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Antioxidant, α-glucosidase inhibitory, and profiling metabolites on different parts of mangrove *Sonneratia x urama*

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ABSTRACT

Sonneratia (Lythraceae), a mangrove plant genus, is a source of metabolites and has been used in traditional medicine. This study investigated the phytochemical content, antioxidant, and α-glucosidase inhibitory activities of different plant parts of *Sonneratia x urama* extracts and profiled metabolites in the most active extract. The result showed that the fruit, root, and stem bark of *S. x urama* extract contained high phenolics. The highest total phenolic content (TPC) (460.77±1.71 mgGAE/g dry extract) and total flavonoid contents (TFC) (16.18±0.08 mgQE/g dry extract) were recorded in stem bark extract compared to other extracts. This extract also showed the highest antioxidant capacity based on DPPH, FRAP, and ABTS methods with 4838.31±7.77, 2586.95±3.23, and 1953.83±11.35 µmolTE/g dry extract, respectively. α-glucosidase inhibitory assay showed that the stembark of *S. x urama* has the highest activity with IC_{50} 64.07±7.23 µg/mL. Furthermore, LC-MS/MS was used to profile the metabolites of the stem bark extract. Stem bark extract contained several putative compounds such as 3,4'-di-O-methyl ellagic acid, ellagic acid, hallactone B, luteolin 7-O-glucuronide, 3,4-dihydroxy mandelic acid, chelirubine, gallic acid, etc. These findings suggested that the stem bark, fruit, and root of *S. x urama* can be a potential source of antioxidant and antidiabetes agents.

1. Introduction

Diabetes is a class of metabolic disorders marked by increased blood sugar levels (hyperglycemia) caused by deficiencies or impaired secretion of insulin [1]. Hyperglycemia induces reactive oxygen species (ROS), which leads to oxidative stress [2]. Diabetes-related

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chronic hyperglycemia is connected to long-term harm, malfunction, and damage of different organs, especially the heart, blood vessels, kidneys, eyes, and nerves [1]. The International Diabetic Federation reports that in 2021, 537 million people aged 20-79 years have diabetes, which is expected to increase to 643 million in 2030 and 783 million in 2045[3]. Some diabetes drugs have lowered blood glucose levels, but they cause side effects such as excessive hypoglycemia, weight gain, nausea, bloating, headache, pharyngitis, diarrhea, and others [4]. However, the increasing prevalence of hyperglycemia and the side effects of commercial diabetes drugs have increased the need to find new drugs to control blood glucose levels. Therefore, plants or herbal medicine are becoming a good source of new diabetes drugs with little or no side effects [5,6].

Mangrove plants grow in tropical and subtropical regions along rivers, estuaries, and shorelines [7]. They produce primary metabolites like proteins, amino acids, and carbohydrates necessary for life. In contrast, secondary metabolites such as alkaloids, phenolics, steroids, and terpenoids have pharmacological, ecological, and toxicological effects [8].

Sonneratia, a mangrove plant genus, belongs to the family Lythraceae and extends from East Africa to Indo-Malaya, tropical Australia, Micronesia, and Melanesia [9]. Various parts of several *Sonneratia* species, fruit, bark, and leaves, have been used in traditional medicine to arrest hemorrhage, treat asthma, hepatitis, febrifuge, swelling, sprains, and diabetes [8,10]. Several species of *Sonneratia* e.g *S. ovata, S. caseolaris, S. paracaseolaris, S. apetala, S. hainanensis* have been studied about chemical constituents, and the results have included a variety of structure compounds, including phenolics [11], terpenoids [11–14], alkaloids [15], and flavonoid compounds [13]. Extract and chemical compounds from *Sonneratia* plants have been reported to contribute to antioxidant activity [16,17], antiaging [11], antibacterial [18], anticancer[19], and anti-diabetes activities[20,21]. Extract of some *Sonneratia* species showed α-glucosidase inhibitory activities [19,22], and antidiabetes in vivo [23–26] .

Sonneratia x urama is a natural hybrid of *S. alba* and *S. lanceolata*. *S. x urama* tree can reach 10-20 m high, and has a spreading and dense canopy, flowering and fruiting throughout the year [27]. It has been reported to grow in Indonesia, Australia, and Papua New Guinea [28], besides *S. caseolaris, S. alba,* and *S. ovata*, which were reportedly distributed in Indonesia [29].

In the preliminary test, we found the presence of phytochemicals such as flavonoids, alkaloids, tannins, saponins, and terpenoids in the fruit, root, and stembark of *S. x urama*. However, studies on chemical compounds, antioxidants, and antidiabetes from *S. x urama* are not yet available. Therefore, this study evaluated the phytochemical content such as TPC (total phenolic content) and TFC (total flavonoid content), antioxidant capacities based on DPPH (2,2–diphenyl picrylhydrazyl), FRAP (Ferric Reducing Antioxidant Power), ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid), α-glucosidase inhibitory activity on different parts of *S. x urama* and identification the metabolites based on LCMS/MS in the most active extract of *S. x urama*.

2. Materials And Methods

2.1. Plant materials

Sonneratia x urama was collected from Barito Kuala Regency, South Kalimantan, Indonesia. The plant was identified by Dr. Gunawan from the Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Lambung Mangkurat, South Kalimantan, Indonesia. The fruits, roots, and stem bark of *S. x urama* were air-dried and ground into powder.

2.2. Extraction

Fruit (200 grams), root (100 grams), and stembark (200 grams) powder were macerated with methanol (1: 5 w/v) for 24 hours. Each extract was filtered with Whatman filter paper. The residue was remacerated with methanol (3 times). The filtrate was concentrated in a rotary vacuum evaporator and then dried in a water bath to yield the methanol extract of fruit, root, and stem bark of *S. x urama*. Percent yield calculated based on equation (1).

$$\boldsymbol{Yield}\ (\%) = \frac{\textbf{weight extract}}{\textbf{weight sample}}\boldsymbol{x}\ \mathbf{100\%} \quad (1)$$

2.3. Determination of total phenolic content (TPC)

The total phenolic content of fruit, root, and stem bark extract of *S.x urama* was determined using the Folin-Ciocalteu method [30]. A total of 0.5 mL of extract or standard solution with a certain concentration was mixed with 0.5 mL of Folin–Ciocalteu solution (Sigma-Aldrich), 1 mL sodium carbonate solution (7.5 %) (Merck), and 8 mL aquadest in a tube. The mixture was incubated (20 minutes) in a water bath at a temperature of 65▫C and then cooling the tubes in cool water. The absorbance was measured employing a UV–vis spectrophotometer at 765 nm. The standard curve of gallic acid (Sigma-Aldrich) features a 50–175 mg/L concentration. The TPC values were calculated from a linear regression equation, and TPC values were expressed in equivalent to gallic acid (mg GAE)/g dry weight extract.

2.4. Determination of total flavonoid content (TFC)

Determination of total flavonoid content (TFC) based on the aluminium trichloride method, as described by [31]. Two milliliters of sample or standard was added to 2 mL 2% $AlCl_3$ solution (Sigma-Aldrich) and vortexed for 5 seconds. After 30 minutes, the absorbance of solutions was measured using a UV–vis spectrophotometer at 415 nm. The standard curve of quercetine (Sigma-Aldrich) has 2-20 mg/L concentration. The TFC values were calculated from a regression linear equation, and TFC values were expressed to Quercetine equivalent (mg QE)/g dry weight extract.

2.5. Antioxidant capacity based on DPPH method

The DPPH (2,2–diphenyl picrylhydrazyl) radical scavenging activity analysis was described by [32]. A total of 2 mL of extract or standard solutions was added to 2 mL of 0.15 mM DPPH, vortexed for 5 seconds, and incubated for 30 minutes in a dark room. Absorbance was measured using a UV-Vis spectrophotometer at a wavelength of 515 nm. A Trolox standard curve was generated with 5-70 µmol/L concentrations. The percentage inhibition was calculated using equation (2).

$$\boldsymbol{Inhibition}\ (\%) = \frac{(\mathbf{Ac} - \mathbf{As})}{\mathbf{Ac}}\boldsymbol{x}\ \mathbf{100} \qquad \mathbf{(2)}$$

where
Ac = Absorbance of control (DPPH)
As = Absorbance of sample
The antioxidant capacity (DPPH) values were calculated from a linear regression equation and were expressed in µmol Trolox equivalent/g dry weight extract (µmolTE/g).

2.6. Antioxidant capacity based on FRAP method

The FRAP (Ferric Reducing Antioxidant Power) analysis was performed using a modified technique by [33]. FRAP solution was prepared before measurement by mixing 2.5 mL of 10 mM TPTZ reagent with 25 mL of acetate buffer pH 3.6 and 2.5 mL of 20 mM $FeCl_3 \cdot 6H_2O$ and adding distilled water to precisely 100 mL in a flask. A total of 1 mL of extract or standard solution was added with 3 mL of FRAP reagent. The solution was incubated in the dark for 15 minutes, and the absorbance was measured using a UV-Vis spectrophotometer at 598 nm. The $FeSO_4 \cdot 7H_2O$ standard curve was generated at 100-250 µmol/L concentrations. The Trolox standard curve was generated at a 25-75 µmol/L concentration. The antioxidant capacity (FRAP) values were calculated from a linear regression equation and were expressed in µmol Trolox equivalent/g dry weight extract (µmolTE/g).

2.7. Antioxidant capacity based on ABTS method

The ABTS (2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) assay was described by [34]. An ABTS radical cation solution was made by mixing 7 mM ABTS and 2.45 mM potassium persulfate (in 50% (v/v) ethanol) and left overnight at room temperature in the dark. Subsequently, 50% (v/v) ethanol was added to the solution to obtain an absorbance of 0.700 ± 0.005 at 734 nm. A total of 2.5 mL of diluted ABTS radical cation solution and 0.25 mL of extract or standard solution were combined and incubated for 12 minutes in the dark. The absorbance was measured at 734 nm. The Trolox standard curve was generated at a 10-125 µmol/L concentration. The antioxidant capacity (ABTS) values were calculated from a linear regression equation and were expressed in µmol Trolox equivalent/g dry weight extract (µmolTE/g).

2.8. α-glucosidase inhibitory assay

The alpha-glucosidase inhibitory assay was carried out as described by [35]. The α-glucosidase enzyme solution was prepared by homogenizing 1 g of rat intestinal acetone powder (Sigma, St. Louis) with 30 ml of normal saline, then centrifuging at 12,000 rpm for 30 minutes. The supernatant was ready for use in the assay. About 10 µL of different dilutions of extract were reacted with 50 µL phosphate buffer (0.1 M, pH 6.9) and 20 µL maltose (10 mM in phosphate buffer pH 6.9), 80 µL glucose kit, and 20 µL α-glucosidase enzyme. The mixtures were incubated for 10 minutes at 37˚C, and then the absorbance was measured by Victor Nivo Multimode Plate Reader (Revvity) at 520 nm. Inhibition (%) was calculated based on equation (3).

$$\boldsymbol{Inhibition}\ (\%) = \frac{(\mathbf{A\ blank} - \mathbf{A\ sample})}{\mathbf{A\ blank}}\boldsymbol{x}\mathbf{100} \qquad \mathbf{(3)}$$

Where
A blank = Absorbance enzyme reaction – Absorbance blank of enzyme, and
A sample = Absorbance sample reaction – Absorbance blank of sample reaction.
The IC_{50} values were calculated from a nonlinear regression equation and were expressed in µg/mL.

2.9. LC-MS/MS analysis

S. x urama stembark extract (5 mg) was diluted in 1 mL MeOH and filtered through a 0.2 µm nylon membrane. UHPLC Vanquish Tandem Q Exactive Plus Orbitrap HRMS ThermoScientific was used for the analysis. The separation column was an Accucore C18, 100 x 2.1 mm, 1.5 µm (ThermoScientific). H_2O + 0.1% formic acid (A) and acetonitrile + 0.1% formic acid (B) made up the eluent. The following was the programming for the gradient elution: 0–1 min (5% B), 1–25 min (5–95% B), 25–28 min (95% B), and 28–33 min (5% B). The injection volume was 2 µL, and the flow rate was 0.2 mL/min. The mass

spectrometer was run in an electrospray ionization (ESI) source in negative mode and scanning range of m/z 100–1,500 with Chemspider and MzCloud Database.

2.10 Statistical Analysis

Data were presented as mean ± standard deviation (SD) with 3 replications. Statistical analysis was performed using Origin Pro 2024 software. Data were subjected to One Way ANOVA (Analysis of Variance) with α 0.05, followed by the Turkey test to compare differences in significance between samples. Correlation between TPC, TFC, DPPH, FRAP, ABTS and α-glucosidase inhibitory was done using Pearson correlation analysis.

3. Results and Discussion

3.1. Extraction

Table 1. Yield of methanol extract of different parts of *S. x urama*

Extract	Yield	
	Weight (g)	% w/w
Fruit	17.40	8.70
Root	6.68	6.68
Stembark	17.06	8.53

Different parts of *S. x urama* plant were extracted using a methanol solvent. Table 1 showed the yield of the methanol extract of different parts *S. x urama*. Methanol extract of the fruit had the highest yield (8.70%w/w), followed by stem bark with an equivalent yield to fruit (8.53%w/w), and finally, the root of *S. x urama*, which had the lowest yield. The extraction yields might depend on plant organ characteristics and the amount of phytochemical constituents dissolved in methanol.

3.2. Total Phenolics and Flavonoids Content

Table 2 revealed the TPC and TFC values of different parts of *S. x urama*. Methanol can extract phenolic compounds, including flavonoids, from *S. x urama* well. The TPC values of different plant parts of *S. x urama* ranged from 121.58±0.16 to 460.77±1.71 mgGAE/g. Various parts of plant *S. x urama* contain high phenolic compounds, based on criteria TPC > 70 mg GAE/g [36]. The stembark of *S. x urama* had the highest TPC and TFC, followed by root and fruit.

Table 2. The TPC and TFC of *S. x urama.*

Extract	TPC (mgGAE/g)	TFC (mgQE/g)
Fruit	121.58±0.16[a]	8.63±0.11[a]
Root	131.65±0.13[b]	12.68±0.02[b]
Stem bark	460.77±1.71[c]	16.18±0.08[c]

[a,b,c]Mean ± SD (n=3) with the different superscripts in the same column are significantly different ($p < 0.05$).

The TPC value of *S. x urama* fruit was similar to that of *S. caseolaris* fruit (122 mg GAE/g), but the TFC value of *S. x urama* fruit was lower than that of *S. caseolaris* fruit (613 mgQE/g) [37]. The TPC of root *S. x urama* was higher than root *S. caseolaris* (119.44 ± 3.99 mgGAE/g) [38], and TPC in stembark of *S. x urama* was higher than bark *S. alba* (10.248±0.174 mgGAE/g) [39]. The TFC in various parts of *S. x urama* was lower than the bark of *S. alba* [40].

Phenolic compounds, including flavonoids, tannins, lignans, phenolic acids, etc., are known as potent antioxidants, and they can prevent damaged cells or diseases caused by oxidative stress, such as inflammation, cancer, diabetes, and cardiovascular disease [41].

3.3. Antioxidant Capacity

The antioxidant capacity of different parts of *S. x urama* was determined by DPPH, FRAP, and ABTS methods and was expressed in the Trolox equivalents (TE) unit. The DPPH and ABTS methods are based on scavenging free radicals (DPPH) or radical cations (ABTS) by mixed hydrogen atom hydrogen (HAT) and single electron transfer (SET) mechanism from antioxidants. In contrast, FRAP is based on single electron transfer mechanism to reducing Fe^{3+}-TPTZ to Fe^{2+}-TPTZ [41,42].

Table 3 showed that stem bark, root, and fruit extracts of *S. x urama* have high DPPH and ABTS free radical scavenging capacity. The order of antioxidant capacity (DPPH) of *S. x urama* extract is stembark>fruit>root. This is also consistent with the order of antioxidant capacity of *S. x urama* extracts in scavenging ABTS radical cations. Meanwhile, the order of the ability of *S. x urama* extract to reduce Fe^{3+} to Fe^{2+} is stem bark>root>fruit.

Table 3. The antioxidant capacity of *S. x urama*

Extract	DPPH (µmolTE/g)	FRAP (µmolTE/g)	ABTS (µmolTE/g)
Fruit	1232.20±1.60[a]	541.32±0.72[a]	1169.35±4.67[a]
Root	1196.58±2.52[b]	812.14±0.99[b]	708.49±4.67[b]
Stembark	4838.31±7.77[c]	2586.95±3.23[c]	1953.83±11.35[c]

[a,b,c]Mean ± SD (n=3) with the different superscripts in the same column are significantly different ($p < 0.05$).

The antioxidant capacity of DPPH and FRAP of *S. x urama* fruit is smaller than that of *Rhodomyrtus tomentosa* fruit, namely 1419.75 ± 3.48 and 1367.59 ± 9.12 µmol TE/g DW, respectively [32]. Meanwhile, the stem bark of *S. x urama* has a greater antioxidant capacity in both DPPH and FRAP than other extracts of *S.x urama*. The antioxidant capacity by ABTS of the fruit and root of *S.x urama* is smaller than ethanol clove extract (1652.97 ± 109.58 µmolTE/g). In contrast, the stembark extract of *S.x urama* is greater than clove extract [43].

3.4 α-glucosidase inhibitory

The α-glucosidase enzyme plays a key role in carbohydrate metabolism. Inhibition of this enzyme can delay the digestion of disaccharides, leading to malabsorption and a subsequent decrease in postprandial blood glucose levels [44]. Therefore, extracts or chemical compounds that inhibit α-glucosidase may have potential as antidiabetes agents.

Table 4. The in vitro antidiabetes assay based on α-glucosidase inhibitory assay

Sample	% Inhibition	IC_{50} (µg/mL)
Fruit	89.48±4.27[a]	96.42±10.44[a]
Root	88.03±2.80[a]	214.64±14.24[b]
Stembark	89.03±1.42[a]	64.07±7.23[c]
Acarbose	99.61±0.19[b]	57.88±0.88[c]

[a,b,c]Mean ± SD (n=3) with the different superscripts in the same column are significantly different ($p < 0.05$).

Table 4 showed the α-glucosidase inhibitory of different parts of *S.x urama* extract and the positive control, acarbose. Fruit, root, and stembark extract at a final concentration of 625 µg/mL have similar inhibition in the 88.03±2.80 to 89.48±4.27% range. A series concentration of fruit, root, and stem bark of *S.x urama* was tested in an α-glucosidase inhibitory assay and then given the IC_{50}. The stembark extract had the strongest α-glucosidase inhibitory activity, followed by the fruit and root. The IC_{50} of stembark 64.07±7.23 µg/mL was similar (0.9-fold) to the IC_{50} of acarbose. Alpha-glucosidase inhibitory activity of the stem bark extract is 0.9-fold to acarbose activity. Meanwhile, fruit and root were 1.7-fold and 3.7-fold, respectively, weaker than acarbose.

The alpha-glucosidase inhibitory activity of the methanolic extract of the stem bark, root, and fruit of *S. x urama* was stronger compared to the methanolic extract of the bark of *S. apetala* (IC_{50} 0.432 ± 0.010 mg/mL) [22], but weaker than that of the ethanolic extract of *S. ovata* fruits 1.86 µg/mL [45].

3.5 Metabolite profiling of stem bark extract

Metabolite profile analysis aims to determine the components or metabolites present in a sample. Metabolite profiling studies generally separate complex metabolites or extracts using chromatography techniques coupled with a mass spectrometer (MS), such as gas chromatography-mass spectrometry (GC-MS) or liquid chromatography-mass spectrometry (LC-MS). Among these, LC-MS method is the most widely used for analyzing medicinal plants. This technique is not limited by metabolite volatility or stability and does not require sample derivatization [46,47]. Volatile and semi-volatile compounds are typically identified using GC-MS/MS, whereas LC-MS/MS is employed to detect non-volatile and polar metabolites [48].

LC-MS/MS was used to investigate metabolites in the methanolic extract of *S. x urama* stembark, the most active extract. The liquid chromatography profile of methanol stembark extract of *S. x urama* is shown in Fig.1. Some of the chemical compounds present in the methanol extract of stembark have not yet been identified (unknown). The metabolites identified are shown in Table 5.

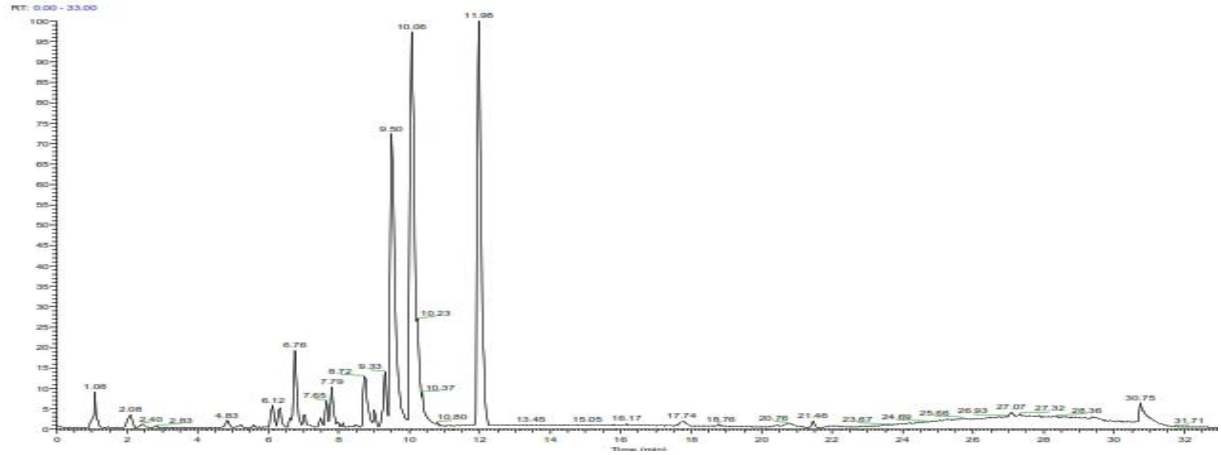

Fig.1. Liquid chromatography profile of methanol stembark extract *S. x urama*.

Table 5. Putative compounds in the stem bark methanol extract of *S. x urama*.

No	RT (min)	Moleculer Formula	Major ion (M-H) m/z	Calc. Moleculer Weight	Putative Compound/metabolite
1	1.086	$C_6 H_{14} O_6$	181.07088	182.07815	Hexitol
2	1.089	$C_5 H_{12} O_5$	151.06024	152.06752	L-(-)-Arabitol
3	1.103	$C_7 H_{14} O_8$	225.06114	226.06822	Glucoheptonic Acid
4	1.107	$C_6 H_{12} O_6$	179.05536	180.06253	Hex-2-ulose
5	1.083	$C_6 H_{12} O_9 S$	259.01254	260.01982	6-O-Sulfo-alpha-D-galactopyranose
6	1.151	$C_7 H_{10} O_7$	205.03479	206.04207	2-methylcitric acid
7	1.159	$C_{20} H_{18} O_{14}$	481.06195	482.06923	1,4,8,9,10,11,12,13-Octahydroxy-3-(hydroxymethyl)-3,4,4a,16a-tetrahydro-1H-dibenzo[f,h]pyrano[3,4-b][1,4]dioxecine-6,15-dione
8	1.176	$C_4 H_6 O_5$	133.01338	134.20660	DL-Malic acid
9	2.067	$C_7 H_6 O_5$	169.01332	170.0206	Gallic acid
10	2.394	$C_{13} H_{16} O_{13} S$	411.02332	412.03059	Turgorin
11	6.12	$C_8 H_8 O_5$	183.02901	184.03628	3,4-dihydroxy mandelic acid
12	6.325	$C_{21} H_{16} N O_5$	361.09595	362.10322	Chelirubine
13	6.389	$C_{34} H_{24} O_{22}$	783.06775	784.07515	Pedunculagin
14	6.735	$C_{41} H_{28} O_{26}$	935.07800	936.08528	Casuarictin
15	7.094	$C_{24} H_{32} O_5 S$	431.19171	432.19899	3,4a,5-Trimethyl-6-{[(2E)-3-(methylsulfanyl)-2-propenoyl]oxy}-4,4a,5,6,7,8,8a,9-octahydronaphtho[2,3-b]furan-4-yl (2E)-2-methyl-2-butenoate
16	7.406	$C_{11} H_{14} O_8 S$	305.03348	306.04075	5-(3,4-Dihydroxyphenyl)-4-hydroxypentanoyl hydrogen sulfate
17	7.487	$C_{21} H_{10} O_{13}$	469.00415	470.01143	3,4-Dihydroxy-5-[(2,3,7,8-tetrahydroxy-5,10-dioxo-5,10-dihydrochromeno[5,4,3-cde]chromen-1-yl)oxy]benzoic acid atau sanguisobic acid dilactone
18	7.595	$C_{22} H_{28} O_{11} S$	499.12753	500.1346	[7-Hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-3-(hydroxymethyl)-6,8-dimethoxy-1,2,3,4-tetrahydro-2-naphthalenyl]methyl hydrogen sulfate
19	7.647	$C_{21} H_{26} O_{10} S$	469.11667	470.12395	1-(10-Butyryl-5,7-dihydroxy-8,8-dimethyl-2-oxo-7,8-dihydro-2H,6H-pyrano[3,2-g]chromen-4-yl)-2-propanyl hydrogen sulfate
20	7.87	$C_{14} H_{10} O_8$	305.02997	306.03724	2-Protocatechuoyl phloroglucinol carboxylic acid
21	8.104	$C_{13} H_{10} O_8$	293.0301	294.03746	Tricrozarin A
22	8.486	$C_{21} H_{18} O_{13}$	477.06686	478.07414	Quercetin-3'-glucorinide
23	8.732	$C_{28} H_{12} O_{16}$	603.00433	604.01161	Gallagic acid
24	8.738	$C_{14} H_6 O_8$	300.99641	302.00569	Ellagic acid
25	9.305	$C_{20} H_{24} O_9 S$	439.10602	440.11333	Hallactone B

26	9.684	$C_{21}H_{18}O_{12}$	461.07175	462.07902	luteolin 7-O-glucuronide
27	10.366	$C_9H_{14}O_4$	185.08101	186.08829	cis-2-Carboxycyclohexyl-acetic acid
28	11.968	$C_{16}H_{10}O_8$	329.02954	330.03682	3,4'-di-O-methyl ellagic acid
29	13.14	$C_{18}H_{34}O_5$	329.23306	330.24034	(-)-pinellic acid
30	14.113	$C_{17}H_{12}O_8$	343.0455	344.05278	3,4,3'-Tri-O-methylellagic acid
31	16.166	$C_{30}H_{48}O_5$	487.34201	488.34929	Asiatic acid
32	18.756	$C_{25}H_{49}O_{12}P$	571.28815	572.29542	(2R)-2-Hydroxy-3-[(hydroxy{[(1S,2R,3R,4S,5S,6R)-2,3,4,5,6-pentahydroxycyclohexyl]oxy}phosphoryl)oxy]propyl palmitate
33	19.811	$C_{39}H_{54}O_7$	633.37801	634.38618	3-{[(2E)-3-(3,4-Dihydroxyphenyl)-2-propenoyl]oxy}-2-hydroxylup-20(29)-en-28-oic acid
34	24.435	$C_{30}H_{48}O_3$	455.35239	456.35966	Oleanolic acid

Most metabolites in stem bark were phenolic compounds, including phenolic acid, flavonoids, and tannins. In addition, some terpenoids, fatty acid, and carbohydrates were in stembark methanol extract. Based on LC-MS/MS analysis, there were dominant compounds i.e 3,4'-di-O-methyl ellagic acid, ellagic acid, hallactone B, luteolin 7-O-glucuronide, 3,4-dihydroxy mandelic acid, chelirubine, and gallic acid. Some of the putative compounds and their related compounds in *S. x urama* have been isolated from *Sonneratia* species. Oleanolic acid has been isolated from the fruit of *S. caseolaris* and *S. ovata* meanwhile luteolin and luteolin 7-O-glycoside have been isolated from *S.caseolaris* [13]. Gallic acids derivated have been isolated from *S. ovata* leaves [14]. Similar chemical compositions are typically found in taxonomically related plants because they are produced by conserved metabolic pathways [49]. Thus, the similar compounds or natural modifications of these compounds are very likely to be found in plants of different species in the same genus.

According to previous research, ellagic acid is an antioxidant, antihepatotoxic, antisteatosic, anti cholestatic, antifibrogenic, antihepatocarcinogenic and antiviral properties [50]. Ellagic acid derivated e.g. 3,3 -di-O-methyl ellagic acid had antioxidant and antimicrobial activities [51]. Chelirubine had antiproliferative and anti-apoptotic activity [52]. Oleanolic acid is α-glucosidase inhibitors with IC_{50} 6.29±0.7 µg/mL [53]. Luteolin is active as an antioxidant, anti-tumor, anti-inflammatory, antibacterial, and analgesic [54]. Luteolin-7-O-glucoride has anti-inflammatory activity [55]. Gallic acid is prospective as an antioxidant [56] and antidiabetes [57].

3.5 Correlation of TPC, TFC, Antioxidant, and α-glucosidase inhibitory

The relationship between TPC, TFC, and antioxidant capacities of different parts of *S. x urama* extracts is shown in Table 6. A positive and very strong correlation existed between TPC and TFC with r=0.85979. It means that the TPC content increases as the TFC increases.

Table 6. Pearson correlation coefficient of TPC, TFC, and antioxidants capacities of *S. x urama*

	TPC	TFC	DPPH	FRAP	ABTS	α-glucosidase inhibitory
TPC	1					
TFC	0.85979	1				
DPPH	0.99938	0.84156	1			
FRAP	0.98902	0.77495	0.99355	1		
ABTS	0.92072	0.59261	0.93362	0.96822	1	
α-glucosidase	-0.62036	-0.2022	-0.64403	-0.72086	-0.86768	1

TPC has a positive and very strong correlation with the antioxidant capacities of DPPH, FRAP, and ABTS, with r=0.99938, r=0.98902, and 0.92072, respectively. It is indicated that TPC has contributed to the antioxidant capacity of *S. x urama*. Furthermore, TFC showed a positive and very strong correlation with antioxidant capacities DPPH (r=0.84156) and FRAP (r=0.77495), and a strong correlation with ABTS (r=0.59261). TPC and TFC

are positively associated with the antioxidant capacity of different parts of *S.x urama*. On the other hand, a negative correlation was recorded on α-glucosidase with antioxidant capacities (DPPH, FRAP, ABTS), TPC, and TFC. It shows an inverse relationship between α-glucosidase with TPC, TFC, DPPH, FRAP, and ABTS. Alpha-glucosidase showed a very strong correlation with ABTS (r= -0.86768), a strong correlation with FRAP (r= -0.72086), and a moderate correlation with DPPH (r= -0.64403).

4. Conclusion

This study showed that different parts of *S. x urama* e.g stembark, fruit, and root, had potent antioxidant and antidiabetes agents. The stembark extract revealed has the highest TPC, TFC, antoxidant capacity (DPPH, FRAP, and ABTS), and α-glucosidase inhibitory activity compared to other extracts. LC-MS/MS analyzed showed that stem bark extract contained several putative compounds such as 3,4'-di-O-methyl ellagic acid, ellagic acid, hallactone B, luteolin 7-O-glucuronide, 3,4-dihydroxy mandelic acid, chelirubine, gallic acid, etc.

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