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A Comprehensive Review On Anti-Microbial And Antioxidant Properties Of Betel Leaf

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Abstract

Piper betel L. is a member of the *Piperaceae* family, which is sometimes referred to as Paan. In Sri Lanka, India, Thailand, Taiwan, and other Southeast Asian nations, it is widely grown.The leaves have a caustic, bittersweet, spicy, and somewhat sweet flavor. It contains a significant number of biomolecules with a range of pharmacological actions, including laxative, carminative, stomachic, anti-helminthic, tonic, and aphrodisiac properties. The leaves are used to treat a variety of conditions, including styptic, bronchitis, ozoena, cough, and foul-smelling mouth. They also clear the throat. In the current investigation, four distinct extracts of piper betel leaves (water, methanol, ethyl acetate, and petroleum ether) were evaluated against four distinct pathogenic bacteria: Escherichia coli, Proteus vulgaris, Staphylococcus aureus, and Streptococcus pyogenes. This current review showed that betel leaves extract, essential oil could inhibit microbial growth and kill various Gram-negative and Gram-positive bacteria as well as fungal species, including those that are multidrug-resistant and cause serious infectious diseases.

Keywords: Piper betle linn.,anti-microbial agent, Piperaceae, Chavicol, Eugenol.

INTRODUCTION

The betel leaf, also known as “Paan” or “Nagvalli” (family: *Piperaceae*), is a perennial creeper that is evergreen. The significance of leaves has been discussed in regard to every aspect of human life, including social, cultural, and religious aspects, and it is still highly relevant today.[1]One of the most valuable medicinal plants is piper betel, whose leaves have been utilized for a variety of therapeutic applications. The huge plant family *Piperaceae*, which includes Piper betel, is also known as Sirih in Malaysia and Indonesia and Paan in India. Since ancient times, betel leaves have been chewed while being wrapped with areca nuts, mineral slaked lime, catechu, flavouring agents, and spices. [2]
The leaves of piper betel are abundant in moisture, protein, lipids, minerals, vitamins, phytochemicals, and antioxidants. It aids in the prevention and treatment of a wide range of illnesses, including halitosis, boils and

abscesses, conjunctivitis, constipation, headache, hysteria, itches, mastitis, mastoiditis, leucorrhoea, otorrhoea, ringworm, gum swelling, rheumatism, abrasion, wounds, and bruises, among others. [3]
Betel leaf contains a major chemical component called eugenol, which has been shown in several animal experiments to have anti-inflammatory qualities[4].In addition to eugenol, betel leaves also include hydroxychavicol, alpha-tocopherol, and allylpyrocatechol, which are significant elements that help raise growth-stimulating hormone (GSH) levels in mouse liver and skin [5,6]

The various parts of Piper betle, notably the leaves, have been linked to its anti-oxidant and anti-inflammatory qualities. In general, leaves were shown to have larger levels of flavonoids and phenols, as well as stronger antioxidant, radical scavenging, and anti-cancer properties [7,8].

Antioxidant, antifungal, antiulcergenic, antiplatelet, antidiabetic, immunomodulatory, antileshmanial, antiamoebic, anti-inflammatory, antifilarial and antimicrobial are some of the properties of betle leaf. Other properties include antifertility [9], antihyperglycemic [10], antidermatophytic [11], antinacepative [12] and radioprotective properties [13].
Kingdom: Plantae
Division : Spermatophyta
Class : Magnoliopsida
Sub-class : Magnolilidae
Order : Piperales
Familia : *Piperaceae*
Genus : Piper
Species : Piper betle L.[14]


CHEMICAL CONSTITUENTS OF BETEL LEAF:

Alkaloids, carbohydrates, amino acids, tannins, and steroidal components were found in leaves after phytochemical analysis.[15] In particular, phenol and terpene-like substances are responsible for the distinctively intense, pungent, aromatic flavour of leaves.[16]

The leaf's constituents include water (85–90%), proteins (3–3.5%), carbs (0.5–6.1%), minerals (2.3–3.3%), fat (0.4–1%), fiber (2.3%), essential oil (0.08–0.2%), tannin (0.1–1.3%), and the alkaloid arakene. Along with other vitamins, it also contains vitamin C (0.005-0.01%), nicotinic acid (0.63-0.89mg/100g), vitamin A (1.9-2.9mg/100g), thiamine (10-70g/100g), and riboflavin (1.9-30g/100g). Other minerals included in it are calcium (0.2-0.5%), iron (0.005-0.007), iodine (3.4 g/100 g), phosphorus (0.5%-0.6%), and potassium (1.1-4.6%).[17]
Compared to older leaves, the fresh, new leaves have considerably higher levels of the enzyme and sugar that breaks down essential oils. Along with being four times more effective as an antibacterial agent than carbolic

acid, betel leaves also contain a substance called "Chavicol." Together with terpenes, it can be found in betel oil as a whitish liquid.[18,19]

Classification	Compounds	Classification	Compounds
Monoterpenes	α-Thujene	**Sesquiterpenes**	δ-Elemene
	α-Pinene		α-Copaene
	Camphene		β-Elemene
	Sabinene		E-β-Caryophyllene
	Myrcene		β-Copaene
	α-Terpinene		γ-Elemene
	β-Phellandrene		Aromadendrene
	1,8-Cineole/Eucalyptol		α-Humulene
	(E)-β-Ocimene		γ-Muurolene
	γ-Terpinene		Germacrene D
	Terpinolene		Germacrene B
	Linalool		β-Selinene
	Terpinen-4-ol		α-Selinene
	α-Terpineol		Bicyclogermacrene
	L-limonene		α-Muurolene
	Linalyl acetate		cis-β-Guaiene
			δ-Cadinene or δ-amorphene
			Palustrol
			Spathulenol
			Caryophyllene oxide
			Globulol
			Viridiflorol
			Cubenol
			α-Cadinol
			Ledene
			α-amorphene
			Cubebene
Phenylpropanoids	Estragole/Methyl chavicol	**Aldehydes**	Undecanal
	Chavicol		Phenyl acetaldehyde
	Anethole/Isoestragole		
	Safrole		
	Chavicol acetate		
	Eugenol		
	Methyl eugenol		
	Acetyl eugenol		
	Phenyl acetaldehyde		

The leave's essential oils include carvacrol, eugenol, chavicol, allylkatekol, cineol, estragol, caryophyllene, cardinene, and p-cymenedan eugenol methylether.[20]

ANTI MICROBIAL ACTIVITY OF BETEL LEAF:

Antibacterial Activity:

Extracts from P. betle Linn leaves have been shown to have antibacterial effects on a number of pathogenic bacteria, including Salmonella typhi, Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa. P. betle Linn's antibacterial properties are a result of its phenolic and alkaloid composition. Eugenol and hydroxychavicol are two phenolic compounds found in P. betle Linn that have been shown to have antibacterial activity by preventing the development of bacterial growth and biofilms. According, the alkaloids found in P. betle Linn, like piperine and pellitorine, show antibacterial activity by rupturing bacterial cell membranes and preventing bacterial development [21].

Antifungal Activity:

Various pathogenic fungi, such as Candida albicans, Aspergillus niger, and Trichophyton mentagrophytes, have been known to be resistant to P. betle Linn leaf extracts. P. betle Linn's antifungal properties are a result of its phenolic and flavonoid composition.The phenolic chemicals found in PBL, like eugenol and hydroxychavicol, have antifungal effect by preventing the growth of fungi and the development of biofilms.The flavonoids found in PBL, like quinazoline and quercetin, have antifungal properties that work by rupturing the fungal cell membrane and preventing the growth of fungi [22].

Antiviral Activity:

Leaf extracts from P. betle Linn have been shown to have antiviral properties against a number of viruses, including the herpes simplex virus (HSV), the human immunodeficiency virus (HIV), and the influenza virus.

P. betle Linn's antiviral properties are a result of its phenolic and flavonoid composition.The phenolic chemicals found in PBL, including as eugenol and hydroxychavicol, have antiviral effect by preventing viral reproduction and access into host cells and the flavonoids found in PBL, such as quercetin and catechin, have antiviral effect by preventing viral reproduction and entrance into host cells [23,24].

Antiparasitic Activity:

Several parasites, including Trypanosoma cruzi, Leishmania donovani, and Plasmodium falciparum, have been shown to be resistant to P. betle Linn leaf extracts. P. betle Linn's antiparasitic properties are a result of its terpenoid and alkaloid composition.The alkaloids found in PBL, like piperine and pellitorine, have antiparasitic effect by rupturing the parasite cell membrane and preventing parasite proliferation.The terpenoids found in PBL, including as caryophyllene and humulene, have antiparasitic effect by rupturing the parasite cell membrane and preventing parasite proliferation [25,26].

Mechanism of Action:

Several bioactive substances, including phenolics, alkaloids, terpenoids, and flavonoids, are thought to be responsible for P. betle Linn's antibacterial action.These substances display antimicrobial activity by rupturing microbial cell membranes, restricting microbial growth, and preventing the development of biofilms.The phenolic chemicals found in PBL, including as eugenol and hydroxychavicol, have antibacterial effect by rupturing microbial cell membranes and preventing microbial development.The alkaloids found in PBL, like piperine and pellitorine, have antibacterial effect by rupturing microbial cell membranes and preventing microbial development. The terpenoids found in PBL, namely caryophyllene and humulene, have the ability to damage microbial cell membranes and inhibit microbial growth [27,28].

Antimicrobial Resistance:

Multidrug resistant (MDR) bacteria have emerged as a result of antimicrobial resistance (AMR), a global public health problem. To fight AMR and safeguard public health, it is essential to develop novel antimicrobial agents. Due to its broad spectrum antibacterial activity and minimal toxicity, P. betle Linn has been suggested as a viable natural antimicrobial agent to treat AMR. However, more research is required to assess the efficacy and security of P. betle Linn extracts as a possible antibacterial agent [29-30].

ANTIOXIDANT ACTIVITY:

The cycle of chemical processes can occur in life because there is oxygen in the air for the oxidation process, which gives energy in the form of ATP [31].

In addition, the oxidation-reduction process in a live body can result in the production of oxygen. The transfer of electrons from one atom to another atom also involves this mechanism [32].

Unpaired single electrons will, however, result in the production of free radicals when there are difficulties with the flow of electrons. Free radicals are molecules, ions, or atoms that contain unpaired electrons in their outer orbitals. Because of this, they are extremely active and can oxidize or reduce other molecules. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are other names for free radicals. The mitochondria, which are by-products of aerobic respiration, are the body's primary source of ROS and RNS [33,34].

Free radicals with an oxygen core include hydroxyl, superoxide anion, alkoxyl, peroxyl, and nitric oxide. Nitric oxide and superoxide radicals have lower reactivity than hydroxyl and alkoxyl radicals, which have half-lives of 1 and 10-9 s, respectively. These two molecules are very reactive and can swiftly attack nearby molecules and inflict significant damage [35,36].

In simple terms, superoxide dismutase (SOD) converts superoxide anion radicals into O2 and H2O2 when O2 activates NADPH oxidase to produce ROS. However, oxidative stress can also result from high levels of ROS or pro-oxidants in the body. This also occurs as a result of the body's insufficient production of antioxidants [37,38]. Acute kidney failure, diabetes, atherosclerosis, preeclampsia, and hypertension are just a few of the disorders that can develop as a result of oxidative stress harming biological cells' ability to operate [39].

Antioxidants are compounds that can act as reducing agents, limit the oxidation of other molecules, and neutralize free radicals. This antioxidant's primary job is to stop the production of ROS from starting a chain reaction [40]. Scavenging by oxidants, transforming harmful free radicals into less harmful initiators, boosting endogenous antioxidant defence systems, and lowering or inhibiting free radical generation are all examples of antioxidant defence mechanisms. These all function by defending the organism against oxidative stress [37]. Both endogenous (made by the body) and exogenous obtained from outside the body, such as dietary supplements) sources of antioxidants exist. Exogenous antioxidants or non-enzymatic antioxidants serve as a secondary line of defence against ROS, while endogenous antioxidants or enzymatic antioxidants serve as the first line of defence [41].

Enzymatic antioxidants can defend the body from oxidative damage since they can break down ROS. The three primary enzymes involved in the defence against ROS are superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidases (GSHPx) [42]. Prokaryotic and eukaryotic cells have SOD as a key ROS defence mechanism. Prokaryotes primarily include iron and manganese, whereas eukaryotes contain copper, zinc, and manganese [43].

Synthetic and natural antioxidants are further separated under exogenous antioxidants. These antioxidant substances interact with ROS to reduce or stop their action [41].

Synthetic antioxidants attack ROS through a number of processes, including the binding of metal ions, the deactivation of singlet oxygen, the transformation of radical into non-radical species, and the absorption of UV light. Synthetic antioxidants include compounds like butylhydroxyanisol (BHA), butylhydroxytoluene (BHT), tert-butylhydroquinone (TBHQ), octyl gallate (OG), and propyl gallate (PG) [44,45].

Natural antioxidants may improve the body's natural antioxidant defenses by neutralizing and inhibiting ROS production [47]. Fruits, leaves, seeds, vegetables, bark, and stems are the primary sources of these natural antioxidants [46].

Phenolic is a secondary metabolite molecule that is made in a number of plant components and has significant antioxidant action. In addition to hydrogen donation, metal ion chelation, singlet oxygen quenching, and free radical scavenging, phenolic antioxidant action also involves other mechanisms. [48,49]

Additionally, flavonoids are crucial in limiting or preventing the damage brought on by free radicals. Flavonoids protect the body against oxidative damage [41].

Natural antioxidants are still being developed today since they offer the same advantages as synthetic antioxidants without the negative side effects [50,51].

Hydrogen atom transfer (HAT) and single electron transfer (SET) methods are the two main categories used to classify methodologies used to measure antioxidant activity. The HAT-based technique measures the capacity of antioxidants to reduce free radical activity by donating hydrogen, whereas the SET-based method measures the capacity of antioxidants for educing various molecules, including free radicals [52].

CONCLUSION:

Studies have shown that betel leaf contains a number of vitamins, including riboflavin, nicotinic acid, vitamin C, and vitamin A. The leaf has a variety of biological functions and functions as a natural antioxidant.Betel leaf compounds inhibit the growth of microorganisms, including gram-positive, gram-negative bacteria, drug-resistant bacteria, and fungi, which cause severe infectious diseases. The leaf produces an enzyme that aids in digestion and exhibits strong antibacterial properties against a wide range of microbes. On the other hand, betel leaf, when used extensively, has numerous medical benefits without any negative consequences, save from pregnancy.

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