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Review Article

A Review on *Piper betle L.*: Antioxidant, Antimicrobial, Extraction and Application in Food Product Development

Sangeetha Karunanithi*, Gnana Moorthy Eswaran U, Proshanta Guha and Prem Prakash Srivastav

Department of Agricultural and Food Engineering, Indian Institute of Technology - Kharagpur, West Bengal, India

***Corresponding Author:** Sangeetha Karunanithi, Department of Agricultural and Food Engineering, Indian Institute of Technology - Kharagpur, West Bengal, India.

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Abstract

Betel leaf (*Piper betle* L.) is a rich source of nutrients which attracts attention. Betel leaves utilized in various form like extract, extract oil and essential oil which contains 20 to 60 major and minor chemical compounds like eugenol (48.41%), estragole (16.12%), α-copaene (6.43%), anethol (2.62%) and eucalyptol (1.58%). This oil has been reported by several clinical studies to have potential roles in disease management. However, 35-70% of betel leaves are lost during processing. Therefore, extraction of valuable compounds from surplus leaves act as one of the post-harvest loss reduction methods. The beneficial effect of betel leave extract is depending on the availability of chemical compounds which varies based on the extraction system. So, selection and application of suitable extraction techniques play a crucial role in the process. The utilization of betel leave in food products development is an emerging strategy in the growing economy. Its importance to explore the application of betel leaves in traditional and modern food system. This review focused on nutrient, potential health benefits, novel extraction methods, recent application of betel leaf oil and extract in food product development for human consumption and food preservation with the aim of providing suggestions for its exploitation.

Keywords: Betel Leaf; Nutrient and Health Benefits; Extraction; Novel Food Products

Abbreviations

AE: Assisted extraction; APC: Ally pyrocatechol; BHA: Butylated hydroxyanisole; BHT: Butylated hydroxytoluene; BL: Betel leaves, C: Carbon, CFU: Colony forming unit; CHV: Chevibetol; CO_2: Carbon dioxide; DNA: Deoxyribonucleic Acid; DPPH: 2,2diphenyl-1-Picrylhydrazyl; Fe (II): Iron(II); g: Gram; GAE: Gallic Acid Equivalent; GC-MS: Gas Chromatography-Mass Spectroscopy; GHz: Giga Hertz; H: Hydrogen; h: Hours, H_2O: Water; H_2O_2: Hydrogen Peroxide; HD: Hydro Distillation; IC_{50}: Inhibitory Concentration; kcal: Kilo Calories; kHz: Kilo Hertz; l: Liter; m: Milli; MHz: Megahertz; mm: Milli Meter; MPa: Mega Pascal; MW: Microwave; NO: Nitrous Oxide; O: Single Oxygen; O_2: Oxygen; OC: Degree Celsius; PBR322: Bolivar and Rodriguez; pH: Hydrogen Potential; ppm: Part Per Million; RH: Relative Humidity; RNA: Ribonucleic acid; RNS: Reactive Nitrogen Species; ROS: Reactive Oxygen Species; SC-CO_2: Super critical Carbon dioxide; SCF: Super Critical Fluid; TPC: Total Phenolic Content; US: Ultrasound; W: Watt; β: Beta; %: Percentage; µ: Micro.

Introduction

Betel leaf (*Piper betle* L.) is a heart-shaped deep green leaf associated with the Piperaceae family with more than 2000 species. Betel leaf is a perennial creeper and produced leaves with glossy nature along with white catkin inflorescence. In catkin of betel leaf, the male plant has dense and cylindrical spikes, where the female plant has pendulous spikes. The plant is attached to the host tree or support by root, which arises from each node. The cultivation is widely distributed in subtropical and tropical areas of the world. There are hundreds of different varieties of betel leaves globally, including 40 varieties from India and 30 varieties from West Bengal. The plant is dioecious, that is male and female plants are different, but all are shade-loving perennial root climbers [1]. However, despite its origin in Malaysia, this vine is also cultivated in other countries such as Bangladesh, Burma, China, India, Malay, Pakistan, Philippines, and Sri Lanka. In India, betel leaf is cultivated in different states such as Orissa, Maharashtra, Tamil Nadu, Uttar Pradesh, and West Bengal [2]. The betel leaf is called Paan which is well understood in almost all the languages in India. This betel leaf is also called with different names according to their mother tongue, such as Saptaseera, Nagurvel, Nagaballi, Sompatra, Tambuli, Tamalapaku, Tambul, Vaksha Patra, Voojangalata, Vettilai. The varieties of betel leaf formed depends on their morphology, micrometrical traits, region of cultivation, size, color, aroma, and taste across the country. Some varieties are Assampatti, Bangla, Banarasi, Bagerhadi, Calcutta, Ghangeta, Magadhi, Mitha, Mysoreale, Nova Cuttak, Karpoorakodi, Kallarkodi, Kariyale, Karapaku, Kapoori, Kauri, Kasi, Pachakodi, Sanchi, Salem, Tellaku, Vellaikodi, etc. [1]. The betel leaf has a strong pungent or sweet taste with a strong aromatic spicy flavor. For example, mild to strong spicy taste in Bangla and Sanchi varieties whereas sweet taste in the Mitha variety. This taste variation among betel leaves is due to chemical compounds, nutritional compounds, and other factors [3]. The presence of essential oil, phenols, and terpenes contribute to aroma characteristics in betel leaf. The phytochemicals, mainly the polyphenolic compounds present in the betel leaf act as a natural antioxidant used to prevent oxidative damage, regulate oxidation, stress-related diseases such as diabetes and cardiovascular disease in the human body. The bioactive compounds present in the betel leaf contributes various activities such as anti-carcinogenicity, antibacterial, antifungal, anti-protozoa, anti-larval, anti-allergic, anti-filarial, anti-diabetic, anti-helminthic, antitumor, anti-depressant, antibacterial, anti-hypotensive, and antimicrobial effects [4].

The incredible characteristic of betel leaves, such as organoleptic, therapeutic, nutritional, functional, antioxidant, antimicrobial properties, and other favorable properties, act as a driving force to the food technologist, food scientist, and food manufacturer to utilize these leaves and formulate novel food products. The compounds present in betel leaf is used for self-life extension and enrichment of food safety factors by incorporating the betel leaf extract and essential oil during processing. Further, the researchers have proposed the possible utilization of betel leaf, extract, and essential oil as a food preservative, and to deliver major crucial nutrients to the consumer by the development of novel food products, formulation of medicines in pharmaceutical industries, development of cosmetic products [5]. However, the perishable nature of betel leaf poses a risk of quick spoilage due to fungal infections during improper processing, storing, and transportation. The spoilage betel leaf around 10% leads to the loss of Rs. 900 million per year in India. Therefore, the researcher has focused on developing the technology to minimize the post-harvest losses by adopting various methods like depetiolation, dehydration, controlling senescence by chemical treatment, modified atmospheric packaging followed by adopting better packaging methods, curing or bleaching the leaves, development of novel products, and extraction of various beneficial compounds such as betel leaf extract and essential oil from the surplus or unsold betel leaves. Therefore, extracting valuable compounds from the betel leaf is vital for better utilization in the food industry. Extraction of beneficial bioactive compounds present in betel leaf accomplished by adopting suitable extraction methods. It includes traditional extraction methods like distillation, solvent extraction, maceration to modern extraction methods, such as accelerated solvent extraction, supercritical extraction, thermal and non-thermal assisted extraction methods with various solvents such as methanol, ethanol, ethyl acetate, and acetone. Such solvents are selected due to their minimum or no toxicity, bio grades, and easy availability for improving the extraction yield [6]. The process involved in betel leaf for extracting valuable components (essential oil) is depicted in figure 1. The essential betel leaf oil has a remarkable aromatic and medicinal property, with a potential industrial future. Exploration of this betel leaf with the well-coordinated effort from the farmers, traders, scientists, and policymakers is required to reduce post-harvest losses, enhance the national economy, and generate employment opportunities.

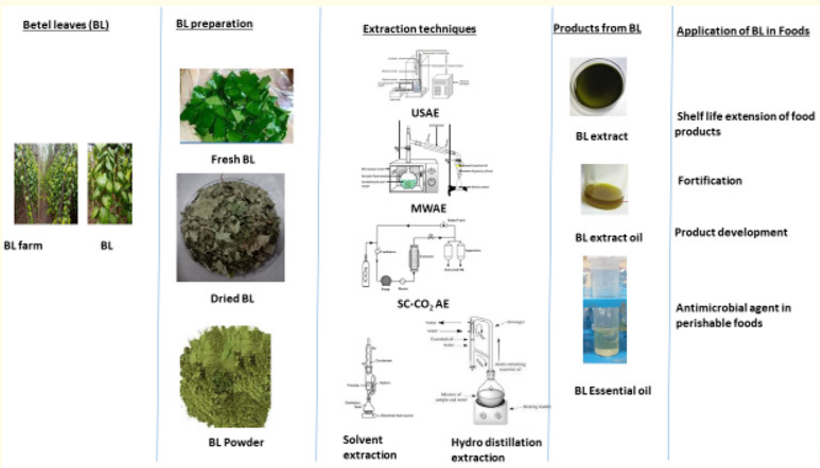

Figure 1: Betel leaves processing for extraction and its utilization in foods.

There is no single article reviewing the complete information of betel leaf and its products as discussed above. So, the aim of the present review is mainly concentrating and compiling the updated information from literature about all the relevant work carried out on shelf life enhancement techniques and novel product development. This review provides all possible and valuable information about the betel leaf.

Nutritional features of betel leaf

Betel leaf contains enormous nutritive value including vitamins, minerals, enzymes, protein, essential oil, and bioactive compounds, which are highly beneficial for treating diseases such as liver, brain, and heart diseases which is depicted in table 1 [1,2].

Nutrients	Unit	Quantity
Energy	Kcal/100g	44
Moisture	%	85 to 90
Protein	%	3-3.5
Fat	%	0.8-0.98
Fibers,	%	2-3
Carbohydrate	%	0.5 to 6.10
Vitamin C	%	0.005 – 0.0
Vitamin A	mg/100g	1.9 to 2.9
Nicotinic acid	mg/100g	0.63 to 0.89
Thiamine	mg/100g	10 to 70
Riboflavin	µg/100g	1.9 to 30
Nitrogen	%	2.0 to 7.0
Phosphorus	%	0.05 to 0.6
Potassium	%	1.1 to 4.6
Calcium	%	2.0 to 0.5
Iron	%	0.005 to 0.007
Iodine	mg/100g	3.2 to 3.4
Essential oil	%	0.08 to 0.2
Chlorophyll	%	0.01 to 0.25
Tannins	%	0.1 to 1.3

Table 1: Nutritional value of betel leaf.

Heath benefits of betel leaf

Products such as betel leaf pieces, betel leaf powder, betel leaf extract, and essential oil can be used in several manufacturing industries to produce superior functional food, drugs, and other products, leading to endless benefits for human health. The betel leaf powder and betel leaf pieces can be used to treat headache, joint pain, arthritis, sour throat, nervous pain, debility, and nervous exhaustion due to its analgesic and cooling effect [7]. It is also used to reduce bad breath, indigestion, cough, asthma, bronchitis, and teeth related issues. The betel leaf juice can be applied to treat endo-parasites, cough, fever, asthma, fatigue, skin and eye-related problems, as well as wound disinfection in children. This betel leaf is also used to treat dental and periodontal diseases through tablets and mouth washers. The betel leaf oil also contains effective biological compounds like phenol, diastase, sugar, and poses antioxidant, antifungal, and inflammatory properties which can be used for treating typhoid, cholera, tuberculosis, stomach ailment, respiratory disinfection by inhibiting the growth of deadly bacteria [8]. The betel leaves are equivalent to cow milk due to their nutritional content (six leaves and a bit of slaked lime equaled with 300 mL of milk) [2]. These leaves improve appetite, milk secretion, wound healing, treatment for lousy smell, stops bleeding in the nose, filariasis, and curing obesity [9]. Betel leaf extract plays a vital role in many aspects, mainly in pharmaceutical science. Betel leaf extract act as a potential antioxidant because it significantly delays and inhibits the oxidation process. Most of the health issues like arthritis, cardiovascular disease, cancer, rheumatoid, Alzheimer's disease, and neurodegenerative disorder are caused by free radicals. The free radicals produced by protein and lipid degradation producing superoxide radical, hydroxyl radical, and 1,1-diphenyl-2 picrylhydrazyl. The antioxidant compound in the betel leaf extract scavenges all those free radicals and prevents diseases caused by oxidation. Betel leaf possesses effective antiseptic, germicidal and other pharmacological properties that also effectively deal with the diseases, such as nausea, vomiting, indigestion, and flatulence.

Phytochemical composition of betel leaf and betel leaf oil

The chemical composition of betel leaf is associated predominantly with phenolic compounds in nature. Betel leaf extract having chemical compounds such as chavibetol, chavibetol acetate, allylpyrocatechol, α-tocopherol, β-carotene, eugenol, hydroxy chavicol, piperol A, and piperol B, etc. The important phytochemical has been listed in table 2. The betel leaf plant also contains terpinene, p-cymene, carvacrol, alley catechol, estragole, oxalic acid, malic acid, amino acid, and chavicol with its derivatives [10]. These major and minor compounds present in the essential oil contribute significant biological activity to the living body [11]. The major volatile compounds and their relative percentage value of essential oil analysed by GC-MS revealed that it had 33 chemical compounds [12]. These compounds attribute various medicinal and aromatic properties. Alcohol, aldehydes, alkanes, alkenes, ester, ketones, and amines were the major volatile compounds present in essential oil. Tamluk Mitha variety of betel leaf essential oil had 46 chemical compounds [13]. Similarly, the vellaikodi variety provided essential oil with 65 chemical compounds in betel leaf essential oil which produces specific biological activity. The betel leaf essential oil has higher oxygenated monoterpenes (eugenol and linalool),

Chemical Compounds	Quantity
Acetyl eugenol	14.05%
Allylpyrocatechol diacetate	0.71%
Allylpyrocatechol monoacetate	0.23%
Anethol	2.62%
Camphene	0.48%
Caryophyllene	1.30%
Chavibetol	53%
Chavibetol acetate	15.5%,
Chavicol	11.08%
Estragole	16.12%
Eucalyptol	1.58%
Eugenol	48.41%
Eugenol acetate	28%
Limonene	1.06%
Linalool	12.42%
Methyl acetate	1.45%
Pinene	0.21%
Safrole	25.67%
α-copaene	6.43%
α-pinene	0.21%
β-cubebene	13.60%
1,8 cineol	0.04%
3-methoxy cinnamaldehyde	1.38%

Table 2: Important chemical compounds of betel leaves.

sesquiterpene hydrocarbons, and monoterpenes hydrocarbons at minor concentrations which impart strong fragrance and aromatic characteristics. The chemical composition of an extracted essential oil varies quantitatively and qualitatively based on its ecological and geographical location, variety of betel vine, country, time of harvesting, and climatic factors. Every phytochemical compounds contributes to biological activity like eugenol act as a superior antioxidant, antifungal, antibacterial, anthelmintic, and nematicidal activity [8]. This eugenol can also act as an aromatic and fragrance agent, leading to a role in the food and cosmetic industry. It is also applicable for the local anesthetic to fill in dentistry temporarily. The next compound anethole acts as a sweet flavoring agent and is effective against fungus, insects, and other microbes [11]. Estragole is used in the food industry as a flavoring substance, food preservatives, and herbal medicinal products. The linalool compounds in betel leaf is used for skin diseases like skin irritation and acts as an anticancer agent. Hydroxy chavicol provides a light smell of creosote and acts as anticarcinogenic, antimutagenic, antioxidant, anti-inflammatory, and gastric ulcer healing activities in the biological system. B-caryophyllenes provide clove like aroma, and black pepper spiciness, used for preventing diabetes, prevent anxiety, and Alzheimer like disease. Iso-eugenol provides floral odor used in baked foods, chewing gums, flavoring agents in non-alcoholic drinks [14]. Safrole provides spicy taste and odor, which is used for detoxifying the body and used in beverages and candy preparation in the food industry. From the above discussion, it can be concluded that betel leaf and betel leaf essential oil have superior biochemical compounds. These compound leads to enormous beneficial effects in biological, organoleptic, and functional properties which can be used in food, pharma, and medical industry.

Antioxidant potential of betel leaf

Antioxidants are compounds present in natural and synthetic forms that can inhibit oxidation by scavenging or breaking down the oxidative reactive species [15]. Reactive oxygen species contains unstable oxygen molecules that can react with cells which causes damages to RNA, DNA, and protein present in the biological body. Free radicals are molecules with single or multiple unpaired electrons in their outer shells. These free radicals are produced due to adenosine triphosphate by the mitochondria organelle in the body while cells use oxygen to generate energy. During energy generation, two by-products are obtained: reactive nitrogen species (RNS) and reactive oxygen species (ROS). These by-products play a crucial activity in both beneficial and toxic effects based on the concentration level. High concentrations of ROS and RNS causes oxidative stress which triggers the damage of all cell structures. The antioxidant is the compound that can be used to counteract oxidative stress and alleviate its effects on the health of the biological system. This antioxidant is used to prevent the diseases caused by oxidative stress and is free from the side effects. This antioxidant activity can prevent deadly diseases such as cancerous disease, cardiovascular disease, neurodegenerative disease, Parkinson and Alzheimer's disease caused by free radicals**.** There are synthetic antioxidants such as BHA (Butylated hydroxyanisole), and BHT (butylated hydroxytoluene) used in food and pharmaceuticals which produces toxic effects. To overcome these cons, attempts were made to extract natural antioxidants from plant sources such as polyphenols, saponins, and tannins [11]. Antioxidant activities of the extract were analyzed by the maximal inhibitory concentration of 50% scavenging of DPPH radicals. The lower IC_{50} value indicates the higher antioxidants concentration of extract because the concentration of the antioxidant compound present in the extract can quench free radicals via transferring the hydrogen or electron atom to DPPH free radicle. The antioxidant activity correlates to the phenolic compounds present in extracts and flavonoid content which comprises the number of hydroxyl groups in their molecular structure, such as eugenol, hydroxyl chavicol, and gallic acid which strongly contribute to the antioxidant activities. Higher antioxidant activity of extract linked to higher extraction yield of major compounds such as eugenol, hydroxyl chavicol, and gallic acid [15]. The various extracting solvent influences much on the extraction yield of antioxidant compounds from the betel leaf. The high polarity solvent can produce more extraction yield of antioxidant compounds. Methanol extract produced a high concentration of antioxidant compounds [16]. The extraction of antioxidant, polyphenolic compounds, and bioactive compounds with different solvents and concluded that the highest total phenolic compounds of betel leaf extract were found to be 0.29 to 2.62 mg/GAE/gdw (milligram of gallic acid equivalent per gram in dry weight) for Banarasi Paan variety with 80% methanol as a solvent and the highest DPPH scavenging activity of 133 mg/GAE/gdw was found for Calcutta Paan variety with solvent of 80% ethanol [11]. From this study, we can conclude that polarity of solvent influences much on the extraction of bioactive compounds. The highest polyphenolic compounds with the more DPPH scavenging activities indicate the extract's maximum antioxidant presence [11]. The maximum free radicals scavenging activity of 89.46% inhibition was found when the betel leaf extracted with ethanol solvent. The antioxidative properties of betel leaf extract are high due to catechol at higher concentrations [15]. These APC compounds of 1.23% are used for preventing the lipid peroxide induced by Fe (II) and rat brain homogenates and damage of PBR322 plasmid DNA caused by gamma rays. These evidence shows that betel leaf extract's ability to scavenge H_2O_2 and O_2 radical species leads to a superior antioxidative effect. Antioxidant activity of betel leaf extract compounds, i.e., eugenol, has been compared with nitrous oxide (NO) and hydroxyl radical assays. The result shows that the antioxidant activity of eugenol was found to be superior (IC_{50} =114.34 ± 0.46 µg/mL) than nitrous oxide, which has hydroxyl radical scavenging of IC_{50} > 1000 µg/mL [16].

Antimicrobial activities of betel leaf

The antimicrobial activities of betel leaf extract against some mastitis bacteria such as *Staphylococcus aureus* and *Streptococcus agalactiae* has been studied based on the inhibitory zone method with the control sample of Iodip at 10% [17]. The betel leaf extract at 30% concentration shows the inhibition zone diameter for *Staphylococcus aureus* of 10.20 ± 0.03 mm, *Streptococcus agalactiae* of 8.12 ± 0.65 mm, *E. Coli* of 9.23 ± 0.19 mm. This inhibition zone of betel leaf extract is the same as the inhibition zone of 10% Iodip (synthetic antimicrobial agent). The highest inhibition zone formed by betel leaf extract is due to active compounds in the form of saponins, flavonoids, tannins, alkaloids, and terpenoids. As the concentration of betel leaf extract increased, there was a gradual increase in the inhibitory zone diameter. The antibacterial activity or inhibition zone is different for different microorganisms based on the bacterial resistant capabilities and the microorganism's cell wall characteristics. This higher diameter of the inhibitory zone represents the higher antimicrobial activity of the extract [7]. This antimicrobial activity is also influenced by independent factors such as extraction time and temperature. As the temperature and time increased to 80^{o}C up to 120 minutes, the inhibition zone diameter reduced to 5.89 mm. This reduction of the inhibition zone diameter due to physical and chemical changes occurs during the higher extraction temperature. Therefore, the optimum temperature of 60^{o}C at 120 minutes produced the highest inhibitory zone of 8.20 ± 014 mm for *Staphylococcus aureus* bacteria [5]. The betel leaf extract stored at room temperature of 28^{o}C produces less inhibitory power of 4.56 ± 0.14 mm on the third day compared to 6.36 ± 0.33 mm of the inhibitory zone on the same day for the refrigerated (4^{o}C) storage extract [9]. This study indicates that the storage condition of betel leaf extracts influences antimicrobial activities against *Streptococcus agalactiae* followed by *E. Coli* and *Staphylococcus aureus*. The effect of betel leaf extract which is extracted by methanol solvent on minimal inhibitory concentration and minimal bactericidal concentration against selected bacterial pathogens study shows that the lowest minimal inhibitory concentration of 0.1 µL/mL and minimal bactericidal concentration of 0.2 µL/mL of betel leaf extract for *Salmonella typhi* and highest minimal inhibitory concentration of 12.8 µL/mL and minimal bactericidal concentration of 6.4 µL/mL of betel leaf extract for *Pseudomonas aeruginosa* [18]. This study concludes that the betel leaf extracted by methanol can be used to treat the infections caused by pathogenic bacteria such as *E. Coli, Bacillus cereus, Pseudomonas aeruginosa,* and *Salmonella typhi*. The antimicrobial activity of betel leaf extract is also based on its bioactive compounds such as polyphenol and sterol compounds in abundance and the interaction of betel leaf extract with the bacterial cell wall, which leads to the destruction of bacterial compounds. The studies showed that the ethanolic extract of betel leaf could be used as antimicrobial agents in food products to extend the shelf life. The betel leaf extract has the highest concentration of fatty acids such as stearic acid, palmitic acid, and hydroxy fatty acid esters, leading to the potential antimicrobial activity against pathogenic microorganisms [19]. Flavonoids are the polyphenolic compounds that cause the best antibacterial activity. Also, it gives positive benefits to human health and acts as an anti-inflammatory, antitumor, antihemolytic, antiviral, and antioxidative properties.

Essential oil from betel leaf

As there is a massive demand for food availability due to population growth, there is a concern for minimally processed fresh food products, leading to significant losses, food safety, and quality challenges. So, those products have promoted the use of naturally occurring substances that pose beneficial antimicrobial and other health promoting substances such as essential oil [17]. Essential oils can be extracted from spices, herbs, and plants due to the presence of numerous bioactive compounds which possess antimicrobial properties. The betel leaves has been disposed as a waste material during improper processing and storage condition. Curing and bleaching of betel leaf produce 25% rejected leaves as non-consumable in the cottage industries located in India. So, extraction of valuable compounds like essential oil from surplus leaves, unsold leaves, de-chlorophyll leaves, or stale leaves plays a significant role in reducing post-harvest losses. This betel leaf volatile essential oil possesses enormous beneficial properties such as medicinal properties, organoleptic, and other desirable properties. The essential oil is made of a large number of volatile compounds, mainly secondary metabolites of the complex composition having specific odor. The betel leaf oil contributes various medicinal values such as pain relief and enhances healing properties. This essential oil also contributes various crucial biological activities such as antioxidant, antifungal, antidiabetic, antiamoebic, antimicrobial, anti-inflammatory, and other allied properties. This essential oil is used in medicinal, stimulant, tonic, aromatic, and other valuable products [15]. Such applications indicate the crucial industrial aspects as ingredients for producing various products such as food, flavor, fragrance, and pharmaceutical industrial products. The chemical compounds of essential oil from betel leaf with antioxidant activity mitigates oxidation and stress-related chronic disease. Apart from the medicinal value, the betel leaf essential oil is used to develop novel food products and non-food products.

Extraction methods of essential oil from betel leaf

The selection and design of appropriate extraction technology are important to receive the extract with all the essential compounds. This selection process influences the extraction yield, effectiveness of the antioxidant activity, quantity, quality aspect of phytochemicals such as total phenolic and flavonoid content. This essential oil is extracted by standard methods such as expression, maceration, percolation, and solvent extraction. Other techniques like hydro distillation, steam distillation, ultrasound-assisted, microwave-assisted hydro distillation, or supercritical fluid extraction methods are also employed. However, the hydro distillation method is widely used for essential oil extraction due to its easy, simple, low cost, and environmentally friendly characteristics. The different varieties of betel leaf produce different oil yields such as Mitha (2%), Bangla (1.7%), and Sanchi (0.8%) essential oil [20]. These essential oils and their constituents vary qualitatively and quantitatively. These changes are based on geographical and climate conditions etc. Such as varieties, soil type, temperature, humidity, and agronomic practices table 3. Shows that application of novel non thermal methods for extraction of essential oil from betel leaf.

S. No	Extract	Methods	Conditions	Result	Reference
1	EO	Curing assisted HD	Extraction time (140 min), extraction temperature (100°C) and leaf to water ratio (1:1.5 g/L)	0.48% EO yield from cured BL than 0.35% from uncured BL	[12]
2	EO	Ultrasound-assisted HD	Power level of 100 W, 37 ± 3 kHz, pretreatment of 90 minutes and leaf-to-water ratio of 1:2.	Highest oil yield of 0.25% than 0.2% in control	[13]
3	EO	Microwave assisted HD	2.45 GHz, 500W at 0.33L/W	Highest yield in less time (1.41% w/w dry basis in 50 minute than 210 min for control)	[10]
4	EO	Microwave assisted HD	2.45 GHz, 500 W and 0.33 L/W ratio in less extraction time	Highest yield of oil 0.348 %	[6]
5	BL extract oil	Supercritical CO_2 extraction	Temperature 40.0°C, Pressure-19 MPa and Flowrate- 7.00 ml/min.	0.228 g of global oil yield and 8.21 % of Eugenol	[14]
6	BL extract oil	Supercritical CO_2 extraction	78°C temperature, 30 MPa pressure, 8 ml/min of flowrate.	7.05% of oil yield and 791.709 mg GAE/g of TPC.	[3]
7	BL extract oil	Supercritical CO_2 extraction	80°c and 20 MPa, flow rate of CO_2 at 4 ml/min.	Highest oil yield of 6.456%	[11]
8	BL extract	Ultrasound-assisted extraction	Frequency of 37 kHz with a constant power of 400 W, temperature of 50°C, ratio of 1:20 g/ml and 80% ethanol, extraction period of 30 min	Highest TPC of 307 mg GAE/g dw as 212 mg GAE/g dw in control	[4]

Table 3: Extraction techniques used for recovering BL essential oil (EO) and extract.

Maceration method

Maceration is one of the extraction processes where the sample is prepared either powder or leaves placed inside the maceration chamber to proceed with the extraction process. The solvent at a specified quantity is added from the chamber's top until the sample is completely covered with solvent. Here, there are two independent factors: agitation speed and contact time, periodic changes of solvent at a specified interval, which influence the extraction yield. This process enhances the mass transfer rate, which ultimately improves oil yield and other biochemical compounds. Then the extract is collected by filtration or decantation process. Subsequently, the filtrate is placed into the rotary evaporator or H2O bath to remove the extraction solvents present in the desired extract. This method of extraction is very simple, and it is used for heat sensitive plant materials. For three days, one kg of betel leaf powder was kept in a maceration chamber containing 21 liters of 70% ethanol [21]. The solvent was replaced at a regular interval of 24 hours. Then the extract was filtered out and subjected to the rotary evaporator at 40 to 50 ^{0}C to evaporate the solvent entirely. From these studies, we can conclude that the maceration method produced extract with significantly better quality, but it took a long time for the extraction process to complete as well as there is a susceptibility for microbial growth and rancidity of extract.

Solvent extraction method

The betel leaf oil has been extracted using ethanol as a solvent which produced the strongest antibacterial activity against *Staphylococcus aureus* and *E. Coli* than the acetate solvent extraction and H_2O solvent extraction methods [22]. Extraction medium also influences the antibacterial activity of betel leaf extract as the ethanol obtained more amount of chavicol, eugenol, caryophyllene than acetone and H_2O solvent extraction. Clearly, the parameter which influence the yield of extraction may be listed as: the mass of the material, the quantity of solvent, type of solvent, texture of the material, fineness or coarseness of materials, temperature of extraction, and extraction time [23]. The oil yield mainly depends upon the solvent type and extraction time and temperature are the most influencing parameter for maximizing the oil yield. Optimization of these parameters is essential for concluding the accurate, independent values to get the desired impact on extraction, determining the possibility of interaction among the selected independent variable, and reducing the number of experimental runs. The optimization of the oil extraction parameter with 4 factors 3 levels using box-behnken response surface design to achieve the maximum yield of oil (10.94%) has been done. The optimum conditions for the above yield (10.94%) was material quantity (2g), solvent quantity (281.4 mL), n-hexane solvent, the temperature of extract (72^{0}C), and contact time of 3 hours [14]. Similarly, the independent variable by response surface box Behnken design such as extraction time of 6 hours, the particle size of 10 mm mesh with a solid-liquid ratio of 1:40 g/mL produced maximum oil yield of 0.22% [12].

Aqueous extraction method

The aqueous extraction method has been compared with the hexane solvent extraction method for both oil yield and the antimicrobial activity of betel leaf extract [17]. It has been concluded that the aqueous extraction method produced a higher oil yield (1.57g of oil) than the hexane extraction method (1.23g of oil) under similar conditions. The higher extractability in the aqueous method is due to the higher polarity of the molecules than ethanol, and polar compounds are extracted easily compared to nonpolar compounds. The aqueous extraction process gives higher antimicrobial activity due to the higher polar compounds in H_2O and shorter chain compared to ethanol. So, the water has a higher capability to extract polar compounds like aromatic carboxylic acid. Similarly, the 2,5-dimethylbenzoic acid yield was higher (91.51%) with the aqueous extraction process compared to the ethanol extraction process (76.22%). These compounds also induce the highest antimicrobial activity. So, they concluded that the aqueous extraction method is suitable for extracting betel leaf solute due to its merits, like green and eco-friendly technology. The highest betel leaf extract yield and polyphenol content was received when the steam is injected into the sample with 1:10 of sample: water ratio. There was also positive correlation with antioxidant activity (1C50 = 17.4 ppm) and antifungal activity against Candida albicans (MIC = 0.5%) [15]. From this, it is clear that the sample: H2O ratio is the most significant parameter responsible for the maximum yield with more antioxidant and antifungal activity.

Curing assisted extraction

Consumption of betel leaf had irritation due to high pungency, which could be removed using curing treatment. The cured betel leaf produced the highest essential oil with a yield of 0.22 ± 0.02% than noncured betel leaf yield of 0.18 ± 0.01% due to the highly porous structure formed during the curing process and enhanced mass transfer rate [12]. This study shows that pretreatment like curing enhances the oil yield or extraction yield followed by hydro distillation techniques. Also, these curing treatments produce the extract with an abundant quantity of bioactive compounds as mentioned in previous curing subtopics. These compounds are responsible for crucial biological properties like antimicrobial, antidiabetic, anti - inflammatory properties.

Supercritical fluid assisted extraction

There are wide variety of techniques available for the extraction of biological compounds. Most of them involve high heat or temperature, which may damage the heat sensitive compounds, time-consuming, lengthy operating procedure, and require higher solvent quantity. Further trace of the toxic compounds were also formed in the extract due to incomplete removal of solvent. So, there is a demand to overcome those limitations that are highly desirable. One such technology is supercritical fluid extraction (SCFE), which produces high-quality extract, free from toxic residues, compared to other conventional methods. In SCFE, carbon dioxide (CO_2) is used as a solvent for the extraction process. The SCF extraction process with important independent variables, such as pressure (10 to 30 mpa) and temperature (40 to 80^{0}C), and the results indicated that the oil yield rose as the temperature increases while decreasing of pressure [11]. Similarly, antioxidant activity of extract of SCF extraction, showed more activity by increasing pressure at a constant temperature. As the temperature increased, the antioxidant activity of the extract decreased simultaneously. Meanwhile, the antioxidant activity is enhanced by reducing temperature while increasing the pressure and vice versa because the increasing temperature in the extraction process results in reducing CO_2 density, which leads to the drop solvent power [14]**.** The less antioxidant activity is achieved while enhancing the temperature due to oxidation of easily oxidizable compounds [11]. Compared to the soxhlet extraction techniques, the SC-CO_2 produced less oil yield due to high oil solubility. However, this SC-CO_2 extraction method resulted as higher antioxidant value despite of low oil yield. Similarly, the extraction parameters has been optimized in the SC-CO_2 process to get the maximum yield [3]. To recover the oil yield of 7.05% and total phenolic content of 791.71 mg gallic acid equivalent/gram of the sample, the extraction parameters to set at 30 MPa pressure, 78^{0}C temperature, the flow rate of CO_2 is 8 mL/min when particle size kept at 355 mm and extraction time of 3 hours. This study concludes that the pressure and flow rate play a significant role in extracting oil and total phenolic content using CO_2 as a solvent in supercritical fluid extraction technology.

Ultrasound assisted extraction

Apart from the traditional technology like maceration, hexane extraction, and mechanical extraction, the extraction yield improved by novel assisted techniques. Various novel techniques like microwave, ohmic heating, SCF, irradiation, etc. Are available for enhancing the extraction yield. One such technology is ultrasound technology. This ultrasound (US) technique improves extraction efficiency due to the acoustic cavitation of ultrasound and its mechanical effect. These implosive cavitation bubbles produce shockwaves generated by inter-particle collision at high velocity and macro turbulence, enhancing diffusivity of mass transfer rate. These multiple mechanisms happened from acoustic cavitation near the surface layer, breakdown of cells, and erosion to enhance the recovery of the crucial compounds from the samples [4]. Finally, the ultrasound assisted extraction method improves the extraction of bioactive compounds such as tannins, steroids, flavonoids, saponin, total phenolic, and flavonoid content from the sample. The effect of ultra-sonic bath system on the extraction process at constant ultrasound power of 400 W with a frequency of 37 kHz for 30 minutes which leads to structural alteration and disintegration of the membrane holding the bioactive compounds [13]. Then the treated samples were subjected to maceration with independent factors like temperature, the concentration of solvent, and solute to solvent ratio and found that the maximum yield of 13.88% with total phenolic content of 311.21 mg GAE per g, 97.75% of antioxidant activity was obtained when treated at 51.60 ^{0}C with 78.74% ethanol, and solute to solvent ratio of 1:21.85 g/ml compared to conventional maceration extraction which produces the extraction yield of 10.96%. The author also received saponins, tannins, and major phenolic compounds with amended peak areas in the ultrasound assisted extraction process. It concludes that the ultrasound assisted extraction process is a superior technology pretreatment for extracting betel leaf compounds due to enhanced mass transfers rate with less energy consumption and less extraction time. The extraction of betel leaf compounds with different methods like sonication, soxhlet, and maceration method [4]. It has been concluded that sonication techniques produce the highest flavonoid and phenolic content, followed by maceration and soxhlet extraction techniques. Also, sonication technology showed highest free radical scavenging activity in terms of IC_{50} is 5.35 ± 0.3 µg/mL followed by maceration techniques of IC_{50} is 5.53 to 0.07 µg/mL) and soxhlet method is 5.83 ± 0.16 µg/mL). The highest radical scavenging activity of the extract is due to the highest content of eugenol and eugenol acetate in the extract.

Microwave-assisted extraction

Another important pretreatment technology to overcome the cons of traditional technology is microwave-assisted extraction (MAE) technology. The microwave is a type of electromagnetic wave of non-ionizing radiation with frequencies ranging from 300 MHz to 300 GHz. This microwave radiation energy penetrates the food particle then reacts with the polar compounds to produce heat energy. This microwave energy can heat the entire mass of biological substances simultaneously at a high heat transfer rate. These microwave-assisted extraction processes have considerable merits like reducing extraction time, less solvent requirement, and faster energy transfer at the selective heating process. MWE methods tooks only 30 minutes to extract the oil yield of 0.42% from the sample by microwave assisted hydro-distillation, whereas conventional hydro-distillation methods took 180 minutes for producing 0.39% of oil yield from the sample (orange peel) [6]. The microwave-assisted hydro-distillation acts as an energy-efficient and time-reducing method. It takes only 18 minutes to get the first drop of oil, and the extraction process is completed within 50 minutes with a yield of 1.41%. These results were comparable to conventional hydro-distillation methods, where it takes 45 minutes to get the first drop of oil, and the process takes 210 minutes to complete the extraction. The ultimate benefit of microwave assisted hydro-distillation method is to reduce the extraction time and extract 90% of compounds present in the sample within 50 minutes [10]. The microwave oven operated at 2.45 GHz frequency with the highest power output of 1000 W in the above method. This study suggested to use microwave assisted hydro-distillation to recover maximum yield and reduce energy consumption in the process of extraction.

Application of betel leaf extract in food and beverages

Betel leaf is possessing biochemical compounds which have beneficial effect in the biological system. Due to these characteristics of betel leaf, it can be widely used in the food and beverages industry to provide enhanced product quality and health benefits by preventing disease-causing elements table 4. depicted the utilization of betel leaf in the form of essential oil and extract for product development. That apart, the addition of betel leaf extract to beverages provides a preventive and curative powers to the food and beverage products with extended shelf life due to active compounds such as chavicol and eugenol. Shelf life extension of food products was due to the antimicrobial and antibacterial effect of betel leaf. In the current decade, more people prefer to have convenient food with high safety concerns. Most processed foods are spoilt easily if the manufacture does not add preservatives to them. There are some chemical preservatives called benzoic acid, sorbic acid in Jam, jelly, pickles, and paste that may cause various health hazards. So, the public is more eager about the natural preservative added products. Betel leaf has a potential antiseptic, antimicrobial and antibacterial activity against food spoilage microorganisms which makes it a good natural preservative.

S. No	Source	Product	Quantity	Result	Reference
1	Betel leaf (BL) flour	Broiler meat	1%	Lower cholesterol to 14 mg/dl	[31]
3	BL extract	Tilapia slices	400 ppm	Preserve tilapia slices up to 12 days.	[22]
4	BL slurry	Sev	30%	The β- carotene and vitamin c and other nutritional content improved by 1973.07 µg/100g and 18.36 mg/100g	[26]
5	BL essential oil	Raw apple juice	0.19 µl/ml	Shelf life of treated juice was extended by 6 days	[32]
6	BL extract	Hokkien noodles	15%	Best quality and sensory acceptability	[27]
7	BL essential oil	Tomato paste	0.25 mg/g	Extended the shelf life by 14 days	[20]
8	BL extract (Ethanol)	Nile tilapia (oreochromis niloticus) fillets	400 ppm,	Sensorial acceptable up to 12 days at 4°c	[33]
9	BL Essential oil	Novel cup cake	0.005 %	Best quality and sensory acceptability	[29]
10	BL Essential oil	Sapota juice	0.3 µl/ml	Food preservative & shelf life up to 30 days	[21]
11	BL	Ghee	1.50%	Sensorial superior with higher flavor and color	[23]
12	BL incorporated ice	Sardine muscle	0.1%	14 days for sardines stored in ice containing BL extract.	[34]
13	BL extract	Dahi	0.50%	Superior quality up to 7 day of storage	[19]
14	BL extract	Goat milk shrikhand	2%	Overall acceptability increased	[28]
15	BL distillate	Mango beverage	1%	Sensorial superior with higher flavor and color	[5]
16	BL extract	Meat	3%	Preserve the meat for up to 20 days	[9]
17	BL distillate	Whey based watermelon beverage	2%	Increases the deliciousness and nutritional value of the product. Preserves up to 20 days	[35]
18	BL extract	Fruit squashes	30%	Preserves up to 60 days	[8]
19	BL extract	Instant ginger	2%	Increase antioxidant strength by 6.642%	[36]
20	BL	Uttapam batter	One piece	Prevent over fermentation due to suppression of gas forming organisms	[37]
21	BL extract	Khoa	0.5%	Preserves up to 9 days	[18]
22	BL extract	Raw milk	0.5%	Extended the shelf life of raw milk by 5 hours	[30]
23	BL extract	Kulfi	15%	Best in overall acceptability	[38]

Table 4: Application of betel leave as a potential source in food products.

Snacks products

The betel leaf is very nutritious and poses various health benefits, which is can be used as an ingredient in the production of snacks items. The betel leaf added cutlet, ladoo, and namkeen were compared with mint leaf added products in terms of sensory characteristics by T-test with 5-point hedonic scale. The experiment revealed that organoleptic acceptability of betel leaf added namkeen and ladoo was high compared to mint leaf added food products [24]. The utilization of betel leaf in day-to-day life provides to overcome the deficiency of iron and calcium micronutrients through various recipes. The utilization of betel leaf offers economic as well as health benefits.

The food product namely coconut burfi, cutlet, and muthia with addition of betel leaf and the betel leaf added coconut, burfi showed higher nutritional values, such as protein 11.49g, carotene 114.05 µg, folic acid 51.89g and iron 5.80 mg per 100g, compared to spinach added food product [25]. The Khakhra with incorporation of betel leaf powder at different concentrations of 5, 7.5, 10% shows that among the concentration, the 5% betel leaf powder added Khakhra gave highly acceptable sensory characteristics and extend shelf life around 60 days under the ambient temperature [26]. This betel leaf added Khakhra also revealed the highest nutritional constitutes, such as 12.81g of protein, 2.79 mg of vitamin C, 2.23g of ash, 2.97g of crude fiber, 69.66g of carbohydrate, 378.68 µg of β-carotene, 215.85 mg of calcium and 7.30 mg of iron per 100g product. That apart, betel leaf extract incorporated aloevera gel, betel leaf essential oil added potato chips, sago starch-based edible film by adding essential oil and extract of betel leaf has been developed [27]. All the novel products based on betel leaf extract can also be taken up as supplementary food in the pharmaceutical industry for cancer treatment.

Solid foods

The properties of noodles has been enhanced by the addition of betel leaf [27]. As the percentage of betel leaf extract increased, the food product's hardness decreased due to the interaction of phenolic compounds present in betel leaf on molecules for reassociation of amylose. The betel leaf compounds interact with the starch amylose chain and inhibit the aggregation of amylose via hydrogen bonding in the dough, leading to the enlargement of free volume in the noodle matrix. This interaction reaction provides enhanced elongation flexibility, which leads to softening the texture of noodles and increases the adhesiveness due to better hydration of the starch molecules. The noodles incorporated with 15% betel leaf extract produced the result of best acceptability among the panel. From these studies, we can conclude that the addition of betel leaf extract on the food products leads to modification of the starch compounds causing a positive quality effect in terms of softness.

The traditional sweet like Khoa has been preserved with addition of 0.5% aqueous extract of betel leaf [18]. They concluded that the betel leaf added Khoa had extended shelf life and other important antimicrobial and antioxidant effects. Milk products i.e., Shrikant prepared with sapota pulp and betel leaf extract with different concentrations [28]. The sensory characteristics show that 30% sugar blended chakka, sapota pulp, and betel leaf in the ratio of 83: 15: 2, respectively produced the highest score of overall acceptability (8.47) of goat milk Shrikant with the highest acceptable taste, flavors, consistency, color and appearance characteristics. It is very well known that the betel leaf oil has more health benefits and provides various beneficial properties. Therefore, it is used to manufacture food products as one of the ingredients. The cupcake prepared by adding betel leaf oil at different concentrations followed by sensory evaluation with 9 points hedonic scale and found that 0.05% (v/w) oil added novel cupcake had the highest value of consumer preference in terms of overall acceptability [29]. They concluded that the developed novel cupcake was profitable and created self-sustaining entrepreneurship compared to other cupcakes available in the market. Due to its medicinal stimulant, aromatic and other beneficial properties, the betel leaf oil can be widely used to prepare food products. Similarly, several other novel food product was developed at IIT, Kharagpur, such as ice cream, halva, cupcakes, suji, chocolate, and biscuit with the addition of 0.01 to 0.5% concentration of essential oil extracted from betel leaf [9,29].

Liquid foods

The whey-based mango beverage with mango juice 12%, sugar 7%, betel leaf distillate at different concentrations of 0, 1, 2, 3% [5]. The sensory characteristics of beverage observed that the overall acceptability rate depends on concentration of betel leaf distillate which influence color, appearance, mouthfeel, and flavor with a 9-point hedonic scale. Among all the beverages, the beverages added with 2% of betel leaf distillate were most acceptable and liked by panel members. The effect of betel leaf extract on qualities of dahi and observed that the pH of Dahi decreased from 4.40 to 4.03 [19]. The titrable acidity was increased for the control dahi at the end of the seventh day of storage. In contrast, the dahi added with 0.5% betel leaf extract showed decreases and increases of pH and acidity, respectively. This also reduced firmness and consistency due to exhibiting characteristics of the phenolic compound present in the betel leaf on the starter culture. The addition of betel leaf is responsible for superior control of the quality characteristics in food products. The researcher also used the betel leaf extract to preserve milk due to the high content of phenolic and polyphenolic compounds due to antimicrobial and antioxidant activity [30].

Slurry foods

The shelf life of chili bo or chili slurry with the addition of betel leaf extract at different concentrations (0 to 1.75 mg/ml) [7]. In that study, the chili bo with the highest concentration of betel leaf extract showed a 6% reduction in the aerobic microbial count. In contrast, chili bo without betel leaf extract showed a 2.4% reduction of the aerobic microbial count. Also, the yeast and molds were lesser (5.22 log CFU/ml) than the control sample (5.31 log CFU/ml) at the end of the seventh day of storage. This reduction of microorganisms is due to the presence of fatty acids, hydroxy fatty acid ester, and hydroxy chavicol, which act as antimicrobial properties. Clearly, betel leaf extract exhibits a great antimicrobial activity in food. Food product such as tomato paste is a processed ingredient used in every food, and it is more susceptible to Mycotoxin production i.e., Aspergillus flavus causes spoilage of tomato paste. The microemulsion of betel leaf essential oil exhibited superior antifungal efficacy in tomato paste against Aspergillus flavus [20]. From this, we can conclude that the microemulsion of betel leaf essential oil can be used as natural preservatives, producing the best storage life of food products. Addition of 0.25 mg/g of betel leaf essential oil to the tomato paste during the accelerated storage studies under 89 ± 1.2% RH at 39 ± 1.0OC and found it to be a more acceptable concentration based on the fuzzy logic approach of sensory evaluation and it extended the self-life by 14 days [20]. Apart from the edible food products, there is a significant concern for the development of non-edible products, such as skin emollients, tooth powder, toothpaste, Paan masala, mouth fresheners, deodorants, antiseptic lotion, facial cream, cold drinks, appetizers, digestive agents, carminative mixture herbal shampoo, tonics, and other products. Therefore, research and development on product development from the surplus betel leaves would help to reduce considerable quantity of post-harvest losses.

Future studies

The green betel leaves as a valuable by-product because of their abundance and potential use of extract or volatile essential oil (EO) acquired during the extraction procedure. The use of the leaf extract/EO that is covered in the aforementioned section has received very few reports. Given the dearth of study in this field, researchers have focused on its potential application in a variety of processes, including food application, pharmaceutical industries, cosmetic industries, etc. By using cutting-edge preservation techniques which is useful and practical in the future of industry, it is possible to reduce the post-harvest losses of betel leaves. To lessen these losses of betel leaves, more inventive technologies and scientific research are needed. The majority of Indians are either directly or indirectly dependent on every process like production, processing, packaging, handling, shipping, and marketing of betel leaves. The national and state governments need to work together to establish a Research and Development Board and take more appropriate actions for supporting various projects and provide subsidy. This can assist to regulate betel leaf prices, promote export-focused operations and cultivation, enhance preservation methods, and utilize waste and byproducts. The efforts of farmers, traders, scientists, technicians, researchers, administrators, policymakers can increase the economy and employment possibilities related to betel leaves. This can be achieved by developing industrial-scale greenhouse culture, product development center, cool storage facilities, continuous curing equipment, medical considerations, and marketing. Apart from these, the researcher has to focus on the application of novel technology like cold plasma, high pressure processing for minimizing the losses and maximizing the beneficial bioactive compounds.

Conclusion

Betel leaf is a rich source of phenolic compounds, which have a wide range of medicinal applications and are responsible for a variety of health benefits. As a result, there is an increasing interest in using EO and betel leaf extract in a variety of industrial applications, including food supplements, the cosmetics and pharmaceutical industries. The highly effective bioactive chemicals found in betel leaves and its derivative products are in high demand in worldwide. This review discussed the recently used extraction techniques and product description, both of which have a substantial impact on the growth of the manufacturer's economic worth. Considering the biological properties of betel leaf such as its antibacterial, antioxidant, and anti-cancer effects, it is clear that this plant has great potential as a green medicine in the future. This review also discussed the conventional and modern technology for extraction of betel leaf compounds like essential oil, potential as a bio preservative and products development which create the way for entrepreneurship development. By reading this article, the technical readers can understand the latest research carried out on various aspects of betel leaf. This article provides almost all the vital information in a single place pertaining to betel leaf products used for development of food.

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