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Research Article

Phytoconstituents, antioxidant, and cholinesterase inhibitory activities of the leaves and stem extracts of *Artocarpus sericicarpus*

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Abstract

The study aimed to investigate the antioxidant and cholinesterase inhibitory activities of the leaves and stems of *Artocarpus sericicarpus* and to analyse the phenolic compounds in the extracts. The modified Ellman's method was used to determine the cholinesterase inhibitory activities against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes. The antioxidant properties were evaluated using DPPH and ABTS methods. The total phenolic content (TPC) was measured by spectrometric assay, and compound identification was carried out by LC-MS/MS analysis. The results showed that the leaf and stem extracts of *A. sericicarpus* exerted significant inhibitory effects against AChE and BChE, as well as antioxidant activities. The stem ethanolic extract exhibited the highest potency against AChE and BChE with IC_{50} values of 5.81 and 11.46 µg/mL, respectively. The leaf and stem ethanolic extracts gave higher antioxidant activities and TPC compared to the water-based extracts. The LC-MS/MS analysis indicated the presence of phenolic compounds, such as flavones, flavonols, flavanones, prenylated chalcones, and xanthones in the extracts.

Keywords

Artocarpus sericicarpus, cholinesterase inhibitor, antioxidant, phenolic compounds

Introduction

Among several neurological disorders, Alzheimer's disease (AD) is a progressive neurodegenerative disease that commonly affects elderly people. It is reported that more than 50 million people are suffering from AD worldwide, and the number is expected to increase every year (Prince et al. 2013; Alzheimer's Association 2023). AD causes progressive and irreversible memory decline, cognitive impairment, behavioral changes, and limitations on daily life tasks (Dipiro et al. 2020). Despite the complexity and incomplete understanding of the pathogenesis of AD, two major hypotheses, the amyloid cascade and the cholinergic, are currently being considered with regard to the underlying molecular mechanism (Breijyeh and Karaman 2020). The cholinergic hypothesis suggests that the neurodegenerative mechanism is a decline of the neurotransmitter acetylcholine (ACh) in the brain. The medications

currently prescribed for AD patients are targeted to increase the brain's acetylcholine levels, which are essential for central cholinergic transmission. ACh is degraded by two catabolic cholinesterase enzymes, acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) into a choline and an acetyl group after being transported across neural synapses (Marucci et al. 2021; Zhou and Huang 2022). Therefore, inhibition of these enzymes will prevent the hydrolysis of acetylcholine increasing the concentration of ACh in the brain. Growing evidence showed the relation between oxidative stress and AD. The overproduction of reactive oxygen species (ROS) or deficiency of antioxidants causes oxidative stress that damages the brain cells and causes AD to develop into dementia. Oxidative stress also contributes to the existence of the toxic peptide β-amyloid in the brain (Sinyor et al. 2020; Tamagno et al. 2021) Therefore, strategies for the treatment of AD have involved the use of antioxidants (Pritam et al. 2022).

Medicinal plants have been used widely as a source of therapeutic substances. Plant secondary metabolites have played a significant role in the development of medicine for various therapeutic targets, including neurological disorders (John et al. 2022; Wang et al. 2022). The genus *Artocarpus* (Family Moraceae) comprises more than fifty species of evergreen and deciduous trees, and more than half of *Artocarpus* species can be found in South East Asia, such as in Indonesia, Malaysia, Thailand, and Brunei Darussalam. Economically, the genus is of appreciable importance as a source of edible fruit such as *Artocarpus heterophyllus* (jackfruit), *Artocarpus champeden* (chempedak), and *Artocarpus communis* (breadfruit). In addition to its edible fruits, the wood is valued for making furniture, musical instruments, building construction, and boats. The plant is also widely used in folk medicine, such as to treat skin diseases, toothache, edema, malaria fever, chest pain, diabetes, and diarrhea (Jagtap and Bapat 2010; Lathiff et al. 2021). The *Artocarpus* genus is a source of phenolic compounds, including flavonoids, stilbenoids, chalcones, and xanthones that exhibit various biological activities (Hakim et al. 2006; Jagtap and Bapat 2010; Lathiff et al. 2021). Several arylbenzofurans isolated from *Artocarpus lakoocha* showed promising AChE inhibitory activity (Namdaung et al. 2008). In continuation of the search for cholinesterase inhibitors from Indonesian medicinal plants, we are interested in studying the potency of *A. sericicarpus* as a cholinesterase inhibitor and antioxidant. The study of *A. sericicarpus*, in terms of chemical composition as well as biological activities, is limited. The stembark extract of *A. sericicarpus* has been reported as an antimalarial agent. There is no report on the potency of *A. sericicarpus* as a cholinesterase inhibitor.

Materials and methods

Plant material

The leaves and stem of *A. sericicarpus* were collected from Balikpapan Botanical Garden, East Kalimantan, Indonesia in 2015. The voucher specimens (BPN-03) were kept at the Institute of Tropical Diseases, Universitas Airlangga. The plant was identified by Purwodadi Botanical Garden, East Java, Indonesia, with identification letter number: 0074/IPH.06/HM/XII/2015.

Chemicals

The reagents used for cholinesterase assays were acetylcholinesterase from electric eel (AChE type VI-S), acetylthiocholine iodide (ATCI), horse-serum butyrylcholinesterase (BChE), butyrylthiocholine iodide (BTCI), 5,5′-dithiobis[2-nitrobenzoic acid] (DTNB), bovine serum albumin (BSA), Tris buffer, and galantamine. The chemicals used for antioxidant assays were 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), and potassium persulfate. Folin-Ciocalteu's phenol reagent, sodium carbonate, and standard gallic acid were used for the determination of total phenolics. All reagents were obtained from Sigma-Aldrich.

Preparation of extracts

Freshly collected leaves and stems of *A. sericicarpus* were air-dried at room temperature for approximately seven days and then pulverized. Ten grams of the powdered leaves and stems were each extracted with ethanol using maceration protocol. The samples were soaked in the solvent (100 mL) for 24 hours, followed by vacuum filtration. The extraction process was repeated twice. Another extraction was carried out in water. Ten grams of the powdered leaves and stems were each soaked in water (100 mL) in an ultrasonic bath for 3 × 10 mins, frequency 50 Hz. The extract and residue were then separated by filtration. The residue was re-extracted using the same protocol twice. All collected filtrates from the ethanolic and water extracts were evaporated in a rotary evaporator to obtain crude ethanolic and water extracts.

Cholinesterase inhibitory assay

The assay was performed using a modified Ellman's protocol as has been reported in our previous publications (Ellman et al. 1961; Suciati et al. 2020, 2021, 2023; Aristyawan et al. 2022). Solution of extracts was prepared in methanol at a concentration of 10 mg/mL, then diluted with water to achieve a serial concentration of samples containing not more than 10% of methanol at 0.1–500 μg/mL (Mathew and Subramaniam 2014). In a 96-microwell plate, 25 μL of samples were mixed with 25 μL of 1.5 mM ATCI or 1.5 mM BTCI, 125 μL of 3 mM DTNB, 50 μL Tris buffer, and 25 μL of 0.22 U/mL AChE or BChE. The solutions were placed in a microplate reader (Thermo Scientific Multiskan FC) and shaken for 30 s before measurement. The absorbances were measured at 405 nm every 5 s for 2 mins before and after the addition of the enzymes. Experiments were performed in triplicates. Galantamine at 0.001–10 μg/mL in 10% methanol was used as a standard and 10% methanol was used as a control. The percentage of inhibition was then calculated with the equation below:

$$\%\ inhibition = \frac{(\text{Mean velocity of control} - \text{Mean velocity of sample})}{(\text{Mean velocity of control})}\ x\ 100$$

The 50% inhibitory concentration (IC_{50}) was calculated using GraphPad Prism 8.0 software (Dotmatics, USA) using log concentrations as axis and % inhibition as ordinate.

DPPH radical scavenging assay

The DPPH assay was carried out according to the modified method developed by Herald et al. (2012) and Lee et al. (2015). The extracts were diluted in methanol to obtain concentrations ranging from 0.5–30 µg/mL. The 0.25 mM DPPH solution was prepared by dissolving DPPH powder in methanol. Standard gallic acid was dissolved in methanol at 0.5–5 µg/mL. The samples (100 µL) and standard gallic acid were combined with 100 µL of DPPH in 96 microwell plates. As a control, DPPH reagent (100 µL) was mixed with methanol (100 µL), while methanol (200 µL) was used as a blank. The mixtures were then incubated in the dark at room temperature for 30 mins. The solutions were shaken for 30 s in a microplate reader (Thermo Scientific Multiskan FC), and the absorbances (A) were measured at 517 nm. The DPPH scavenging activity was calculated using the following formula.

$$\text{DPPH Radical Scavenging activity}\ (\%) = \frac{(\text{A control} - \text{A sample})}{(\text{A control})}\ x\ 100$$

ABTS radical scavenging assay

The ABTS assay was performed based on Lee et al. (2015) with some modifications. ABTS solution prepared in deionized wáter (5 ml, 7 mM) was mixed with potassium persulfate (88 μL, 140 nM). To produce ABTS radical, the mixture was kept in the dark at room temperature for 16 h. Sample solutions with concentration ranging from 0.5–30 μg/mL was prepared in methanol. The samples (100 μL) and ABTS (100 μL) were placed in a 96-well microplate, and incubated for 6 min in the dark at room temperature. The plates were shaken for 30 s in a microplate reader, followed by an absorbance (A) measurement at 734 nm. Gallic acid was used as standard at concentrations of 0.5–5 µg/mL in methanol. Experiments were carried out in triplicates, and the ABTS radical scavenging effect was calculated using following equation.

$$\text{ABTS Radical Scavenging activity}\ (\%) = \frac{(\text{A control} - \text{A sample})}{(\text{A control})}\ x\ 100$$

Determination of Total Phenolic Content (TPC)

The TPC of the extracts was measured using a slightly modified method developed by Zhang et al. (2006). In a 96-well microplate, twenty-five microlitres of serial dilution of gallic acid (25–500 µg/mL) or samples (1000 µg/mL) were added, followed by 75 µL of water and 25 µL of Folin & Ciocalteu's phenol reagent. The mixture was incubated at room temperature for 6 minutes. After that, 100 µL of Na_2CO_3 solution (75 g/L) was added to each well, followed by 90 minutes of incubation in the dark at room temperature. The mixtures were agitated for 30 s, and the absorbances were measured at 765 nm in a microplate reader (Thermo Scientific Multiskan FC). The TPC of samples was reported as milligrams of gallic acid equivalents (GAE) per gram extract.

LC-MS/MS analysis

The LC-MS/MS analysis was performed using Agilent 1260 Infinity Series HPLC connected to a QTOF 6540 UHD accurate mass spectrometer. The chromatographic separation was carried out with an analytical C-18 column (Phenomenex Luna C18(2), 150 × 4.6 mm, 5 µm, USA). A 10 µL sample solution (10 mg/mL in methanol) was introduced into the LC system and eluted with a solvent combination of water containing 0.1% formic acid (A), and acetonitrile with 0.1% formic acid (B). A linear gradient from 5 to 95% B in 30 mins, and hold on at this ratio for 10 mins at a flow rate of 0.5 mL/min. The ion source parameter was performed in positive mode with a mass range of *m/z* 100–1,000 amu. The ESI-MS condition parameters were as follows: drying gas (N2) 7 L/min; dry gas temperature at 350 °C; capillary voltage +3,500 V; and nebulizer pressure at 30 psig. Fragmentations were performed using auto MS/MS with collision energies at 10, 20, and 40 eV. Compound identification was carried out by comparing the MS data, MS/MS fragmentation profiles, and molecular formula with the literature data and databases such as Human Metabolome and MetFrag (https://msbi.ipb-halle.de/MetFrag/) with a maximum error of 5 ppm was accepted (Aristyawan et al. 2022; Suciati et al. 2023).

To perform a GNPS analysis the LC-QTOF-MS/MS data were converted to mmol file format using MSConvert software. The data were then transferred to the GNPS server (gnps.ucsd.edu) to generate the chemical networking map (ID = 79727b25f7a4487d904ba114b79a4319). The networks were created where edges were filtered to have a cosine score above 0.7 and more than 6 matched peaks. Precursor ion mass tolerance was set to 0.2 Da, while MS/MS fragment ion tolerance was set at 0.5 Da. The molecular networking data were visualized with Cytoscape software version 3.9.1. A ball-and-stick layout where nodes represent parent mass and cosine score was reflected by edge thickness (Nothia et al. 2020; Li et al. 2022; Putri et al. 2023; Suciati et al. 2023).

Results and discussion

Cholinesterase (ChE) inhibitory activities

The leaves and stem extracts were screened against AChE and BChE enzymes based on the modified Ellman's method. The cholinesterase inhibitory activity of the extracts expressed as IC_{50} values, calculated from the regression equations obtained from the activity of samples at different concentrations, was found to increase dose-dependently (Fig. 1). Overall, the leaves and stem extracts showed higher inhibition against AChE compared to BChE enzymes. The stem ethanolic extract gave the lowest IC_{50} values against AChE and BChE enzymes at 5.81 µg/mL and 11.46 µg/mL, respectively (Table 1). This data suggested that the stem extract is more potential as cholinesterase inhibitor compared to the leaves extract.

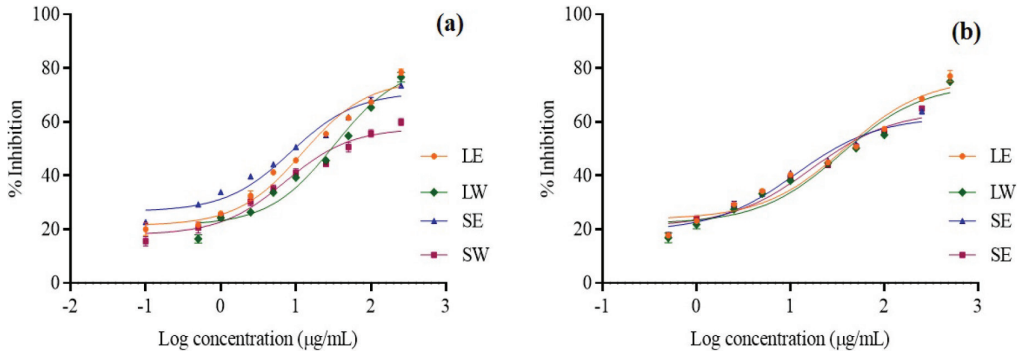

Figure 1. Concentration-dependent response of *A. sericicarpus* extracts against AChE (**a**) and BChE (**b**); each value is expressed as means ± SEM (n = 3). LE : leaves ethanolic extract; LW: leaves water extract; SE: stem ethanolic extract; SW: stem water extract

Antioxidant activity

Table 1. ChE inhibitory activity, antioxidant, and total phenolic contents (TPC) of *A. sericicarpus* extracts.

Sample[a]	IC_{50} (µg/mL)[b]				TPC[b] (mg GAE/g extract)
	AChE	BChE	DPPH	ABTS	
LE	12.31 ± 0.88	22.20 ± 0.60	10.54 ± 0.23	8.74 ± 0.03	217.23 ± 0.80
LW	32.41 ± 1.36	35.06 ± 0.23	17.61 ± 0.56	11.32 ± 0.03	157.61 ± 0.95
SE	5.81 ± 0.1	11.46 ± 0.10	14.42 ± 0.47	8.62 ± 0.32	215.60 ± 1.08
SW	8.10 ± 0.41	16.84 ± 0.26	17.43 ± 0.79	11.74 ± 0.13	140.80 ± 1.87
Gal	0.20 ± 0.01	1.33 ± 0.02	ND	ND	ND
GA	ND	ND	2.76 ± 0.02	0.97 ± 0.03	ND

[a]LE : leaves ethanolic extract; LW: leaves water extract; SE: stem ethanolic extract; SW: stem water extract, Gal: Galantamine; GA: Gallic acid.
[b]Data presented as mean ± SEM of three experiments, each carried out in triplicates.

The antioxidant activity of the extracts was evaluated by DPPH and ABTS tests. Table 1 shows the antioxidant activity of the studied extracts, expressed in terms of the amount of extract required to reduce into 50% the DPPH or ABTS concentration (IC_{50}). Both extracts showed similar strength of antioxidant activity in both DPPH and ABTS tests with IC_{50} values of 8.62–17.61 µg/mL. In general, the leaf and stem ethanolic extracts showed higher antioxidant capacity compared to the water-based extracts. The measurement of radical scavenging activity of the extracts at various concentrations suggested that the leaf and stem extracts of *A. sericicarpus* exhibited concentration-dependent antiradical activities in both DPPH and ABTS assays (Fig. 2).

Phytochemical analysis

The total phenolic contents (TPC) in the extracts were evaluated using a Folin-Ciocalteu reagent. The gallic acid standard curve equation (y = 0.0056× + 0.0492, R^2 = 0.9994) was used for the calculation of the TPC content in the extracts. The results as can be seen from Table 1 showed that the ethanolic extracts of the leaves and stems contain higher amounts of phenolic compounds compared to the water extracts. In order to identify the phenolic components in the ethanolic extracts, an LC-MS/MS analysis was carried out. The base peak chromatograms (BPC) of the extracts in the positive ion mode are presented in Fig. 3.

To analyze the difference between the leaves and the stem extracts in terms of chemical composition, a molecular networking study was carried out. The GNPS molecular networking (Fig. 4) shows the cluster of compounds present in the leaves and stem extracts. The green dots represent compounds identified in the leaves extract, the blue dots for compounds present in the stem extract, and the red dots for compounds identified in both leaves and stem extracts. The molecular networking analysis, as well as the base peak chromatograms, indicated that there are several compounds present in both the leaves and stem extracts. However, the difference between the two extracts is apparent. Fig. 4b shows an example of compound clusters that indicate the difference between the leaves and stem extracts. The molecular ions at m/z 611.162, 449.108, and 465.103 identified as rutin, kaempferol glucoside, and isoquercetin, respectively, are only present in the leaves extract, meanwhile the molecular ions at m/z 435.143, 437.159, 503.207, and 503.208 later identified as artobiloxanthone, artonin E, artonin B, and artonin A were only detected in the stem extract. Several sphingolipids compounds such as sphingosine, sphinganine and phyto-

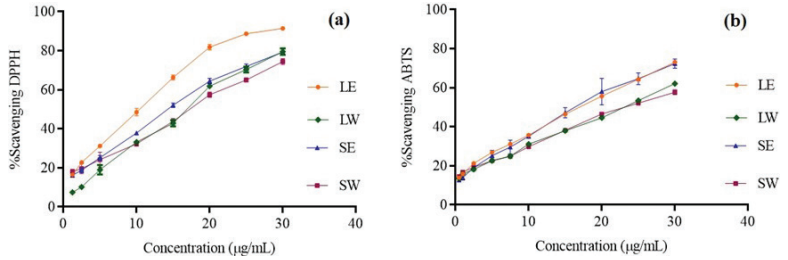

Figure 2. Radical scavenging effect of *A. sericicarpus* extracts in DPPH (**a**) and ABTS (**b**) assays; each value is expressed as means ± SEM (n = 3). LE : leaves ethanolic extract; LW: leaves water extract; SE: stem ethanolic extract; SW: stem water extract.

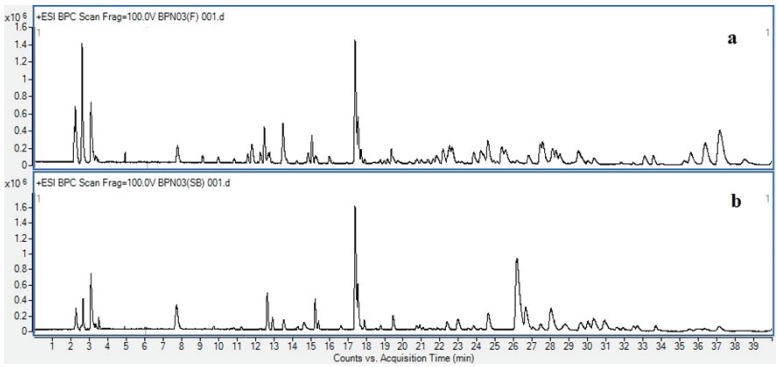

Figure 3. Base peak chromatograms (BPC) of the **a.** leaves and **b.** stem ethanolic extracts of *A. sericicarpus*.

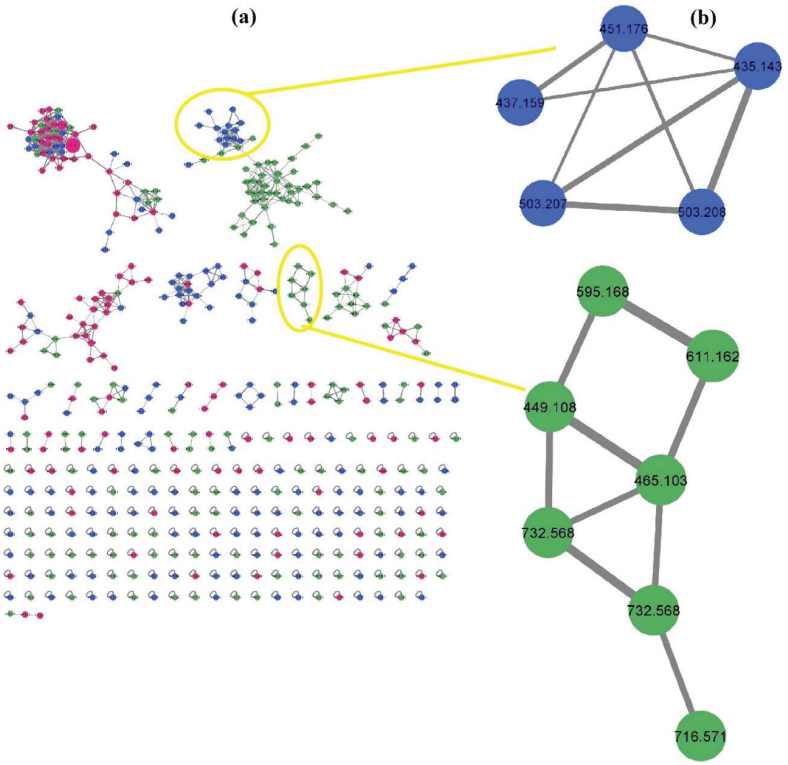

Figure 4. Molecular networking of the compounds from the leaves and stem extracts of *A. sericicarpus* (**a**) with expansion of selected clusters (**b**).

sphingosine can be detected in both extracts. Identified phenolic compounds from the extracts are presented in Tables 2, 3. Paratocarpins B–E and J–L were identified in the ethanolic extract of *A. sericicarpus* leaves. Paratocarpins are isoprenoid-substituted chalcones that were firstly reported from *Paratocarpus venenosa* Zoll (Syn. *Artocarpus venenosa*) (Hano et al. 1995a, 1995b). Prenylated chalcones were also reported from various *Artocarpus* spp., such as *A. lowii*, *A. bracteate*, *A. anisophyllus*, *A. fulvicortex*, and *A. elasticus* (Hakim et al. 2006; Jagtap and Bapat 2010; Lathiff et al. 2021; Zhai et al. 2022). Other phenolic compounds found in our samples are artonins A, B, E, J, K, M, and P, as well as artobiloxanthone, identified in the stem ethanolic extract. These compounds have also been reported from various *Artocarpus* species (Hakim et al. 2006; Jagtap and Bapat 2010; Lathiff et al. 2021).

Relation between phenolic contents, antioxidant, and ChE inhibitory activities

Phenolic compounds have been well-documented to play a significant role in the antioxidant activities of medicinal plants. The redox capacity of the phenolic compound is the primary contributor to its antioxidant activity, enabling it to effectively scavenge and counteract free radicals, break down peroxide, and extinguish singlet or triplet oxygen. Research findings indicate that the antioxidative potential of phenolic compounds is contingent upon the number and configuration of hydroxyl groups present in the compound (Jothy et al. 2012). Statistical analysis was carried out to evaluate the correlation between the total phenolic contents (TPC) of extracts and the antioxidant capacity as well as the ChE inhibitory activity. The Pearson's correlation showed a strong negative correlation between the ABTS radical scavenging

Table 2. LC-MS/MS analysis of phenolic compounds identified in the leaf ethanolic extract of *A. sericicarpus*.

RT[a] (mins)	$[M+H]^+$	Product ions *m/z*	Formula	Exact mass	Diff (ppm)	Proposed Compounds
9.984	355.1029	163.0385, 145.0285, 135.0438, 117.0326, 89.0381	$C_{16}H_{18}O_9$	355.1024	-1.52	Chlorogenic acid
9.986	163.0391	145.0278, 135.0438, 117.0336, 89.0379, 77.0382	$C_9H_6O_3$	163.0390	-0.79	Umbelliferone
11.815	611.1624	465.1022, 345.0609, 303.0502, 255.0862, 129.0539, 85.0280	$C_{27}H_{30}O_{16}$	611.1607	-2.84	Rutin
12.455	449.1086	349.0291, 287.0553, 139.0654, 95.0836	$C_{21}H_{20}O_{11}$	449.1087	-1.7	Kaempferol glucoside
12.473	465.1031	303.0500, 145.0491, 127.0388, 85.0274, 69.0320	$C_{21}H_{20}O_{12}$	465.1028	-0.75	Isoquercetin
15.313	517.1713	499.1622, 337.1083, 283.0613, 127.0407, 85.0280	$C_{26}H_{28}O_{11}$	517.1704	-1.67	Luteone glucoside
19.157	427.2115	409.2032, 337.1449, 299.1657, 257.1549, 227.1067, 185.0963, 71.0495	$C_{25}H_{30}O_6$	427.2115	0.04	Broussoflavan A
19.436	409.2012	353.1403, 257.1551, 231.1031, 201.0920, 173.0964, 123.0442, 69.0699	$C_{25}H_{28}O_5$	409.2010	-0.61	Paratocarpin J
21.349	423.1808	271.1329, 253.1232, 201.0927, 137.0234	$C_{25}H_{26}O_6$	423.1802	-1.38	Kuwanon F
22.526	409.2015	391.1921, 337.1450, 257.1546, 239.1441, 185.0965, 157.1019, 123.0433	$C_{25}H_{28}O_5$	409.2010	-1.34	Paratocarpin D
22.669	409.2017	337.1448, 257.1550, 239.1441, 185.0966, 185.0969, 123.0433	$C_{25}H_{28}O_5$	409.2010	-1.83	Paratocarpin E
25.548	339.1231	283.0618, 189.0919, 165.0186, 123.0089	$C_{20}H_{18}O_5$	339.1227	-1.18	Paratocarpin K
25.58	409.2015	353.1403, 257.1548, 201.0920, 69.0697	$C_{25}H_{28}O_5$	409.2010	-1.34	Paratocarpin L
27.581	391.1910	373.1820, 281.1551, 263.1440, 239.1446, 221.1338, 197.0974, 169.1015, 119.0489	$C_{25}H_{26}O_4$	391.1904	-1.57	Paratocarpin B
28.298	391.1912	337.1450, 241.1599, 209.0969, 185.0964, 155.0865, 137.0238, 69.0698	$C_{25}H_{26}O_4$	391.1904	-2.08	Paratocarpin C

Table 3. LC-MS/MS analysis of phenolic compounds identified in the stem ethanolic extract of *A. sericicarpus*.

RT[a] (mins)	$[M+H]^+$	Product ions *m/z*	Formula	Exact mass	Diff (ppm)	Proposed Compounds
13.537	583.1804	437.1241, 301.0711, 191.0334, 129.0545, 85.0280, 71.0487	$C_{30}H_{30}O_{12}$	583.1810	1.03	Epicatechin 3-*O*-(2-trans-cinnamoyl-beta-D-allopyranoside)
22.173	437.1609	395.1127, 381.0959, 363.0812, 339.0500, 113.0561, 79.0168	$C_{25}H_{24}O_7$	437.1595	-3.25	Artonin J
22.402	383.1137	365.1026, 341.0668, 323.0563, 295.0603, 83.0856	$C_{21}H_{18}O_7$	383.1125	-3.06	Artonin K
26.193	435.1432	393.0982, 321.0393, 219.0291, 163.0379, 121.0282	$C_{25}H_{22}O_7$	435.1438	1.45	Artobiloxanthone
26.667	437.1587	381.0978, 363.0873, 335.0914, 283.0949, 189.0178	$C_{25}H_{24}O_7$	437.1595	1.78	Artonin E
31.612	503.2081	461.1608, 447.1446, 405.0976, 231.0827, 139.1107	$C_{30}H_{30}O_7$	503.2064	-3.32	Artonin A
32.083	449.1246	407.0736, 393.0974, 379.0817, 337.0723, 67.0358	$C_{25}H_{20}O_8$	449.1231	-3.35	Artonin M
32.702	503.2070	447.1450, 405.0976, 311.2965, 261.0760, 213.0554, 55.0161	$C_{30}H_{30}O_7$	503.2064	-1.13	Artonin B
36.124	503.2072	447.1452, 373.1676, 191,0297, 79.0522	$C_{30}H_{30}O_7$	503.2064	-1.53	Artonin P

activity and the TPC of extract (r = -0.996, p = 0.004). This indicates that the higher the TPC value of extract the lower the IC_{50} value in the ABTS radical scavenging activity. The correlation is considered significant if $p \leq 0.05$. A strong correlation was also observed between total phenols and the deactivation of DPPH radicals, although the correlation was not statistically significant (r = -0.869, p = 0.131). There were weak correlations between total phenols and the ChE inhibitory activity in both AChE and BChE enzymes (r = -0.378, p = 0.622, r = -0.377, p = 0.623, respectively).

The findings of our study are in accordance with those reported in the previous study of *Artocarpus* spp. The antioxidant potential of several *Artocarpus* has been reported (Buddhisuharto et al. 2021; Hawari et al. 2021). The seed, peel and pulp of *A. heterophyllus* showed DPPH radical scavenging activity due to its phenolic and flavonoid compounds. Antioxidant activity was also reported from the fruit and stem bark extract of *A. altilis* as well as the seed extract of *A. hirsutus*. Isolated compounds with antioxidant capacity of *Artocarpus* have also been reported (Lathiff et al. 2021) Isobavachalcone, 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone, and 4-hydroxyonchocarpin from *A. lowii* gave strong radical scavenging activity in the ABTS, DPPH and FRAP assays (Abdullah et al. 2017). Another chalcones, elastichalcone B and cycloartocarpesin isolated from *A. elasticus* showed promising antioxidant activity in the TLC bioautography assay against DPPH and in the 96-well microplate reader with IC_{50} values of 11.30 and 11.89 μg/mL, respectively (Ramli et al. 2013). Several artobiloxanthones isolated from *A. obtusus* and *A. anisophyllus* showed significant antioxidant properties in the DPPH assay (Hashim et al. 2012; Lathiff et al. 2015). These findings suggest the promising antioxidant activity of flavones, chalcones and xanthones from *Artocarpus* spp. Reports on ChE inhibitory activity of *Artocarpus* is limited. Arylbenzofurans and methyl ether analogs from *A. lakoocha* were reported as potent cholinesterase inhibitor with IC_{50} values ranging from 0.87–1.10 μM. The lower correlation between the total phenolic content of the extract and the ChE inhibitory activities suggested that only specific type of phenolic compounds can interact with AChE and BChE enzymes. To the best of our knowledge, there is no report on the antioxidant and ChE inhibitory activity of *A. sericicarpus*.

Conclusions

Artocarpus sericicarpus leaf and stem extracts exhibited significant cholinesterase inhibitory activity against AChE and BChE, as well as antioxidant activity. The ethanolic extracts of the leaves and stems were more effective as antioxidants and cholinesterase inhibitors than their water-based counterparts. The phenolic compounds, such as flavones, flavonols, flavanones, chalcones, and xanthones present in the extracts, may contribute to the antioxidant and cholinesterase inhibitory activities of the extracts.

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