Antioxidant and Antidiabetic from Rhizophora mucronata Derived from Sambera Beach, East Kalimantan, Indonesia

by Usman Usman

Submission date: 30-Oct-2023 03:13PM (UTC+0700)
Submission ID: 2207692693
File name: Artikel_Usman_et_al_2023_TJNPR.pdf (250.18K)
Word count: 5025
Character count: 27980

Trop J Nat Prod Res, October 2023; 7(10):4921-4926
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Antioxidant and Antidiabetic from *Rhizophora mucronata* Derived from Sambera Beach, East Kalimantan, Indonesia

Usman Usman[1]*, Muh. Amir Masruhim[1], Pintaka Kusumaningtiyas[1], Erwin Erwin[2], Dewi E. Bulan[3]

[1]*Master Study Program of Chemistry Education, Faculty of Teacher Training and Education, Mulawarman University, Samarinda, East Kalimantan, Indonesia*
[2]*Department of Chemistry, Faculty of Mathematics and Natural Sciences, Mulawarman University, Samarinda, East Kalimantan, Indonesia*
[3]*Department of Aquatic Resource Management, Faculty of Fisheries and Marine Sciences, Mulawarman University, Samarinda, East Kalimantan, Indonesia*

ARTICLE INFO

Article history:
Received 02 September 2023
Revised 09 October 2023
Accepted 19 October 2023
Published online 01 November 2023

ABSTRACT

This study aims to evaluate the bioactive compounds, antioxidant, and antidiabetic properties of methanol, dichloromethane, and ethyl acetate extracts of *Rhizophora mucronata* mangrove leaves. The *R. mucronata* leaf samples (1 kg) were extracted with methanol, followed by liquid-liquid partition extraction with dichloromethane, and finally ethyl acetate solvent. The extraction procedure was repeated three times for one 24-hour period. The phytochemical content of the three extracts was determined using the color test method, followed by an antioxidant activity test using the DPPH (1,1-diphenyl-2-picrylhydrazyl) method, and an Oral Glucose Tolerance Test (OGTT) to detect antidiabetic activity. The phytochemical contents of methanol, dichloromethane, and ethyl acetate extracts of *R. mucronata* mangrove leaves are alkaloids, flavonoids, phenolic compounds, triterpenoids, steroids, saponins, and tannins. The antioxidant activity of the ethyl acetate extract is categorized as extremely strong, with an IC_{50} value of 34.64 ppm. In addition, the ethyl acetate extracts reduced blood glucose levels in mice by 57.64% after 24 hours. The mangrove plant *R. mucronata* from the Sambera beach, particularly the ethyl acetate extract, has the potential to be developed as a natural antioxidant and alternative anti-diabetic medicine.

Keywords: DPPH scavenging activity, Mangrove Plants, Oral glucose tolerance test, Phytochemical screening

Introduction

The mangrove forest in Indonesia is one of the largest mangrove forest areas in the world.[1] Therefore, researchers in the field of natural organic chemistry and herbal medicine are interested in learning more about how mangrove forests might be used as a source of antibiotics. In recent years, the demand for herbal medicine by people with diabetes has increased, along with the increasing amount of diabetes in Indonesia. Data from the International Diabetes Federation (IDF) shows that the amount of diabetes in Indonesia in 2019 was estimated to reach 10.7 million people. By 2045, it is expected to increase to 16.7 million people.[2] Therefore, research towards a diabetic cure is still ongoing.

The mangrove plant is a type of plant that is widely used by the community as a traditional medicine to cure various diseases. These diseases include diarrhea, malaria, smallpox, asthma, diabetes, fever, swelling, rheumatism, skin diseases, hepatitis, diuretics, leprosy, antitumor, leukemia, anticancer, antiviral, and mumps.[3–5] Parts of mangrove plants that are utilized as medicinal materials are root tissue, stem wood, bark, leaves, twigs, flowers, and fruits.[6,7]

*Corresponding author. E mail: sainusman@ymail.com
Tel: +62 813-4710-5831

Citation: Usman U, Amir Masruhim M, Kusumaningtiyas P, Erwin E, Bulan DE. Antioxidant and Antidiabetic from *Rhizophora mucronata* Derived from Sambera Beach, East Kalimantan, Indonesia. Trop J Nat Prod Res. 2023; 7(10):4921-4926. http://www.doi.org/10.26538/tjnpr/v7i10.31.

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

Mangrove plants are rich in secondary metabolites such as alkaloids, polyphenols, flavonoids, tannins, saponins, triterpenes, anthraquinones, catechins, glucose, proteins, steroids, phenolic compounds, and glycosides that have antioxidant and antidiabetic activities. These mangrove plant species include *Avicennia marina, Acanthus ilicifolius, Ceriops tagal, Rhizophora mucronata, Rhizophora apiculata, Sonneratia alba, Sonneratia caseolaris, Xylocarpus granatum,* and *Nypa fruticans*.[8–10] There has been very little study of the bioactivity of the mangrove species, *R. mucronata* from Sambera Beach in East Kalimantan, Indonesia. Therefore, it is important to investigate the potential of this species in order to identify the bioactive compounds with antioxidant and antidiabetic activities, which can subsequently be developed as natural herbal medicines.

The present study was therefore conducted to investigate the antioxidant and antidiabetic potentials of the active chemical compounds from *Rhizophora mucronata* obtained from Sambera Beach, East Kalimantan, Indonesia.

Materials and Methods

Equipment and Reagents

This equipment used in this research includes digital analytical balance (XPR106DUHQ), rotary evaporator (RE301A-W, Yamato Scientific Co.Ltd.Japan), vortex (Labnet Vortex Mixer VX-200), incubator (Memmert Incubator I IN 55 PLUS), pH meter (Lutron PH-208), and UV-Vis spectrophotometer (Shimadzu UV-Vis UV-1280). The reagents for phytochemical testing (alkaloids, flavonoids, phenolic compounds, steroids, triterpenoids, tannins, and saponins), methanol, dichloromethane, ethyl acetate, H_2SO_4, and $FeCl_3$ were purchased by Merck (Darmstadt, Germany). CMC-Na and 1,1-diphenyl-2-picrylhidrazyl were supplied by Sigma Aldrich (USA). Glibenclamide 5 mg as a test drug was produced by PT. First Medipharma (Sidoarjo, Indonesia).

Sample Collection and preparation

The leaves of *R. mucronata* were collected in February 2022 from Sambera Beach (0°14'44.8"S, 117°25'00.6"E), East Kalimantan, Indonesia (Figure 1). The mangrove leaves were rinsed under running water to remove dirt attached to the leaves and then cut into small pieces. The dried samples were separated and then pulverized into fine powder with a size of 90 mesh. The mangrove leaf powder was prepared to be used for the subsequent procedures.

Extraction

About 1 kg of *R. mucronata* mangrove leaf powder was extracted by maceration method and filtered every 24 hours three times using 70% methanol solvent (powder and solvent ratio of 1:10). The methanol extract obtained was combined and then the solvent was evaporated with a rotary evaporator at 40°C at 1 atm pressure, until a thick blackish green methanol extract was obtained. Dichloromethane and ethyl acetate were used to extract a portion of the methanol extract by liquid-liquid partition. Furthermore, the methanol, dichloromethane, and ethyl acetate extracts were prepared for the phytochemical, antioxidant, and antidiabetic analysis.

Phytochemical Test

Phytochemical screening of methanol, dichloromethane, and ethyl acetate extracts was carried out qualitatively using modified standard procedures. Alkaloids, flavonoids, phenolics, steroids, triterpenoids, tannins, and saponins were the phytochemicals that were identified.[11–13]

Antioxidant test

The antioxidant activity of the methanol, dichloromethane, and ethyl acetate extracts of *R. muronata* leaf extracts and vitamin C (standard drug) were evaluated *in vitro* using the DPPH (1,1-diphenyl-2-picrylhidrazyl) method following the procedure described by Senhaji *et al*. with slight modifications.[14] An aliquot of 2 mL of each of methanol, dichloromethane, or ethyl acetate extract was made in four concentrations (20, 40, 60, and 80 ppm), while vitamin C was prepared in concentrations of 2, 4, 6, and 8 ppm. All samples were mixed continuously with 2 ml of DPPH (50 ppm) solution. After being incubated for 30 minutes in the dark at room temperature, the absorbance of the three extracts and vitamin C were measured using a UV-Vis spectrophotometer at a wavelength of 517 nm.[14] The percentage of antioxidant activity or the percentage of DPPH inhibition of the methanol, dichloromethane, and ethyl acetate extracts and vitamin C were calculated using the following formula presented in Equation 1.

$$\text{DPPH \% inhibition} = \frac{\text{Absorbance of Control} - \text{Absorbance of Sample}}{\text{Absorbance of Control}} \times 100\% \quad (1)$$

Then a linear regression curve was made by plotting the percentage data of DPPH inhibition against the concentrations of the three extracts as well as the concentration of vitamin C. The IC_{50} value (as an indicator of antioxidant activity) of the methanol, dichloromethane, and ethyl acetate extracts and vitamin C was calculated using the regression equation of the linear regression curve obtained.[15]

Antidiabetic test

The antidiabetic activity of the various extracts was evaluated using the oral glucose tolerance test (OGTT) method. The mice used were male mice with a body weight of 150-200 grams and were divided into 5 groups, each group consisting of 5 mice. Before treatment, all mice were fasted for 18 hours, and blood samples were taken from a vein in the tail of the mice using a glucometer to determine fasting/initial blood glucose levels. Then all groups were given 50% glucose monohydrate solution orally, except for the negative control group. After induction of glucose monohydrate for 180 minutes, the mice's blood glucose levels were measured again and mice that were already hyperglycemic (blood glucose level > 200 mg/dl) were selected as treatment samples. The mice in Group 1 (negative control) received 1% CMC-Na (Sodium-Carboxymethyl Cellulose) suspension. Group 2 (positive control) was the group of mice that were given glibenclamide suspension at a dose of 10 mg/kg BW. A 300 mg/kg BW methanol extract of mangrove leaves was administered to group 3 (D1) mice. In Group 4 (D2), mice were treated with methanol extract of mangrove leaves at a dose of 600 mg/kg body weight, and in Group 5 (D3), mice were treated with methanol extract of mangrove leaves at a dose of 1,200 mg/kg body weight. The same thing also applies to treatments using dichloromethane and ethyl acetate. Measurement of blood glucose levels in mice was carried out after the treatment group (negative control, positive control, methanol extract, dichloromethane, and ethyl acetate extract of mangrove *R. mucronata* leaves) at 8, 16, and 24 hours to determine the decrease in blood glucose levels in mice. Furthermore, the percentage of decrease in blood glucose levels of mice was calculated using the following formula equation 2.[16]

$$\text{DBGL} = \frac{\text{Glucose level after (IGM)}}{\text{Final blood glucose level}} \times 100\% \quad (2)$$

% DBGL is the percentage decrease in blood glucose level and IGM is the induction of glucose monohydrate.

Figure 1: Location of *R. mucronata* sampling in Sambera beach, East Kalimantan, Indonesia (www.coordinatesmarker.com)

Results and Discussion

Phytochemical analysis

The results (Table 1) of the phytochemical screening of the methanol, dichloromethane, and ethyl acetate extracts of the mangrove leaves of *R. mucronata* showed the presence of secondary metabolites, such as alkaloids, flavonoids, phenolics, steroids, triterpenoids, tannins, and saponins. The results of the phytochemical as presented in Table 1 showed that the methanol *R. muronata* leaf extract contained alkaloids, flavonoids, triterpenoids, and saponins. Meanwhile, the dichloromethane extract contained flavonoids, steroids, and tannins, while the ethyl acetate extract contained phytochemicals, such as alkaloids, flavonoids, phenolics, triterpenoids, tannins, and saponins. Previous researchers have reported that *R. muronata* mangrove leaf extracts contain phenolics, flavonoids, tannins, saponins, terpenoids, dihydro flavonols, caffeic acid, vanillic acid, p-hydroxybenzoic acid, alkaloids, coumarins, quinones, resins, phytosterols, xanthoprotins, pigments (chlorophyll and carotenoids), and glucose.[17–20] The other research by Bulan *et al* 2022.[21] revealed that the methanol extract of mangrove leaves of *R. mucronata*, *R. stylosa*, and *R. apiculata* contains compounds such as alkaloids, cardiac glycosides, saponins, phenolics, tannins, steroids, and terpenoids. Meanwhile ethyl acetate extracts of the third mangrove leaf species (*R. mucronata, R. stylosa, and R. apiculata*) contained compounds such as alkaloids, cardiac glycosides, saponins, phenolics, flavonoids, tannins, steroids, and terpenoids.[21] Phytochemical analysis of five mangrove leaf species, mainly *Bruguiera cylindrica*, *Aegiceras corniculatum*, *Acrostichum aureum*, *Avicennia alba*, and *R. mucronata*, all contain secondary metabolites, such as flavonoids, saponins, terpenoids, steroids, phenolics, tannins, and anthraquinones.[22,23]

Antioxidant Activity of Rhizophora mucronata

This study used the DPPH method to assess the antioxidant activity of methanol, dichloromethane, and ethyl acetate extracts of *R. mucronata* mangrove leaves, and vitamin C (standard drug). The concentrations of methanol, dichloromethane, and ethyl acetate extracts of *R. muronata* mangrove leaves and vitamin C were then plotted against the percentage of DPPH inhibition (Figure 2). The antioxidant activity of compounds or extracts is usually expressed by the IC_{50} value. A linear regression

equation can be used to determine the IC_{50}, which is the concentration of antioxidant compounds required to reduce DPPH radicals by 50%. The IC_{50} describes the relationship between extract/compound concentration and the degree of inhibition. The lower the IC_{50} value obtained, the stronger the antioxidant activity of the compound.[24] Antioxidant activity is classified as very strong in extracts with IC_{50} values <50 ppm, strong in extracts with IC_{50} values of 50 to 100 ppm, moderate in extracts with IC_{50} values of 100 to 150 ppm, weak in extracts with IC_{50} values of 150 to 200 ppm, and inactive in extracts with IC_{50} values of >200 ppm.[25]

The results of the calculation of IC_{50} values for methanol, dichloromethane, and ethyl acetate mangrove extracts of *R. muronata* and vitamin C (standard drug) are presented in Table 3. The antioxidant activity properties of vitamin C and ethyl acetate extracts are in the very strong category, with IC_{50} values of 5.41 and 34.64 ppm, respectively, while the antioxidant activity properties of the *R. mucronata* mangrove dichloromethane leaf extract are in the strong category, with an IC_{50} value of 93.25 ppm. Meanwhile, the antioxidant activity of methanol extract is included in the medium category with an IC_{50} value of 100.64 ppm. Ethyl acetate and methanol extracts of *R. mucronata*, *R. stylosa*, and *R. apiculata* have been reported to show strong DPPH scavenging activity.[25] The activity is due to the presence of phytochemical compounds contained in the three mangrove plant species. Therefore, the three *Rhizophora* species can be developed as natural antioxidants.[21] The difference in antioxidant activity of the three *R. mucronata* mangrove leaf extracts is due to differences in the composition of chemically active compounds that each extract possesses. Differences in the composition of these active compounds can provide synergistic effects between compounds resulting in increased antioxidant activity. Active chemical compounds such as phenolics, flavonoids, anthocyanins, tannins, and other phenolic compounds contained in the extract are directly linked to antioxidant activity.[16,26]

Secondary metabolites contained in mangrove species of *R. mucronata* include alkaloids, flavonoids, phenolics, steroids, tannins, and terpenoids that show strong antioxidant properties.[27,28] It has been reported that the methanol extract of mangrove leaves of *R. mucronata* showed strong antioxidant activity with an IC_{50} value of 47.39 ± 0.43 /mL. The presence of flavonoid compounds, such as catechins in the methanol extract of *R. mucronata* mangrove leaves is thought to be responsible for cholinesterase inhibitory and antioxidant activity.[29] Chlorophyll a, chlorophyll b, beta-carotene, lutein, neoxanthin, pheophytin a, and violaxanthin are pigment profiles in the leaves of mangrove plants of *R. mucronata*.[30] All identified pigments have strong antioxidant potential, especially as free radical scavengers and Nrf-2 stimulants. The mechanism of action of these pigments is by interacting with each other to inactivate antioxidant enzymes and inhibit the expression of oxidative stress proteins.[30]

Antidiabetic activity of Rhizophora mucronata

Measurement of mice blood glucose levels was done using the oral glucose tolerance test (OGTT) method. The results of the calculation of the percentage reduction in blood glucose levels of mice in each treatment group, namely negative control, positive control, methanol, dichloromethane, and ethyl acetate leaf extracts of *R. muronata* are presented in Table 4.

According to the results in Table 4 and Figure 3, the positive control glibenclamide (dose of 10 mg/kg BW) had the highest percentage decrease in blood glucose levels in mice, followed by ethyl acetate extract in the D3 treatment group (dose of 1,200 mg/kg BW). Following that are methanol extract in treatment group D2 (dose of 600 mg/kg BW), and dichloromethane extract in treatment group D3 (dose of 1,200 mg/kg BW).

Table 1: Phytochemical content of extracts of methanol, dichloromethane, and ethyl acetate of *Rhizophora mucronata* mangrove leaves.

No.	Phytochemical Test	The extract and observations		
		Methanol	Dichloromethane	Ethyl Acetate
1.	Alkaloids	(+)	(-)	(+)
2.	Flavanoids	(+)	(+)	(+)
3.	Phenolics Compounds	(-)	(-)	(+)
4.	Steroids	(-)	(+)	(-)
5.	Triterpenoids	(+)	(-)	(+)
6.	Tannins	(-)	(+)	(+)
7.	Saponins	(+)	(-)	(+)

- = Absent + = Present

Table 2: The percentage of DPPH inhibition of methanol, dichloromethane, and ethyl acetate extracts of *Rhizophora muronata* leaves and vitamin C at various concentrations.

Extract	Absorbance (517 nm)				Percentage of DPPH inhibition			
	20 ppm	40 ppm	60 ppm	80 ppm	20 ppm	40 ppm	60 ppm	80 ppm
Methanol	0.205	0.195	0.174	0.156	22.64	26.42	33.96	41.13
Dichloromethane	0.203	0.189	0.158	0.148	23.40	28.68	40.38	44.15
Ethyl Acetate	0.154	0.125	0.095	0.058	41.89	52.83	64.15	78.11
	Absorbance (517 nm)				Percentage of DPPH inhibition			
	2 ppm	4 ppm	6 ppm	8 ppm	2 ppm	4 ppm	6 ppm	8 ppm
Vitamin C	0.219	0.167	0.114	0.071	17.36	36.97	56.98	73.21

DPPH: 1,1-diphenyl-2-picrylhydrazy

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

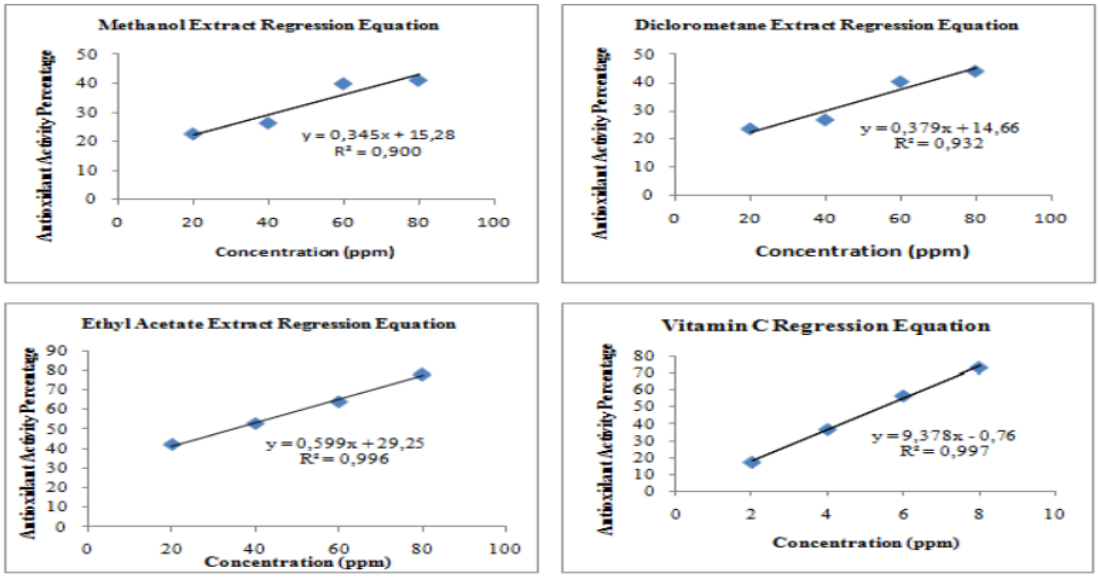

Figure 2: The graph of linear regression equation of methanol, dichloromethane, ethyl acetate extracts, and vitamin C

Table 3: The IC_{50} values of *R. muronata* mangrove leaf extracts and vitamin C determined by linier regression equation

Extract	Regression Equation	IC_{50} Value (ppm)
Methanol	y = 0.345x + 15.28	100.64
Dichloromethane	y = 0.379x + 14.66	93.25
Ethyl Acetate	y = 0.599x + 29.25	34.64
Vitamin C	y = 9.378x - 0.76	5.41

The highest decrease in glucose levels was observed in the positive control group (glibenclamide). This is because glibenclamide can stimulate pancreatic beta cells to secrete insulin and increase the sensitivity of peripheral cells to increased insulin levels.[31]
The decrease in mice blood glucose levels observed in treatment groups D1, D2, and D3 in methanol, dichloromethane, and ethyl acetate extracts of *R. mucronata* mangrove leaves is due to the content of secondary metabolites, such as alkaloids, flavonoids, steroids, tannins, and saponins contained in the three mangrove leaf extracts.[32] These secondary metabolites are thought to have a role in reducing blood glucose levels in mice.[33] Mangrove fruit extract of *R. mucronata* with doses of 125, 250, and 500 mg/kg BW was able to reduce the blood glucose levels of diabetic rats.[32,33] Compared to the treatment group that received mangrove fruit extract from *R. mucronata* species, glibenclamide at a dose of 5 mg/kg BW was more effective in lowering blood sugar levels.[32] Flavonoids, steroids, saponins, and tannins are among the secondary metabolites found in the mangrove fruit extract of *R. mucronata* that are expected to lower blood sugar levels.[33] Alkaloids saponins can have hypoglycemic effects because they can stimulate insulin secretion from pancreatic beta cells.[34] Flavonoids and tannins can reduce blood glucose levels by capturing free radicals and reducing the increase in oxidative stress that occurs in diabetes to control blood glucose.[35,36] Secondary metabolites from ethanol extracts, chloroform, and mangrove root fractions of *R. mucronata* species showed antidiabetic activity.[37,38] The mechanism of antidiabetic activity of mangrove bark extract of *R. mucronata* species is by increasing insulin secretion, and restraining the digestion and absorption of carbohydrates.[39,40]

Conclusion

The secondary metabolite compounds contained in the methanol, dichloromethane, and ethyl acetate extracts from *R. mucronata* mangrove leaves are linked to antioxidant and antidiabetic activities. With an IC_{50} value of 34.64 ppm, the antioxidant activity of the ethyl acetate extract is classified as extremely robust. Furthermore, after 24 hours, the ethyl acetate extracts decreased blood glucose levels in mice by 57.64%. The ethyl acetate extract of the mangrove plant *R. mucronata* from Sambera beach, East Kalimantan has the potential to be developed as a natural antioxidant and alternative anti-diabetic therapy.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgments

The authors would like to thank PIU IsDB Mulawarman University Indonesia for funding this research through the Higher Education Research Grant Program and the Pharmacy Research Laboratory of Mulawarman University for the facilities provided to carry out this research.

Table 4: Percentage reduction in blood glucose levels of mice in the treatment groups after 24 hours

Treatment Group	Fasting Glucose Level (mg/dl)	Blood Glucose Level After IGM (mg/dl)	Blood Glucose Level After Treatment (mg/dl)	The Percentage of Blood Glucose Level Reduction (%)
Negative Control (CMC-Na 1 %)	85.7	-	-	-
Positive Control (Glibenclamide; Dose 10 mg/kg bw)	97.3	276	107	61.23
Methanol Extract				
D1 (*R. mucronata* Leaf Extract; Dose 300 mg/kg bw)	95.7	285.7	170.3	40.39
D2 (*R. mucronata* Leaf Extract; Dose 600 mg/kg bw)	97	276.3	158.3	42.71
D3 (*R. mucronata* Leaf Extract; Dose 1.200 mg/kg bw)	92.7	269	162	39.78
Dichloromethane Extract				
D1 (*R. mucronata* Leaf Extract; Dose 300 mg/kg bw)	99.3	276.3	224.4	18.78
D2 (*R. mucronata* Leaf Extract; Dose 600 mg/kg bw)	93.7	306.3	229.7	25.01
D3 (*R. mucronata* Leaf Extract; Dose 1.200 mg/kg bw)	99.3	259.7	178	21.81
Ethyl Acetate Extract				
D1 (*R. mucronata* Leaf Extract; Dose 300 mg/kg bw)	94.3	268	193	27.99
D2 (*R. mucronata* Leaf Extract; Dose 600 mg/kg bw)	96.7	274	178	35.04
D3 (*R. mucronata* Leaf Extract; Dose 1.200 mg/kg bw)	96	279.3	118.3	57.64

IGM: Induction of glucose monohydrate

References

1. The Ministry of Environment and Forestry. Mangrove area in Indonesia. 2021; 2 p.
2. Atlas IDFD. International Diabetes Federation. The Lancet. 1955. 266; 134–137 p.
3. Dossou-Yovo HO, Vodouhè FG. Ethnobotanical survey of mangrove plant species used as medicine from Ouidah to grand-popo districts, southern Benin. Am J Ethnomedicine. 2017; 4 (18): 1-6. https://doi.org/10.21767/2348-9502.100008.
4. Usman U, Kusumaningtyas P, Sukemi S, Erwin E. An Evaluation of the Antidiabetic and Antimicrobial Activity of an Ethanolic Extract from Rhizophora mucronata Leaf. J Sains dan Kesehat. 2023; 5(4): 541–549.
5. Barman AK, Ahmed T, Das H, Biswas B, Ali M, Acharyya R, et al. Evaluation of antidiabetic potential of extract of Sonneratia caseolaris (L.) Engl. leaves against alloxan-induced diabetes in mice. Trop J Nat Prod Res. 2021; 5(1): 77–83.
6. Arora K, Nagpal M, Jain U, Jat RC, Jain S. Mangroves: A novel gregarious phyto medicine for diabetes. Int J Res Dev Pharm Life Sci. 2014; 3(6): 1244–1257.
7. Revathi P, Senthinath TJ, Thirumalaikolundusubramanian P, Prabhu N. An overview of antidiabetic profile of mangrove plants. Int J Pharm Pharm Sci. 2014; 6(3): 1–5.
8. Das SC, Das S, Tah J. Mangrove Forests and People's Livelihoods BT- Mangroves: Biodiversity, Livelihoods and Conservation. In: Das SC, Pullaiah, Ashton EC, editors. Singapore: Springer Nature Singapore; 2022; 153–173 p. Available from: https://doi.org/10.1007/978-981-19-0519-3_7
9. Aljaghthmi OH, Heba HM, Zeid IMA. Antihyperglycemic properties of mangrove plants (*Rhizophora mucronata* and *Avicennia marina*): an overview. Adv Biol Res (Rennes). 2017; 11(4): 161–170.
10. Sachithanandam V, Lalitha P, Parthiban A, Mageswaran T, Manmadhan K, Sridhar R. A review on antidiabetic properties of Indian mangrove plants with reference to island ecosystem. Evidence-based Complement Altern Med. 2019; vol. 2019: 1-21. https://doi.org/10.1155/2019/4305148.
11. Kenneth-Obosi O, Babayemi OJ. Qualitative and quantitative evaluation of phytochemical constituents of selected horticultural and medicinal plants in Nigeria. Int J Homeopath Med. 2017; 3(1):1-8.
12. Kachkoul R, Houssaini TS, El Habbani R, Miyah Y, Mohim M, Lahrichi A. Phytochemical screening and inhibitory activity of oxalocalcic crystallization of Arbutus unedo L. leaves. Heliyon. 2018; 4(12): 430-437. https://doi.org/10.1016/j.heliyon.2018.e01011.
13. Shaikh JR, Patil M. Qualitative tests for preliminary phytochemical screening: An overview. Int J Chem Stud. 2020; 8(2): 603–608.
14. Senhaji B, Chebli B, Mayad E, Hamdouch A, Heimeur N, Chahid A, et al. Phytochemical screening, quantitative analysis and antioxidant activity of Asteriscus imbricatus and Pulicaria mauritanica organic extracts. Int Food Res J. 2017; 24(6): 2482–2489.
15. Aarthia M, Laasri FE, Moussa SI, Ullah R, Bari A, Saeed Ali S, et al. Phytochemistry, antioxidant activity, antiproliferative effect, and acute toxicity testing of two Moroccan aristolochia species. Evidence-Based Complement Altern Med. 2019; Vol. 2019:1-8. pages. https://doi.org/10.1155/2019/9710876.
16. Sahnouni F, Aicha D, Saim S, Djilali B, Menadi S. Tropical Journal of Natural Product Research Original Research Article Phytochemical Content, Antioxidant and Antibacterial Activities of Three Red Macroalgae from Algerian West Coast. Trop J Nat Prod Res. 2021; 5(2): 336-341. https://doi.org/10.26538/tjnpr/v5i2/21.
17. Akasia AI, Putra I, Putra ING. Skrining fitokimia ekstrak daun mangrove Rhizophora mucronata dan Rhizophora apiculata yang dikoleksi dari kawasan mangrove Desa Tuban, Bali. J Mar Res Technol. 2021;4(1): 16–22.
18. Babuselvam M, Uthiresan K, Ravikumar S, Uthiraselvam M, Rajabudeen E. Scientific evaluation of aqueous extracts of fresh and dried leaves from *Rhizophora mucronata* lamk (Rhizophoracea) in Rats. African J Pharm Pharmacol. 2012; 6(11): 814–817.
19. Abidin NAZ, Halim NHA, Me R. Basic study of chemical constituents in Rhizophora species. In: The Open Conference Proceedings J. 2013; 4 (Suppl-2, M7) 27-28. Faculty of Applied Science, Universiti Teknologi MARA Negeri Sembilan, Ka. Malaysia.
20. Gurudeeban S, Kaliamurthi S, Thirugnanasamb R. Positive regulation of Rhizophora mucronata Poir extracts on blood glucose and lipid profile in diabetic rats. [Online] 2016; 2(2:10): 2-8. Available from: https://api.semanticscholar.org/CorpusID:52238046
21. Bulan DE, Nurfadilah N, Syahrir MR, Mismawati A, Torambung AK, Rachmawati M. Phytochemical composition and antioxidant activity of leaf extracts from three Rhizophora

species from Bontang Waters, Indonesia. Trop J Nat Prod Res. 2022; 6(8): 1178-1182
22. Kumari CS, Yasmin N, Hussain MR, Babuselvam M. Invitro anti-inflammatory and anti-artheritic property of Rhizopora mucronata leaves. Int J Pharma Sci Res. 2015; 6(3): 482–485.
23. Zou Y, Lu Y, Wei D. Antioxidant activity of a flavonoid-rich extract of Hypericum perforatum L. in vitro. J Agric Food Chem. 2004; 52(16): 5032–5039.
24. Arbiastutie Y, Diba F, Masriani M. Cytotoxicity Activity of Several Medicinal Plants Grow in Mangrove Forest against Human's Cervical (HELA), Breast (T47D), and Colorectal (WiDr) Cancer Cell Lines. Int J Nutr Pharmacol Neurol Dis. 2022; 12(2): 46–50.
25. Molyneux P. The use of the stable free radical diphenylpicrylhydrazyl (DPPH) for estimating antioxidant activity. Songklanakarin J sci technol. 2004; 26(2): 211–219.
26. Muharni M, Ferlinahayati F, Yohandini H. Antioxidant, antibacterial, total phenolic and flavonoid contents of sungkai leaves (Paronema canescens). Trop J Nat Prod Res. 2021; 5(3): 528–533.
27. Bandaranayake WM. Bioactivities, bioactive compounds and chemical constituents of Mangrove Plants. Wetl Ecol Manag. 2002; 10: 421–452.
28. Sahidin I, Nohong N, Manggau MA, Arfan A, Wahyuni W, Meylani I, et al. Phytochemical profile and biological activities of ethylacetate extract of peanut (Arachis hypogaea L.) stems: In vitro and in silico studies with bibliometric analysis. Indones J Sci Technol. 2023; 8(2): 217-242. IJOST Sept 2023. DOI - 17509/ijost.v8i254822 [Internet].
29. Suganthy N, Devi KP. In vitro antioxidant and anti-cholinesterase activities of Rhizophora mucronata. Pharm Biol. 2016; 54(1): 118–129.
30. Rumengan A, Mandiangan E, Tanod W, Paransa DS, Paruntu C, Mantiri D. Identification of pigment profiles and antioxidant activity of Rhizophora mucronata mangrove leaves origin Lembeh, North Sulawesi, Indonesia. Biodiversitas J Biol Divers. 2021; 22(7): 2805-2816. DOI: 10.13057/biodiv/d220730.
31. Liem S, Yuliet Y, Khumaidi A. Uji Aktivitas Antidiabetes Kombinasi Glibenklamid Dan Ekstrak Daun Salam (Syzygium Polyanthumwight.) Terhadap Mencit (Mus Musculus) Yang Diinduksi Aloksan. Farm Galen. 2015; 1(1): 42–47.
32. Tran N, Bao P, Le L. Bioactive Compounds in Anti-Diabetic Plants: From Herbal Medicine to Modern Drug Discovery. Biology (Basel). 2020; 9:252 : 1-31.
33. Shehadeh MB, Gary S, Abu-Odeh AM. Plants secondary metabolites as blood glucose-lowering molecules. Molec. 2021; 26(14): 4333. doi: 10.3390/molecules26144333
34. Mu'nisa A, Rosi KA. Effect of Giving Mangrove Fruit Extract (Rhizopora mucronata) on Reducing Blood Sugar Levels in Mice (*Mus musculus*). 2017; 34–38.
35. Hardoko H, Suprayitno E, Puspitasari Y. Study of ripe Rhizophora mucronata fruit flour as functional food for antidiabetic. Int Food Res J. 2015; 22: 953–959.
36. Patel D, Kumar R, Laloo DD, Hemalatha S. Natural medicines from plant source used for therapy of diabetes mellitus: An overview of its pharmacological aspects. Asian Pacific J Trop Dis. 2012; 2: 239–250.
37. Widowati W. Potential of antioxidants as antidiabetics. Kedokt Maranatha. 2008; 7(2 12 2–202.
38. Ario R, Tachibana S. Preliminary studies of Indonesian eugenia polyantha leaf extracts as inhibitors of key enzymes for Type 2 diabetes. J Med Sci. 2013; 13: 103–110.
39. Eldeen IMS, Effendy MAW. Antimicrobial agents from mangrove plants and their endophytes. 872-882. Available from: https://api.semanticscholar.org/Corpus 29842729
40. Usman, Masruhim MA, F, Erika, Nurdin M, Kuncoro H. Antidiabetic activity of leaf extract from three types of mangrove originating from Sambera coastal region Indonesia. Res J Pharm Technol. 2019; 12(4): 1707–1712.

Antioxidant and Antidiabetic from Rhizophora mucronata Derived from Sambera Beach, East Kalimantan, Indonesia

ORIGINALITY REPORT

15%	0%	11%	9%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to National University of Singapore Student Paper	1%
2	Submitted to iGroup Student Paper	1%
3	Submitted to Universitas Tanjungpura Student Paper	1%
4	Yustika Alfani, Siva Hamdani, Hesti Renggana. "AKTIVITAS ANTIDIABETES DARI TANAMAN FAMILI MYRTACEAE DENGAN INDUKSI ALOKSAN", Jurnal Ilmiah As-Syifaa, 2021 Publication	1%
5	Nael Abutaha, Fahd A. AL-mekhlafi, Mohamed A. Wadaan. "Phytochemical Analysis and antibacterial activity of Washingtonia filifera (Lindl.) H. Wendl. fruit extract from Saudi Arabia", Journal of King Saud University - Science, 2023 Publication	<1%

6	Thirunavukkarasu Palaniyandi, Asha Sivaji, Ramanathan Thirugnanasambandam, Priya Durairaj et al. "Isolation and identification of Anti-Oxidant Fraction from Active Extract of Rhizophora mucronata Poir. Leaves", Pharmaceutical Chemistry Journal, 2020 Publication	<1 %
7	Submitted to Badan PPSDM Kesehatan Kementerian Kesehatan Student Paper	<1 %
8	Submitted to Mahidol University Student Paper	<1 %
9	Submitted to University of Massachusetts Student Paper	<1 %
10	ERDONG YUAN. "PREPARATION AND ANTIOXIDANT ACTIVITY OF CAMELLIANIN A FROM *ADINANDRA NITIDA* LEAVES", Journal of Food Processing and Preservation, 10/2008 Publication	<1 %
11	Khadija Faddladdeen, Soad Shaker Ali, Safia Bahshwan, Nasra Ayuob. "Thymoquinone Preserves Pancreatic Islets Structure Through Upregulation of Pancreatic β-Catenin in Hypothyroid Rats", Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 2021 Publication	<1 %

12	O. Bakr Riham, A. Mohamed Shaza, E. Waly Nermien. "Phytochemical and biological investigation of Eugenia uniflora L. cultivated in Egypt", Journal of Pharmacognosy and Phytotherapy, 2017 Publication	<1 %
13	Isam M. Abu Zeid, Abdul Rahman A. FarajAlla. "Chapter 35 Borassus flabellifer L. Palmyra Palm (Daleeb): Biochemistry, Functions and Utilization", Springer Science and Business Media LLC, 2019 Publication	<1 %
14	Submitted to University of Namibia Student Paper	<1 %
15	Submitted to Sultan Qaboos University Student Paper	<1 %
16	Submitted to University of Messina Student Paper	<1 %
17	Nilesh Lakshman Dahibhate, Devendra Kumar, Kundan Kumar. " Determination of Bioactive Polyphenols in Mangrove Species and Their anti- Activities by Ultra-High-Performance Liquid Chromatography – Electrospray Ionization – Tandem Mass Spectrometry (UPLC-ESI-MS/MS) ", Analytical Letters, 2020 Publication	<1 %

18	Sully M. Cruz, Nereida Marroquín, Luis E. Alvarez, Dora E. Chang, Armando Cáceres. "Evaluation of Mangrove (Rhizophora mangle L.) products as coloring, antimicrobial and antioxidant agents", International Journal of Phytocosmetics and Natural Ingredients, 2015 Publication	<1 %
19	Submitted to Udayana University Student Paper	<1 %
20	Submitted to University of Stellenbosch, South Africa Student Paper	<1 %
21	Submitted to University of Teesside Student Paper	<1 %
22	Veena Sharma. "Prophylactic Efficacy of Coriandrum sativum (Coriander) on Testis of Lead-Exposed Mice", Biological Trace Element Research, 11/10/2009 Publication	<1 %
23	Submitted to Wageningen University Student Paper	<1 %
24	Jin Dai, Junli Hao, Yuhang Chen, Yuru Guo et al. "Empagliflozin Modify gut microbiota in db/db Mice Correlating with the Improvement of Glucose and Lipid Metabolism", Research Square Platform LLC, 2023 Publication	<1 %

25	Keita Nakagawa, Kazuki Watanabe, Koji Mizutani, Kohei Takeda et al. "Genetic Analysis of Exacerbated Healing Responses after Periodontal Therapy due to Type 2 Diabetes: Clinical and in vivo Studies", Research Square Platform LLC, 2023 Publication	<1%
26	Natarajan Suganthy, Dicson Sheeja Malar, Kasi Pandima Devi. "Rhizophora mucronata attenuates beta-amyloid induced cognitive dysfunction, oxidative stress and cholinergic deficit in Alzheimer's disease animal model", Metabolic Brain Disease, 2016 Publication	<1%
27	Submitted to Southern New Hampshire University - Continuing Education Student Paper	<1%
28	Nebula, Murukesh, H. S. Harisankar, and N. Chandramohanakumar. "Metabolites and bioactivities of Rhizophoraceae mangroves", Natural Products and Bioprospecting, 2013. Publication	<1%
29	Ramalingam Saravanan, Leelavinothan Pari. "Succinic acid monoethyl ester, a novel insulinotropic agent: Effect on lipid composition and lipid peroxidation in streptozotocin–nicotin-amide induced type 2	<1%

diabetic rats", Molecular and Cellular Biochemistry, 2006
Publication

30	Submitted to University of Hertfordshire Student Paper	<1%
31	Eman E. Yassien, Moaz M. Hamed, Usama Ramadan Abdelmohsen, Hanaa M. Hassan, Hanaa S. S. Gazwi. "In vitro antioxidant, antibacterial, and antihyperlipidemic potential of ethanolic Avicennia marina leaves extract supported by metabolic profiling", Environmental Science and Pollution Research, 2021 Publication	<1%
32	Ulfah Amalia, Yudomenggolo Sastro Darmanto, Sumardianto, Laras Rianingsih. "Chemical Characteristics of Fish Nugget with Mangrove Fruit Flour Substitution", Aquatic Procedia, 2016 Publication	<1%
33	Wiwit Denny Fitriana, Sri Banun Titi Istiqomah, Taslim Ersam, Sri Fatmawati. "The relationship of secondary metabolites: A study of Indonesian traditional herbal medicine (Jamu) for post partum maternal care use", AIP Publishing, 2018 Publication	<1%

34	Submitted to Dominican University of California Student Paper	<1%
35	K.A. Ferey, C. Fauris, G.P. Husson, R. Vilagines. "Cytotoxicity assessment of chlorinated bacteria in water using the RNA synthesis inhibition method", Toxicology, 2000 Publication	<1%
36	Submitted to University of Huddersfield Student Paper	<1%
37	Dineshkumar Saravanan, Seethalakshmi Avudaiappan. "Association between Admission Blood Glucose Levels and Clinical Outcomes among Diabetic Adults Admitted to a Tertiary Care Hospital in Chennai, India: A Retrospective Study", JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH, 2023 Publication	<1%
38	Sudhir Chandra Das, Shreya Das, Jagatpati Tah. "Chapter 7 Mangrove Forests and People's Livelihoods", Springer Science and Business Media LLC, 2022 Publication	<1%
39	Jayasinghe, L.. "Geranylated phenolic constituents from the fruits of Artocarpus nobilis", Phytochemistry, 200607 Publication	<1%

40	Jiwan S. Sidhu, Tasleem A. Zafar. "Chapter 28 Fruits of Indian Subcontinent and Their Health Benefits", Springer Science and Business Media LLC, 2020 Publication	<1%
41	Submitted to Taylor's Education Group Student Paper	<1%
42	Vahideh Abdi, Iman Sourinejad, Morteza Yousefzadi, Zahra Ghasemi. "Biosynthesis of Silver Nanoparticles from the Mangrove Rhizophora mucronata: Its Characterization and Antibacterial Potential", Iranian Journal of Science and Technology, Transactions A: Science, 2019 Publication	<1%
43	Harikrishna Devalapally, Kombu Subramanian Rajan, RaghuRam Rao Akkinepally, Rama Krishna Devarakonda. "Safety, Pharmacokinetics and Biodistribution Studies of a β-galactoside Prodrug of Doxorubicin for Improvement of Tumor Selective Chemotherapy", Drug Development and Industrial Pharmacy, 2008 Publication	<1%
44	Shalaka S. Vaidya, H. Vinaya, Supriya S. Mahajan. "Microwave-assisted synthesis, pharmacological evaluation, and QSAR	<1%

studies of 1,3-diaryl-2-propen-1-ones", Medicinal Chemistry Research, 2012
Publication

45 Center for the Evaluation of Risks to Human Reproduction. "NTP-CERHR Expert Panel report on the reproductive and developmental toxicity of methanol", Reproductive Toxicology, 200405 <1%
Publication

46 Dong-Qi Tang, Shun Lu, Yu-Ping Sun, Enda Rodrigues, Wayne Chou, Cheryl Yang, Li-Zhen Cao, Lung-Ji Chang, Li-Jun Yang. "Reprogramming liver-stem WB cells into functional insulin-producing cells by persistent expression of Pdx1- and Pdx1-VP16 mediated by lentiviral vectors", Laboratory Investigation, 2005 <1%
Publication

47 Mrunmai Tapadia, Stuart Johnson, Ranjeet Utikar, Philip Newsholme, Rodrigo Carlessi. "Antidiabetic effects and mechanisms of action of γ-conglutin from lupin seeds", Journal of Functional Foods, 2021 <1%
Publication

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	Off		