PHCOG RES. REVIEW ARTICLE

Review on *Polygonum minus*. Huds, a commonly used food additive in Southeast Asia

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ABSTRACT

Polygonum minus (Polygonaceae), generally known as 'kesum' in Malaysia is among the most commonly used food additive, flavoring agent and traditionally used to treat stomach and body aches. Raw or cooked leaves of *P. minus* are used in digestive disorders in the form of a decoction and the oil is used for dandruff. The pharmacological studies on *P. minus* have demonstrated antioxidant, *in vitro* LDL oxidation inhibition, antiulcer activity, analgesic activity, anti-inflammatory activity, *in vitro* antiplatelet aggregation activity, antimicrobial activity, digestive enhancing property and cytotoxic activity. The spectroscopic studies of essential oil of *P. minus* showed the presence of about 69 compounds, which are responsible for the aroma. The phytochemical studies showed presence of flavonoids and essential oils. This review is an effort to update the botanical, phytochemical, pharmacological and toxicological data of the plant *P. minus*.

Key words: Antioxidant, antiulcer, phytoconstituents, *polygonum*

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INTRODUCTION

Every plant on earth is useful to mankind either directly or indirectly. Many plants have created history in the treatment of diseases. The classical examples include opium for pain management, digitalis for cardiac failure and cinchona for malaria. With the recognition of the role of antioxidants in many diseases, there was a worldwide search for natural antioxidants. Plants containing these principles are nowadays screened for a variety of pharmacological properties. The plant *Polygonum minus* is not an exception in this context as it is reported to have a high content of antioxidants and hence has gained great attention. In Malaysia it is known as "kesum" and also commonly known as "laksa leaves." In Malaysia, it is a part of several types of fresh vegetables that are consumed raw, as "ulam" or equivalent to salad in other countries. These include "selom" (*Oenanthe javanica;* Apiaceae) and "pegaga" (*Centella asiatica;* Mackinlayaceae). Most of these herbs are believed to be associated with antioxidant activities and have many beneficial effects.[1] Kesum has many claims with regards to its traditional uses. Raw or cooked leaves and seeds of *P. minus* are used in digestive disorders in the form of a decoction and the oil is used in dandruff. But it is more commonly used as a flavoring agent. This review is focused on the botanical, phytochemical, pharmacological and toxicological aspects of *P. minus*.

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PLANT PROFILE

Synonym	: *Persicaria minor* (Huds.)
Kingdom	: Plantae
Superdivision	: Spermatophyta
Division	: Magnoliophyta
Class	: Magnoliopsida
Order	: Polygonales
Family	: Polygonaceae
Genus	: *Polygonum*
Species	: *Polygonum minus* Huds.

Polygonum minus is generally known as phakphai in Thailand, Kleiner Knöterich in German and Chakhong-machain Manipuri (India). *P. minus* originated from Southeast Asian countries namely Malaysia, Thailand, Vietnam and Indonesia. It grows wild in damp areas near the ditches,

river banks and lakes. It survives well on cool and hilly areas.[2] The plant also grows in India and Sri Lanka, up to 800-900 meters above sea level.

Morphology

This plant [Figure 1] achieves a height of 1.0 m on the lowlands and 1.5 m on the hilly areas. It is a slender twining shrub, frequently climbing up on tall trees. The leaves are long and lanceolate measuring about 5-7 cm long and 0.5-2.0 cm wide. The dark green leaves are aromatic and arranged alternately on a stem. The anatomy and micromorphology of the leaves of *P. minus* have been described by Bunawan *et al*.[3] The stem is cylindrical, green and slightly reddish having short internodes with nodes that are easily rooted.[2] However one more type of kesum that is vertical-growing is also available. For commercial production, the vertical type is more suitable for efficient field maintenance and harvesting.[2]

Phytochemistry

P. minus has not has been subjected to much phytochemical studies as there are only a few reports available on its chemical constituents. To date there are reports on identification and isolation of flavonoids and essential oil.

The flavonoids reported in are flavonols: Myricetin [3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)-4-chromenone] and quercetin [2-(3,4-dihydroxyphenyl) -3,5,7-trihydroxy-4 *H*-chromen-4-one]; a methyl flavonol [6,7-4',5'-dimethylenedioxy-3,5,3'-trimethoxyflavone] and a flavone [6,7-methylenedioxy- 5,3',4',5'-tetramethoxyflavone].[4,5]

Kesum has high levels of essential oil (72.54%), which contains aliphatic aldehydes (87%).[4] Decanal (24.36%) and dodecanal (48.18%) are major aliphatic aldehydes present in Kesum, others include 1-decanol (2.49%), 1-dodecanol (2.44%), undecanal (1.77%), tetradecanal (1.42%), 1-undecanol (1.41%), nonanal (0.86%), 1-nonanol (0.76%), and β-caryophyllene (0.18%).[6] The essential oil in the leaves of the plant, which is responsible for the aroma is reported to contain 69 compounds that have been identified by gas chromatography and mass spectroscopy.[6] The compounds found in the essential oil include geraniol [(*trans*)-3,7-dimethyl-2,6-octadien-1-ol] and geranial/citral (3,7-dimethylocta-2,6-dienal).[7] These compounds are responsible for the fragrance and are found to be antimicrobial, antioxidant, immunostimulant and anti-carcinogenic.[8] Vimala *et al*., reported the presence of oxalic acid in leaves and this may be responsible for the digestive enhancement activity.[9] Pharmacological properties of the selected phytoconstituents of *P. minus* are listed in Table 1.[9-27]

Figure 1: Morphology of the *Polygonum minus*

Pharmacological effects

Pre-clinical studies

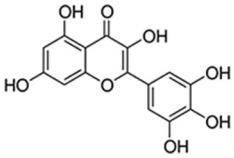
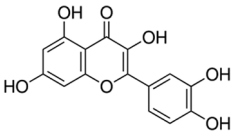
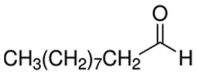
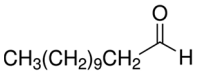
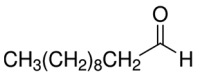
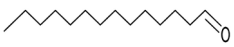
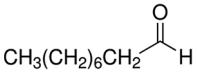
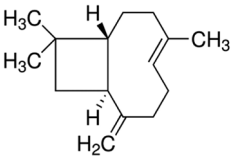
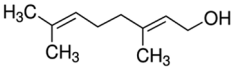
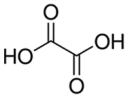
Antioxidant capacity

Antioxidant activity of the *P. minus* was reported by many researchers using DPPH radical scavenging, TBARS and FRAP assay. The high polyphenol content, vitamin C and β carotene was suggested to be responsible for the antioxidant activity of *P. minus*.[6,28] The aqueous, methanol and ethanol extracts have been reported to possess high antioxidant potential, comparable with synthetic antioxidant such as butylhydroxytoluene (BHT) and gallic acid.[29-34] The Total Phenolic Content (TPC) of the methanol and ethanol extracts of the leaves of *P. minus* were reported to be 31.38 mg and 21.06 mg Gallic Acid Equivalent (GAE) per g of the extract, respectively. The aqueous extract of leaves of *P. minus* showed a significant antioxidant property and high TPC (2800.6 mg/100 g GAE).[9] TPC of the aqueous, methanol, and ethanol extracts of the whole plant of *P. minus were* reported to be 55.5 mg, 122.1 mg and 207 mg GAE per g, respectively.[31,35,36] The total ascorbic acid content was found to be 0.54 mg/g FW (fresh weight) and the flavonoid content was found to be 2.46 mg/G DW (dry weight).[32]

Role in LDL oxidation

The inhibitory action of *P. minus* on LDL oxidation induced by collagen was reported by Saputri and Jantan, 2011.[36] The LDL oxidation activity of the various concentrations of methanol extract of *P. minus* was measured against copper mediated oxidation in isolated human LDL. It was further reported that this inhibition was dose dependent and an increase in the concentration of the extract showed higher inhibition.[36] This study confirms the correlation between high phenolic content and inhibition of LDL oxidation.

Table 1: Pharmacological properties of selected phytoconstituents of *P. minus*

Compound name	Chemical structure	Properties
Myricetin		An antioxidant, which reduce the incidence of prostate and pancreatic cancer,[10] nocturnal melatonin level[11] and also attenuate the LDL cholesterol level.[12]
Quercetin		Flavonoid, which has wide variety of the pharmacological properties including antiviral,[13] anti-asthmatic,[14] anti-cancer,[15] anti-inflammatory[16] and hypotensive properties.[17]
Decanal		An antioxidant with antimicrobial activity[18]
Dodecanal/Lauric aldehyde		An antioxidant with antimicrobial activity[19,20]
Undecanal		An antioxidant with antifertility activity[21]
Tetradecanal/Myristaldehyde		Natural bioactive lipid modulator and antioxidant[22,23]
Nonanal		An antioxidant with antidiarrhoeal activity[24]
β-caryophyllene		An antioxidant with antileishmanial activity[25,26]
Geraniol		Natural favoring agent with antioxidant and chemoprotective effects[27]
Oxalic acid		Natural mineral supplement with digestive enhancing activity[9]

Anti-platelet aggregation activity

The inhibitory potential of the methanol extract of *P. minus* on human platelet aggregation was reported by Saputri and Jantan, 2011.[36] The inhibitory potential was measured against various platelet aggregation inducers, namely arachidonic acid (AA), adenosine diphosphate (ADP) and collagen. It was reported that this extract was not much effective against AA and ADP induced platelet aggregation as the % of inhibition was 25.6 ± 0.8 and 24.0 ± 2.1 respectively.[36]

Gastro-protective activity

The aqueous extract of whole plant of *P. minus* was assessed for its ulcer prevention properties against an ethanol induction model.[37] The results showed significant inhibition of ulcerated areas in rats pretreated with *P. minus* and this effect was dose dependent and the extract (250 mg/kg) was equally effective as omeprazole (20 mg/kg).The gastro-protective effect of the bioactive fraction (EA: MeOH = 1:1) of *P. minus* leaves may be due to alteration inmucus production, hexoseamine levels and PGE2 synthesis in rodents.[38] Christapher *et al.,* also studied the antiulcer effect of methanol and aqueous extracts of leaves of *P. minus* in rodents using pyloric ligation model. The methanol extract of *P. minus* has significant gastro-protective (antiulcer) effect at the dose of 200 mg/kg BW whereas aqueous extracts of *P. minus* did not showed any gastro-protective in Wistar rats.[39]

Antimicrobial activity

The plant extracts were screened against various bacteria, viruses and fungi. The antibacterial activity was mainly done on *Helicobacter pylori* that that causes duodenal ulcer. It has been reported that petroleum ether, methanol and chloroform extract of *P. minus* produced high inhibition zones against *H. pylori*, however no inhibition zone was observed with aqueous extract.[40] Musa *et al.*, reported the antibacterial activity of *P. minus* against 10 isolated pathogenic fish bacteria.[41] Further, it has been

demonstrated that *P. minus* was slightly more effective than control in preventing microbial growth in refrigerated duck meatballs.[42] The antiviral activity of ethanol extract of *P. minus* was tested against *Herpes simplex* virus type-1(HSV-1) and *Vesicular stomatitis* virus (VSV), where it has shown strong antiviral activity against HSV-1and weak activity against VSV.[28]

Johnny *et al.,* studied the antifungal activities of the 15 selected Malaysian plants including *P. minus* against *Colletotrichum gloeosporioides* isolated from mango. Different extracting solvents were used and methanol extract of *P. minus* showed effective inhibition of radical growth as compared to chloroform and acetone.[43] Traditionally, *P. minus* is mixed with a little kerosene and applied as a paste on the skin to get rid of the fungal infections.[44]

Digestive enhancing activity

Vimala *et al.,* demonstrated the presence of oxalic acid in *P. minus* at 200 nm by High-Performance Liquid Chromatography (HPLC) method. Oxalic acid is a proven digestive aid and this rationalizes the traditional use of kesum as a digestive system stimulant.[9,45]

Cytotoxicity and genotoxicity

Many species of the genus *Polygonum viz. P. bistorta*, *P. avicular* and *P. multiflorum* have been reported to be cytotoxic against a variety of cancer cell lines.[46-48] *P. avicular* has been reported to be effective against cervical cancer cell line. Likewise *P. minus* also demonstrated cytotoxic effect against Hela cells (CD_{50}:0.1 mg/ml). However when tested against normal lung fibroblast cell line (Hs888Lu), both ethanol and aqueous extracts did not show any effective inhibition.[31] Wan-Ibrahim evaluated 20 Malaysian medicinal plants, which includes *P. minus* for genotoxic effects on human lymphocytes. Concentrations up to 2000 μg/mL were tested and at the highest concentration *P. minus* caused moderate DNA damage, *i.e.* the strand breaks was 31.4%.[49]

Immunomodulatory effect

George *et al.,* studied immunomodulatory property of aqueous extract of *P. minus* on Swiss albino mice using *in vivo* carbon clearance assay and reported the dose (200 and 400 mg/kg) dependent increase in phagocytic index. This study showed that the phagocytic index of 400 mg/kg body weight is comparable to standard drug Levamisole at 2.5 mg/kg of body weight.[50]

Antiproliferative activity

Ghazali *et al*., studied the antiproliferative effect of various solvent extracts of *P. minus* using *in vitro* MTT assay against HepG2, WRL68, HeLA, HCT 116, MCF-7 and Chang cell lines. In this study ethanol extract showed lowest IC_{50} of 32.25 ± 3.72 μg/ml towards HepG2 cell lines with minimum toxicity in WRL68 normal embryonic liver cells whereas methanol extract showed moderate antiproliferative activity against HCT 116 cell lines (IC_{50} = 56.23 ± 3.2 μg/ml).[51] This study also demonstrate direct correlation between antioxidant capacity and antiproliferative effect of a fraction of ethyl acetate extract.

Anti-inflammatory and analgesic activity

Christapher *et al.,* studied the anti-inflammatory and analgesic activity effect of methanol and aqueous extracts of leaves of *P. minus* in rodents. The study demonstrated that the aqueous extract possesses analgesic activity in formalin test, acetic acid-induced writhing, tail immersion test and anti-inflammatory activity in carrageenan induced inflammation whereas the methanolic extract showed analgesic activity but no anti-inflammatory activity.[39]

Cognitive enhancing effect

George *et al.,* studied the effect of water extract of *P. minus* on the learning and memory and reported that the extract has the activity against scopolamine induced cognition deficit in Barnes maze rat model.[52]

Clinical studies

Sexual performance and well-being

Jay *et al.,* conducted a clinical trial on *Eurycoma longifolia* (200 mg daily) in combination with water extract of *P. minus* (100 mg daily). Randomized, double blind, and placebo- controlled parallel design study was conducted on healthy male volunteers of age 45-65 years. The study showed that the combination is more effective than placebo in enhancing sexual performance in healthy volunteers.[53]

Clinical safety data

Toxicity to liver and kidney is the major concern of consumption of natural product. *P. minus* was found to be safe to liver and kidney even for prolonged use (100 mg daily/12 weeks). The basic laboratory values for liver and kidney including albumin, AST, ALT, alkaline phosphatase, bilirubin, Blood Urea Nitrogen (BUN), creatinine, and calculated Glomerular Filtration Rate (GFR) did not show any significant change in the study period.[53]

Toxicity data

Choudhary *et al*., studied the acute and sub-acute toxic effects of aqueous extract of *P. minus* on wistar rats for 28 days oral administration and reported that the no-observed adverse- effect level (NOAEL) is more than 1000 mg/kg of the body weight.[54] This study may suggests the safety of raw leaf consumption along with other food in the south east Asia region.

CONCLUSION

Plants containing antioxidant principles are nowadays, extensively screened for various pharmacological activities. *P. minus* is abundantly available in Southeast Asia and possesses high antioxidant activity. This plant has been long used in traditional medicine and Malay cuisine. The pharmacological activities rationalize the traditional claims about this plant. However the scientific data about this plant and its identified phytoconstituents are limited with respect to its pharmacological activities, pharmacokinetics and clinical trials. Exploration of pharmacological properties, bioactivity- guided isolation of active principles of *P. minus* and studies on their structure-activity relationships, mechanisms of actions, pharmacokinetics and toxicity are required for the development of *P. minus* as a successful therapeutic agent. Furthermore, clinical studies also can be conducted with standardized extracts or fractions.

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