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**Phytochemistry and pharmacological potentiality of
Betelvine (*Piper betle* L.): Review article**

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Abstract

Betelvine (*Piper betle* L) is a perennial, dioecious, evergreen creeper belonging to the family Piperaceae, grown commercially for its fresh leaves. Since antiquity betelvine has been used as a religious, recreational and medicinal plant in Southeast Asia and often referred as "Green Gold" in India. Betle leaves, which are most commonly used plant part, are pungent with aromatic flavor and are widely consumed as masticatory with its mild stimulant activity. Experimental studies revealed the presence of active principles like hydroxychavicol, allylpyrocatechol and eugenol in leaf essential oil and tannins, anthraquinones, flavonoids, alkaloids, phenols and terpenoids in leaf extracts which possess diverse biological and pharmacological effects such as antibacterial, antifungal, larvicidal, antiprotozoal, nematocidal, anticarcinogenic, gastroprotective effects, free radical scavenging, antioxidant, anti-inflammatory hepatoprotective, antiulcer and immunomodulatory activities. In this review, an attempt has been made to summarize the phytochemical composition and scientifically validated pharmacological properties of betel leaf. Thus, it creates a platform for pharmaceutical companies interested in formulating a plant based natural drug for specific targeted ailments.

Keywords: Betelvine, Green Gold, masticatory, phytochemistry

Introduction

Piper betle Linn., (Family Piperaceae) a perennial, shade loving and evergreen dioecious climber commonly known as the betelvine is an important medicinal and recreational plant in Southeast Asia^[1]. The crop is believed to have been originated in Eastern Malaysia and distributed in Southeast Asian countries, and cultivated in India, Sri Lanka, Bangladesh, Burma and Nepal^[2, 3]. Betel leaf cultivation has vast potential as it plays an important role in economics and also securing livelihood of people in South Asia^[3, 4]. Betel leaf is the most valued plant part, which has an important socio-cultural uses, besides having significant medicinal properties and nutritional values^[5]. In India it is customary to offer betle leaves to guests along with additives like arecanut on various socio-cultural and religious occasions as a mark of respect (referred to as tumbol)^[6]. Leaves are chewed as post meal mouth freshner along with arecanut, slacked lime and other additives which is known as betle quid. Betelvine is extensively used as an important medicinal plant in the traditional system of medicine of Southeast Asian countries for the treatment of various diseases like bad breath, boils and abscesses, conjunctivitis, constipation, headache, itches, mastitis, mastoiditis, leucorrhoea, otorrhoea, swelling of gum, rheumatism, cuts and injuries^[7]. Betel leaves are also reported to possess anticancer, antimutagenic, anti-amoebic, anti-giardial, anti-inflammatory, mosquito larvicidal, antimicrobial, immunomodulatory, antiulcerogenic, radioprotective, antileishmanial, and antifungal activities^[8]. Leaves were often heated and applied to the chest to relieve cough and asthma^[9]. The leaves were used to relieve throat pain^[10]. The essential oil from betel leaves was used as gargle or inhalation in diphtheria and respiratory catarah^[11].

Phytochemistry of betel leaves

The aroma of betel leaf is due to the presence of essential oils, consisting of phenols and terpenes. The fresh new leaves contain much more amount of essential oil, diastase enzyme and sugar as compare to old leaves. The 'Chavicol' present in betel leaf is a potent antiseptic agent as compared to carbolic acid^[2, 12, 13]. Betel leaf is a second most popular daily consumption item in Asia, which contribute the best oral hygiene to oral cavity^[14]. The

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chewing of *paan* develops red colour in the mouth due to oxidation of lime, and the mild stimulant activity is owed with the presence of betel quid, however the betel leaf gives mouth a fresh feel after chewing *paan*. Betel leaves chewing increases the salivation in turn increases the amount of peroxidase, lysozyme and antibodies to combat against bacterial growth in the oral cavity. It also enhances the gastric juice, pancreatic lipase secretion which helps in digestion process.

The betel leaves contains a wide variety of biologically active compounds whose concentration depends on the genotype, season and climatic conditions. The various phytochemicals found in the betel plants are chavibetol, chavicol, hydroxychavicol, estragole, eugenol, methyl eugenol, hydroxycatechol, caryophyllene, eugenol methyl ether, cadinene, γ -lactone, allyl catechol, p-cymene, cepharadione A, dotriacontanoic acid, tritriacontane, p-cymene, terpinene, eucalyptol, carvacrol, sesquiterpenes, cadinene, caryophyllene, dotriacontanoic acid, hentriacontane, pentatriacontane, stearic acid, n-triacontanol, triotriacontane, piperlonguminine, allylpyrocatechol diacetate, isoeugenol, 1, 8-cineol, α -pinene, β -pinene, sitosterol, β -sitosteryl palmitate, γ -sitosterol, stigmaterol, ursolic acid, ursolic acid 3 β -acetate. The phytochemical analysis of leaves also revealed the presence of alkaloids, carbohydrates, tannins, amino acids and steroidal components [2, 15]. The essential oil extracted from stalk, leaf, stem and root constitutes safrole, and the fruit essential oil constitute β -phellandrene [16].

Pharmacological effects of betel leaves

Since antiquity betel leaf has been described as an aromatic stimulo-carminative, astringent and aphrodisiac. The aromatic volatile essential oil extracted from fresh betel leaves contains a phenol called chavicol, which has a powerful antiseptic properties. Due to the presence of various phytochemicals, the leaf has great potency to act as natural anti-oxidant. The anti-oxidant property is correlated with different biological activities like hepatoprotective, antidiabetic, antiarthritis, anti-stroke and anticancer properties, since free radicals are involved in all these diseases [17]. Chewing betel leaves helps to maintain the level of ascorbic acid in the saliva. Ascorbic acid being an excellent antioxidant, scavenge the free radicals in the body, thus preventing oral cancer [18]. The betel leaf extracts have an effective anti-diabetic property as they regulate the blood sugar levels [19].

The aqueous and alcoholic extracts of fresh betel leaves showed effective inhibitory action against various types of microorganisms including several gram positive and gram negative bacteria such as *Micrococcus pyogenes*, *M. luteus*, *B.subtilis*, *Staphylococcus aureus*, *S.pyogenes*, *Diplococcus pneumoniae*, *E.coli*, *Vibrio comma*, *Pseudomonas aeruginosa* and also showed antifungal activity against *Aspergillus niger* and *A.oryzae* [20, 21, 22]. The betel leaf extracts had profound antioxidant activity [23], and also showed highest free radical scavenging activity with percent residual rate of absorbance (%RRA) of 15% which is comparable to vitamin E&C widely used in Antiwrinkle cosmetics among 13 aromatic oils from Thai medicinal plants [24]. The antioxidative and antihemolytic activities of betel leaf extracts were attributed to the high concentration and combined activity of flavonoids and polyphenols [25]. The spray dried betel leaf powder serves as a potential source for treatment of Type-2 diabetes [26]. The leaf infusion and different cream formulation of betel leaves showed potential antiseptic activity and antidermatophytic activity respectively [27, 28]. The gastroprotective activity of hot

water extracts of betel leaves showed the protection against indomethacin induced gastric ulceration due to antioxidative and mucin protecting properties [17]. The betel leaf extract had shown antifertility and antiestrogenic effects in female rats [29]. The histological study using a rat model had shown antihepatotoxic effect against carbon tetrachloride (CCl₄) induced liver injury by declining alpha smooth muscle actin (alpha-sma) expression by betel leaf extract [30]. Similarly, the *P. betle* leaf extract can effectively prevent γ -ray induced lipid peroxidation and thus possess radio protective activity [31]. The immunomodulatory and antidepressant activity were also reported in trials conducted on mice using alcoholic extracts of betel leaf [32, 33]. Analgesic and anti-inflammatory activities of leaf extracts were proved on a dose dependent manner in a rat model [34]. The essential oil derived from fresh leaves of *P.betle* proved to be effective against wide spectrum of microbes and aflotoxins which is due to the presence of multiple components of essential oil [35]. Anticarcinogenic properties of betel leaf were also reported [36].

Conclusion

Piper betle a traditional medicinal plant known very well throughout the world as a potent source for novel therapeutic usage. The betel leaves are the rich source of nutrients, antioxidants and various groups of phytochemicals makes it fit for future usage as a prominent source for treating various conditions. In this review, an attempt has been made to throw a light on the biomolecule constituents of essential oil and leaf extracts of betel vine and their validated pharmacological and nutraceutical properties. There is a need to intensify the studies on standardisation and stabilisation of betel leaf extracts which paves a path for its future therapeutic usage. Thus, creating a platform for pharmaceutical companies interested in formulating a plant based natural drug for specific targeted ailments.

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