicrobial activity, antioxidant activity, antidiabetic, anticancer activity, etc. justify its bioprospecting for future green medicine. It can be concluded that the betel vine keeps promising as a natural reservoir with regard to its nutritional, pharmacological and economical aspects for the rapidly growing human population.

Comment [P4]: Error

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Comment [P5]: Revise space error

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