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Short Communication

Canarium odontophyllum Miq. (Dabai) Leaf Phytoextracts and Their Medicinal Properties

Muhammad Wahizul Haswan Abdul Aziz^{1,2}, Siti Fathiah Masre¹, Dayang Fredalina Basri³ and Ahmad Rohi Ghazali^{1*}

¹Centre for Toxicology and Health Risk Studies (CORE), Faculty of Health Sciences, Universiti Kebangsaan Malaysia, 50300 UKM, Kuala Lumpur, Malaysia ²Department of Para-clinical Sciences, Faculty of Medicine and Health Sciences, Universiti Malaysia Sarawak, 94300 UNIMAS, Kota Samarahan, Sarawak, Malaysia

³Centre for Diagnostic, Therapeutic & Investigative Studies (CODTIS), Faculty of Health Sciences, Universiti Kebangsaan Malaysia, 50300 UKM Kuala Lumpur, Malaysia

ABSTRACT

Canarium odontophyllum Miq., renowned locally as "dabai," is an endemic plant in Sarawak, Malaysia. Most people, especially in rural areas, consume this plant to maintain their health. A few medicinal studies have investigated *C. odontophyllum* Miq.'s biological properties to substantiate its use as nutraceuticals and health supplements. Crude extracts from *C. odontophyllum* Miq. demonstrated various medicinal properties, including antibacterial, antimalarial, antioxidant, anticancer, antidiabetic, and antihypertensive. In addition, numerous phytoextracts studies have revealed the existence of a variety of beneficial compounds, including flavonoids, tannins, and terpenoids. However, despite various biological activities of *C. odontophyllum* Miq., there is currently no analysis summarizing the medicinal properties of its leaf. Thus, this short communication attempts to narrate the medicinal properties of *C. odontophyllum* Miq. leaf and their phytoextracts

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E-mail addresses:

amwhaswan@unimas.my (Muhammad Wahizul Haswan Abdul Aziz) sitifathiah@ukm.edu.my (Siti Fathiah Masre) dayang@ukm.edu.my (Dayang Fredalina Basri) rohi@ukm.edu.my (Ahmad Rohi Ghazali) * Corresponding author responsible. In conclusion, we summarized *C. odontophyllum* Miq. leaf promising therapeutic effects with their phytoextracts and a step closer to developing it as potential nutraceuticals and health supplements to fulfill social interest.

Keywords: Canarium odontophyllum Miq., dabai, flavonoids, medicinal properties, phytoextracts, terpenoids

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INTRODUCTION

Borneo, Asia's largest island, is split politically between three countries: Malaysia, Brunei, and Indonesia to the north and south. The East Malaysian states of Sabah and Sarawak make up about 26% of the island in the north. Borneo is home to one of the world's oldest rainforests, rich in biodiversity and providing a plentiful supply of fruits and vegetables, especially in rural areas. Over the centuries, older generations have used wild plants for medicinal purposes, especially in traditional medicine. It is because they are rich sources of biologically active compounds. However, wild plants have been neglected over time, and the full potential use of the plants is not well explored. Plants are the main source for drug development, according to Craig (1999), and about 80% of the world's population uses plant extracts as conventional medicine for their immediate health care needs. *Canarium odontophyllum* Miq. or renowned locally as "dabai," is an endemic plant in Sarawak, Malaysia, and devoured as a snack food by the natives to maintain health and well-being (Latiff et al., 2000). However, *C. odontophyllum* Miq. is classified as an underutilized

fruit and has not been fully explored due to lack of promotion. Our literature survey showed that only several scientific studies had been conducted to date to investigate the medicinal properties of *C. odontophyllum* Miq. leaf (Figure 1).

Hence, the present short communication attempts to narrate the medicinal properties of *C*. *odontophyllum* Miq. leaf and their phytoextracts to establish a scientific foundation for the medicinal use of *C*. *odontophyllum* Miq. leaf as nutraceuticals.



Figure 1. Canarium odontophyllum Miq. leaf

METHODOLOGY

This study was created by collecting and consulting recent articles on *C. odontophyllum* Miq. Leaf's medicinal uses and scientific evidence. Journals and electronic databases from PubMed, Elsevier, Google Web, Google Scholar, Web of Science, and Springer were used to gather all the knowledge about the leaf of this plant. Only texts written in English from January 2014 to December 2020 were considered for this study. Search on *C. odontophyllum* Miq. was done using combinations of keywords, including: '*Canarium odontophyllum* Miq.,' '*C. odontophyllum* leaf,' 'biological activity,' 'phytoconstituents,' 'phytochemical,' and 'phytoextract.' The plant's scientific name was validated using The Plant List (www.theplantlist.org). The structural formulae were drawn and checked from Chemspider (https://www.chemspider.com) and PubChem (https://pubchem.ncbi.nlm.nih. gov/) based on the reported chemical constituents from *C. odontophyllum* Miq.

MEDICINAL PROPERTIES OF C. odontophyllum Miq. LEAF

As outlined in Table 1, results from various studies indicated that *C. odontophyllum* Miq. leaf possessed many potentials, including antibacterial, antimalarial, antioxidant, anticancer, hypoglycemic, and vasorelaxant properties.

Antioxidant Capacity

The initial study to investigate the antioxidant efficacy of C. odontophyllum Miq. leaf was performed by Basri et al. (2014). The ferric reducing/antioxidant power (FRAP) assay screened the C. odontophyllum Miq. leaf aqueous, methanol, and acetone extracts antioxidant capacity. All C. odontophyllum Miq. leaf extracts were found to exhibit dosedependent antioxidant potential. Acetone extract exhibited the uppermost antioxidant capacity of $355.26 \,\mu\text{M}$ FeSO₄.7H₂O at 50 μ g/ml. In contrast, methanol extract exhibited moderate antioxidant activity (281.15 µM FeSO₄.7H₂O at 50 µg/ml) (no significant difference from that acetone extract), followed by aqueous extract with 140.29 µM FeSO₄.7H₂O at 50 µg/ml. Preliminarily, their findings showed that *C. odontophyllum* Miq. leaf extracts could provide a natural source of antioxidant constituents for medical use and health benefits. Furthermore, Budin et al. (2018) demonstrated that the C. odontophyllum Miq. leaf aqueous extract possesses the capability to decrease oxidative stress markers [malondialdehyde (MDA) reduced by 15.38%, protein carbonyl reduced by 35.26%, glutathione (GSH) increased by 12.5%, superoxide dismutase (SOD) increased by 20.29% and glutathione peroxidase (GPx) increased by 10.53%] in streptozotocin-induced diabetic rat's liver. This antioxidant capacity opened a wide possibility of more medicinal properties of the leaf.

Antibacterial Effects

Antibacterial derived from plants has immense medicinal potential, as they could fulfill the role with fewer adverse effects that are frequently related to synthetic antimicrobials. Today, continuous further discovery and production of antibacterial plant-derived products are needed. Basri and Nor (2014) performed *in vitro* antibacterial activity of *C. odontophyllum* Miq. and found methanol and acetone leaf extracts effective (MIC value 0.195 mg/ml) against *Staphylococcus aureus* ATCC 25923. Several studies on acetone and methanol extracts showed that methicillin-resistant *Staphylococcus aureus* (MRSA) was sensitive to the extracts (Basri & Sandra, 2016; Basri et al., 2016; Shamsuddin et al., 2018). However, more research is needed to identify and isolate the antibacterial compounds from the *C. odontophyllum* Miq. leaf. Thus, the leaf extract could open more possibilities to discover new, clinically useful antibacterial compounds.

Table 1 <i>Reported medicin</i> o	al properties of Ca	Table 1 <i>Reported medicinal properties of</i> Canarium odontophyllum <i>Miq. leaf</i>			
Medicinal properties	Solvent of extract(s)	Experimental model	Result	Conclusion	Researchers (Year)
Antioxidant	Aqueous Methanol Acetone	FRAP assay was done on aqueous, methanol, and acetone extracts to screen theirs in vitro antioxidant capacity.	All leaf extracts exhibited dose- dependent antioxidant potential with acetone extract (highest), methanol extract (moderate), and aqueous extract (lowest antioxidant power).	Preliminarily shown that <i>C. odontophyllum</i> leaf extracts contain antioxidant constituents.	Basri et al. (2014)
	Aqueous	The diabetic induced rats were treated with the extract (300 mg/kg/day for 28 days) in comparison to the control group. In addition, for diabetic induction, 65 mg/kg of streptozotocin (STZ) was given intravenously.	Oxidative stress testing indicated lower protein carbonyl and MDA levels, significantly (p<0.05) elevated activity of GSH, GPx, and SOD than the untreated diabetic group.	<i>C. odontophyllum</i> leaf aqueous extract protects against liver damage in diabetic rats.	Budin et al. (2018)
Antibacterial	Methanol Acetone	For growth inhibition, the extracts were tested against Bacillus cereus, Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa.	Methanol and acetone extract inhibited <i>S. aureus</i> growth.	Both extracts contain potentially therapeutic compounds against <i>S.</i> <i>aureus</i> .	Basri and Nor (2014)
	Methanol Acetone	The broth microdilution method was used to test the antibacterial properties of extracts against MRSA.	Minimum inhibitory concentrations (MIC) values obtained were $312.5 \mu g/mL$ (methanol) and $156.25 \mu g/mL$ (acetone). Minimum bactericidal concentrations (MBC) were 625 $\mu g/mL$ (methanol) and $312.5 \mu g/mL$ mL (acetone).	Both extracts showed the anti-MRSA effect that is comparable to vancomycin.	Basri and Sandra (2016)

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Medicinal properties	Solvent of extract(s)	Experimental model	Result	Conclusion	Researchers (Year)
	Acetone	Post-antibiotic effect (PAE) was done for extract against MRSA ATCC 33591. In addition, MIC and MBC values were determined.	With an identical MIC and MBC value of 1250 g/ml, C. <i>odontophylum</i> leaf acetone extract was bactericidal against MRSA ATCC 33591. In addition, the extract demonstrated extended PAE time $(0.85 \pm 1.74$ hours) compared to oxacillin $(0.18 \pm 2.43$ hours) against MRSA.	Extract exhibited bacteriostatic activity as well as a long-lasting antibacterial effect.	Basri et al. (2016)
	Acetone	MIC, MBC, and TKA analyses against MRSA (ATCC 33591 and Mu50).	MIC/MBC ratio showed the bacteriostatic effect of extract against both MRSA strains. The extract inhibited MRSA growth at low concentrations.	The extract inhibited the growth of MRSA and might be explored as an anti-MRSA agent.	Shamsuddin et al. (2018)
Antimalarial	Methanol	Ex-vivo antimalarial activity of extracts (methanol, acetone, and aqueous) was evaluated on <i>Plasmodium berghei</i> NK65 infected erythrocytes. In addition, Plasmodium lactate dehydrogenase (pLDH) and SYBR green I fluorescence assay were done.	Methanol extract showed the lowest IC ₅₀ values ($0.0004 \ \mu g/m$]) from pLDH Assay and SYBR green I fluorescence assay ($0.002 \ \mu g/m$]) compared to positive control chloroquine 0.0011 $\mu g/m$ l (pLDH assay) and 0.029 $\mu g/m$ l (SYBR green I fluorescence assay).	<i>C. odontophyllum</i> leaf methanol extract showed promising antimalarial activity and could be developed into a schizonticidal agent.	Ishak et al. (2020)
Cytotoxic/ Anticancer	Methanol Acetone Aqueous	Cytotoxicity (MTT assay) of extracts against human colorectal carcinoma cells HCT 116 was carried out.	A fiter a 24-hour treatment with extracts, IC_{30} values were obtained (methanol 0.10 ± 0.011 mg/mL, acetone 0.08 ± 0.003 mg/mL, aqueous 0.40 ± 0.162 mg/mL).	According to this preliminary finding, <i>C</i> . <i>odontophyllum</i> leaf extracts have promising anticancer properties.	Basri et al. (2015)

Dabai Leaf Phytoextracts Medicinal Properties

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Medicinal properties	Solvent of extract(s)	Experimental model	Result	Conclusion	Researchers (Year)
	Acetone	The Ames test was used to determine the extract mutagenicity and antimutagenicity.	No mutagenesis activity was detected from the extract. However, the presence of the metabolic activator S9 system resulted in the highest antimutagenic action with inhibition of 62.38% (TA98) and 58.24% (TA100).	The extract had strong inhibitory effects on mutagenicity, and it also showed antimutagenic activity and, therefore, could be developed as an anticancer agent.	Ghazali et al. (2017)
Antidiabetic	Aqueous	Diabetic-induced rats were treated with extract orally 300 mg/kg/day for 28 days compared to diabetic control. In addition, 65 mg/kg of STZ was given intraperitoneally to induce diabetes.	The extract-treated diabetic group had lower (p<0.05) fasting blood glucose levels than the diabetic control.	The aqueous extract can reduce blood glucose levels.	Saari et al. (2017)
Vasorelaxation/ Antihypertension	Aqueous	Isolated thoracic aortic rings were positioned between two tungsten wires coupled to an isometric force transducer after being suspended in a tissue bath. A data capture system was used to record the changes in tension.	The extract elicited relaxation in endothelium-intact and endothelium-denuded aortic rings.	The extract has a vasorelaxant effect mediated by the inhibition of calcium channels.	Basri et al. (2018)

Table 1 (conitnue)

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Antimalarial

We cannot afford to ignore the hunt for antimalarial drugs derived from plant sources. Furthermore, essential antimalarial medications today, such as artemisinin and quinine, have been isolated from plants (Bhatnagar & Das, 2007). Similarly, the *C. odontophyllum* Miq. methanol leaves extract showed the lowest plasmodium lactate dehydrogenase (pLDH) assay half-maximal inhibitory concentration (IC_{50}) values. It was the most potent against the schizont stage of *Plasmodium berghei* NK65. The methanol extract also exhibits promising antimalarial activity and the potential to be a schizonticidal agent (Ishak et al., 2020).

Anticancer Agents

Many attempts have also been made to find the correlation between the phytoextracts' antioxidant properties and their potential for anticancer. While no conclusive evidence of such correlation has been found, it has been suggested that phytoextracts antioxidant activity is also an indicator of its anticancer potential. The dabai fruit has excellent potential to be exploited as a nutraceutical due to its nutrient-rich and antioxidant capabilities. Thus, the initial study to investigate the antioxidant efficacy in leaf extracts of C. odontophyllum Miq. was done by Basri et al. (2014). In another preliminary study, all three extracts showed cytotoxic activity after 24 hrs treatment with acetone extract at an IC₅₀ value of 0.08 \pm 0.003 mg/mL against human colorectal cancer cells (HCT 116) compared to methanol and aqueous extracts with IC₅₀ values of 0.10 ± 0.011 mg/mL and 0.40 ± 0.162 mg/mL, respectively (Basri et al., 2015). These studies could provide an insight into its promising anticancer activity. Furthermore, the extract may also be developed as a chemopreventive agent based on its significant antimutagenic activity demonstrated, where C. odontophyllum Miq. leaf acetone extract in the presence of the metabolic activator S9 system with inhibition percentage greater than 50% in both bacteria Salmonella typhimurium strains TA98 and TA100 (Ghazali et al., 2017).

Antidiabetic

The aqueous extract of *C. odontophyllum* Miq. leaf (300 mg/kg for 28 days) induced a significant reduction in glucose level. The fasting blood glucose of the diabetic group treated with *C. odontophyllum* Miq. was significantly lower than the diabetic group (p<0.05). The original manuscript stated no exact values, but according to their bar chart, the values were roughly 34 mmol/L and 21 mmol/L for the diabetic and treated groups, respectively. The discovery implied that the *C. odontophyllum* Miq. leaf aqueous extract could lower blood glucose levels in diabetic rats (Saari et al., 2017). *C. odontophyllum* Miq. leaf could also be exploited as a new prospective with many medicinal properties in nutraceutical products.

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Vasorelaxation and Antihypertensive

With the elevated incidence of hypertension, researchers aim for alternative therapies from plant origins for their phytoextract compounds with vasorelaxant and hypotensive properties. The aqueous extract of *C. odontophyllum* Miq. leaf was studied on isolated thoracic aortic rings suspended in a tissue bath. The extract had an EC₅₀ of 5.89 mg/ml in the endothelium-denuded aorta ring and 8.36 mg/ml in the endothelium-intact aortic ring. The extract (3–15 mg/ml) induced relaxation in endothelium-intact and endothelium-denuded aortic rings precontracted with phenylephrine. Therefore, the study suggested that the vasorelaxant effect of the extract was endothelium-independent and could be developed as a hypotensive agent (Basri et al., 2018).

MAJOR PHYTOEXTRACTS IN C. odontophyllum Miq. LEAF

Phytoextracts are naturally present in almost all plants. With fibers and nutrients, phytoextracts in plants serve as a protection mechanism against disease. Table 2 shows the phytoextracts in *C. odontophyllum* Miq. leaf. The major constituents of the extracts are flavonoids, tannins, and terpenoids. Flavonoids are compounds that possess many biological features that benefit human health. In diets, flavonoids supply an abundance of natural antioxidants to humans. In the best of situations, flavonoids neutralize free radicals' adverse effects and thereby tend to resist certain disorders. In addition, they interact with various cellular targets such as antioxidants and free-radical scavenger activities, providing anti-inflammatory, antiviral, antibacterial, anti-aging, and notably anticancer properties (Karak, 2019). Tannins are a type of polyphenolic compound with complex plant structures. Its molecular weights are typically greater than 500 Da. Several natural tannins and related compounds have been reported to have various medicinal activities, including antioxidant, antitumor, antidiabetic, and antibacterial (Zou et al., 2014; Pajari et al., 2016; Singh et al., 2018).

Terpenoids are secondary metabolites with carbon backbone-containing molecular structures of isoprene (2-methylbuta-1,3-diene) units. In growth and development, thousands of terpenoids produced by plants have no discernible role, thus classifying them as 'secondary' metabolites. Important medicinal activities are shown by the terpenoids group, such as antiviral, antibacterial, antimalarial, anti-inflammatory, cholesterol synthesis inhibition, and anticancer (Mahato & Sen, 1997). According to Basri and Nor (2014), saponin and phenolic compounds were only detected in methanol and aqueous extracts. None of the extracts contained alkaloids. However, there have yet been no single bioactive compounds extracted from *C. odontophyllum* Miq. leaf from all previous studies.

Dabai Leaf Phytoextracts Medicinal Properties

Phytoextracts	Acetone	Methanol	Aqueous
Alkaloids	-	-	-
Flavonoids	+	+	+
Tannins	+	+	+
Terpenoids	+	+	+
Saponin	-	+	+
Phenolic compound	-	+	+

 Table 2

 Phytoextracts in Canarium odontophyllum Miq. leaf

- = not detected, + = detected

HEALTH BENEFITS OF C. odontophyllum Miq. LEAF

Further laboratory research and clinical studies should be carried out to assess relevant biochemical markers and specific phytoextracts to understand the mechanism of medicinal actions. As for its anticancer properties, other investigatory activities must be carried out in several different animal tumor systems for more conclusive findings and further scientific validation. It is also essential to understand that *C. odontophyllum* Miq. can be effective in isolation and could have a potential effect when given in combination with other herbs or medicines. However, the review findings are very favorable for using *C. odontophyllum* Miq. leaf as a multi-purpose therapeutic agent. There are currently some limitations in the existing literature, and further clinical trials should be carried out to promote its use of remedial use, thus fulfilling social interest.

CONCLUSION

C. odontophyllum Miq. leaf possesses many medicinal properties. Their role is played by the phytoextracts found in the leaf itself. Therefore, *C. odontophyllum* Miq. leaf would offer promising therapeutic effects and, in the future, be developed as potential nutraceuticals and health supplements.

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