Chemical Composition and Biological Activities of Nepalese Piper betle L.

Article · March 2012

CITATIONS
2

READS
3,416

2 authors:

Prabodh Satyal
University of Alabama in Huntsville
69 PUBLICATIONS **172** CITATIONS
SEE PROFILE

William N Setzer
University of Alabama in Huntsville
466 PUBLICATIONS **4,714** CITATIONS
SEE PROFILE

Chemical Composition and Biological Activities of Nepalese *Piper betle* L.

Prabodh Satyal, PhD graduate student

and William N Setzer, Professor of Chemistry

Betel: *Piper betle* L., Synonym *Chavica betle* Miq.

Other common names: English: betel leaf; Nepali/ Hindi: paan; Malyalam: vetta, vettila

Botanical family: Piperaceae

Odor description: Strong aromatic smell

Distribution of species

There are around 2000 species of *Piper betle* distributed worldwide (Mabberley, 1997), of which 10 species are available in Nepal. *Piper betle* is currently distributed in Africa, western Asia, Himalaya, India, southeast Asia, Malaysia, China, Nepal, and Sri Lanka (Press et al, 2002; Thanh et al, 2002). In Nepal, the plant is widely cultivated at altitudes of 150-1400 m.

Piper betle is a perennial, climbing vine that has a deep green heart-shaped leaf. It is one of the most famous spices in Nepal, India, and China, and is cultivated for chewing and for traditional aesthetical uses (Periyanayagam et al, 2011).

Traditional medicinal uses

Betel is traditionally used in eye and skin diseases (Farnsworth and Bunyapraphatsara, 1992). The leaves of the plant have been used in Ayurvedic medicine and more recently the leaf essential oil has been reputed to demonstrate anthelmintic, aphrodisiac, carminative, and laxative properties. Yunani believes that it works as a styptic and vulnerary drug (Herbal Medicine Research Centre, 2005).

Essential oil composition

Chemical profile for *Piper betle* leaf essential oil from Nepal	
Chemical Family	Components
Monoterpenes	*trans*-sabinene hydrate (tr)
Sesquiterpenes	(*E*)-caryophyllene (0.4%), δ-cadinene (tr), α-humulene (tr), γ-muurolene (tr)
Alcohols	α-cadinol (tr), τ-muurolol (tr)
Esters	methyl salicylate (tr), chavibetol acetate (11.7%), allylpyrocatechol diacetate (6.2%)
Aldehydes	*n*-decanal (tr)
Phenols[a]	chavicol (0.4%), eugenol (0.4%), chavibetol[b] (80.5%), methyl eugenol (0.4%)
Piper betle leaf essential oil from Nepal was analyzed by using the GC -MS method (Satyal et al, 2012) at the University of Alabama in Huntsville. The yield of the oil was 0.1% pale yellow color on hydro-distillation using Clevenger type apparatus. "tr" indicates trace component <0.05%	

[a] The phenolic components likely play a role as antioxidants (Suppakul et al, 2006).

[b] Chavibetol is an isomer of eugenol.

Biological activity

Antifungal, antiseptic, anthelmintic, and antihypertensive properties are exhibited by betel leaf chloroform extract (Evans et al, 1984). Using the serial microbroth dilution method (Satyal et al, 2012), marginal antimicrobial activity of chavibetol-rich betel leaf oil was observed with minimum inhibitory concentrations (MIC) on *Staphylococus aureus* (MIC = 625 µg/mL), *Bacillus cereus* (MIC = 625 µg/mL), *Escherichia coli* (MIC = 625 µg/mL), *Pseudomonas aeruginosa* (MIC =625 µg/mL), *Aspergillus niger* (MIC = 313 µg/mL), and *Candida albicans* (MIC = 1250 µg/mL).

Insecticidal activity

Safrole-rich *Piper betel* essential oil exhibits insecticidal activity against the common housefly, *Musca domestica* (Mohottalage, 2007).

Cytotoxic activity

In vitro cytotoxic activity is also exhibited by chavibetol-rich *Piper betel* leaf oil on MCF-7 human breast adenocarcinoma cells with 100% killing at 100 µg/mL. The cytotoxic activity of betel leaf extracts and essential oils can be attributed to phenylpropanoids such as hydroxychavicol (Chakrabroty et al, 2012) and chavibetol. In contrast with the observed cytotoxic activity in adenocarcinoma cells, brine shrimp lethality (Satyal et al, 2012) was not shown by *Piper betel* leaf oil.

Volatile chemical composition and chemotypes

The following chemotypes have been recorded from various parts of the world.

- Chavicol chemotype: Indian 'Sagar Bangla' cultivar (Garg and Jain, 1996).
- Isoeugenol chemotype: Indian *Piper betle* 'Meetha' cultivar (Kumar et al, 2007), and Vietnamese betel sample (Thanh et al, 2002).
- Eugenol chemotype: 'Kapoori' cultivar (Kumar et al, 2009), and 'Kapoori' and 'Bangla' cultivars from India (Rawat et al, 1989).
- Germacrene D chemotype: Indian *Piper betle* var. *sirungamani*1 (Periyanayagam et al, 2011).
- Safrole chemotype: Sri Lankan *Piper betle* leaf essential oil (Mohottalage et al, 2007), South Indian sample (Jirovetz et al, 1999), Indian 'Desawari' betel, and 'Sanchi' cultivar of India (Rawat et al, 1989).
- Anethole chemotype: 'Meetha' *Piper betle* cultivar from India (Rawat et al, 1989).
- Chavibetol chemotype: Philippine sample (Rimando et al, 1987), Malaysian sample (Jantan et al, 1994), and our sample from Nepal.
- The major component of Taiwanese betel floral essential oil is safrole (28%) (Truyen and Chan, 1999). The major component of the Vietnamese betel rhizome is α-cadinol (Thanh et al, 2002).

The variation in essential oil composition is not unexpected because the plants often produce different qualitative and quantitative amounts of phytochemicals when grown in different geographical locations of the world. This difference could be attributed to differences in environmental, climatic, and ecological conditions of each specific geographic area.

Therapeutic actions

Antioxidant activity is observed in *Piper betle* leaf oil-chemotype not indicated-(Arambewela et al, 2006). In India, antihistaminic properties are also observed with ethanol extracts of *Piper betle* (Hajare et al, 2011). *Piper betle* is used as an anthelmintic, astringent, blood purifier, stimulant, and tonic, and for diabetes, excessive thirst, fever, loss of appetite, nasal inhalation, nausea, and worms (Irani, 2005). In skin care it is used for boils, dandruff, discoloration of the skin, eczema, leprosy, skin disease, tetanus, urticaria, and wounds, and it is also used in hair care (Irani, 2005).

Safety

Piper betle has been linked to oral (lip, mouth, and tongue) cancer in areas where it is chewed excessively. It has been demonstrated, however, that adjuncts such as tobacco and areca nut are carcinogenic, but *Piper betle* alone is devoid of carcinogenic properties (Guha, 2006; Rai et al, 2011). Dyspepsia and pyorrhea have also been observed in individuals who chew betel to excess (Deoda, 2008). Pregnant women have been advised not to use the essential oil (Irani, 2005). Note, however, that safrole is a known carcinogen (Wislocki et al, 1977) and safrole-rich chemotypes may, therefore, be a risk and should be avoided.

Core aromatherapy uses (Irani, 2005)

Antiseptic: The *Piper betle* essential oil is a powerful antiseptic.

Astringent: The essential oil of *Piper betle* is used as a strong astringent.

Nervous system: *Piper betle* essential oil has been used as a primary stimulant for the central nervous system followed by a kind of inebriety in large doses.

Oral care: *Piper betle* essential oil is used to remove mouth odor and improves the voice.

Sugumaran et al proved that *Piper betle* essential oil can serve as an antimicrobial agent against dental pathogens (Sugumaran et al, 2011).

Cultural importance

In Hindu culture, betel leaf and areca nut play an important role in various ritual ceremonies. Money is paid to a priest by inserting it into the betel leaf. In Vietnamese culture, people believe betel leaf initiates conversation. During Vietnamese weddings, betel leaf and areca nut are traditionally exchanged to indicate the strong love relationship between the bride and groom.

Other uses of betel leaf (Deoda, 2008)

Headache: It can relieve severe headache upon application to the painful region.

Urinary complicacy: Leaf juice is mixed with dilute milk and sweetened slightly to assist in easing urination.

Nervous system: Leaf juice is helpful in nervous pain and nervous exhaustion. Mix betel leaf juice with honey and use as a tonic to the nervous system.

Cough and sore throat: Leaf juice mixed with honey can relieve an irritating cough and sore throat.

Pulmonary infection: Pulmonary infection in childhood and old age can be treated by warming leaves that have been soaked in mustard oil and applying to the chest to relieve cough and difficulty in breathing.

Constipation: Insertion of betel leaf dipped in castor oil into the rectum instantly relieves constipation.

Breast-feeding: Lactation of nursing mothers can be improved by applying to the breast betel leaf mixed with cooking oil or mustard oil.

Inflammation: Applying betel leaf to the joints and testes can reduce arthritis and orchitis, respectively.

Wound care: The juice of a few leaves should be extracted and applied to a wound prior to applying a bandage. This promotes healing time to just two days with a single application.

Boils: A leaf is gently warmed until it softens. Then a layer of castor oil is applied to the boil, which allows for the transfer of the essential oil to the boil. Next, the oiled leaf is applied to the boil for several hours. Upon several applications, the boil will rupture and the purulent material will drain out of the boil. Betel leaf prepared in this way may be applied at bedtime and removed the following morning.

Acknowledgement

Prabodh Satyal is grateful to Tribhuvan University for helping with the plant collection and access to laboratory facilities, and to Mr. Akash Deo for collection of the essential oil. William N. Setzer is grateful to an anonymous private donor for the gift of the GC/MS instrumentation. The authors would also like to express gratitude to Tilak Gautam for identifying plants for the project and Dr. Bernhard Vogler for technical assistance.

References

Arambewela L, Arawwawala M, Rajapaksa D. (2006). *Piper betle*: A potential natural antioxidant. *International Journal of Food Science and Technology*. 41, p10-14.

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, p239-245.

Chakraborti J B, Mahato S K, Joshi K et al. (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, p88-89.

Deoda R. (2008). *Piper betle.* Available: http://p-cognosy.blogspot.com/2008/08/piper-betle.html Last accessed 4th July 2012.

Evans P, Bowers W, Funk E. (1984). Identification of fungicidal and nematocidal components in the leaves of *Piper betle* (Piperaceae). *Journal of Agricultural and Food Chemistry*. 32, p1254-1256.

Farnsworth N R, Bunyapraphatsara N. (1992). *Thai Medicinal Plants*. Mahidol University, Thailand: Medicinal Plant Information Center, Faculty of Pharmacy. p402.

Garg S C, Jain R. (1992). Biological activity of the essential oil of *Piper betle* L. *Journal of Essential Oil Research*. 4, p601-606.

Garg S C, Jain R. (1996). Volatile constituents of the essential oil of *Piper betle* L. (Cultivar Sagar Bangla). *Indian Journal of Chemistry*. 35B, p874-875.

Guha P. (2006). Betel leaf: The neglected green gold of India. *Journal of Human Ecology*. 19, p87-93.

Hajare R, Darvhekar V, Shewale A et al. (2011). Evaluation of antihistaminic activity of *Piper betle* leaf in guinea pig. *African Journal of Pharmacy and Pharmacology*. 5, p113-117.

Herbal Medicine Research Centre. (2005). *Compendium of Medicinal Plants Used in Malaysia.* Kuala Lumpur: Herbal Medicine Research Centre. p225.

Irani F. (2005). An encounter with Ayurveda Aromatherapy. *National Assn. for Holistic Aromatherapy Journal*. (3/4), p29-35.

Jantan IB, Ahmad AR, Ahmad AS et al. (1994). A comparative study of the essential oils of five *Piper* species from peninsular Malaysia. *Flavour and Fragrance Journal*. 9, p339-342.

Jirovetz L, Puschmann C, Buchbauer G et al. (1999). Analysis of the essential oil of *Piper betle* L. leaves from South-India using GC/FID, GC/MS and olfactometry. *Scientia Pharmaceutica*. 67, p305-312.

Kumar R, Singh S, Kulshrestha R et al. (2007). Volatile constituents of essential oil of betel leaf (*Piper betle*, Linn) Cv. Meetha. *Indian Perfumer.* 51, p55-56.

Kumar R, Singh S, Agarwal S C et al. (2009). Chemical composition and antimicrobial activity of essential oil of *Piper betle* (L.) Cv. Kapoori leaves. *Indian Perfumer.* 53, p38-40.

Mabberley D J. (1997). *The Plant Book*, 2nd Ed. Cambridge: Cambridge University Press. p560.

Mohottalage S, Tabacchi R, Guerin P M. (2007). Components from Sri Lankan *Piper betle* L. leaf oil and their analogues showing toxicity against the housefly, *Musca domestica*. *Flavour and Fragrance Journal*. 22, p130-138.

Periyanayagam K, Mubeen M, Saleem M et al. (2011). Phytochemical studies and GC/MS analysis on the isolated essential oil from the leaves of *Piper betle* L. var. *sirugamani*1 (SGM1). *Journal of Pharmacy Research*. 4, p2411-2413.

Press J R, Shrestha K K, Sutton D A. (2000). *Annotated Checklist of the Flowering Plants of Nepal*. London: The Natural History Museum, http://www.efloras.org/florataxon.aspx?flora_id=110&taxon_id=200012019 Last retrieved on 5th May 2012.

Rai M P, Thilakchand K R, Palatty P L et al. (2011). *Piper betel* 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*. 12, p2149-2156.

Rawat A K S, Tripathi R D, Khan A J et al. (1989). Essential oil components as markers for identification of *Piper betle* L. cultivers. *Biochemical Systematics and Ecology*. 17, p35-38.

Rimando A M, Han B H, Park J H et al. (1986). Studies on the constituents of Philippine *Piper betle* Leaves. *Archives of Pharmacal Research.* 9, p93-97.

Suppakul P, Sanla-Ead N, Phoopuritham P. (2006). Antimicrobial and antioxidant activities of betel oil. *Kasetsart Journal (Natural Science)*. 40 (Suppl.), p91-100.

Satyal P, Paudel P, Lamichhane B et al. (2012). Volatile constituents and biological activities of the leaf essential oil of *Jasminum mesnyi* growing in Nepal. *Journal of Chemical Pharmaceutical Research*. 4, p437-439.

Sugumaran M, Suresh G M, Shankarnarayanan K et al. (2011). Chemical composition and antimicrobial activity of vellaikodi variety of *Piper betle* Linn leaf oil against dental pathogens. *International Journal of PharmTech Research*. 3, p2135-2139.

Thanh L, Dung N X, Luu H V et al. (2002). Chemical composition of the leaf oil from *Piper betle* L. cultivated in Vietnam. *Journal of Essential Oil-Bearing Plants*. 5, p38-42.

Truyen L, Chan N. (1999). *National Institute of Materia Medica Medicinal Plants in Vietnam*. Hanoi: Science and Technology Publishing House. p179-184.

Wislocki P G, Miller E C, Miller J A et al. (1977). Carcinogenic and mutagenic activities of safrole, 1′-hydroxysafrole, and some known or possible metabolites. *Cancer Research*. 37, p1883-1891.

Prabodh Satyal received his B.Sc. and M.Sc. degrees in organic chemistry from Tribhuvan University, Nepal. He is pursuing a Ph.D. degree in Biotechnology Science and Engineering from the University of Alabama in Huntsville. He has studied the chemical composition of 100 kinds of essential oils from the Himalayan range of Nepal with 18 different bioassays. Before joining Dr. Setzer's lab, he worked as a Lecturer of Chemistry at Kathmandu University for three years. In his PhD work, he is looking for therapeutically important novel volatile components in essential oils.

Will Setzer received his B.S. degree in chemistry from Harvey Mudd College and his Ph.D. degree in organic chemistry from the University of Arizona. He has been studying phytochemistry, natural products drug discovery, and chemical ecology for more than 20 years. He is currently Professor and Chair of the Chemistry Department at the University of Alabama in Huntsville.