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# Traditional and functional uses of betel leaf (*Piper betle* L.) pertaining to food sector: a review

# Arnab Roy1,2,\*, Proshanta Guha1

- <sup>1</sup> Agricultural and Food Engineering Department, Indian Institute of Technology, Kharagpur, West Midnapur, West Bengal, India
- <sup>2</sup> Department of Food Technology, School of Engineering and Technology, Mizoram University, Tanhril, Aizawl, Mizoram, India

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# ABSTRACT

Betel leaf (*Piper betle* L.) is a commercial crop, which is traditionally consumed in the raw state as a mouth freshener and stimulant in Southeast Asia since antiquity. It possesses various functional and medicinal properties, such as antimicrobial, antioxidant, anti-diabetic, anti-carcinogenic etc. The leaf contains essential oil, which has a unique aroma contributing flavour and fragrance. This essential oil is a mixture of concentrated phytochemicals, among which the major components are estragole, chavicol, chavibetol, \(\mathcal{B}\)-cubebene, and caryophyllene. In different scientific researches, betel leaf extracts or essential oil were described for its numerous beneficial functional properties, contributed by these bioactive compounds. However, some health hazards may occur, when the leaf is consumed along with areca nut and tobacco. This review article provides an overview of the current status of betel leaf and its essential oil for its utilization as a bioactive ingredient in the food system.

Keywords: Betel leaf, traditional use, essential oil, bio-active compounds, functional properties.

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#### INTRODUCTION

Since the antiquity, betel leaf (*Piper betle* L.) is being used for ceremonial, religious and medicinal values in Southeast Asia (Guha, 1997). Different varieties of betel leaf are generally found in this region. It is widely consumed in India in the form of 'Paan' or betel quid. A quid is prepared with green or decolorized betel leaf incorporating many other ingredients, such as slaked lime, areca nut chips, catechu, aniseed, clove, sweeteners, and tobacco etc. The quid is chewed to get stimulating, mouth freshening and digestive effects (Guha, 2006; Garg et al., 2014). Moreover, offering 'Paan' to guests during various religious, social and cultural occasions is considered as a mark of respect in India, Bangladesh, Pakistan, and many other countries (Guha, 1997; Harborne, 1994).

The term 'essential oil' refers to the group of plant-based secondary metabolites that is odoriferous like any other essence or fragrant materials (White and Eiserle, 1961). Essential oils of the plants are concentrated hydrophobic liquids, contain scarcely

<sup>\*</sup> For correspondence: A. Roy (Email: <a href="mailto:arnabroy.agfe@gmail.com">arnabroy.agfe@gmail.com</a>)

water-soluble, both volatile and non-volatile components, which are generally lipophilic (Donsì and Ferrari, 2016). These components are classified under phenolic acids, flavonoids, isoflavones, alkaloids, carotenoids, monoterpenes and aldehydes (Seow et al., 2014). The secondary metabolites contained in these oils are intended to offer specific host defensive function (Bennett and Wallsgrove, 1994), which is also true in the case of phenolic compound rich essential oils. These oils are mostly found at the specialized plant cells, such as osmophores, glandular trichomes, ducts and cavities (Venkatachalam et al., 1984), which are extracted by using simple to complex extraction techniques (Nakatsu et al., 2000). The essential oils mostly offer broader ranges of anti-allergic, anticancer, insecticidal, antimicrobial and antioxidant activities (Seow et al., 2014), which qualify these oils to be natural food preservative having high consumer demand. Such consumer demand for natural products necessitates the development of an alternative food preservative to retard microbial spoilage (Mandal et al., 2014; Roy et al., 2016) without any adverse health effect. Apart from being potential natural food preservatives, these oils also carry a potential future in the innovative food packaging sector due to its antimicrobial and antioxidant activities (Asbahani et al., 2015), besides being a potential and attractive flavouring substance for the food and beverage industries as well.

Despite the increasing scientific interest and advancement in betel leaf and its essential oil research, there is a lack of summarized data on traditional uses, chemical compositions, functional activities, and commercial product development scenario. In the context of such scientific research, this review article tries to summarize all the possible information on betel leaf and its essential oil justifying wider possibilities for its use as a natural source for food preservation and packaging.

#### GEOGRAPHIC DISTRIBUTION AND AGRO-CLIMATE

Betel leaf (*Piper betle* L.) is an aromatic creeper, which belongs to *Piperaceae* family comprising approximately 10 genera sprawling over 2000 species (Chakraborty and Shah, 2011). This plant is familiar with different vernacular names such as 'Paan' in India, 'Trau' in Vietnam and 'Plue' in Thailand (Rai et al., 2011). It is abundantly grown in Southeast Asian countries for commercial purpose. India, Srilanka, Bangladesh, Malaysia, Burma, Nepal, Myanmar and Thailand are the major cultivators of the vine (Guha, 2006). The leaves of the plant are economically important for being used as the principal component in betel quid (Paan). It is consumed by more than 15-20 million people on a daily basis only in India, whereas the number is over two billion worldwide (Guha, 2007).

This is a dioecious and shade loving perennial root climber plant bearing heart-shaped green leaves. The leaves are about 5 to 15 cm long and 3 to 10 cm broad. It acuminates at the apex and unequally cradles at the base. Five to seven numbers of lateral veins curving from the base to apex are well observed in the leaves. Microscopic image of betel leaf indicates the presence of abundant rounded oil cells filled with a brownish secretion (Muhammed, 2007). This brownish secretion is essential oil fixed in the oil cells contributing around 2% (dry basis) of the leaf (Guha, 2006).

Cultivation of this plant requires stable soil moisture, high humidity and mild temperature, which is not always available in the natural environment. Fluctuations in these environmental parameters proved to be detrimental to the plant. Therefore, it is cultivated inside an artificially constructed hut-like structure, which maintains the plant growing parameters within suitable range imitating the natural ecological condition (Guha, 2006). In India, the structure is often called as 'Boroj', which is constructed using paddy straw, jute sticks, bamboo stems, leaves and petioles of banana to provide the shaded and humid environment. The dimensions of the structure remain within the range of 2 to 3 m in height, 10 to 20 m in length and 5 to 15 m in width. The plant is cultivated through vegetative propagation from the cuttings of 3 to 5 years old vines.

Both the leaves and the oil are highly valuable commercial commodities much intended in many places in the Asian countries. Therefore, attempts are being made to cultivate this plant with modern agro-technologies. However, long before the modern cultivation of betel leaf started, it was popular for its various traditional uses as mentioned in the ancient texts.

# TRADITIONAL USES

Apart from the socio-cultural use, betel leaf is also well known for its traditional claims in different medical conditions. The ancient Indian medicine system 'Ayurveda' has been an integral part of Indian culture and 'Herbal Materia Medica'. Documentation of betel leaf chewing in the ancient Sanskrit texts like 'Charaka and Sushruta Samhita' (600-400 BC), establishes its status of ancient use. It is well referred as "Tambool" in different Sanskrit scriptures including 'Charaka and Sushruta Samhita', 'Astanga Hridayam', 'Bhabaprakasha', 'Hariyamsa', 'Varahapurana', 'Panchatantra and Jataka tales' (Kumar, 1999). Most of these scripts highlighted the medicinal properties of betel vine. Juice and decoction of the leaf are mainly used as traditional medicine. The betel leaf extract is often recommended as an adjuvant in 'Ayurveda'. Apart from its independent use as medicine, betel leaf extract was also used in various Ayurvedic formulations in order to improve the medicinal effects (Kumar, 1999; Shastri, 1962). In 'Sushrut Samhita' (ch 28-46; 279-280) (Singhal and Chunekar, 1980), and 'Bhavaprakasa' (sloka 180-183), (Mishra and Vaisya, 1969), betel leaves are mentioned as aromatic and nonslimy. It offers a sharp, hot, acrid and astringent taste, which is an appetizer as well. It acts on the two major consequences, 'pitta' and 'vata', which are described in 'Ayurveda' as the diseased state of the human body. It is also reported to act on the different oral disease including voice disorder, oral itching, and bad odour, and also used to promote extra salivary secretion (Kumar, 1999). That apart, it is also mentioned to offer aphrodisiac effect (Murthy, 1995). These claims are well justified with the specific use that has been described in the ancient texts. Chewing of betel leaf is recommended while going to attend a social gathering, after getting up from the bed (preferably in daytime), after vomiting and at the time of cohabiting (Kumar, 1999). Chewing of betel leaf at the cohabiting justifies its aphrodisiac effect. Besides, the use of betel leaf quid at a social gathering is possibly due to its strong odour that acts as a mouth freshener and keeps away the possible oral bad odour. Its mild stimulating action also gave a refreshing effect. Reports are also available in the ancient Indian medicinal texts referring its role providing strength to heart and regulating the blood pressure (Murthy, 1995). Use of betel leaf as an antimicrobial and anti-inflammatory agent is also described in different texts (Sharma, 1995). Apart from this, other biological activities such as antioxidant, anti-diabetic, gastroprotective, anti-nociceptive, insecticidal etc. activities of betel leaf have also been reported (Srinivasan et al., 2016). This plant serves as a common ingredient during the preparation of several indigenous medicines in Asian countries. Apart from the strong ethnomedicinal claims, this plant is very little explored as compared to similar Indian traditional plants like 'Tulsi' (Ocimum sanctum) etc. Presence of bioactive chemicals in the betel leaf matrix can be correlated with its traditional claims. The existence of these bioactive chemicals is well demonstrated in several scientific literatures.

Despite the huge consumption pattern, a major surplus of betel leaf is often found during the rainy season. In India, a minimum 10% surplus of the gross production of betel leaf is wasted during the rainy season every year. This wastage can be minimized by different means, such as extraction of essential oil.

## **ESSENTIAL OIL OF BETEL LEAF**

Betel leaf (*Piper betle* L.) contains a significant amount of essential oil (about 2.0% dry basis) in its juicy leaves (Guha, 2007). It is a concentrated form of phytochemicals offering enormous functional activity. Betel leaf essential oil (BLEO) contains a number of chemical constituents including a significant amount of various phenolic compounds. The major chemical components of

essential oil of betel leaf (Tamluk Mitha variety) include estragole, chavicol, chavibetol,  $\beta$ -cubebene, and caryophyllene. Besides, other components like eucalyptol,  $\alpha$ -cubebene,  $\beta$ -elemene,  $\gamma$ -muurolene, elixene,  $\delta$ -cadinene, 4-Allylphenyl acetate are also present in trace amount (Basak and Guha, 2015). This essential oil with a pungent smell offers a wide spectrum of antimicrobial activity against both fungal and bacterial strains (Basak and Guha, 2017; Roy and Guha, 2018). Being a treasure house of antimicrobial compounds, the research interest with essential oil of betel leaf is increasing day by day. As BLEO is an edible plant-based essential oil, it may be considered as generally recognized as safe (GRAS) material. The uniqueness of betel leaf essential oil lies upon its antimicrobial and antioxidant potential. Thus, it can also be exploited for active food packaging. Apart from this, the unique spicy smell can enhance the flavour of some particular food articles.

#### **CHEMICAL COMPOSITIONS**

The chemicals associated with betel leaf are predominantly phenolic in nature. Chloroform extract of betel leaf contains an array of compounds including chavibetol, chavibetol acetate, chavicol, allylpyrocatechol, and allylpyrocatechol diacetate (Chang et al., 2002; Evans et al., 1984). Other bioactive compounds like  $\alpha$ -tocopherol,  $\beta$ -carotene, eugenol, and hydroxychavicol are also well distributed in betel leaf (Bhide et al., 1991). Piperbetol, methylpiperbetol, piperol A and piperol B are the betel leaf specific chemicals (Zeng et al., 1997) found is this leaf. That apart, phenylpropanoid, cinnamoyl, and six flavonoids derivatives are also reported to found in both aqueous and ethanolic extracts if the leaf (Ferrereset al., 2014).

Indian betel leaf variety 'Bangla', 'Mitha', and 'Mysore' contains similar phytochemical profiling. It contains chevibetol along with allylpyrocatechol and their respective glucosides. However, the concentrations of chevibetol and allylpyrocatechol were significantly less in the Mitha and Mysore varieties (Ratheeet al., 2006). Ethyl acetate extract of *Piper betle* contains hexadecanoic acid, eugenol, and phytol (Srinivasan et al., 2016). Moreover, the root of the plant also contains a number of bioactive compounds. For example, the shade-dried betel vine root extracted with water followed by n-butanol showed the presence of triterpenes and β-sitosterol (Saeed et al., 1993).

#### SCIENTIFIC EXPLANATION OF THE ETHNOMEDICINAL CLAIMS

## **Antimicrobial activity**

The antimicrobial activity is one of the most important properties of a food preservative. It protects the food articles from the harmful effects of microbes. Betel leaf contains chavibetol, chavibetol acetate, chavicol, allylpyrocatechol, and allylpyrocatechol diacetate etc. Presence of these bioactive compounds is the main reason for its antimicrobial efficacy (Evans et al., 1984). Various microorganisms, such as *Streptococcus mitis*, *Streptococcus sanguis*, *Actinomyces viscosus*, and *Staphylococcus mutans* are prevalent in our oral cavity, which contributes to dental plaque and tooth decay. It has been reported that, crude aqueous extract of betel leaf exhibited excellent antimicrobial activity against these oral pathogenic strains, which are the early colonizers of dental plaque (Fathilah et al., 2000). In another study, the effects of betel leaf extract against oral pathogenic strain confirm its traditional use in voice disorder, oral itching, and bad odour. It was also reported that the crude extract of betel leaf caused damages to the plasma cell membrane and coagulated the nucleoid of *Staphylococcus mutans*. The extract inhibited the glucosyltransferase activity, which affected the glucan formation. Thus, leads the environment to become less conducive for bacterial growth. Besides, changing the ultrastructure of *Staphylococcus mutans*, the extract also reduced the acid producing properties of the bacteria, which suggests it possess anti-cariogenic activities (Thurairajah and Rahim, 2007). It is quite interesting to observe that, different extracts of different solvents, such as, hexane, chloroform and methanol showed anti-

quorum sensing properties against *Pseudomonas aeruginosa*, *Escherichia coli*, and *Chromobacterium violaceum* (Datta et al., 2016; Tan et al., 2013) This is further supported by another recent report which explains the mitigation of virulence factors and biofilm formation by the microbes. It was achieved using the bioactive metabolite 'phytol' present in *Piper betle*, through quorum sensing of a nosocomial (originated in a hospital) pathogen *Serratia marcescens* (Srinivasan et al., 2016).

A recently published research also reported the inhibition of bioluminescence and biofilm production of *Vibrio harveyi*, using *Piper betle* ethyl acetate extract (PBE). This harmful microbe is a potent producer of pathogenic biofilm, which resists the effect of disinfectants, chemicals, multiple antimicrobials, and even biocides (Srinivasan et al., 2017). Furthermore, the potential antimicrobial effect of ethanol extract of betel leaves was reported by Hoque et al., (2011), where the inhibition of the growth was observed for a few foodborne pathogens, such as *Staphylococcus aureus*, *Escherichia coli*, *Vibrio cholerae* and *Shigella dysenteriae*. The minimum inhibitory concentration (MIC) was found to be ranging from 0.625% (w/v) to 0.75% (w/v). A recent study by Roy and Guha (2018) also reported the antimicrobial efficacy, where nanoemulsion prepared with essential oil of betel leaf showed in-vitro inhibition of a few foodborne pathogens, such as *Escherichia coli*, *Bacillus cereus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa and Klebsiella pneumonia*. The MIC was found to be ranging from 0.5 to 1.25 µl/ml and minimum bactericidal concentration (MBC) was 1.0 to 2.5 µl/ml. These reports suggest that betel leaf can be used as a potential natural antimicrobial substance for food preservation unlike synthetic chemicals, which are reported to possess numerous harmful side effects.

## **Antioxidant activity**

The antioxidant activity is another important functional property of betel leaf. It has been reported by a large number of researchers. Dasgupta and De, (2004) have reported that the aqueous extract of betel leaf showed potent antioxidant activity which was better than tea polyphenols. It prevented lipid peroxidation in an in-vitro system. Similar results were also reported by Wong et al. (2006). They expressed the total polyphenol content (TPC) in terms of gallic acid equivalent (GAE) and antioxidant activity as Trolox equivalent antioxidant capacity (TEAC). The antioxidant activity was determined by DPPH (1,1-diphenyl-2-picrylhydrazyl) free radical scavenging assay and FRAP (ferric reducing antioxidant potential) assays. The TPC was found to be 16-23 mg/g GAE, whereas, TEAC<sub>DPPH</sub> and TEAC<sub>FRAP</sub> were found as 80-120 µmol/g and 170-210 mol/g Trolox equivalent respectively. On the other hand, the ethanolic extract of betel leaf exhibited a high level of total phenolic content (TPC) and total flavonoid content (TFC), which makes betel leaf a potential source of natural antioxidant (Maisuthisakul et al., 2007). These results were further confirmed by Nouri et al. (2014), where methanolic (90%) and ethanolic (90%) extracts of betel leaf showed maximum phenolic contents of 205.2 and 202.9 mg GAE/g dry weight, respectively. Among them, ethanolic extract exhibited the highest percentage of DPPH free radical inhibition.

Chakraborty and Shah (2011) also have reported the antioxidant activity of betel leaf extract obtained with four different solvents, such as water, methanol, ethyl acetate, and petroleum ether. All these samples showed antioxidant activity which was determined by four different methods, such as DPPH photometric assay, ferric ion reductive ability, superoxide radical scavenging, and hydroxyl radical scavenging assay. In another study, Arambewela et al. (2006) reported the antioxidant potential of betel leaf using hot water extract (HWE), cold ethanolic extract (CEE) and essential oil (EO) of the leaf. The antioxidant effects of the samples were also compared with commonly used synthetic antioxidant 'BHT (butylated hydroxytoluene)'. It was found that the effectiveness of CEE was higher than that of BHT, for initial free radical scavenging activity. From these studies, it can be suggested that betel leaf is a natural source of better potential antioxidant than synthetic chemicals.

# Digestive and gastro protective properties

Chewing of betel leaf is traditionally claimed to improve the digestive effect, besides stimulating salivary gland secretion. Early investigation revealed that taking orally administered betel leaf provides significant stimulatory influence on digestive enzymes of the pancreas, and also on intestinal mucosa and bile production in rats (Prabhu et al., 1995). Modern scientific research explored that betel leaf extract also has a gastroprotective effect (Arawwawala et al., 2014). Ethanolic extract of the leaf also exhibited gastro protective activity on gastric lesions experimentally induced in rats. Furthermore, oral administration of betel leaf ethanolic extract at a dose of 200 mg/kg body weight for ten consecutive days resulted in a significant protective activity against indomethacin-induced gastric lesions in rats (Majumdar et al., 2002). In a similar study, administration of betel leaf ethanolic extract at a dose of 150 mg/kg body weight daily for ten days resulted in significant healing effect against induced peptic ulcer in albino rats (Majumdar et al., 2003).

#### Wound healing properties

A study in the early 90s, the wound healing property of betel leaf extract was reported. During the study, aqueous extract of the leaves was evaporated and the dried residue (1%) was mixed with white soft paraffin and applied on the wounds of laboratory rabbits. The wound contracted in ten days and healed in fourteen days (Santhanam and Nagarajan, 1990). In a study, Saeed et al., (1993) observed antiplatelet and anti-inflammatory activities of triterpenes and β-sitosterol was, which were isolated from betel leaf. Arachidonic acid (1.7 mM), ADP (2.2 μM) and platelet activating factor (PAF, 0.8 μM) were used to induce aggregation. Triterpenes inhibited arachidonic acid and PAF induced aggregation, whereas β-sitosterol inhibited all three types of platelet aggregation. In a separate study, piperol A, piperol B, piperbetol and methylpiperbetol were isolated from the leaves. These active ingredients selectively inhibited the aggregation induced by platelet-activating factor (PAF) of washed 'rabbit platelets', (Zeng et al., 1997). In another study, the application of betel leaf extract showed wound healing activity over skin excision wounds of streptozotocin Sprague-Dawley rats (Keat et al., 2010). A recent study demonstrates the activity of aqueous extract of *P. betle*, which decreased the oxidative stress and 11β hydroxysteroid dehydrogenase-1 (11β HSD-1) expression. Thus, leading to rapid wound healing of diabetic wounds (Ghazali et al., 2016).

## Antidiabetic activity

The antidiabetic activity of betel leaf extract is also scientifically proven. In a study by Arambewela et al., (2005), significant lowering of blood glucose level was observed, when hot water extract (HWE) and cold ethanolic extract (CEE) of betel leaf were administered orally in a dose-dependent manner in normoglycaemic and streptozotocin (STZ)-induced diabetic rats. In another streptozotocin-induced diabetic rat model study, a significant reduction in blood glucose level was observed when treated with orally administered betel leaf suspension (75 and 150 mg/kg of body weight) for thirty days. Furthermore, reduction in glycosylated haemoglobin was also observed and activities of liver enzymes, such as glucose-6-phosphatase and fructose-1,6-bisphosphatase were decreased (Santhakumari et al., 2006).

#### **Anticancer activity**

Apart from the wound healing activity, betel leaf extract also scientifically reported to provide an anticancer effect in both *in vitro* and *in vivo* prostate cancer models. Aqueous extract of betel leaves reduced the tumor growth in an animal tumor model. This extract was administrated for eight weeks in rats, which successfully inhibited DMBA (7,12-dimethylbenz(a)anthracene)-induced mammary carcinogenesis (Rao et al., 1985). Bhide et al. (1991) also studied the chemopreventive effect of some of the

constituents of betel leaf extract. These constituents, such as α-tocopherol, β-carotene, eugenol and hydroxychavicol, successfully reduced the number of papilloma (small wart-like growth on the skin or on the mucous membrane) on benzo[a]pyrene induced forestomach neoplasia (new, abnormal growth of tissue) in male Swiss mice. In another report, this research group further explored the chemopreventive effect of betel leaf extract (BLE) and its constituents on DMBA-induced skin tumors in mice (Azuine et al., 1991). Ethyl acetate extract of *Piper betle* also offered anticancer activities. This extract inhibited breast cancer cell (MCF-7 cell) proliferation (rapid reproduction of a cell)., by increasing the activities of catalase and superoxide dismutase (Abrahim et al., 2012). Furthermore, hydroxychavicol, isolated from the alcoholic extract of betel leaf, induced apoptosis of CML cells. The apoptosis happens due to the loss of the mitochondrial membrane and release of inner contents, which also overrides the imatinib resistance of the cells (Chakraborty et al., 2012). This hydroxychavicol is also reported to act against prostate cancer and oral KB carcinoma cells. It induces the cell cycle arrest and apoptosis of oral KB carcinoma cells (Chang et al., 2002). In another study, significant inhibition of growth of human prostate xenograft was also observed with oral doses of betel leaf extract in mice (Paranjpe et al., 2013). From these studies, it can be suggested that betel leaf and its components possess potential anticancer effects.

## Various other disease inhibition properties

Recent studies also exhibited a direct relation of betel leaf extracts with neurodegenerative diseases. Valentão et al. (2010) reported acetylcholinesterase inhibitory capacity betel leaf extract. The same research group later reported anti-cholinesterase activity of phenolic compounds isolated from betel leaf in both aqueous and ethanolic extract (Ferreres et al., 2014). Hydroxychavicol was found to be the major compound in both the extracts. Their report also concluded that aqueous extract of betel leaf offered an enormous number of other bioactive compounds. This aqueous extract over a concentration of 500 µg/ml exerted a cytotoxic effect to human neuroblastoma (one type of cancer cells) cells. Thus, *Piper betle* possesses a positive impact on the prevention and treatment of neurodegenerative diseases (Ferreres et al., 2014). Apart from this, modern research has also opened several new therapeutic possibilities of betel leaf extract to control allergic diseases by inhibiting the production of allergic mediators. Wirotesangthong et al. (2008) have reported that the ethanolic extract of *Piper betle* inhibited the production of allergic mediators by bone marrow-derived mast cells and lung epithelial cells. As mentioned earlier, betel leaf contains hydroxychavicol which is also a potent xanthine oxidase inhibitor, which is involved in purine metabolism. Thus, inhibiting xanthine oxidase reduces the production of uric acid, which is a root cause of various ailments like a kidney stone, rheumatism etc. The effectiveness of hydroxychavicol to treat the hyperuricemia is even superior to that of the clinically used drug, allopurinol (Murata et al., 2009).

#### APPLICATIONS IN THE FOOD AND BEVERAGE SECTORS

From the aforementioned discussions of the profilatic and curative attributes of betel leaf, it is clearly proved that this edible leaf and its components have several beneficial effects on human health beyond basic nutrition. Therefore, when any food article is developed by incorporating betel leaf or its components would surely provide the above benefits, such as antimicrobial, antioxidant, antidiabetic, anticarcinogenic etc. However, not many products are available in the market or known to the food sector so far. But some scientific studies have shown the use of betel leaf or its components in food packaging and production. For example, it was reported that sago starch films were prepared using different levels of betel leaf extract which showed antibacterial activity. It also showed water vapour and oxygen permeation properties, besides protection from ultraviolet radiation. These properties were enhanced with an increased level of betel leaf extract. The starch films were also reported to show increased seal strength and elongation but decreased tensile strength with the increased level of the extract (Nouri and

Nafchi, 2014). Therefore, such composite films may open up a new horizon in the edible food packaging sector. The same research group also reported a structural modification of noodles by incorporating betel leaf extract at different levels. It resulted in softer noodles having better sensory attributes with higher levels of betel leaf extract (Nouri et al., 2015). Roy and Guha (2015) prepared a cupcake fortified with essential oil of betel leaf which enhanced the organoleptic properties of the final product. In another study, Vernekar and Vijayalaxmi (2018) reported that the nutritional values of 'papad' was increased by incorporating dehydrated betel leaf powder. Basak (2018a, 2018b) has also suggested the use of essential oil of betel leaf for extending the shelf life of tomato paste and raw apple juice which also enhanced organoleptic properties of the products. These research studies though suggested the use of betel leaf and its components in the food and beverage sectors, but there are a few concerns related to human health associated with betel leaf chewing.

## RECENT CONCERN ON THE TOXICITY OF BETEL QUID

In a country like India, after tea and coffee, the consumption pattern of betel guid is in the second position, on a daily basis (Muruganandam et al., 2017). Consumers prefer to chew betel leaf with slaked lime, areca nut, tobacco etc. Consumption of betel quid is reported to have a high risk of toxicity. The toxicity is due to the added ingredients associated with quid making. The deadliest component of betel quid is raw betel nut or areca nut (Areca catechu). Chewing of betel nut is proved to be a causative agent for several harmful health effects (Chen et al., 2017). Observing such adverse effects on human health, the International Agency for Research on Cancer (IARC) enlisted betel nut as a potent carcinogenic to human beings (IARC, 2004). Betel nut chewing is also reported to be associated with an increased risk of arterial stiffness (Wei et al., 2017). During betel quid consumption, mild addiction of betel nut is also observed while consumed with tobacco, which has high addictive potential. The symptoms are most prevalent in Adolescents (Milgrom et al., 2016). It is interesting to observe that, individually betel leaf does not possess any toxicity, therefore, have a wider possibility to be used in food, medicine, and cosmetic industries. Both invitro and in-vivo studies have suggested nontoxic properties of Piper betle. Oral supplementation of betel leaf extract (1, 5 and 10 mg/kg body weight) did not cause any oxidative damage (Choudhary and Kale, 2002). With the increasing awareness among consumers about the toxic effects, the possibility of use of areca nut and tobacco may decline for betel guid making in near future. Consequently, the use of betel leaf may also decline, though without any allegation. Thus, searching alternative uses of betel leaf and its derived products, like essential oil, may open up new opportunities to support the betel leaf cultivators, processors and traders as well.

#### **CONCLUSIONS**

There is a growing awareness among consumers to use natural substances over synthetic preservatives in the food and beverage industries. Essential oils are potential alternatives to synthetic chemicals for food preservation. From this study, it can be concluded that betel leaf is a significant source of essential oil. This essential oil contains an enormous number of bioactive compounds, such as phenols, flavonoids, alkaloids etc. These bioactive compounds are mainly responsible for various functional properties, like, antimicrobial, antioxidant, antidiabetic, anti-inflammatory, anti-carcinogenic etc. These functional properties have attracted a huge focus of the researchers to explore betel leaf and its essential oil. It was quite interesting to observe that betel leaf extract with different solvents offered different functional activity. So that, to get a specific release of different bioactive ingredients specific solvents are used. From this study, it can be suggested that the various beneficial properties of betel leaf and its components in different forms may be utilized as a food ingredient, food preservative, sensory quality enhancer, packaging material etc. in food and beverage sectors.

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## **REFERENCES**

- Abrahim, N. N., Kanthimathi, M. S., Abdul-Aziz, A. 2012. Piper betle shows antioxidant activities, inhibits MCF-7 cell proliferation and increases activities of catalase and superoxide dismutase. BMC Complementary and Alternative Medicine, 12(1), 1195. https://doi.org/10.1186/1472-6882-12-220
- Arambewela, L. S. R., Arawwawala, L. D. A. M., Ratnasooriya, W. D. 2005. Antidiabetic activities of aqueous and ethanolic extracts of Piper betle leaves in rats. Journal of Ethnopharmacology, 102(2), 239–245. https://doi.org/10.1016/j.jep.2005.06.016
- Arambewela, L., Arawwawala, M., Rajapaksa, D. 2006. Piper betle: A potential natural antioxidant. International Journal of Food Science and Technology, 41(SUPPL. 1), 10–14. https://doi.org/10.1111/j.1365-2621.2006.01227.x
- Arawwawala, L. D. A. M., Arambewela, L. S. R., Ratnasooriya, W. D. 2014. Gastroprotective effect of Piper betle Linn. leaves grown in Sri Lanka. Journal of Ayurveda and Integrative Medicine, 5(1), 38–42. https://doi.org/10.4103/0975-9476.128855
- Asbahani, A. El, Miladi, K., Badri, W., Sala, M., Addi, E. H. A., Casabianca, H., Mousadik, A. El, Hartmann, D., Jilale, A., Renaud, F.N.R., Elaissari, A. 2015. Essential oils: From extraction to encapsulation. International Journal of Pharmaceutics, 483(1–2), 220–243. https://doi.org/10.1016/j.ijpharm.2014.12.069
- Azuine, M. A., Amonkar, A. J., Bhide, S. V. 1991. Chemopreventive efficacy of betel leaf extract and its constituents on 7,12-dimethylbenz(a)anthracene induced carcinogenesis and their effect on drug detoxification system in mouse skin. Indian Journal of Experimental Biology, 29(4), 346–351.
- Bakkali, F., Averbeck, S., Averbeck, D., Idaomar, M. 2008. Biological effects of essential oils A review. Food and Chemical Toxicology, 46(2), 446–475. https://doi.org/10.1016/j.fct.2007.09.106
- Basak, S. 2018a. Shelf Life Extension of Tomato Paste Through Organoleptically Acceptable Concentration of Betel Leaf Essential Oil Under Accelerated Storage Environment. Journal of Food Science, 83(5), 1396–1403. https://doi.org/10.1111/1750-3841.14133
- Basak, S. 2018b. The use of fuzzy logic to determine the concentration of betel leaf essential oil and its potency as a juice preservative. Food Chemistry, 240(August 2017), 1113–1120. https://doi.org/10.1016/j.foodchem.2017.08.047
- Basak, S., Guha, P. 2015. Modelling the effect of essential oil of betel leaf (Piper betle L.) on germination, growth, and apparent lag time of Penicillium expansum on semi-synthetic media. International Journal of Food Microbiology, 215, 171–178. https://doi.org/10.1016/j.ijfoodmicro.2015.09.019
- Basak, S., Guha, P. 2017. Betel leaf (Piper betle L.) essential oil microemulsion: Characterization and antifungal activity on growth, and apparent lag time of Aspergillus flavus in tomato paste. LWT Food Science and Technology, 75, 616–623. https://doi.org/10.1016/j.lwt.2016.10.021

- Bennett, R. N., Wallsgrove, R. M. 1994. Secondary metabolites in plant defence mechanisms. New Phytologist, 127(4), 617–633. https://doi.org/10.1111/j.1469-8137.1994.tb02968.x
- Bhide, S. V, Zariwala, M. B., Amonkar, A. J., Azuine, M. A. 1991. Chemopreventive efficacy of a betel leaf extract against benzo[a]pyrene-induced forestomach tumors in mice. Journal of Ethnopharmacology, 34(2–3), 207–213.
- Chakraborty, D., Shah, B. 2011. Antimicrobial, anti-oxidative and anti-hemolytic activity of Piper betle leaf extracts. International Journal of Pharmacy and Pharmaceutical Sciences, 3(3), 192–199.
- Chakraborty, J. B., Mahato, S. K., Joshi, K., Shinde, V., Rakshit, S., Biswas, N., Choudhury (Mukherjee), I., Mandal, L., Ganguly, D., Chowdhury A. A., Chaudhuri, J., Paul, K., Pal, B. C., Vinayagam, J., Pal, C., Manna, A., Jaisankar, P., Chaudhuri, U., Konar, A., Roy, S., Bandyopadhyay, S. 2012. Hydroxychavicol, a Piper betle leaf component, induces apoptosis of CML cells through mitochondrial reactive oxygen species-dependent JNK and endothelial nitric oxide synthase activation and overrides imatinib resistance. Cancer Science, 103(1), 88–99. https://doi.org/10.1111/j.1349-7006.2011.02107.x
- Chang, M. C., Uang, B. J., Wu, H. L., Lee, J. J., Hahn, L. J., Jeng, J. H. 2002. Inducing the cell cycle arrest and apoptosis of oral KB carcinoma cells by hydroxychavicol: roles of glutathione and reactive oxygen species. British Journal of Pharmacology, 135(3), 619–630. https://doi.org/10.1038/sj.bjp.0704492
- Chen, G., Hsieh, M. Y., Chen, A. W. G., Kao, N. H. L., Chen, M. K. 2017. The effectiveness of school educating program for betel quid chewing: A pilot study in Papua New Guinea. Journal of the Chinese Medical Association. https://doi.org/10.1016/j.jcma.2017.10.001
- Choudhary, D., Kale, R. K. 2002. Antioxidant and non-toxic properties of Piper betle leaf extract: in vitro and in vivo studies. Phytotherapy Research, 16(5), 461–466. https://doi.org/10.1002/ptr.1015
- Dasgupta, N., De, B. 2004. Antioxidant activity of Piper betle L. leaf extract in vitro. Food Chemistry, 88(2), 219–224. https://doi.org/10.1016/j.foodchem.2004.01.036
- Datta, S., Jana, D., Maity, T. R., Samanta, A., Banerjee, R. 2016. Piper betle leaf extract affects the quorum sensing and hence virulence of Pseudomonas aeruginosa PAO1. 3 Biotech, 6(1), 18. https://doi.org/10.1007/s13205-015-0348-8
- Donsì, F., Ferrari, G. 2016. Essential oil nanoemulsions as antimicrobial agents in food. Journal of Biotechnology, 233, 106–120. https://doi.org/10.1016/j.jbiotec.2016.07.005
- Evans, P. H., Bowers, W. S., Funk, E. J. 1984. Identification of Fungicidal and Nematocidal Components in the Leaves of Piper betle (piperaceae). Journal of Agricultural and Food Chemistry, 32(6), 1254–1256. https://doi.org/10.1021/jf00126a011
- Fathilah, A., Bakri, M., Rahim, Z. H. A. 2000. Pasca Sidang Symposium on National Health Sciences 3rd, 29-30 April. Faculty of Health Sciences, University Kebangsaan Malaysia, 216–219.
- Ferreres, F., Oliveira, A. P., Gil-Izquierdo, A., Valentão, P., Andrade, P. B. 2014. Piper betle Leaves: Profiling Phenolic Compounds by HPLC/DAD-ESI/MS n and Anti-cholinesterase Activity. Phytochemical Analysis, 25(5), 453–460. https://doi.org/10.1002/pca.2515
- Garg, A., Chaturvedi, P., Gupta, P. C. 2014. A review of the systemic adverse effects of areca nut or betel nut. Indian Journal of Medical and Paediatric Oncology, 35(1), 3–9. https://doi.org/10.4103/0971-5851.133702
- Ghazali, N. A., Elmy, A., Yuen, L. C., Sani, N. Z., Das, S., Suhaimi, F., Yusof, R., Yusoff, N. H., Thent, Z. C. 2016. Piper betle leaves induces wound healing activity via proliferation of fibroblasts and reducing 11β hydroxysteriod dehydrogenase-1

- expression in diabetic rat. Journal of Ayurveda and Integrative Medicine, 7(4), 198–208. https://doi.org/10.1016/j.jaim.2016.08.008
- Guha, P. 1997. Status Report on Production, Processing and Marketing of Betel Leaf (Piper betle L.). Agricultural and Food Engineering Department, IIT, Kharagpur, India (1997).
- Guha, P. 2006. Betel Leaf: The Neglected Green Gold of India. Journal of Human Ecology, 19(2), 87-93.
- Guha, P. 2007. Extraction of essential oil: An appropriate rural technology for minimizing wastage of surplus betel leaves. AMA, Agricultural Mechanization in Asia, Africa and Latin America.
- Harborne, J. B. 1994. Indian Medicinal Plants. A Compendium of 500 Species. Vol.1; Edited by P. K. Warrier, V. P. K. Nambiar and C. Ramankutty. Journal of Pharmacy and Pharmacology, 46(11), 935–935. https://doi.org/10.1111/j.2042-7158.1994.tb05722.x
- Hoque, M. M., Rattila, S., Shishir, M. A., Bari, M. L., Inatsu, Y., Kawamoto, S. 2011. Antibacterial Activity of Ethanol Extract of Betel Leaf (Piper betle L.) Against Some Food Borne Pathogens. Bangladesh Journal of Microbiology, 28(2), 58–63. https://doi.org/10.3329/bjm.v28i2.11817
- IARC. 2004. Betel-quid and Areca-nut Chewing and Some Areca-nut-derived Nitrosamines. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, 85, 1–427. https://doi.org/10.1002/food.19940380335
- Keat, E. C., Razak, S. S., Fadil, N. M., Yusof, F. M., Chan, L. H., Chyi, F. K., Teoh, S. L., Das, S., Latiff, A. A., Mazlan, M. 2010. The effect of Piper betle extract on the wound healing process in experimentally induced diabetic rats. La Clinica Terapeutica, 161(2), 117–120.
- Kumar, N. 1999. Betelvine (Piper betle L.) Cultivation: A unique case of plant establishment under anthropogenically regulated microclimatic condition. Indian Journal of History of Science, 34(1), 19–32.
- Maisuthisakul, P., Suttajit, M., Pongsawatmanit, R. 2007. Assessment of phenolic content and free radical-scavenging capacity of some Thai indigenous plants. Food Chemistry, 100(4), 1409–1418. https://doi.org/10.1016/j.foodchem.2005.11.032
- Majumdar, B., Chaudhuri, S. R., Ray, A., Bandyopadhyay, S. K. 2002. Potent antiulcerogenic activity of ethanol extract of leaf of Piper betle Linn by antioxidative mechanism. Indian Journal of Clinical Biochemistry: IJCB, 17(1), 49–57. https://doi.org/10.1007/BF02867942
- Majumdar, B., Ray Chaudhuri, S. G., Ray, A., Bandyopadhyay, S. K. 2003. Effect of ethanol extract of Piper betle Linn leaf on healing of NSAID-induced experimental ulcer--a novel role of free radical scavenging action. Indian Journal of Experimental Biology, 41(4), 311–315.
- Mandal, S. M., Roy, A., Ghosh, A. K., Hazra, T. K., Basak, A., Franco, O. L. 2014. Challenges and future prospects of antibiotic therapy: from peptides to phages utilization. Frontiers in Pharmacology, 5, 105. https://doi.org/10.3389/fphar.2014.00105
- Milgrom, P., Tut, O. K., Gallen, M., Mancl, L., Spillane, N., Chi, D. L., Ramsay, D. S. 2016. Symptoms with betel nut and betel nut with tobacco among Micronesian youth. Addictive Behaviors, 53, 120–124. https://doi.org/10.1016/j.addbeh.2015.10.011
- Mishra, B., Vaisya, R. 1969. Bhavaprakasa of Sri Bhava Mishra. Chowkhamba Sanskrit Series. Varanasi, India.
- Muhammed, A. M. 2007. P-96: Isolation, structure elucidation and properties of secondary metabolites in plants, 118–162.

- Murata, K., Nakao, K., Hirata, N., Namba, K., Nomi, T., Kitamura, Y., Moriyama, K., Shintani, T., Iinuma, M., Matsuda, H. 2009. Hydroxychavicol: a potent xanthine oxidase inhibitor obtained from the leaves of betel, Piper betle. Journal of Natural Medicines, 63(3), 355–359. https://doi.org/10.1007/s11418-009-0331-y
- Murthy, K. R. S. 1995. Vagbhatta's Astanga Hrdayam. Krishnadas Academy, Varanasi, India.
- Muruganandam, L., Krishna, A., Reddy, J., Nirmala, G. S. 2017. Optimization studies on extraction of phytocomponents from betel leaves. Resource-Efficient Technologies. https://doi.org/10.1016/j.reffit.2017.02.007
- Nakatsu, T., Lupo, A. T., Chinn, J. W., Kang, R. K. L. 2000. Biological activity of essential oils and their constituents. Studies in Natural Products Chemistry, 21, 571–631. https://doi.org/10.1016/S1572-5995(00)80014-9
- Nouri, L., Nafchi, A. M. 2014. Antibacterial, mechanical, and barrier properties of sago starch film incorporated with betel leaves extract. International Journal of Biological Macromolecules, 66, 254–259. https://doi.org/10.1016/j.ijbiomac.2014.02.044
- Nouri, L., Nafchi, A. M., Karim, A. A. 2014. Phytochemical, antioxidant, antibacterial, and α-amylase inhibitory properties of different extracts from betel leaves. Industrial Crops and Products, 62, 47–52. https://doi.org/10.1016/j.indcrop.2014.08.015
- Nouri, L., Nafchi, A. M., Karim, A. A. 2015. Mechanical and Sensory Evaluation of Noodles Incorporated with Betel Leaf Extract. International Journal of Food Engineering, 11(2), 221–227. https://doi.org/10.1515/ijfe-2014-0183
- Paranjpe, R., Gundala, S. R., Lakshminarayana, N., Sagwal, A., Asif, G., Pandey, A., Aneja, R. 2013. Piper betle leaf extract: anticancer benefits and bio-guided fractionation to identify active principles for prostate cancer management. Carcinogenesis, 34(7), 1558–1566. https://doi.org/10.1093/carcin/bgt066
- Prabhu, M. S., Platel, K., Saraswathi, G., Srinivasan, K. 1995. Effect of orally administered betel leaf (Piper betle Linn.) on digestive enzymes of pancreas and intestinal mucosa and on bile production in rats. Indian Journal of Experimental Biology, 33(10), 752–756.
- Rai, M. P., Thilakchand, K. R., Palatty, P. L., Rao, P., Rao, S., Bhat, H. P., Baliga, M. S. 2011. Piper betle Linn (betel vine), the maligned Southeast Asian medicinal plant possesses cancer preventive effects: time to reconsider the wronged opinion. Asian Pacific Journal of Cancer Prevention: APJCP, 12(9), 2149–2156.
- Rao, A. R., Sinha, A., Selvan, R. S. 1985. Inhibitory action of Piper betle on the initiation of 7,12-dimethylbenz[a]anthracene-induced mammary carcinogenesis in rats. Cancer Letters, 26(2), 207–214.
- Rathee, J. S., Patro, B. S., Mula, S., Gamre, S., Chattopadhyay, S. 2006. Antioxidant Activity of Piper betle Leaf Extract and Its Constituents. Journal of Agricultural and Food Chemistry, 54(24), 9046–9054. https://doi.org/10.1021/jf061679e
- Roy, A., Guha, P. 2015. Development of a novel cup cake with unique properties of essential oil of betel leaf (Piper betle L.) for sustainable entrepreneurship. Journal of Food Science and Technology, 52(August), 4885–4894. https://doi.org/10.1007/s13197-014-1540-2
- Roy, A., Guha, P. 2018. Formulation and characterization of betel leaf (Piper betle L.) essential oil based nanoemulsion and its in vitro antibacterial efficacy against selected food pathogens. Journal of Food Processing and Preservation, 42(6), 1–7. https://doi.org/10.1111/jfpp.13617
- Roy, A., Shrivastava, S. L., Mandal, S. M. 2016. Self-assembled carbohydrate nanostructures: synthesis strategies to functional application in food. In Novel Approaches of Nanotechnology in Food (pp. 133–164). Elsevier. https://doi.org/10.1016/B978-0-12-804308-0.00005-4

- Saeed, S. A., Farnaz, S., Simjee, R. U., Malik, A. 1993. Triterpenes and B-sitosterol from Piper betle: isolation, antiplatelet and anti-inflammatory effects. Biochemical Society Transactions, 21(4), 462S.
- Santhakumari, P., Prakasam, A., Pugalendi, K. V. 2006. Antihyperglycemic Activity of Piper betle Leaf on Streptozotocin-Induced Diabetic Rats. Journal of Medicinal Food, 9(1), 108–112. https://doi.org/10.1089/jmf.2006.9.108
- Santhanam, G., Nagarajan, S. 1990. Wound healing activity of Curcuma aromatica and Piper betle. Fitoterapia, 61(5), 458–459.
- Seow, Y. X., Yeo, C. R., Chung, H. L., Yuk, H. G. 2014. Plant Essential Oils as Active Antimicrobial Agents. Critical Reviews in Food Science and Nutrition, 54(5), 625–644. https://doi.org/10.1080/10408398.2011.599504
- Sharma, P. V. 1995. Dravyaguna Vijnana. Vol. II Vegetable Drugs, Chaukhamba Sanskrit Bhawan, Varanasi, India.
- Shastri, S. N. 1962. Charaka samhita of agnivesha revised by charak and drahabala. Chowkhamba Vidya Bhawan, Varanasi, India.
- Singhal, G. D., Chunekar, K. C. 1980. Pharmaceutical consideration in ancient Indian surgery (Based on the chapters of 28-46 of Sutra-Sthana of Susruta Samhita). Chowkhamba Orientalia, Varanasi, India.
- Srinivasan, R., Devi, K. R., Kannappan, A., Pandian, S. K., Ravi, A. V. 2016. Piper betle and its bioactive metabolite phytol mitigates quorum sensing mediated virulence factors and biofilm of nosocomial pathogen Serratia marcescens in vitro. Journal of Ethnopharmacology, 193, 592–603. https://doi.org/10.1016/j.jep.2016.10.017
- Srinivasan, R., Santhakumari, S., Ravi, A. V. 2017. In vitro antibiofilm efficacy of Piper betle against quorum sensing mediated biofilm formation of luminescent Vibrio harveyi. Microbial Pathogenesis, 110, 232–239. https://doi.org/10.1016/j.micpath.2017.07.001
- Tan, L., Yin, W.-F., Chan, K.-G. 2013. Piper nigrum, Piper betle and Gnetum gnemon Natural Food Sources with Anti-Quorum Sensing Properties. Sensors, 13(3), 3975–3985. https://doi.org/10.3390/s130303975
- Thurairajah, N., Rahim, Z. H. 2007. The Crude Aqueous Extract of Piper betle L. and its Antibacterial Effect Towards Streptococcus mutans. American Journal of Biochemistry and Biotechnology, 3(1).
- Valentão, P., Gonçalves, R. F., Belo, C., De Pinho, P. G., Andrade, P. B., Ferreres, F. 2010. Improving the knowledge on Piper betle: Targeted metabolite analysis and effect on acetylcholinesterase. Journal of Separation Science, 33(20), 3168–3176. https://doi.org/10.1002/jssc.201000429
- Venkatachalam, K. V., Kjonaas, R., Croteau, R. 1984. Development and Essential Oil Content of Secretory Glands of Sage (Salvia officinalis). Plant Physiology, 76(1), 148–150.
- Vernekar, A. A., Vijayalaxmi, K. G. 2018. Development of Papad from dehydrated betel leaves (Piper betle L.) Powder. International Journal of Food Science and Nutrition, 3(5), 33–38.
- Wei, Y. T., Chou, Y.T., Yang, Y.C., Chou, C.Y., Lu, F.H., Chang, C.J., Wu, J.S. 2017. Betel nut chewing associated with increased risk of arterial stiffness. Drug and Alcohol Dependence, 180, 1–6. https://doi.org/10.1016/j.drugalcdep.2017.07.035
- White, L., Eiserle, R. 1961. Essential Oils. Perfume and Flavoring Materials. Industrial Engineering Chemistry, 53(6), 421–427. https://doi.org/10.1021/ie50618a019

- Wirotesangthong, M., Inagaki, N., Tanaka, H., Thanakijcharoenpath, W., Nagai, H. 2008. Inhibitory effects of Piper betle on production of allergic mediators by bone marrow-derived mast cells and lung epithelial cells. International Immunopharmacology, 8(3), 453–457. https://doi.org/10.1016/j.intimp.2007.11.005
- Wong, S. P., Leong, L. P., William Koh, J. H. 2006. Antioxidant activities of aqueous extracts of selected plants. Food Chemistry, 99(4), 775–783. https://doi.org/10.1016/j.foodchem.2005.07.058
- Zeng, H.W., Jiang, Y.Y., Cai, D.G., Bian, J., Long, K., Chen, Z.L. 1997. Piperbetol, Methylpiperbetol, Piperol A and Piperol B: A New Series of Highly Specific PAF Receptor Agonists from Piper betle. Planta Medica, 63(04), 296–298. https://doi.org/10.1055/s-2006-957685



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