Pharmacogn J. 2019; 11(2): 429-438
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com | www.journalonweb.com/pj | www.phcog.net

Review Article

Syzygium polyanthum (Wight) Walp: A Potential Phytomedicine

Azlini Ismail[1*], Wan Amir Nizam Wan Ahmad[2]

ABSTRACT
Ethnomedicinal plant is one of the important sources for drug discovery. *Syzygium polyanthum* (Wight) Walp is one of the ethnomedicinal plants that is currently gaining attention for its various pharmacological potentials. This review evaluates its traditional uses, chemical profiles, toxicological aspects, nutritional values, as well as its pharmacological properties. From our literature search in Science Direct, Scopus, and Google Scholar databases, it was found that *S. polyanthum* has valuable therapeutic potentials including antidiabetic, antihypertensive, antimicrobial, antioxidant, anticancer, antitumor, antidiarrheal, acetylcholinesterase inhibitory, and dental plaque inhibition properties. However, few research areas, especially its toxicological profiles, mechanism of actions, as well as identification of its bioactive compound, require more in-depth studies.
Keywords: Chemical, Nutritional, Pharmacological, *Syzygium polyanthum,* Toxicological

Azlini Ismail[1], Wan Amir Nizam Wan Ahmad[2]

[1]Department of Fundamental Dental and Medical Sciences, Kulliyyah of Dentistry, International Islamic University Malaysia, Kuantan, Pahang, MALAYSIA. [2]Biomedicine Program, School of Health Sciences, Health Campus, Universiti Sains Malaysia, Kelantan, MALAYSIA.

Correspondence

Dr. Azlini Ismail

Department of Fundamental Dental and Medical Sciences, Kulliyyah of Dentistry, International Islamic University Malaysia, Kuantan Campus, Indera Mahkota, 25200 Kuantan, Pahang, MALAYSIA.

E-mail: dr_azlini@iium.edu.my

Phone no: +6014-5010081

History
- Submission Date: 04-09-2018;
- Review completed: 27-11-2018;
- Accepted Date: 19-12-2018

DOI : 10.5530/pj.2019.11.67

Article Available online
http://www.phcogj.com/v11/i2

COMMON NAMES AND PLANT TAXONOMY

Syzygium polyanthum (Wight) Walp is well known among Malaysians as "*salam*", "*serai kayu*", or "*samak kelat*", whereas in Indonesia, the plant is commonly recognized as "*ubar serai*", "*meselengan*", "*manting*", Indonesia laurel, or Indonesian bay leaf.[1] The scientific name *S. polyanthum* was usually used in synonymous with *Eugenia polyantha*.[2] According to the Archive of "Catalogue of Life",[3] this plant belongs to *Plantae* kingdom, *Magnoliophyta* phylum, *Magnoliopsida* class, *Myrtales* order, *Myrtaceae* family, *Syzygium* genus, and *S. polyanthum* (Wight) Walp species.

TRADITIONAL USES

Leaves, fruits, and barks of *S. polyanthum* are traditionally used for various medicinal and nonmedicinal purposes. The roots and the fruits are consumed to reverse the hangover effect with alcohol, whereas the leaves are traditionally consumed for treating various illnesses such as diabetes mellitus, hypertension, gastritis, ulcers, diarrhea, skin diseases, as well as infections.[4,5] People in Riau, Sumatra, Indonesia, has reported to add *S. polyanthum* leaves as one of the ingredients in their soups, and it was consumed for treating hypertension.[6] Another alternative way of preparing remedies from *S. polyanthum* leaves is by preparing leaf decoction, usually by boiling few pieces of *S. polyanthum* leaves in plain water until they become concentrated.

Apart from its medicinal use, the young shoots of *S. polyanthum* are consumed in its raw form as salad, or locally known among Malay as "ulam" and, sometimes, the mature leaves are used to enhance flavor in various local Malay dishes. Until now, it has been recognized as one of the well-known culinary additives in Indonesia.[7] Besides the leaves, the ripe or unripe fruits of this plant are edible, and the taste is usually described as "sweet-sour."[8] The fruits can be harvested during fruiting season between April and June in the northeastern part of Thailand.[8] Other than the leaves and fruits, barks of *S. polyanthum* can be used to dye nets in order to enhance their strength.

PLANT DISTRIBUTION

S. polyanthum is distributed in South-East Asian countries, including Malaysia,[9] Thailand,[8] Indonesia,[4,5] and Singapore.[10] The plant can be found on hilly areas and in the forests. However, in certain rural areas, the plant is planted in the field and garden, near to the residential area.

PLANT MORPHOLOGY

The plant's height may reach up to 25 m. The root is straight and the trunk is rounded with lush branch [Figure 1a]. The leaf shape is elliptical with length ranging from 5 to 15 cm and width ranging from 3 to 8 cm [Figure 1b]. The base and the end of the leaf are pointy. The upper part of the leaf is dark green with lighter green on the lower part. The leaf petiole is about 0.5–1 cm. The white-colored flowers are small with fragrance [Figure 1c]. The fruit is round with a diameter of 8–9 mm. The unripe fruit is green in color [Figure 1d], and the ripe fruit [Figure 1e] is dark red in color. The brown-colored seed is round with a diameter of 1 mm.

Cite this article: Ismail A, Wan Ahmad WAN. *Syzygium polyanthum* (Wight) Walp: A potential phytomedicine. Pharmacog J. 2019;11(2):429-38.

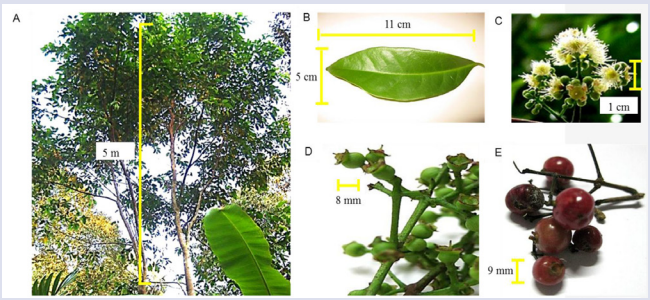

Figure 1: *S. polyanthum* (Wight.) Walp. (a) whole plant, (b) leaf, (c) flowers, (d) unripe fruits, and (e) ripe fruits

CHEMICAL PROFILES

Several studies have revealed the phytochemical components of *S. polyanthum*, but majority of these studies focused on the leaf part of the plant. A preliminary phytochemical screening study conducted by Kusuma *et al.*[11] revealed that the leaves and unripe fruits of *S. polyanthum* contain carbohydrates, tannins, alkaloids, steroids, triterpenoids, and flavonoids, while the ripe fruits contain saponins, carbohydrates, tannins, alkaloids, triterpenoids, and flavonoids. In fact, several studies have quantified the total phenolics and total flavonoids in various types of extracts from barks and leaves of *S. polyanthum*. Lelono *et al.*[4] found that methanolic–water extract from *S. polyanthum* bark had the greatest total phenolic content (TPC) in comparison with both methanolic and water extracts, when measured as catechin and gallic acid equivalents. On the contrary, methanolic extract from *S. polyanthum* bark exhibited the highest total flavonoid content (TFC), when measured as rutin and flavonol equivalents in comparison with methanolic–water and water extracts. When the TPC of *S. polyanthum* leaves was compared with that of *S. polyanthum* barks from previous studies, the TPC of the former[12,13] was found lower than the latter.[4]

Caffeic acid, gallic acid,[13] and 4-allyl-1,2-dihydroxybenzene (hydroxychavicol)[2] were the three phenolic compounds previously identified in *S. polyanthum* leaves. Instrumental analyses using high-performance liquid chromatography and liquid chromatography mass spectrometry showed the presence of both caffeic acid and gallic acid in the methanolic extract of *S. polyanthum* leaves;[13] meanwhile, hydroxychavicol was isolated via bioassay-guided fractionation of ethyl acetate layer from the hydroalcoholic extract of *S. polyanthum* leaves for lipase inhibitory action.[2] Three hydroxyl benzoic acid derivatives (1) 3,4,5-trihydroxy benzoic acid (gallic acid), (2) 4-hydroxy-3-methoxy benzoic acid, and (3) 4-hydroxy-3,5-dimethoxy benzoic acid were identified from fractionation of the methanol–water extract of *S. polyanthum* leaves.[7] Compounds 1–3 have basic phenolic structure with benzoic acid moiety; however, only compounds 2–3 have alpha-glucosidase inhibitory activity, a key enzyme for type 2 diabetes.

Other than that, squalene, a triterpenoid, was detected by using gas chromatography-mass spectrometry analysis on methanol[14,15] and n-hexane[15] extracts of *S. polyanthum* leaves. Hamad *et al.*[15] have also identified n-hentriacontane, a long chain alkane hydrocarbon, a major volatile compound in n-hexane extract of *S. polyanthum* leaves. Another major compound found in ethanolic extract of *S. polyanthum* leaves is phytol, an acyclic diterpene alcohol.[16] A recent study by Rahim *et al.*[17] also detected the presence of these two compounds (squalene and phytol) in various types of *S. polyanthum* leaf extracts (n-hexane, ethyl acetate, and methanol). The major composition of these three extracts is sesquiterpenes, but other components such as other types of terpenes (monoterpenes, diterpenes, and triterpenes), phenolics, aldehydes, hydrocarbons, and fatty acids were also identified. The same study also highlighted the presence of some bioactive compounds with varying pharmacological activities such as hentriacontane (anti-inflammatory), palmitic acid (anti-inflammatory and antibacterial), nerolidol (anti-inflammatory, antinociceptive, antifungal, and antiulcer), linalool (antibacterial, anti-inflammatory, antidiabetic, and hepatoprotective), α-pinene (anti-inflammatory, antibacterial, and hypotensive), α-tocopherol and β-tocopherol (antioxidant), as well as the two major compounds, squalene (antioxidant, antitumor, and chemopreventive effect), and phytol (anti-inflammatory, anticancer, antimicrobial, antioxidant, and antinociceptive).[17]

A latest isolation study by Setyawati *et al.*[18] to find skin-whitening compound managed to isolate four compounds from methanolic extract of *S. polyanthum* leaves; the first compound was identified as 1-(2,3,5-trihydroxy-4-methylphenyl)hexane-1-one; the second compound was identified as 1-(2,3,5-trihydroxy methylphenyl)octane-1-one; and the third compound was identified as (4E)-1-(2,3,5-trihydroxy-4-methylphenyl)decan-1-one. These three compounds are novel, while the fourth isolated compound was 1-(2,3,5-trihydroxy-4-methylphenyl)decan-1-one, a known compound. Compounds 1–4 significantly decreased melanin biosynthesis and were able to inhibit tyrosinase, two important properties for skin whitening.

Other than analysis on the crude extract, there are also ongoing researches on the identification of volatile compounds from the essential oil of *S. polyanthum* leaves. Hydrodistillation of *S. polyanthum* dried leaves produced essential oil with major composition of α-pinene, octanal, and α-caryophyllene.[19] Another recent study had identified few major constituents in the essential oil of *S. polyanthum* leaves such as cis-4-decanal, 1-decyl aldehyde, and capryl aldehyde.[20] In addition, few bioactive compounds from terpene group such as α-humulene, α-copaene, α-selinene, α-zingiberene, β-caryophyllene, and caryophyllene oxide were among the identified compounds in the essential oil of this plant. Phytochemical components in the extract and essential oil of *S. polyanthum* leaves are shown in Table 1.

NUTRITIONAL CONTENT

The nutritional aspect of *S. polyanthum* is also an important aspect to be studied as the leaves are edible and regularly being incorporated in local Malay dishes. Karim *et al.*[21] had determined the content of Vitamins (B2, B3, and C) in *S. polyanthum* leaves. It was found that every 100 mg of dry powder of *S. polyanthum* leaves contains 1.24 mg riboflavin (Vitamin B2), 0.58 mg niacin (Vitamin B3), and 0.40 mg of ascorbic acid (Vitamin C), with the total vitamin content of 2.22 mg.[21] The human body requires vitamins in trace amount in order to maintain normal physiological functions; therefore, deficiencies of vitamin may lead to various detrimental consequences such as scurvy due to the lack of Vitamin C and pellagra for niacin deficiency.

TOXICOLOGICAL ASPECTS

Investigation on the toxicological aspect is another integral issue in evaluating the potential of any phytomedicine. Kusuma *et al.*[11] previously conducted a cytotoxicity test using brine shrimp (*Artemia salina) larvae. The test usually serves* as a preliminary assessment assay in evaluating the potential toxicity of a plant extract prior to toxicity evaluation in higher animals. Kusuma *et al.*[11] reported that the ethanol extract of *S. polyanthum* leaves has LC_{50} (lethal concentration that causes 50% morbidity in total brine shrimp larvae) of more than 1000 μg/ml. An extract was considered as practically nontoxic if the LC_{50} in brine shrimp lethality test was more than 500 μg/ml.[22] Therefore, the leaf extract was considered as non-

Table 1: Phytochemical components in the essential oil and extract of *Syzygium polyanthum* leaves

n	Types of sample	Compounds	Instrumentation	References
1	Essential oil from hydrodistillation of leaves	Aldehyde	GCMS	19
		• Octanal		
		Terpenes		
		• α-pinene		
		• α-caryophyllene		
		Aldehyde	GCMS	20
		• Cis-4-decanal		
		• 1-decyl aldehyde		
		• Capryl aldehyde		
		Terpenes		
		• α-humulene (α-caryophyllene)		
		• α-copaene		
		• α-selinene		
		• α-zingiberene		
		• β- caryophyllene		
		• Caryophyllene oxide		
2	Leaf extract	Phenolics	HPLC and LCMS	13
		• Caffeic acid		
		• Gallic acid		
		Phenolics	NMR and ESI-MS	2
		• 4-allyl-1,2-dihydroxybenzene (hydroxychavicol)		
		Phenolics	Preparative HPLC	7
		• 3,4,5-trihydroxy benzoic acid (gallic acid)		
		• 4-hydroxy-3-methoxy benzoic acid		
		• 4-hydroxy-3,5-dimethoxy benzoic acid		
		Terpenes	GCMS	14
		• Squalene		
		Alkane	GCMS	15,17
		• Hentriacontane		
		Diterpene alcohol	GCMS	16
		• Phytol		
		Acyclic alkene	GCMS	17
		• 1H cyclopropa[a]naphthalene		
		Aldehydes		
		• n-heptanal		
		• Octanal		
		Alkanes		
		• Heptane		
		• Eicosane		
		• n-pentacosane		
		Bicyclic aromatic hydrocarbon		
		• Selina-4,11-diene (naphthalene)		
		Diol		
		• Propylene glycol		
		Fatty acid		
		• Palmitic acid		
		• Stearic acid		

Continue...

Table 1: Cont'd.

	• Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl) (palmitin) Fatty acid ester • Methyl oleate • Methyl palmitate Lignan • 9,12,15-Octadecatrien-1-ol Methylated phenols (tocopherols) • α-tocopherol • β-tocopherol • γ-tocopherol Oxygenated terpenes • Caryophyllene oxide Peroxides • Humulene epoxide II Phenolics • Pyrogallol Steroidal • β-sitosterol Saturated terpenoid alkane • Pentadecane, 2,6,10,14-tetramethyl- Terpenes • Azulene • Farnesol • α-copaene • δ-cadinene • α-cubebene • α-pinene • α-panasinsene • β-panasinsene • α-humulene • β-selinene • 2-isopropenyl-4a,8-dimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (α-selinene) • Linalool • Neophytadiene • Nerolidol • Valencene Unclassified • 2-cyclohexen-3-ol-1-one, 2-[1-iminoethyl]- • 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one		
	Unclassified • 1-(2,3,5-trihydroxy-4-methylphenyl)hexane-1-one • 1-(2,3,5-trihydroxy methylphenyl)octane-1-one • (4E)-1-(2,3,5-trihydroxy-4-methylphenyl)decan-1-one • 1-(2,3,5-trihydroxy-4-methylphenyl)decan-1-one	NMR and MALDI-TOF–MS	18

GCMS=Gas chromatography mass spectrometry, HPLC=High-performance liquid chromatography, MALDI-TOF-MS=Matrix assisted laser desorption/ionization-time-of-flight-mass spectrometry, NMR=Nuclear magnetic resonance, ESI-MS=Electron spray ionization-mass spectrometry

toxic. The test also indicated the safety of fruits because the study also revealed the LC_{50} of more than 1000 µg/ml for unripe fruits and 747.45 µg/ml for ripe fruits.[11]

Perumal *et al.*[12] tested the cytotoxicity of *S. polyanthum* leaf extracts on normal Vero cell lines which were derived from the kidney of African green monkeys using 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay. The colorimetric MTT assay determines the viability of cells reflected by the action of succinate dehydrogenase enzyme on yellow tetrazolium dye, the MTT. The formation of insoluble purple formazan salts indicates the number of viable cells present. This study showed that the inhibitory concentration of *S. polyanthum* leaf extract that caused 50% (IC_{50}) of cytotoxicity of Vero cell lines was 53.50 µg/ml.[12] Therefore, the extract was noncytotoxic because it has IC_{50} value of more than 20 µg/ml.[23] Another MTT assay of methanolic extract of *S. polyanthum* leaf at a concentration of 25–200 µg/mL has also been tested on B16 melanoma cells for 72 h.[18] Even at the highest concentration of 200 µg/mL, the methanolic extract of *S. polyanthum* leaves showed high cell viability.

PHARMACOLOGICAL PROPERTIES

The pharmacological properties of the ripe and unripe fruits, the barks, and mostly the leaves of *S. polyanthum* were widely studied. Currently, *S. polyanthum* leaves were reported to have antioxidant, antidiabetic, antimicrobial, antihypertensive, antitumor, antidiarrheal, acetylcholinesterase inhibitory, and lipase inhibitory activities. A summary of these pharmacological properties is outlined in Table 2.

Antioxidant

Plant is one of the rich sources of antioxidant; it can scavenge free radicals, which is known to contribute in the development of cancer and atherosclerosis by inducing oxidative damage to lipids, proteins, and nucleic acids. Enormous antioxidant studies have been conducted on various parts of *S. polyanthum* including the leaves, the ripe and unripe fruits, as well as the bark. The most commonly employed method was using the diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay,[27-29] followed by other methods such as ferric-reducing assay (FRAP),[10,26,27] beta carotene bleaching assay,[7,12,25] and 2,2-azino-bis(3-ethylbenzothiozoline-6-sulphonic acid) cation radical scavenging (ABTS) assay.[27]

Majority of antioxidant studies on this plant have focused on the leaf parts which were extracted by using various solvents from various ranges of polarity. Aqueous extract of *S. polyanthum* leaves exhibited relatively high DPPH radical scavenging activity as compared to the other 24 tested plant extracts.[10] Ethanolic extract of *S. polyanthum* leaves at 50 and 100 ppm exhibited good DPPH radical scavenging activity of 82.00% and 83.00%, respectively, as compared to 95.00% radical scavenging activity by ascorbic acid as the reference compound.[11]Few other studies reported almost similar values of EC_{50}, for instance, 20.90 ± 0.26,[12] 24.09,[13] and 21.24 ± 1.14 µg/ml[24] for methanolic extracts of *S. polyanthum* leaves.

In a few more comprehensive studies that compared the level of antioxidant activity of leaf extracts, methanolic extract has exhibited the strongest DPPH scavenging activity, followed by water, petroleum ether, and chloroform extracts.[27] Another study has similarly shown that the methanolic extract had the highest antioxidant activity, followed by ethyl acetate, dichloromethane, and hexane extracts.[28] A latest study also supported this whereby the authors found that methanolic extract has highest antioxidant activities compared to ethyl acetate and hexane extracts.[29]

Other than DPPH assay, the FRAP assay is another common assay to demonstrate the antioxidant activity of an extract/compound. Wong *et al.*[10] had shown that aqueous extract of *S. polyanthum* leaves exhibited relatively strong ferric ion-reducing activity as compared to the other 24 tested plant extracts. Later studies compared the ferric ion-reducing activity of different types of *S. polyanthum* leaf extracts. Ethanolic (50%) extract of *S. polyanthum* leaves was found to have higher reducing capability compared to water and hexane extract.[26] In agreement with that, another study using similar assay showed that methanolic extract of *S. polyanthum* leaves had the greatest reducing power followed by water, chloroform, and petroleum ether extract.[27]

The less common antioxidant studies tested for *S. polyanthum* leaf extract were using β-carotene/linoleic acid bleaching and ABTS assay. Previous researches using β-carotene/linoleic acid bleaching assay have shown that the methanolic[12] and water[25] extracts of *S. polyanthum* leaves exhibited almost similar antioxidant activity as compared to the reference synthetic antioxidant compound, the butylated hydroxytoluene.[12,25] Similarly, ABTS assay proved that methanolic extract of *S. polyanthum* leaves also has the highest antioxidant capacity, followed by chloroform extract, water extract, and petroleum ether extract.[27] Altogether, the findings of DPPH, FRAP, and ABTS assays indicated that the antioxidant compounds of *S. polyanthum* leaves were more concentrated in polar solvents.

Besides leaves, the ripe and unripe fruits of *S. polyanthum* were also tested and both showed very good antioxidant activity compared to ascorbic acid as the reference compound.[11] The ripe and unripe fruits of *S. polyanthum* at 100 ppm possess 90.00% and 88.00% DPPH radical scavenging activity as compared to 95.00% DPPH radical scavenging activity of ascorbic acid.[11]

Not only fruits, but also the bark of this plant was also tested for antioxidant activity. The methanolic, methanolic–water, and the water extracts of *S. polyanthum* bark exhibited DPPH scavenging activity with EC_{50} value of 0.34 ± 0.16, 0.18 ± 0.04, and 0.35 ± 0.11 mg/ml, respectively.[4] Meanwhile, by using hydrogen peroxide scavenging method, the methanolic, methanolic-water, and the water extracts of *S. polyanthum* bark exhibited hydrogen peroxide radical scavenging activity of 28.00 ± 0.54%, 15.00 ± 4.22%, and 74.00 ± 0.53%, respectively.[4] In the meantime, by using β-carotene bleaching assay, the methanolic, methanolic-water, and the water extracts of *S. polyanthum* bark exhibited protection from β-carotene bleaching with percentages of 76.43 ± 0.91%, 85.72 ± 0.57%, and 74.33 ± 0.53%, respectively.[4]

Antidiabetic

Diabetes mellitus is one of the most prevailing metabolic disorders with complications such as nephropathy, retinopathy, impotency, stroke, and heart attack.[42] Patients with diabetes usually suffer from hyperglycemic condition as a consequence of insufficient insulin secretion or excessive glucagon secretion and even insulin resistance.[1,7] In a preliminary survey conducted among diabetic outpatients attending Health Community Centre Sering in Medan, Indonesia, it was noted that the most commonly used herb as a traditional remedy for diabetes mellitus was *S. polyanthum* (57.1%).[1]

An intraperitoneal glucose tolerance test on normal Sprague Dawley (SD) rats has shown that petroleum ether, chloroform and methanolic extracts of S. polyanthum leaves did not significantly alter the normal rat's glucose tolerance.[1] In an acute hypoglycemic test on nondiabetic rats, administration of methanolic extract of *S. polyanthum* leaves at dosages from 125 mg/kg to 1 g/kg did not significantly reduce blood glucose level of nondiabetic rats.[14] However, in both alloxan-[7,30] and streptozotocin-[1] induced diabetic rats, *S. polyanthum* leaf extract was shown to significantly lower blood glucose levels of these two diabetic rat models. Lelono[7] had shown that 21-day daily treatment with aqueous extract of *S. polyanthum* leaves at doses of 100, 200, and 300 mg/kg significantly reduced the blood glucose levels of alloxan-induced diabetic rats. In fact,

Table 2: Summary of pharmacological activities of *Syzygium polyanthum* leaves, stem, fruits, and barks

n	Biological activity	Part of plant used	Solvents	Findings	References
1	Antioxidant	Leaf	Water	**DPPH test:** Water extract of leaves has relatively high antioxidant activity reflected by the high scavenging activity as compared to the other 24 tested edible plants **Ferric ion test:** Water extract of leaves has relatively strong ferric ion-reducing activity as compared to the other 24 tested plants	10
			Ethanol	**DPPH test**: 50 and 100 ppm of ethanolic extract of leaves exhibited 82.00% and 83.00% of radical scavenging activity as compared to 95.00% radical scavenging activity by ascorbic acid as a reference compound	11
			Methanol	**DPPH test:** Methanolic extract of leaves exhibited antioxidant activity with the EC_{50} value of 20.9±0.26 µg/ml **Reducing power:** Methanolic extract of leaves exhibited reducing power with EC_{50} of 77.55±0.76 µg/ml **β-carotene/linoleic acid bleaching assay:** Methanolic extract of leaves exhibited greatest inhibition of rates (91.43±2.52%) almost similar to reference synthetic antioxidant compound, the BHT with rates of 92.69±3.15%	12
			Methanol	**DPPH radical scavenging test**: Methanolic extract of leaves have mild antioxidant activity with IC_{50} value of 24.09 µg/ml as compared to standard quercetin with IC_{50} value of 90.85 µg/ml	13
			Methanol and ethyl acetate	**DPPH radical scavenging test:** Methanolic extract of leaves has antioxidant activity with IC_{50} value of 21.24±1.14 µg/ml, while the ethyl acetate extract has lower IC_{50} value of 13.70±0.24 µg/ml	24
			Water	**β-carotene/linoleic acid bleaching assay:** Water extract of leaves exhibited almost similar antioxidant activity as compared to the reference synthetic antioxidant compound, the BHT	25
			Ethanol (50%), water, and hexane	**FRAP assay:** Ethanolic (50%) extract of leaves has higher reducing capability compared to water and hexane extracts	26
			Methanol, water, petroleum ether, and chloroform	**DPPH radical scavenging test:** Methanolic extract of leaves has the highest antioxidant activity in methanol extract, followed by water, petroleum ether, and chloroform extracts **FRAP assay:** Methanolic extract of leaves had the greatest reducing power followed by water, chloroform, and petroleum ether extracts **ABTS assay:** Methanolic extract of leaves also has the highest antioxidant capacity, followed by chloroform, water, and petroleum ether extracts	27
			Methanol, ethyl acetate, dichloromethane, and hexane	**DPPH radical scavenging test:** Highest antioxidant activity was observed in methanolic extract of leaves, followed by ethyl acetate, dichloromethane, and hexane extracts	28
			Methanol, ethyl acetate, and hexane	**DPPH radical scavenging test:** Methanolic extract of leaves has the highest antioxidant activities compared to ethyl acetate and then hexane extract	29
		Fruits (ripe)	Ethanol	**DPPH test:** Ethanolic extract of ripe fruits at 50 and 100 ppm possesses 88.00% and 90.00% radical scavenging activity, respectively, as compared to 95% radical scavenging activity by a reference compound, ascorbic acid	11
		Fruits (unripe)	Ethanol	**DPPH test**: Unripe fruit ethanol extract at 50 and 100 ppm possessed 84.00% and 88.00% radical scavenging activity, as compared to 95.00% radical scavenging activity by a reference compound, the ascorbic acid	11
		Bark	Methanol, methanol-water and water	DPPH test: Bark methanol, methanol-water, and water extract exhibited DPPH scavenging activity with EC_{50} value of 0.34±0.16 mg/ml, 0.18±0.04 mg/ml, and 0.35±0.11 mg/ml Hydrogen peroxide radical scavenging activity: Bark methanol, methanolic–water, and water extracts exhibited activity of 28.00±0.54%, 15.00±4.22%, and 74.00±0.53%, respectively β-carotene bleaching assay: Bark methanol, methanol-water, and water extracts exhibited protection from β-carotene bleaching with percentages of 76.43±0.91%, 85.72±0.57%, and 74.33±0.53%.	4

Continued...

Table 2: Cont'd.

2	Anti-diabetic	Leaf	Methanol, methanol-water and water	Leaves water extract (100, 200 and 300 mg/kg) significantly reduced blood glucose levels of alloxan-induced diabetic rats after 21 days of treatment Leaves methanol-water extract exhibited the best inhibition of alpha-glucosidase activity compared to methanol and water extracts Two active compounds (4-hydroxy-3-methoxy-benzoic acid and 4-hydroxy-3, 5-dimethoxy-benzoic acid) obtained from bioassay-guided fractionation of the methanolic–water extract of the leaves have inhibitory activity against alpha-glucosidase *in vitro*	7
			Petroleum ether, chloroform, methanol and water	Single-dose administration of methanolic extracts of leaves (1.00 g/kg) significantly reduced the blood glucose level in streptozotocin-induced diabetic rats after 7 h of administration	1
			Methanol	Repeated dose (twice daily) administration of the leaves methanol extract at 250, 500 and 1000 mg/kg has significantly reduced the fasting blood glucose levels of streptozocin-induced diabetic rats after 6 days Leaves methanol extract inhibited glucose absorption from the intestine and significantly increased glucose uptake in muscle tissue	14
			Water	200 mg/kg of water leaves extract significantly reduced blood glucose level of alloxan-induced diabetic rats as early as 7 days of treatment	30
3	Antihypertensive	Leaf	Methanol and water	Water (20–100 mg/kg) and methanol (40–100 mg/kg) leaves extracts significantly reduced blood pressure of anesthetized normotensive WKY rats and SHR Autonomic nervous system receptors with the mediation of nitric oxide was suggested to be partly involved in causing the reduction in blood pressure	9
				Water and methanol leaves extract at concentrations ranging from 0.1 to 10 mg/ml caused significant vasorelaxation on the isolated thoracic aorta rings from WKY and SHR Autonomic nervous system receptors with the mediation of nitric oxide was suggested to be partly involved in causing the vasorelaxation effect	31
				Single dose of leaves water (2.50 and 3.00 g/kg) and methanol (2.00, 2.50 and 3.00 g/kg) extracts caused significant reduction in blood pressure of SHR rats, but not in WKY rats when acutely administered Leaves methanol extract (2.50 g/kg) caused significant reduction in blood pressure of SHR rats after 2-week of administration, but the significant antihypertensive effect was observed after 3-week of administration for leaves water extract (2.50 g/kg)	32
		Leaf	Ethanol	Leaves ethanol extract at a concentration 100 ppm showed inhibition of ACE by 53.37±0.95% as compared to standard antihypertensive drug captopril by 88.17±2.89%	33
4	Anti-microbial (antibacterial and antifungal)	Leaf and stem	Ethanol	Leaves and stem ethanol extracts possessed anti-microbial activity against *S. aureus*	34
		Leaf	Ethanol	Leaves ethanol extract had antibacterial activity against *S. dysenteriae*, a Gram-negative *bacilli*, with MBC values in the range of 10%–20% w/v	35
		Leaf	Essential oil	Leaves essential oil strongly inhibited *B. subtilis* growth, but it did not inhibit *E. coli*	20
		Fruit (ripe)	Ethanol	Ripened fruit ethanol extract showed good activity on *S. typhi,* a Gram-negative, rod-shaped bacterium, in relative to erythromycin as standard	11
		Leaf	Ethanol	Ethanol leaves extract exhibited anti-fungal activities against *A. alternata* and *C. capsicii*	36
		Leaf and fruit (ripe and unripe)	Ethanol	Leaves, ripe and unripe fruit ethanol extracts at 40, 60 and 80 µg/disk had low-to-moderate activity against *T. mentagrophytes* Good activity of the ripe and unripe fruit ethanol extracts (40, 60, and 80 µg/disc) was observed against *C. albicans*	11
5	Antidiarrheal	Leaf	Ethanol (70%)	Leaves ethanol extract at 10, 20 and 30% have demonstrated anti-diarrheal activity when induced by castor oil. This was shown by significant inhibition of the charcoal transit (marker) as compared to negative control The activity of the highest concentration of extract at 30% were similar to that of reference drug, loperamide hydrochloride at a dose of 10 ml/kg	37

Continued...

Table 2: Cont'd.

				Leaves ethanol extract have antibacterial activity against *S. dysenteriae* Leaves ethanol extract contains potassium with concentration of 2054 ppm (1.03% w/w) which is beneficial to provide for the associated hypokalemic condition due to dysentery	35
6	Anti-cancer	Leaf	Flavonoid fraction	Active flavonoid fraction from the leaves possessed anti-proliferative activity by inducing cell cycle arrest of HB4C5 at G_1 to S phase, whereas the active flavonoid fraction stacked the cell cycle at G_2/M phase	38
7	Anti-tumour	Leaf	Ethanol	Leaves ethanol extract completely suppressed expression of the early-antigen of Epstein-Barr virus which was induced by a tumor promoter, the phorbol 12-myristate 13-acetate	39
8	Dental plaque inhibition	Leaf	Water (decoction)	Leaves water extract decreased plaque indexes by 43.1±4.02% when gargled by a group of patients with fixed orthodontic appliance Treated patients achieved an average hygiene category (31–50), an effect which was comparable to chlorhexidine (42.1±4.3%) a gold standard of antimicrobial agent	40
9	Lipid-lowering	Leaf	Methanol (50%)	50% aqueous methanol leaves extract showed 73% inhibitory activity at 2.75 mg/mL against porcine pancreatic lipase	2
		Leaf	Methanol (80%)	500 µg/ml of leaves methanol extract has inhibitory activity on pancreatic lipase activity by 43.1±4.02%	41
10	Acetylcholin-esterase inhibitor	Leaf	Methanol and ethyl acetate	Leaves methanol and ethyl acetate extracts inhibited acetylcholinesterase activity with the IC_{50} values of 47.30±3.54 µg/ml and 45.10±8.06 µg/ml, respectively, using Ellman colorimetric assay	24

DPPH=2,2-diphenyl-1-picrylhydrazyl, ABTS=2,2-azino-bis(3-ethylbenzothiozoline-6-sulphonic acid), ACE: Angiotensin Converting Enzyme, FRAP=Ferric-reducing assay, SHR=Spontaneously hypertensive rats, WKY=Wistar-Kyoto, MBC=Minimum bactericidal concentration, BHT=Butylated hydroxytoluene, *S. aureus=Staphylococcus aureus, S, dysenteriae=Shigella dysenteriae, B. subtilis=Bacillus subtilis, E. coli=Eschericia coli, S. typhi=Salmonella typhi, A. alternate=Alternaria alternate, C. capsicii=Colletotrichum capsicii, T. mentagrophytes=Trichophyton mentagrophytes, C. albicans=Candida albicans*

the onset for the antidiabetic effect can be seen as early as 7 days of treatment in alloxan-induced diabetic rats when treated with aqueous extract of *S. polyanthum* leaves at 200 mg/kg.[30] In a different diabetic rat model, Widyawati *et al.*[1] showed that an acute single dose of *S. polyanthum* methanolic extract at 1 g/kg can significantly reduce blood glucose level in streptozocin-induced diabetic rats after 7 h of treatment. In another experiment that introduced a repeated dose (twice daily) administration of *S. polyanthum* methanolic extract at tested dose from 250, 500, and 1000 mg/kg, there were significant reductions in the fasting blood glucose levels of streptozocin-induced diabetic rats after 6 days.[14] In fact, the selective antidiabetic effect by *S. polyanthum* leaves only on diabetic rats is one of the noteworthy observations for this plant.

There are few suggested mechanisms of antidiabetic action by *S. polyanthum* leaf extract. This includes (i) inhibiting alpha-glucosidase, (ii) decreasing glucose absorption, and (iii) increasing glucose uptake by muscle. Alpha-glucosidase is an important enzyme which is responsible for breaking down the large polysaccharides into glucose or sucrose. Inhibition of this enzyme will slow down the time for carbohydrate digestion and thus delays the digestion time. This will lower the rate of glucose absorption. Lelono[7] showed that methanol-water extract of *S. polyanthum* leaves exhibited the best inhibition of alpha-glucosidase activity as compared to both methanol and water extracts. In fact, this is further supported by a more recent report that showed the ability of methanolic extract of *S. polyanthum* leaves to significantly decrease the intestinal absorption of glucose and to significantly enhance the abdominal muscle tissue uptake of glucose *in vitro*.[14]

There was also a report that examined the effect of *S. polyanthum* leaf extract in combination with other common antidiabetic plants (*Andrographis paniculata*). An extract mixture of *S. polyanthum* and *A. paniculata* with a ratio of 1:6 displayed largest decrease in blood glucose levels compared to groups treated with single extracts of either *S. polyanthum* or *A. paniculata*.[30] This has indicates for a synergistic effect between the two plants. Andrographolide has been identified as the bioactive antidiabetic compound in *A. paniculata*. Meanwhile, for *S. polyanthum*, there were two active compounds (4-hydroxy-3-methoxy-benzoic acid and 4-hydroxy-3, 5-dimethoxy-benzoic acid) obtained from bioassay-guided fractionation of the methanolic–water extract of *S. polyanthum* leaves with inhibitory activity against alpha-glucosidase *in vitro*.[7]

Antihypertensive

One of the pertinent areas that is under ongoing investigations is the antihypertensive effect of this plant. A previous study demonstrated that aqueous and methanolic extracts of *S. polyanthum* leaves significantly lowered blood pressure of normal Wistar-Kyoto (WKY) and spontaneously hypertensive rats (SHR) when the extracts were intravenously administered.[9] In order to mimic the traditional mode of consumption, a recent study examined the effects of the two extracts when orally gavaged to conscious WKY and SHR rats.[32] The later study found that an acute administration of aqueous and methanolic leaf extract via oral route significantly lowered the blood pressure of SHR rats, but not in normal WKY.[32] In the subsequent subacute study, methanolic leaf extract at a dose of 2.50 g/kg when given once on a daily basis caused significant antihypertensive effect in SHR rats; the effect was seen as early as after 2 weeks of administration. In contrast, the antihypertensive effect for the aqueous leaf extract was observed only after 3 weeks of administration.[32]

Recently, the antihypertensive research was extended into the search of its mechanism of action. Studies have shown the possibility of *S. polyanthum* leaf extract to cause antihypertensive effect via vasorelaxation and by inhibiting angiotensin-converting enzyme (ACE). *In vitro* study by Ismail and Wan Ahmad[31] demonstrated significant vasorelaxation effect by aqueous and methanolic extracts of *S. polyanthum* leaves on thoracic aorta rings isolated from WKY and SHR. These researches

have also suggested that autonomic receptors and nitric oxide may partly be involved in causing vasorelaxation[31] and antihypertensive effects.[9] Other than vasorelaxation, inhibiting ACE, an enzyme important for the conversion of angiotensin I to angiotensin II, was one of the identified mechanisms of antihypertensive action by *S. polyanthum* leaf extract.[33] Muthia *et al.*[33] showed that ethanolic extract of *S. polyanthum* leaves at a concentration of 100 ppm has ACE inhibitory action of 53.37±0.95% as compared to standard antihypertensive drug captopril by 88.17±2.89%.

In addition, *in vitro* and *in vivo* studies on rats have shown some significant structural improvement of kidney, an important organ for blood pressure regulation as well as on aorta. Studies have shown that the morphology of kidney and aorta of SHR was significantly ameliorated when daily treated with the methanolic extract of *S. polyanthum* leaves for 4 week[43] and 6 weeks,[44] almost comparable to the kidney and aorta of normal WKY rats. Other than that, contractility response to precontractile agent phenylephrine was reduced in the femoral artery of SHR when treated with methanolic extract of *S. polyanthum* leaves. This finding is important as it is indicative of a less hypersensitive artery.[44]

Antimicrobial

The high incidence of increased resistance against microorganisms has paved interest into searching alternative antimicrobial therapeutics, especially from plant sources. Extracts from leaves, fruits, as well as essential oil of *S. polyanthum* have been tested with various bacteria and fungi. Ethanolic extracts of *S. polyanthum* leaves and stem have antibacterial activity against *Staphylococcus aureus*, a Gram-positive, round-shaped bacterium.[34] Another study has reported that ethanolic extract of *S. polyanthum* leaves was active against *Shigella dysenteriae*, a Gram-negative bacillus, with minimum bactericidal concentration values ranging from 10% to 20% w/v.[35] Essential oil of *S. polyanthum* leaves strongly inhibited the growth of *Bacillus subtilis* but not *Eschericia coli*.[20] Ripened fruit extract of *S. polyanthum* showed good activity toward *Salmonella typhi,* a Gram-negative, rod-shaped bacterium, in relative to erythromycin as standard.[11]

Besides action on bacterium, *S. polyanthum* have some actions on certain fungi. For instance, ethanolic extract of *S. polyanthum* leaves inhibited the growth of *Alternaria alternate* and *Colletotrichum capsicii* using the filter paper disc diffusion technique.[36] Extracts of *S. polyanthum* leaves and ripe and unripe fruits from 40, 60, and 80 µg/disc demonstrated antifungal activities, ranging from low to moderate against *Trichophyton mentagrophytes*, a fungus that causes dermatophytosis.[11] Good activity of *S. polyanthum* ripe and unripe fruit extracts (40, 60, and 80 µg/disc) was observed against *Candida albicans*, but not that with *S. polyanthum* leaves. This may suggest the therapeutic potential of *S. polyanthum* ripe and unripe fruit extracts for vaginal yeast infection, skin and diaper rashes, as well diseases caused by *Candida*.[11]

Antidiarrheal

Ethanolic extract of *S. polyanthum* leaves at 10%, 20%, and 30% has demonstrated antidiarrheal activity which was induced by castor oil.[37] The extracts at these tested concentrations significantly inhibited the transit of charcoal which was used as a marker, as compared to the negative control (carboxymethylcellulose). The activity of the highest concentration of extract which was at 30% was similar to that of reference drug, loperamide hydrochloride, at a dose of 10 ml/kg.[37]

Apart from these findings, Fitri *et al.*[35] had shown that *S. polyanthum* leaves have antibacterial activity against *Shigella dysenteriae*, an infective agent that causes shigellosis or bacillary dysentery, an inflammation of the intestines, causing severe diarrhea with the presence of blood or mucus. Another crucial finding was that ethanolic extract of *S. polyanthum* leaves contains potassium at a concentration of 2054 ppm (1.03% w/w).[35] This is beneficial to provide for the associated hypokalemic condition due to dysentery. The suggested potassium intake in patients with hypokalemia dysentery is 1170 ppm.

Anticancer

Flavonoid fraction from *S. polyanthum* leaves was reported to be cytotoxic to mouse colon 26 adenocarcinoma cells and HB4C5 human hybridoma from BALB/c mice.[38] By using specific assays for apoptosis such as caspase 3-gene expression and annexin-flow cytometry analyses, Sulistiyani *et al.*[38] suggested that the effect of cell proliferation inhibition was not due to apoptosis; instead of that, the active flavonoid fraction of *S. polyanthum* in fact stacked the cell cycle at G_2/M phase.

Antitumor

Ali *et al.*[39] had shown that the ethanolic extract of *S. polyanthum* leaves was able to completely suppress the expression of the early antigen of Epstein–Barr virus which was induced by a tumor promoter, the phorbol 12-myristate 13-acetate. Partial suppression by the ethanolic extract of *S. polyanthum* leaves was observed at low concentrations of 12.5 and 25 µg/ml, indicative of a strong antitumor-promoting activity on this plant extract.

Dental plaque inhibition

S. polyanthum leaves may have some potential usages in dentistry.[5] Avriliyanti *et al.*[40] had shown that aqueous decoction of *S. polyanthum* leaves at a concentration of 60% has the ability to decrease plaque indexes by 43.1±4.02% when the decoction was gargled by a group of patients with fixed orthodontic appliance. These patients have actually achieved an average hygiene category (31%–50%) in which the effect was comparable to chlorhexidine (42.1±4.3%), a gold standard of antimicrobial agent.

Lipase inhibitory

Several studies have shown the potential use of *S. polyanthum* leaves in treating and preventing obesity.[2,41] Kato *et al.*[2] showed that 50% aqueous-methanolic leaf extract at 2.75 mg/ml showed 73% inhibitory activity against porcine pancreatic lipase, an enzyme which is important for fat digestion. Hydroxychavicol and another two new dimers have been identified as the active compounds responsible for the lipase inhibitory action by *S. polyanthum* leaves.[2] Alias *et al.*[41] in a recent study on 24 crude plant extracts reported that *S. polyanthum* leaf extract has a medium inhibitory activity of 38.20±6.50% against porcine lipase in comparison with the other 23 crude plant extracts. Nevertheless, this finding made this plant interesting to be a part of food additive in the treatment and prevention of obesity.

Acetylcholinesterase inhibitor

Acetylcholinesterase inhibitor inhibits acetylcholinesterase from cleaving the acetylcholine, thus prolonging the action of acetylcholine at the synaptic junction. Darusman *et al.*[24] had shown that the methanolic and the ethyl acetate extracts of *S. polyanthum* leaves inhibited acetylcholinesterase activity with the IC_{50} values of 47.30 ± 3.54 µg/ml and 45.10 ± 8.06 µg/ml, respectively, using Ellman colorimetric assay. This activity is mainly important for the potential treatment of Alzheimer's disease, a neurodegenerative disorder which is caused by degenerating cholinergic neurons and a decrease in acetylcholine concentration.

Future recommendations

This review supports the various therapeutic potentials of *S. polyanthum*. However, there is necessity to extend the research in few areas: (1) to discover the active compounds responsible for these therapeutic effects,

(2) to study the mechanism of its action, and (3) to comprehensively evaluate its toxicological aspects.

CONFLICTS OF INTEREST

There are no conflicts of interest.

ACKNOWLEDGMENT

The study was supported by the Research Initiative Grant Scheme (RIGS15-039-0039) from International Islamic University Malaysia.

Financial support and sponsorship

The study was supported by the Research Initiative Grant Scheme (RIGS15-039-0039) from International Islamic University Malaysia.

REFERENCES

1. Widyawati T, Purnawan WW, Atangwho IJ, Yusoff NA, Ahmad M, Asmawi MZ. Anti-diabetic activity of *Syzygium polyanthum* (Wight) leaf extract, the most commonly used herb among diabetic patients in Medan, North Sumatera, Indonesia. Int J Pharm Sci Res 2015;6:1698.
2. Kato E, Nakagomi R, Gunawan-Puteri MD, Kawabata J. Identification of hydroxychavicol and its dimers, the lipase inhibitors contained in the Indonesian spice, *Eugenia polyantha*. Food Chem 2013;136:1239-42.
3. Roskov Y, Kunze T, Paglinawan L, Orrell T, Nicolson D, Culham A, *et al*. Catalogue of Life 2013 Annual Checklist; 2013. Available from: http://www.catalogueoflife.org/annual-checklist/2013/. [Last accessed on 2015 May 11].
4. Lelono RA, Tachibana S, Itoh K. *In vitro* antioxidative activities and polyphenol content of *Eugenia polyantha* wight grown in Indonesia. Pak J Biol Sci 2009;12:1564-70.
5. Sumono A, Wulan AS. The use of bay leaf (*Eugenia polyantha* wight) in dentistry. Dent J 2008;41:147-50.
6. Grosvenor PW, Gothard PK, McWilliam NC, Supriono A, Gray DO. Medicinal plants from Riau province, Sumatra, Indonesia. Part 1: Uses. J Ethnopharmacol 1995;45:75-95.
7. Lelono RA. Extracts as inhibitors of key enzymes for type 2 diabetes. J Med Sci 2013;13:103-10.
8. Suksri S, Premcharoen S, Thawatphan C, Sangthongprow S. Ethnobotany in bung khong long non-hunting area, Northeast Thailand. Kasetsart J (Nat Sci) 2005;39:519-33.
9. Ismail A, Mohamed M, Sulaiman SA, Wan Ahmad WA. Autonomic nervous system mediates the hypotensive effects of aqueous and residual methanolic extracts of *Syzygium polyanthum* (Wight) walp. Var. *Polyanthum* leaves in anaesthetized rats. Evid Based Complement Alternat Med 2013;2013:716532.
10. Wong SP, Leong LP, Koh JH. Antioxidant activities of aqueous extracts of selected plants. Food Chem 2006;99:775-83.
11. Kusuma IW, Kuspradini H, Arung ET, Aryani F, Min YH, Kim JS, *et al*. Biological activity and phytochemical analysis of three indonesian medicinal plants, *Murraya koenigii*, *Syzygium polyanthum* and *Zingiber purpurea*. J Acupunct Meridian Stud 2011;4:75-9.
12. Perumal S, Mahmud R, Piaru SP, Chai LW, Ramanathan S. Potential antiradical activity and cytotoxicity assessment of *Ziziphus mauritiana* and *Syzygium polyanthum*. Int J Pharmacol 2012;8:535-41.
13. Har LW, Ismail IS. Antioxidant activity, total phenolics and total flavonoids of *Syzygium polyanthum* (Wight) walp leaves. Int J Med Aromat Plants 2012;2:219-28.
14. Widyawati T, Yusoff NA, Asmawi MZ, Ahmad M. Antihyperglycemic effect of methanol extract of *Syzygium polyanthum* (Wight.) leaf in streptozotocin-induced diabetic rats. Nutrients 2015;7:7764-80.
15. Hamad A, Mahardika MG, Istifah I, Hartanti D. Antimicrobial and volatile compounds study of four spices commonly used in Indonesian culinary. J Food Pharm Sci 2016;4:1-5.
16. Wahjuni S, Wita IW. Hypoglycemic and antioxidant effects of *Syzygium polyanthum* leaves extract on alloxan induced hyperglycemic wistar rats. Bali Med J 2017;3:113-6.
17. Rahim EN, Ismail A, Omar MN, Rahmat UN, Ahmad WA. GC-MS analysis of phytochemical compounds in *Syzygium polyanthum* leaves extracted using ultrasound-assisted method. Pharmacogn J 2018;10:110-9.
18. Setyawati A, Hirabayashi K, Yamauchi K, Hattori H, Mitsunaga T, Batubara I, *et al*. Melanogenesis inhibitory activity of components from Salam leaf (*Syzygium polyanthum*) extract. J Nat Med 2018; 72(2):1-7.
19. Nur Amalina A, Natanamurugaraj G, Mashitah M, Nurul Ashikin A. Chemical composition, antioxidant and antibacterial activities of *Syzygium polyanthum* (Wight) Walp. essential oils. Open Conf Proc J 2013;4:139.
20. Hamad A, Mahardika M, Yuliani I, Hartanti D. Chemical constituents and antimicrobial activities of essential oils of *Syzygium polyanthum* and *Syzygium aromaticum*. Rasayan J Chem 2017;10:564-9.
21. Karim S, Kasthuri L, Nadiatul N. Vitamins and mineral contents of ten selected weeds and local plants of Kelantan, Malaysia. Int J Biol Pharm Allied Sci 2017;6:161-74.
22. Moshi MJ, Innocent E, Magadula JJ, Otieno DF, Weisheit A, Mbabazi PK, *et al*. Brine shrimp toxicity of some plants used as traditional medicines in Kagera region, North Western Tanzania. Tanzan J Health Res 2010;12:63-7.
23. Kuete V, Krusche B, Youns M, Voukeng I, Fankam AG, Tankeo S, *et al*. Cytotoxicity of some Cameroonian spices and selected medicinal plant extracts. J Ethnopharmacol 2011;134:803-12.
24. Darusman LK, Wahyuni WT, Alwi F. Acetylcholinesterase inhibition and antioxidant activity of *Syzygium cumini*, *S. aromaticum* and *S. polyanthum* from Indonesia. J Biol Sci 2013;13:412-6.
25. Othman A, Mukhtar NJ, Ismail NS, Chang SK. Phenolics, flavonoids content and antioxidant activities of 4 Malaysian herbal plants. Int Food Res J 2014;21:759-66.
26. Safriani N, Arpi N, Erfiza NM. Potency of curry (*Murayya koeniigi*) and salam (*Eugenia polyantha*) leaves as natural antioxidant sources. Pak J Nutr 2015;14:131.
27. Widyawati T, Roslan NA, Yusoff NA, Asmawi MZ, Ahmad M. The evaluation of antioxidant and free radical scavenging activities of *Eugenia polyantha* leaves extracts. Int J Chem Tech Res 2016;9:465-71.
28. Hidayati MD, Ersam T, Shimizu K, Fatmawati S. Antioxidant activity of *Syzygium polyanthum* wight extracts. Indones J Chem 2017;17:49-53.
29. Ramdhania Z, Insanu M, Gunarti N, Wirasutisna K, Sukrasno S, Hartati R. Antioxidant activity from ten species of *Myrtaceae*. Asian J Pharm Clin Res 2017; Special Issue (May) :1-7.
30. Widharna RM, Tamayanti WD, Hendriati L, Hamid IS, Widjajakusuma EC. Antidiabetic effect of the aqueous extract mixture of *Andrographis paniculata* and *Syzygium polyanthum* Leaf. Eur J Med Plants 2015;6:82.
31. Ismail A, Wan Ahmad WA. Autonomic receptors and nitric-oxide involvements in mediating vasorelaxation effect induced by *Syzygium polyanthum* leaves extract. Pharmacognosy Res 2017;9:S9-14.
32. Ismail A, Ramli NS, Mohamed M, Wan Ahmad WA. Acute and sub-acute antihypertensive effects of *Syzygium polyanthum* leaf extracts with determination of gallic acid using HPLC analysis. Pharmacogn J 2018;10:663-71.
33. Muthia R, Suganda A, Sukandar E. Angiotensin-1 converting enzyme (ACE) inhibitory activity of several Indonesian medicinal plants. Res J Pharm Biol Chem Sci 2017;8:192-9.
34. Grosvenor PW, Supriono A, Gray DO. Medicinal plants from Riau province, Sumatra, Indonesia. Part 2: Antibacterial and antifungal activity. J Ethnopharmacol 1995;45:97-111.
35. Fitri S, Ramdhani D, Mustarichie R. Comparative study on activities of anti bacillary dysentry *Shigella dysenteriae* of *Syzygium polyanthum* and *Dracaena angustifolia* leaves ethanol extracts. Asian J Pharm Clin Res 2017;10:348-52.
36. Mohamed S, Saka S, El-Sharkawy SH, Ali AM, Muid S. Antimycotic screening of 58 Malaysian plants against plant pathogens. Pest Sci 1996;47:259-64.
37. Malik A, Ahmad AR. Anti-diarrheal activity of ethanolic extract of bay leaves (*Syzygium polyanthum* [Wight.] Walp). Int Res J Pharm 2013;4:106-8.
38. Sulistiyani SF, Wahyuni WT, Sugahara T, Tachibana S, Syaefudin. Cellular mechanism of the cytotoxic effect of extracts from *Syzygium polyanthum* leaves. Am J Drug Discov Dev 2014;4:90-101.
39. Ali AM, Mooi LY, Yih Yih K, Norhanom AW, Mat Saleh K, Lajis NH, *et al*. Anti-tumor promoting activity of some Malaysian traditional vegetable (ulam) extracts by immunoblotting analysis of Raji cells. Nat Prod Sci 2000;6:147-50.
40. Avriliyanti F, Suparwitri S, Alhasyimi AA. Rinsing effect of 60% bay leaf (*Syzygium polyanthum* wight) aqueous decoction on the accumulation of dental plaque during fixed orthodontic treatment. Dent J 2017;50:1-5.
41. Alias N, Leow T, Ali M, Tajudin A, Salleh A, Rahman R. Anti-obesity potential of selected tropical plants via pancreatic lipase inhibition. Adv Obes Weight Manag Control 2017;6:1-11.
42. Blair M. Diabetes mellitus review. Urol Nurs 2016;36:27-36.
43. Ramli NS, Muhammad NA, Safuan S, Noordin L, Wan Ahmad WAN. Preliminary evaluation on the effect of methanolic extract from *Syzygium polyanthum* on improvement of hypertensive-renal damage among spontaneous hypertensive rat models. Ann Microsc 2017;16:15-22.
44. Wan Ahmad WAN, Jamal N, Rahmat U, Ramli NS, Muhammad NA, Noordin L. Evaluation of *Syzygium polyanthum* leaves methanol extract as antihypertensive agent in rat. Int J Cardiol 2017;249:S10.

Cite this article: Ismail A, Wan Ahmad WAN. *Syzygium polyanthum* (Wight) Walp: A potential phytomedicine. Phcog Rev Pharmacog J. 2019;11(2):429-8.