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Review: *Parkia speciosa* as Valuable, Miracle of Nature

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Authors' contributions

This work was carried out in collaboration between both authors. Author NAZ did the literature search for certain part of the manuscript as introduction. Author FM did the literature search and write up of another part of the manuscript such as pharmacology activity. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Parkia speciosa (*P. speciosa*) is traditionally consumed medicinal plant for liver disease, oedema, kidney inflammation, diabetes and as anthelmintic. Recently, there are many reports on antioxidant, antidiabetic, anti-hypertensive, antitumor, antiulcer and antimicrobial potential of various parts of this plant. Furthermore, the potential effect of this plant on cardiovascular system has been reported. This present review aimed to collect the scattered information on pharmacological effect of this plant. A number of possible future studies on the potential of *P. speciosa* related to pharmaceutical product could be successfully conducted with the details provided.

Keywords: Medicinal plant; antimicrobial; antiulcer; antidiabetic; antihypertensive; antioxidant.

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1. INTRODUCTION

Based on ethnobotanical record of Malaysia, *Parkia speciosa* (*P. speciosa*) is categorized under traditional medicinal plant. *P. speciosa* can be found in rainforests, on sandy, loamy and podzolic soils. It also grows wildly in waterlogged locations, freshwater swamp forest and on riverbanks. *P. speciosa* trees can be found in Malaysia, Indonesia, Philippines and Thailand [1]. Seeds of *P. speciosa* can beeaten raw, cooked or roasted. The consumption of *P. speciosa* seeds as ulam is preferred bylocal people in Malaysia. Ulam is a plant which is consumed raw or after a short blanching. The seeds are consumed in traditional medicine as remedies for inflammation, oedema, liver failure, kidney disease, diabetes and to expel intestinal worms [2].

A considerable amount of literature has been published on the morphological characteristic of *P. speciosa*. Studies carried out by Matgomokol since 1995 proved that this plant has been regarded as valuable miracle of nature since ancient time. Morphological characteristic of this plant indicate that the tree usually grows up to 15-40 meters high with bipinnate leaves, pinnae 14-24 pairs, leaflets 31-38 pairs per pinna (42 pairs), oblong. The glands are above the base of petiole, between the junction of the 1-4 distal pair of pinnae, and the junction of the 1-3 distal pairs of leaflets. The flowers are head inflorescences. The tree yields twisted pods in which horizontal seeds with test a are found. The roots are tetrads of xylem alternating with the phloem. There is one layer of cuticle covered stem epidermis. The vascular bundles are 6-7 collateral bundles around the pith. Unicellular pore or 2-3 cells of pore are in the secondary xylem, and xylem rays are uniseriate. The stomata are of typical type found only in the lower epidermis of leaf. There are 2 layers of palisade mesophyll and 4-6 layers of spongy mesophyll [3].

2. CHEMICAL COMPOSITION OF *Parkia speciosa*

Phytochemical screening of *P. speciosa* revealed the presence pharmacologically active compound in the seeds. Almost all parts of the plant showed the presence of phenolic compound [4-5]. To date, only a few studies was done to detect the chemical compound in thepods. Sitosterol, stigmasterol, lupeol, campesterol, and squalene were revealed in the seeds using gas chromatography [6-7]. Lupeol was discovered to exhibit anticarcinogenic activity [8], antinociceptive, and anti-inflammatory properties [9]. *P. speciosa* seeds ethanolic extract exhibit presence of flavonoid such as quercetin, myricetin, luteolin, kaempferol and apigenin. However, none of this flavonoid was detected in the *P. speciosa* seeds methanolic extract using a reversed-phase high performance liquid chromatography [10], but it was noted to be present when screened using a colorimetric assay [11]. This indicates that the phytochemical detection method may influence the outcome of phytochemical revealed in the extract.

Besides, the seeds contain cyclic polysulfides, namely, hexathionine, tetrathiane, trithiolane, pentathiopane, pentathiocane, and tetrathiepane [12] which are responsible for its strong pungent smell and taste. Furthermore, alkaloids and saponins were also found in the plant. Chromatography analysis of the stink bean seeds had identified presence of fatty acids which were undecanoic, myristic, palmitic, oleic, linoleic, elaidic, stearic, stearoic, lauric, arachidonic, and linoleic acids [6]. In the seeds, formation of thiazolidine-4-carboxylic acid, a thioproline, was significantly increased after boiling when detected using gas chromatography-thermal energy analyzer [13]. Thiazolidine-4-carboxylic acid was proven as potential anticarcinogenic agent [14].

3. ANTIOXIDANT ACTIVITY OF *Parkia speciosa*

Antioxidant potential is strongly correlated with reduction of risk in various diseases such as hypertension [15], hyperbilirubinemia [16], stress-induced gastric lesion [17], hyperhomocysteinemia [18], cancer [19], atherosclerosis and diabetes [20]. Hence, much attention has been paid to investigate potential antioxidant source of plants, for future therapeutic use in humans. The frequently used assay to evaluate the antioxidant activity are the total phenolic content, reducing ferric ion antioxidant potential (FRAP) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical-scavenging assays and metal ion chelating assay. Phenolic compounds serve as important constituents of plants and may contribute directly to antioxidative action. Flavanoids had also showed promising antioxidant activity and their effects on human nutrition and health is significant. The

mechanisms of action of flavonoids are through the scavenging or chelating process [21-22]. The FRAP assay was performed to evaluate the antioxidant activity of a compound by measuring its redox property to reduce the ferric ion by single electron donation. As for the DPPH and ABTS assay, the discolouration of DPPH and ABTS solution serves as the indicator for measuring antioxidant potential. Reactive oxygen species contribute to production of oxidative stress and subsequent pathological conditions. Antioxidants reverse the formation of free radical and generate a stable form of radical due to the electron donation by antioxidant agent [23].

Ions ($Fe^{2+)}$ as it acts as most powerful pro-oxidant among the various species of metal ions [24]. Ferrozine can quantitatively form complex with Fe^{2+}. In the presence of chelating agents, the complex formation is disrupted, resulting in a decrease in the red colour of the complex. Measurement of colour reduction therefore allows the estimation of the metal chelating activity of the coexisting chelator. Lower absorbance indicates higher metal chelating activity.

Table 1 summarizes screening studies of the antioxidant properties of *P. speciosa*.The total phenolic content of *P. speciosa* pod extract ranges in between 7.2-25.55 mg GAE/gDW. The determination of TPC was carried out by Folin-Ciocalteu's method, referring to the calibration curve using gallic acid solution as a standard solution. Wonghirundecha et al. [25] had evaluated antioxidant capacity assay for two different types of *P. speciosa* pod which are Sataw-Dan and Sataw-Khao. It was found that the total phenolic and total flavonoid contents of Sataw-Dan pod extract were higher than those of Sataw-Khao pod extract. For antioxidant activity, both stink bean pod extracts had potent antioxidant activity by the radical-scavenging DPPH and ABTS methods, and the metal ion chelating assay. Aisha et al. [26] had conducted antioxidant assay using various extraction solvent. Aisha et al. [26] had concluded that extracts with high total phenols content demonstrated high antioxidant capacity, and vice versa. From Table 1 it can be concluded that methanolic extract of *P. speciosa* pod and seed showed highest phenolic content and antioxidant capacity for DPPH assay. As for the separate extraction of pod and seed, *P. speciosa* pod extract showed higher antioxidant capacity than seed alone. This goes to say *P. speciosa* pod which is regarded as waste material is a potential antioxidant source.

4. ANTIDIABETIC ACTIVITY OF *Parkia speciosa*

Based on the report by World Health Organization, the increase of diabetic patient upto 300 million or more by 2025 remains as an issue of concern [27]. Diabetes mellitus, hasled to severe disease such as retinopathy, neuropathy, nephropathy, heart attack, stroke and peripheral vascular disease [28]. Many plants have been screened for its hypoglycemic property. Plants lower blood glucose level by increasing insulin secretion by pancreas or by inhibiting the intestinal absorption of glucose. Jamaldin and Suhaila [29] revealed that only the chloroform extracts (l g/kg body weight) from both the empty pods and seeds of petai hada strong hypoglycemic activity on diabetic rats. The blood glucose level of alloxan diabetic rats was reduced by 36±6% to 288 mg/100 ml with the oral treatment of 0.4 g/kgBW' pericarp (pod), and by 57±6% to 236 mg/100 ml after the oral treatment with 0.4 g/kgBW petai seed. The onset of *P. speciosa* pharmacological effect is within less than an hour and lasted for at least 24 hours. The hypoglycemic activity of the pericarp (empty pod) andmesocarp (testa) are half of that from the seed which indicate that this waste product can be used as a raw material for the extraction of antidiabetic agent in near future. Another study carried out by Jin and Noor [30] showed that the highest aqueous extract dose of 400 mg/kgbody weight has a significant effect in reducing blood glucose level in normal rats used in the study. A mechanism of hypoglycemic effect was suggested by the synergistic action of p-sitosterol and stigmasterol. They acted directly on the lipoprotein part of the cell membranes, which cause more glucose uptake into the cells, hence resulted in the reduction of glucose concentration in blood. Another study conducted exhibited that pericarp chloroform extracts of *P. speciosa* significantly reduce blood glucose levels in the alloxan-induced diabetic rats [31]. Both this studies clearly demonstrated *P. speciosa* as a potential antidiabetic agent.

Table 1. Antioxidant activity of various part of *Parkia speciosa* plant part

Plant part	Extract	Total phenolic content (mg GAE/g DW)	Total flavonoid content	DPPH assay	ABTS assay (µmol TE/g DW)	Ion metal chelating (µmol EDTAE/ g DW)	FRAP assay	References
Pod	Ethanolic	Sataw-Dan, 84.24 Sataw-Khao-71.39	Sataw-Dan- 5.86 Sataw-Khao-5.38 mg CE/g DW	Sataw-Khao-1218.07 µmol TE/g DW Sataw Dan-920.32 µmol TE/g DW	Sataw-Khao-1610.67 ± 11.88 Sataw Dan-1261.14 ± 17.44	Sataw-Dan-5.86 Sataw-Khao-9.76	NC	Wonghirundecha et al. 2014 [45]
Pod	Methanolic	14.16 ± 0.02	5.28 ± 0.03 mg RE/g DW	IC_{50}= 74.37 µg/ml	NC	NC	NC	Balaji et al. 2015 [46]
Pod	Water	7.2 ± 0.32	NC	357 ± 27 TE/g DW	NC	NC	NC	Aisha et al. 2012 [5]
Pod	n-hexane	16.2 ±0.4	NC	1181 ± 99 TE/g DW	NC	NC	NC	Aisha et al. 2012 [5]
Pod	Water sub extract	255.5 ± 15.7	NC	105 ± 8.0 TE/g DW	NC	NC	NC	Aisha et al. 2012 [5]
Pod and seed	Aqueous	1557.6	NC	7418.3 TE/g DW	NC	NC	1617.3	Ayub Ali et al. 2011 [47]
Pod and seed	Methanolic	2464.3	NC	5936.9 TE/g DW	NC	NC	1898.0	Ayub Ali et al. 2011 [47]
Seed	Ethanol	51.9	20.3	NC	NC	NC	NC	Maisuthisakul et al. 2005 [48]
Seed	Methanol	120	NC	40 TE/g DW	NC	NC	NC	Tangkanakul et al. 2005 [49]
Seed	Aqueous	6.5	NC	67.62 TE/g DW	NC	NC	44.67	Reihani & Azhar 2012 [50]
Leaf	Ethanol	44.7	NC	89.26 TE/g DW	NC	NC	NC	Tangkanakul et al. 2005 [49]
Leaf	Aqueous	22.7	NC	57.4 TE/g DW	NC	NC	NC	Tangkanakul et al. 2005 [49]
Leaf	Aqueous	32.73	NC	22.7 TE/g DW	NC	NC	49.9	Tangkanakul et al. 2005 [49]

NC- Not conducted; CE- Catechin equivalent; RE- Rutin equivalent; DW- Dry weight

5. ANTI-HYPERTENSIVE ACTIVITY OF *Parkia speciosa*

Anti-hypertensive agent is very beneficial in reducing the risk of atherosclerosis, an artery clogging process which causes heart attacks and strokes. The analysis of antihypertensive activities was determined as angiotensin-converting-enzyme (ACE) inhibitory activities [32]. An angiotensin-converting-enzyme inhibitor (ACE inhibitor) is a standard drug used mainly for the treatment of hypertension and congestive heart failure. The mechanism of action for this group of drugs via reducing vascular resistance, as well as a decreasing blood volume, which leads to lowering of blood pressure and decrease of oxygen demand from the heart. These drugs inhibit the angiotensin-converting enzyme, an important element of the renin–angiotensin–aldosterone system.

As for the determination of ACE inhibitory activity, the active peptide from *P. speciosa* seed sample was fractionated according to the molecular mass and the biological activities (antioxidant and antihypertensive). The most active fraction was used for identification of bioactive peptide using mass spectrometry analysis. Results obtained discovered that the protein hydrolysates have the ability to inhibit the ACE in the range of 50.6–80.2%, whereas the non-hydrolysed samples did not show any ACE-inhibitory activities. This result suggested that biological active form of peptides with specific amino acid sequence were produced via enzymatic hydrolysis [33]. However, the parent chain protein could not contribute to ACE inhibition activity might be due to the long and bulky structure. Temperature also played an important role in improving the ACE-inhibitory activity. Results showed that sample produced at an incubation temperature of 25ºC gave a lower inhibitory activity ranging from 51.7% to 57.5%. Bioactive peptide produced at a higher temperature (50ºC), caused an increase in inhibitory potential. Similar trends of increment in inhibitory activity (80.2%) were observed in a sample that had been hydrolysed for 2 h. This is because thermal treatment increases enzyme-protein interactions due to the thermal-induced unfolding of the proteins that eventually enhance the enzymatic hydrolysis in releasing potent bioactive peptides [34]. Hydrolysis process within a 2 h timeframe seems to be the most desired period to produce peptides with a high potency of ACE-inhibitory activity.

5.1 Effects of *Parkia speciosa* on Cardiovascular System

Angiogenesis is the formation of new blood vessel from pre-existing vessels. Angiogenesis plays an important role in the growth and spread of cancer. Angiogenesis is a strictly controlled process in normal human body and regulated by a variety of endogenous angiogenic and angiostatic factors [35]. Angiogenesis proceeds by a series of steps that include endothelial cell activation and breakdown of the basement membrane, followed by the migration, proliferation, and tube formation of endothelial cells. All this process areregulated by numerous factors, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), tumor necrosis factor-α (TNF-α), and interleukin-8 (IL-8) [36]. Aisha et al. [5] reported that *P. speciosa* seed methanolic extract possessed antiangiogenic activity by inhibiting the expression of VEGF and neovascularization in rat aortic rings. Vascular endothelial growth factor (VEGF) is a factor that is involved in pathological angiogenesis or hypervascularization [37] which also plays a crucial role in atherosclerotic lesions [38]. Thus, it plays an essential role in protecting cardiovascular system and inhibiting the development of atherosclerosis.

5.2 Antitumor Effect of *Parkia speciosa*

Previous studies have reported that methanolic extract of *P. speciosa* seeds shows intensity on antimutagenic activity [4]. Factors thought to be influencing antimutagenic activity have been explored in several studies.

Lectin isolated from the *P. speciosa* seeds had shown mitogenic effect on human lymphocytes [39]. There is a large volume of published studies describing the role of lectins. Lectins are highly specific proteins that bind to carbohydrates and are found in many plants, animals, and bacteria which hold great potential for cancer therapy. Lectins can induce apoptosis through different pathways, some being more effective than others in specific celllines. This can be done by stimulating the production of caspases or other proteins involved in the molecular pathway. Such pathways can lead to down-regulation or up-regulation of certain genes involved in apoptotic suppression or induction, respectively. Certain miRNA act as inhibitors of ribosomal inactivating proteins (RIPs) and can be down-regulated through lectin activity thus allowing RIPs to function properly and inhibit neoplastic growth [40].

Table 2. Pharmacological activity of *Pakia speciosa*

Pharmacological activity	References	Study model
Antioxidant activity	4,26,28	*In vitro* FRAP and DPPH assay
Antidiabetic	30	Hypoglycaemic test on animal model
Antihypertensive	32	Angiotensin converting enzyme inhibitory activity
Antiangiogeneic	5	Effect on expression of vascular endothelial growth factor
Antitumor	4	Effect on ribosomal inactivating protein
Antiulcer	44	Ethanol-induced gastric mucosa animal model

6. ANTIMICROBIAL ACTIVITY OF *Parkia speciosa*

A large and growing body of literature has investigated antibacterial property of *P. speciosa* seed that influenced by hexathionine and trithiolane, two cyclic polysulfide compounds [41].

Recent evidence suggested that an aqueous suspension of *P. speciosa* seeds exhibit an ability to suppress the growth of *Aeromonas hydrophila, Staphylococcus aureus, Streptococcus agalactiae, Streptococcus anginosus*, and *Vibrio parahaemolyticus* [42].

A previous study also shown that the ability of the seed extract in methanol to inhibit *H. pylori* growth, while the ethyl acetate extract was effective against *Escherichia coli* [43].

6.1 Antiulcer Effect of *Parkia speciosa*

Al Batran et al. [44] investigated the differential impact of gastroprotective effects of *P. speciosa* against ethanol-induced gastric mucosa in Sprague Dawley rats. The results obtained from the preliminary studies shown gastro protective effects in extract treated rats with upregulation of heat-shock protein 70 and downregulation of pro-apoptotic protein BAX, having significant increases in antioxidant defence enzymes glutathione (GSH) and superoxide dismutase (SOD) [44].

6.2 Toxicity of *Parkia speciosa*

There is lack of toxicity study carried out on *P. speciosa*. To date, there is no single study conducted on the *in vivo* toxicity study of *P. speciosa*. To the best of our knowledge, only Aisha and her team [5] had performed cytotoxicity study of the plant using human umbilical vein endothelial cells (HUVEC). This study demonstrated that the methanolic extract of the fresh pods (100 g/mL) did not exhibit any significant cytotoxic effect on the cell lines. Local people convey information that consumption of *P. speciosa* seeds (up to 30 seeds or equivalent to two long pods) almost every day does not cause any toxic effect [17].

7. CONCLUSION

It is interesting to note that *P. speciosa* has been proven to help promoting health. The present review provide information on pharmacological effect of *P. speciosa* for further exploration on pharmacological activity of this plant.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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