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MINI REVIEW

Chemical constituents and bioactivity of *Piper sarmentosum*: a mini review

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Abstract

Herbs with medicinal potential are important for health and wellness. The main aim of this review article was to disseminate important information regarding the use of *Piper sarmentosum* as natural medicine. *P. sarmentosum* have been reported to possess a varying degree of hypoglycemic, antidiabetic and other additional properties. The antioxidant properties of the herbs may be effective in controlling the oxidative damage. The review article highlights the positive role of traditional herbs as alternative medicine.

1. Introduction

Herbal remedies played an enormously important role in the maintenance of human health throughout the history of mankind. Over 50% of modern clinical are sourced from various plants extracts and have been employed as supplements and nutraceuticals (Bradley, 1992; Sivasubramanian and Brindha, 2014). The genus *Piper*, widely distributed in the tropical and subtropical region of the world, is often used as food flavouring agents, traditional medicines (Burkill, 1966) and pest control agents (Nair and Burke, 1990, Hussain *et al*., 2012). *P. sarmentosum* Roxb. (Piperaceae), locally known as kadok, is a glabrous, creeping terrestrial herb about 20 cm tall. The leaves are dark green and variable in shape and size, usually, heart shape and cordate with 2 -8 cm long petiole (Malaysian Herbal Monograph). Kadok is well known for its medicinal properties, such as its antibacterial, antiprotozoal, antioxidant, antimalarial and hypoglycaemic effects (Zaidan *et al*., 2005). The picture of the plant is shown in Figure 1.

Figure 1. *P. sarmentosum* Roxb. (Malaysian Herbal Monograph)

In the Malay and Indonesian Archipelago, the leaves and roots of this plant are used for the treatment of toothache, fungoid dermatitis on the feet, coughing asthma, and pleurisy (Perry, 1981). In Malaysia, *P. sarmentosum* leaves and roots are applied to the forehead to relieve headache while its decoction is utilized to cure muscle weakness and pain in the bones (Perry, 1981). In Indonesia, *P. sarmentosum* rootlets are chewed with betel nut and the juice is swallowed to treat coughs and asthma. It is also chewed with ginger to treat toothache or chewed with a little nutmeg and ginger to treat pleurisy (Perry, 1981). Warmed leaves coated with coconut oil are applied to the painful chest while the finely ground leaves mixed with a small amount of water are smeared on the throat to treat coughs. In Thailand,

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the roots are used as carminative and stomachic (Perry, 1981) while the fruits and leaves are used as an expectorant (Pongboonrod, 1976; Rukachaisirikul *et al*., 2004). This review describes the chemical constituents of *P. sarmentosum* and its bioactivity as the significant plant of interest. In South-East Asia, the plant has been discovered, however, extensive research to develop further still limited. In Panama, researchers have been working to explore the medicinal potential of this significant plant for its ethnomedical uses and pharmacological activities as this *Piperaceae* family occupying fifth place in Panamanian Flora (Durant-Archibold *et al*., 2018). Due to great demand, scientific studies have been extensively carrying out worldwide. Most of the studies are focusing on biological activities of plant extracts, toxicology based on dosage and marker compound identification. It is believed that herbal product with known quality in terms of phytochemical profile and biological property will increase the value of the particular herbal product significantly. The information provided in this review will be of value not only for the discovery of pharmacological use in new drugs preparation but also to promote the use as the ingredients of traditional medicine.

2. Material and methods

The present review paper considered the literature published prior to 2020 on chemical constituent, pharmacological activities, biological activities and ethnomedicinal uses. This review considered peer-reviewed research papers available at databases as Scopus, Science Direct or Google Scholar.

3. Extraction methods

The separation of compounds from natural products is becoming an important part for food, flavour, fragrance and pharmaceutical industries. Food industries have to deal with handling complex molecules such as chemical constituents or phytochemicals (Tiwari, 1995). Therefore, method of extraction that being employed is important to ensure the quality and quantity of the target compound. There are various methods to extract *P. sarmentosum* and one of them is using soxhlet apparatus (Thitima *et al.,* 2004). Solvent extraction of solid samples, which is commonly known as solid-liquid extraction, but which should be referred to, in a more correct use of the physicochemical terminology, as leaching or lixiviation, is one of the oldest ways of solid sample pretreatment. The most outstanding advantages of conventional Soxhlet are as follows: the sample is repeatedly brought into contact with the fresh portions of the solvent, thereby helping to displace the transfer equilibrium (de Castro and García-Ayuso, 1998).

P. sarmentosum also can be extracted by using reflux (Hussain *et al*., 2008). Reflux is a technique involving the condensation of vapours and the return of this condensate to the system from which it originated (Proestos and Komaitis, 2008).

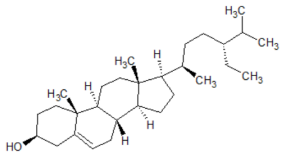
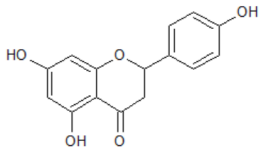
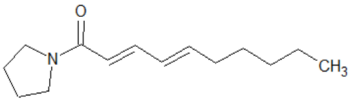
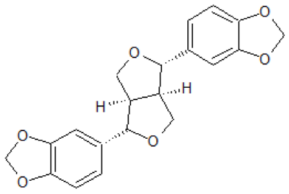
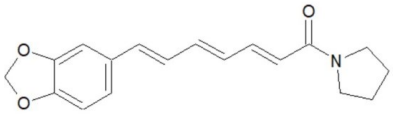
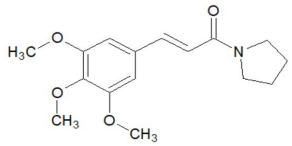
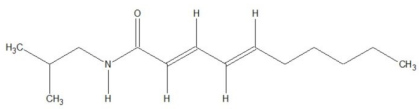
4. Phytochemical constituents of *P. sarmentosum*

P. sarmentosum is rich in bioactive compounds including amides, alkaloids, flavonoids, tannins, saponins, glycosides, terpenoids and phenolic compounds (Mgbeahuruike *et al*., 2017) *P. sarmentosum* is reported to contain the isolation of a number of amides and phenylpropanoids (Likhitwitayawuid *et al*., 1987; Masuda *et al*., 1991; Stohr *et al*., 1999). The chemical constituents of *P. sarmentosum* can be identified using Gas Chromatography-Mass Spectra (GC-MS) and the constituents were identified based on their retention times (R_f) values. The molecular structures of the various compounds found in *P. sarmentosum* are shown in Table 1.

Rukachaisirikul *et al*. (2004) isolated eight amides (pellitorine, guineensine, brachystamide B, sarmentine, brachyamide B, 1-piperettyl pyrrolidine, 3′,4′,5′-trimethoxycinnamoyl pyrrolidine and sarmentosine), two lignans ((+)-asarinin and sesamin) and four other compounds (1-(3,4-methylenedioxyphenyl)-1E-tetradecene, methyl piperate and, a mixture of beta-sitosterol and stigmasterol) from the hexane and methanol extracts of *P. sarmentosum*. New phenylpropanoyl amides (chaplupyrrolidone A, chaplupyrrolidone B and deacetylsarmentamide B) were discovered by Damsud *et al*. (2013) which using bioassay-guided fractions and then further purified by chromatography techniques. Rahman *et al*. (2014) reported the extracts of fruits and leaves of *P. sarmentosum* gave the best matches of 28 compounds in the leaf extract and 24 compounds in the fruit extracts. Interestingly, extensive research was done by Chanprapai and Chavasiri (2017) successfully displayed 63 constituents of *P. sarmentosum* which, accounting of 99.9% of the oil and myristicin was the major components. Other compounds were presents including trans-caryophylle, α-copaene, germacrene-D, β-cubenene and bis-(2-ethylhexyyl) phthalate. Sakilan *et al*.,2019 reported the phytochemicals of *P. sarmentosum* in leaf using ethanolic etxracts and displayed aloocimene, benzene propanoic acid, trans-caryophylle, α-copaene, germacrene-D, cis-methyl isoeugenol,naphthalene, delta-caddinene, 3-(4-methoxyphenyl) propionic acid.

5. Biological activities

Table 1. The molecular structures of the various compounds found in *P. sarmentosum*

Compound	Molecular structure
β-sitosterol	
Naringenin	
Sarmentine	
Sesamin	
1-piperettyl pyrrolidine	
3',4',5'-trimethoxycinnamoyl pyrrolidine	
Pellitorine	

P. sarmentosum being a potential candidate as traditional medicine, the plant has been investigated for a number of activities like antiamoebic (Sawangjiaroen *et al*., 2004), antibacterial, antineoplastic (Toong and Wong (1989), neuromuscular blocking (Rididitid *et al.,* 1998), hypoglycaemic (Peungvicha *et al*., 1998) and antimalarial (Najib *et al*., 1999). Leaf extracts are reported to have antioxidants properties due to flavonoids. Fruit of the plant has shown anti-TB activity and different bioactive amides have been isolated (*Thitima et al*., 2004).

5.1 Antioxidants

Superoxide anion ($O2^-$) is a toxic by-product formed by the univalent reduction of ground-state molecular oxygen (Cunningham *et al*., 1987). Superoxide anion and its reduction products H2O2 and •OH produce a variety of effects on tissue macromolecules and have been implicated as participants in a variety of disease states. Since superoxide anions are produced as toxic by-products of regular biochemical and metabolic reactions in the human biological system, a daily intake of natural antioxidant superoxide scavenger could prevent oxidative damage. A study by Vimala *et al*. (2003) reported that methanolic leaf extracts of *P. sarmentosum* and possessed a natural antioxidant superoxide scavenger, Naringenin. Naringenin belongs to the flavonoid group, 4', 5, 7-Trihydroxyflavanone. The Naringenin compound showed high superoxide scavenging activity that is 75.7% (Vimala *et al*., 2003).

The research by Chanwitheesuk *et al*. (2005) towards 43 edible plants shows that the methanolic extract of the leaves *P. sarmentosum* contain a high level of antioxidant activity with the index of 13.0. Antioxidant activity was determined by measuring the coupled oxidation of carotene and linoleic acid, as described by Hammerschmidt and Pratt (1978). The results suggest that the antioxidant activities of these plants may be attributed to the chemical components present, especially vitamin E and xanthophylls.

5.2 Antimicrobial

Increasing awareness of hazards associated with the use of antibiotics and chemical agents has accelerated investigations into plants and their extracts as new sources of antimicrobial agents. The increasing prevalence of multidrug-resistant strains of microorganism and the recent appearance of strains with reduced susceptibility to antibiotics raises the spectre of untreatable microbial infections and adds urgency to the search for new infection-fighting strategies. The presence of the phytochemicals like flavonoids, tannins, and steroids indicates that *P. sarmentosum* is rich in phenol compounds. Zaidan *et al*. (2005) reported the antibacterial activities of methanol extracts of *P. sarmentosum* leaves against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The research done by Lee *et al*. (2014) showed the methanol extracts of *P. sarmentosum* Roxb give high antibacterial activities against *Escherichia coli, Burkholderia* sp. and *Haemophilus parasuis* in proportion to high amounts of total polyphenol and flavonoid. Chemical compounds such as myristicin and brachyamide B which isolated from the essential oil of *P. sarmentosum* exhibited strong antifungal activity against *Rhizoctonia solani* and *Bipolaris oryzae*. Additionally, Brachyamide B and piperonal also showed strong antibacterial activity against *Xanthomonas oryzae (Xoo)* and *pv. oryzicola (Xoc)* (Chanprapai and Chavasiri, 2017).

The study done by Taweechaisupapong *et al.* (2010) reported the antimicrobial effects of *P. sarmentosum* extracts on *Aggregatibacter actinomycetemcomitans,* an oral microbe, which was tested by the disc diffusion method showed no inhibitory zone. The methanolic fruit

extract of *P. sarmentosum* was found to be effective as antibacterial agents against the causal agent of sheath brown rot, *Pseudomonas fuscovaginae* (Rahman *et al*., 2016). The antibacterial activity of the fruit extract against the pathogenic bacteria *P. fuscovaginae* was measured by the diameter of inhibition zones produced and the MIC and MBC values. The results obtained from this study suggest that the fruit extract of *P. sarmentosum* has a potential to be developed as a novel bactericide.

5.3 Antidepressant

Different type of extracts of *P. sarmentosum* have been investigated for antidepressant-like effect in mice and few parameters were evaluated in the open field test (OFT), force swim test (FST) and tail suspension test (TST). The results indicate that *P. sarmentosum* increased the expression of brain-derived neurotropic factor (BDNF) and effective as an anti-depressant (Qing *et al*., 2017).

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