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By JHONS SUWANDI

Artonin O, a Xanthone Compound from Root Wood of *Artocarpus rigida*

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INTRODUCTION

We have previously reported that from the root bark of *A. rotunda* (Houtt.) Panzer, one of endemic species in Indonesia, obtained from Hutan Raya Bengkulu, has been isolated prenylated flavone, artonin E as well as three xanthone derivatives, artonin O, artonin M and cycloartobiloxanthone, and a geranilated flavone, artoidonesianin L. *A. rigida* is part of *Artocarpus* plant which is also endemic in Indonesia, so the chemistry research about this plant is still interesting. Some organic compounds have successfully been isolated from some parts of *A. rigida* obtained from Keputran Village, Sukoharjo,

Pringsewu Lampung Indonesia. From its root bark, artonin E has been isolated and it has been shown to have good anticancer and antimalaria activities².

In this work, we reported artonin O which has been isolated from root wood of *A. rigida*. The antimicrobial activity of this compound has also been tested against *B. subtilis*.

EXPERIMENTAL

General

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The melting point was determined with Gallenkamp melting point apparatus and is

uncorrected. The UV-Vis spectrum was obtained on Agilent Cary 100 spectrometer and the IR spectrum was measured with Agilent Cary 620 FTIR. The ^1H and ^{13}C NMR spectra were obtained on Agilent spectrometer with DD2 console system at 500 MHz and 125 MHz, respectively. Mass spectrum was measured with Waters mass spectrometer, LCT Premier XE MS. Vacuum liquid chromatography (VLC) was performed using Merck Si-gel 60, thin layer chromatography (TLC) analysis was carried out on pre-coated Si-gel plates (Merck Kieselgel 60 F254, 0.25 mm).

Plant collections

Samples of the root wood of *A. rigida* Blume were collected from Keputran Village, Sukoharjo Pringsewu Lampung and were identified at the Herbarium Bogoriense, Research Centre for Biology, Indonesia Institute of Sciences Bogor, Indonesia and a voucher specimen has been deposited at the herbarium.

Extraction and Isolation

The powder of root wood of *A. rigida* (3 kg) was extracted exhaustively with *n*-hexane (3 x 10 L) and a mixture of methanol-ethylacetate (EtOAc) 1:1 (3 x 10 L). On removal of the solvents by vacuum rotatory evaporator produced methanol/EtOAc

extract (127 g). The methanol/EtOAc extract was then fractionated by Si-gel vacuum liquid chromatography (VLC) and was eluted with EtOAc:*n*-hexane with the ratio from 0 – 100%, to produce 6 main fractions (A-F), A 3.2 g; B 0.6 g, E 7.8 g

Fraction A was then subjected with VLC using Si-gel with eluent of EtOAc:*n*-hexane by increasing the polarity from 10-20%, to produce 5 main fractions based on their TLCs. The fifth fraction (0.33 g) was purified with VLC (Si gel 60 GF₂₅₄, EtOAc:*n*-hexane 3-20%) to yield the main compound, artonin O (compound 1) (29 mg). The fractionation of fraction B was performed with the same way using eluent of EtOAc:*n*-hexane 4-20% to yield 3 main fractions. The fractionation of the third fraction (0.167 g) with VLC using eluent of EtOAc:*n*-hexane 3-20%, the red crystal (4.5 mg) was obtained after being recrystallized with EtOAc:*n*-hexane. This crystal has the same retention time (R_f) with compound 1 based on TLC using three eluent systems. Based on TLC, the total amount of compound 1 obtained was 33.5 mg.

Artonin O (1)

Compound 1, is found to be red needle crystal with melting point of 203-205 °C (decomposed). UV (MeOH) λ_{max} nm (log ϵ): 202 (4.6), 254 (4.3), 317

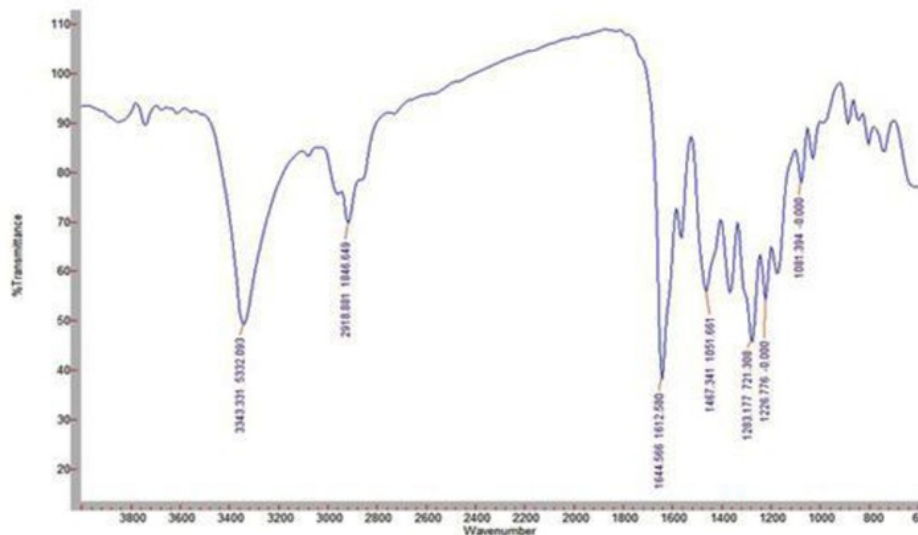


Fig. 1: IR spectrum of isolated compound 1

(4.2); while on the addition of commonly-used shift reagents, did not change the initial spectrum.

The IR (KBr) gave ν_{\max} , cm^{-1} : 3343 (broad), 2918, 1644, 1467, 1283, 1226, and 1081. HRMS m/z (relative intensity): 503.2059 ($M+1$, TOF MS ES+ 1.43e+004.

^1H NMR (CD_3OD) δ (ppm): 1.65; 1.67; 1.77; 1.80 (each for 3H, s, H-17, H-22, 6H, s, for H-18,23 and 3H, s, for 5-13); 2.61 (1H, dd, $J=8$ and 17 Hz, H-9); 3.19 (2H, d, $J=7$ Hz, H-19); 3.75 (1H, d, $J=8.6$ Hz, H-10); 4.54; 4.71 (each for 1H, s, H-12); 5.17; 5.21 (each for 1H, m, H-15 and H-20); 6.46 (1H, s, H-8).

Biological activity

The antibacterial activity test was performed using paper disc method test.

RESULTS AND DISCUSSION

Artonin O

The UV spectrum of compound 1 gave λ_{\max} at 202, 254, and 317 nm in methanol, indicated the characteristic of flavone compound. The maximum absorbance at λ_{\max} 317 nm is a characteristic spectrum of flavone which is the electron excitation on cynamoil group in B ring, known as Band I, while the λ_{\max} at 254 nm is characteristic of electron

excitation of benzoyl group on A ring known as band II.

Fig. 1 shows the IR spectrum of compound 1. There is a broad band at 3343 cm^{-1} which is stretch vibration of hydroxyl group bonded to hydrogen. The band at 2918 cm^{-1} is an indication the presence of C-H aliphatic. The band at 1644 cm^{-1} indicates the present of carbonyl group (C=O) conjugated with C=C bond. The band at 1467 cm^{-1} is the present of C=C aromatic, while the bands at 1283, 1226, 1081 cm^{-1} are indication of stretch of C-O.

The IR spectrum of 1 indicated the similarity with spectrum from standard artonin O. It can be seen by comparing the IR spectra of 1 and the standard in literature (Table 1).

The IR spectrum of compound 1 with band at 3343, 2918, 1644, 1467, 1283, 1226, and 1081 cm^{-1} , and UV spectrum (MeOH) λ_{\max} 202, 254, and 317 nm showed a similar absorption style to artomunoxantrone epoxide (3)⁴, artobiloxanthone (4)⁵, or artonin N (5)⁶ which shows that compound 1 also contains xanthonoid chromophores.

To strengthen the analysis of the structure of the compound isolated, the ^{13}C and ^1H NMR were taken and the spectra of 1 obtained are presented

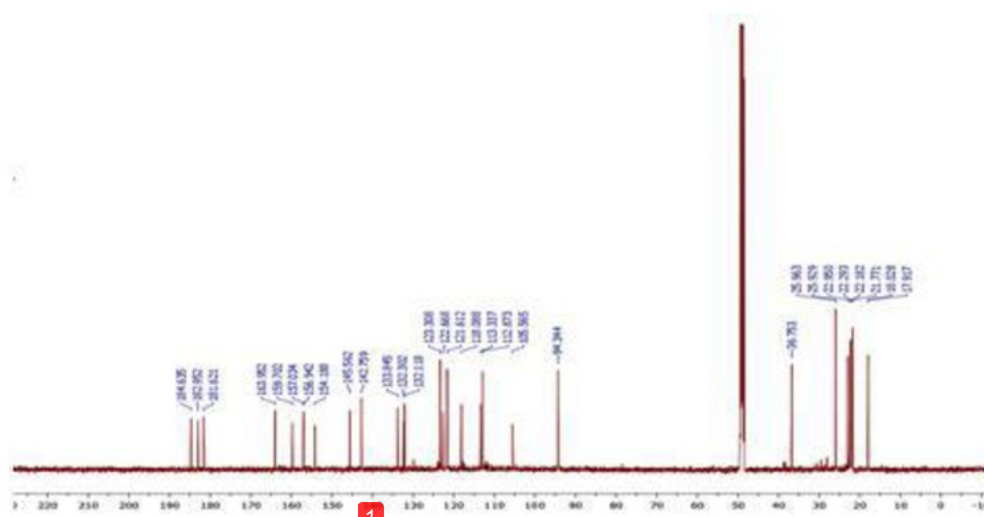


Fig. 2: ^{13}C NMR spectrum of isolated compound 1

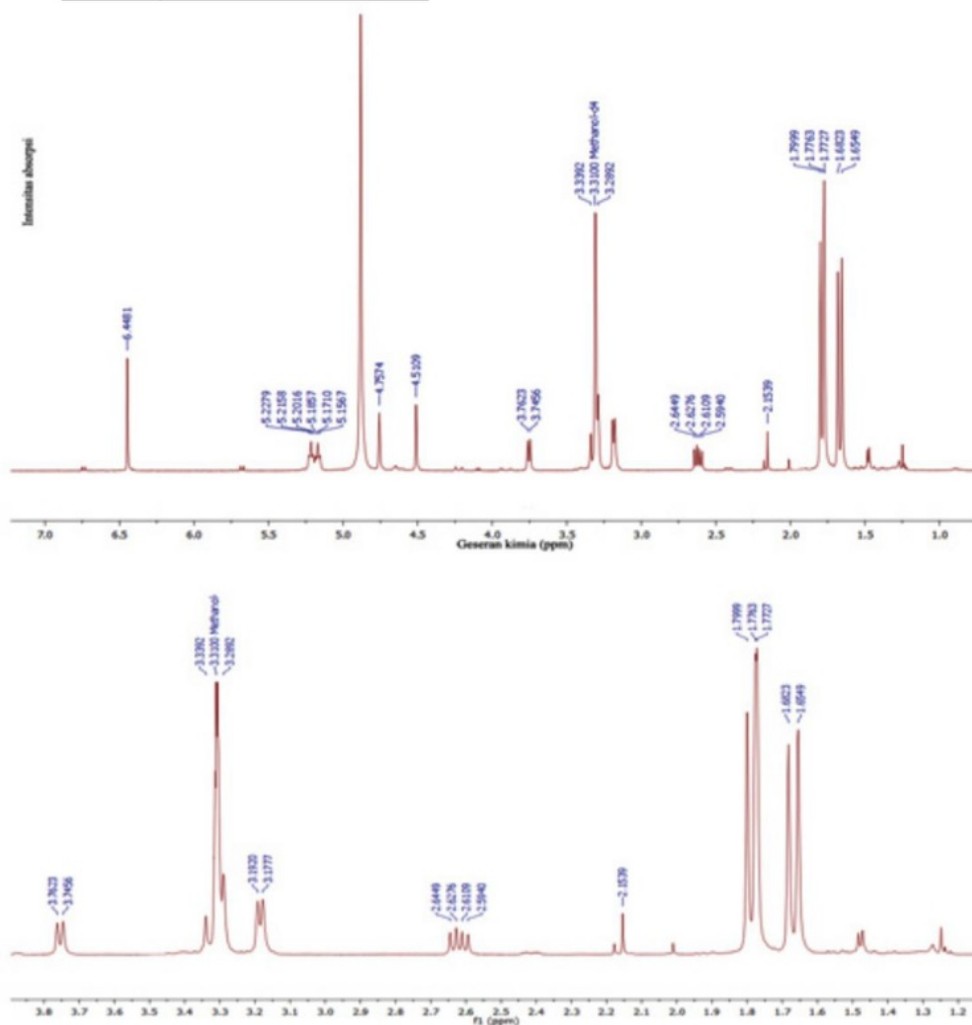
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Table 1: The comparison of IR data of compound 1 (A) and standard (B)

IR (KBr) (cm ⁻¹)	
A	B
3343	3350
2918	2962
1644	1647
1467	1470
1283	1283
1226	1225
1081	1080

in Fig. 2 and 3, respectively. ¹³C NMR spectrum of 1 shows 30 carbon signals. Based on these chemical shifts, at $\delta > 100$ ppm, there are 21 carbon signals which indicate the presence of hybrid orbital sp^2 and there are 9 carbon signals at $\delta < 100$ ppm indicating the presence of hybrid orbital sp^3 .

Each carbon signals at δ 181.6; 182.9; and 184.6 ppm are assigned as carbon from carbonyl group, where the signal at 181.6 ppm is known as C signal of carbonyl from C-4 of a flavone compound, while the other two carbon signals are assigned as carbon from carbonyl group of quinoid structure.



The high resolution mass spectrum shows a signal at $[M+1]^+$, m/z 503. Based on this value, compound 1 is known to a xanthone derived from a flavone with B ring quinonily structured with a frame similar to artonin O, $[M+]$ = 502 with molecular formula of $C_{30}H_{30}O_7$.

Carbon shifts at δ 154.2; 156.9; 157.0; 159.7; and 163.9 ppm indicated the aromatic carbons which bound oxygen. The signals at δ 94.3; 105.6; 113.3; 118.1; 122.7; 132.3; and 145.5 ppm indicate

the presence of aromatic C=C, while signals δ 36.7 and 22.9 ppm indicate the aromatic C-C. The shifts at δ 112.9; 121.6; 123.3; 132.1; 133.8; and 142.7 ppm assigned as C=C aliphatic. The signals at δ 17.9; 18.0; 21.8; 22.2; 22.3; 25.9; and 25.9 are assigned for C-C aliphatic. Based on the data obtained, then the ^{13}C NMR data of compound 1 are suitable for artonin O.

The analyses on the ^{13}C NMR are supported by the 1H NMR of compound 1 (Fig. 3)

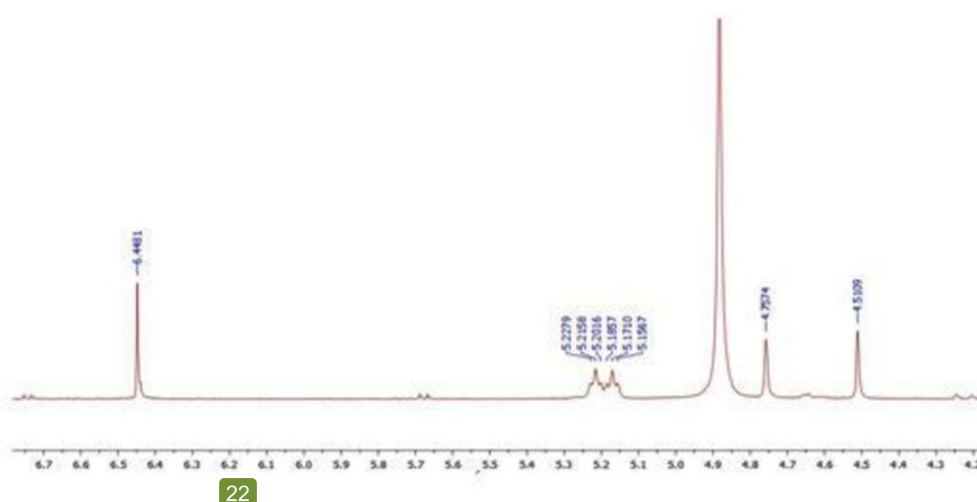


Fig. 3: 1H NMR spectrum of compound 1 (a) normal spectrum and (b) enlarge spectrum

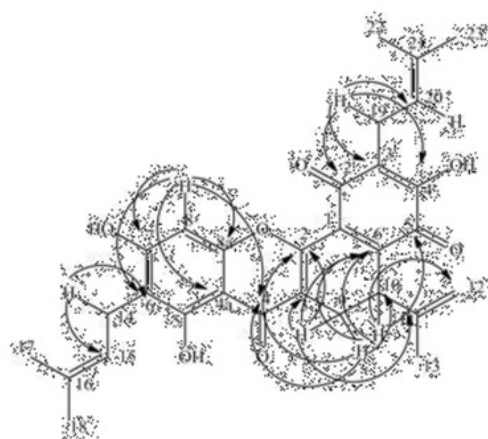


Fig. 4: Some important HMBC correlation of compound 1

which shows some chemical shifts and coupling constants of cyclopropanes of the ABX type. These signals are δ 2.62 (1H, d, J = 8.3 Hz, H-9), 3.33 (H-9b) (covered by solvent signal), and 3.75 (1H, d, J = 8.3 Hz, H-10).

There are also some aromatic protons on signals at δ 6.46 (1H, s, H-8) and some proton signals at δ 1.68 (each at 3H, s, CH_3 -17, and CH_3 -22); 1.88 (3H, s, CH_3 -18); and 1.80 (3H, s, CH_3 -13); 3.18 (2H, d, J = 7.1 Hz, H-19) and 3.34 (2H, d, J = 6.71 Hz, H-14); 5.17 (1H, m, H-15) and 5.21 (1H, m, H-20) which assigned the presence of two 3,3-dimethylallyl groups attached at C-6 and C-3'.

Furthermore, the proton signals of isopropenyl groups appeared at δ 1.78 (3H, s, CH_3 -

1**Table 2: Comparison of ^{13}C NMR and ^1H NMR spectra data compound 1 with artonin O_{3,8}**

No C	^{13}C NMR, δ (ppm)		^1H NMR, δ (ppm)	
	Artonin O (CD ₃ OD)	Compound 1 (CD ₃ OD)	Compound 1 (CD ₃ OD)	Artonin O (CD ₃ OD)
2	157.2	157		
3	118.1	118.1		
4	181.7	181.6		
4a	105.6	105.6		
5	159.7	159.7		
6	113.4	113.3		
7	164	163.9		
8	94.4	94.3	6.46 (1H, s)	6.45
8a	157	156.9		
1'	132.5	132.3		
2'	184.6	184.6		
3'	122.5	122.7		
4'	155.1	154.2		
5'	183.3	182.9		
6'	145.6	145.6		
9	22.9	22.9	2.62 (1Ha, q, J= 8.3 Hz). 3.33(1Hb, covered by solvent signal) 3.75 (1H, d, J=8.3 Hz)	2.61 3.35
10	36.8	36.7	4.75 (1Ha, s)	3.75
11	142.8	142.7	4.51(1Hb, s)	
12	112.9	112.9	1.77(3H, s) 3.34(2H, covered by solvent signal)	4.75 4.54
13	21.8	21.6	5.17 (1H, t, J=7.3 Hz)	1.77
14	22.2	22.2		3.34
15	123.3	123.3	1.65 (3H, s) 1.78 (3H, s)	5.17
16	133.7	133.8	3.18(2H, d, J=7.1 Hz)	
17	25.9	25.9	5.21 (1H, m)	1.65
18	17.9	17.9		1.77
19	22.3	22.3	1.68 (3H, s)	3.19
20	121.8	121.6	1.80 (3H, s)	5.21
21	132.2	132.1		
22	25.9	25.9		1.67
23	18	18		1.8

Table 3: The measurement result of inhibition zone from artonin O against *B. subtilis* with incubation time of 24 hours

Compound	Inhibition Zone (diameter, mm)		
	0.3 mg/disc	0.4 mg/disc	0.5 mg/disc
Artonin O	7	7.5	8.5
Amoxicilline (+)	20	22	22.5
Methanol (-)	0	0	0

23) and signals at δ 4.51; 4.75 (each corresponds to 1H, s, H-12). The comparisons of ^{13}C NMR and ^1H NMR spectra for compound 1 with data on literature for artonin O_{3,8} are tabulated at Table 2.

The deduction was also supported by the HMBC spectrum as shown in Fig. 4.

Bioactivity test

Artonin O has shown to have antibacterial activity toward the growth of *B. subtilis* by the formation of inhibition zone at all concentrations of 0.3; 0.4 and 0.5 mg/disc, with inhibition zone diameters were 7, 7.5 and 8.5 mm, respectively. While amoxicilline used as control positive with concentrations of .05; 0.10; and 0.15 mg/disc, the inhibition zone diameter measured were 20, 22, and 22.5 mm, respectively.

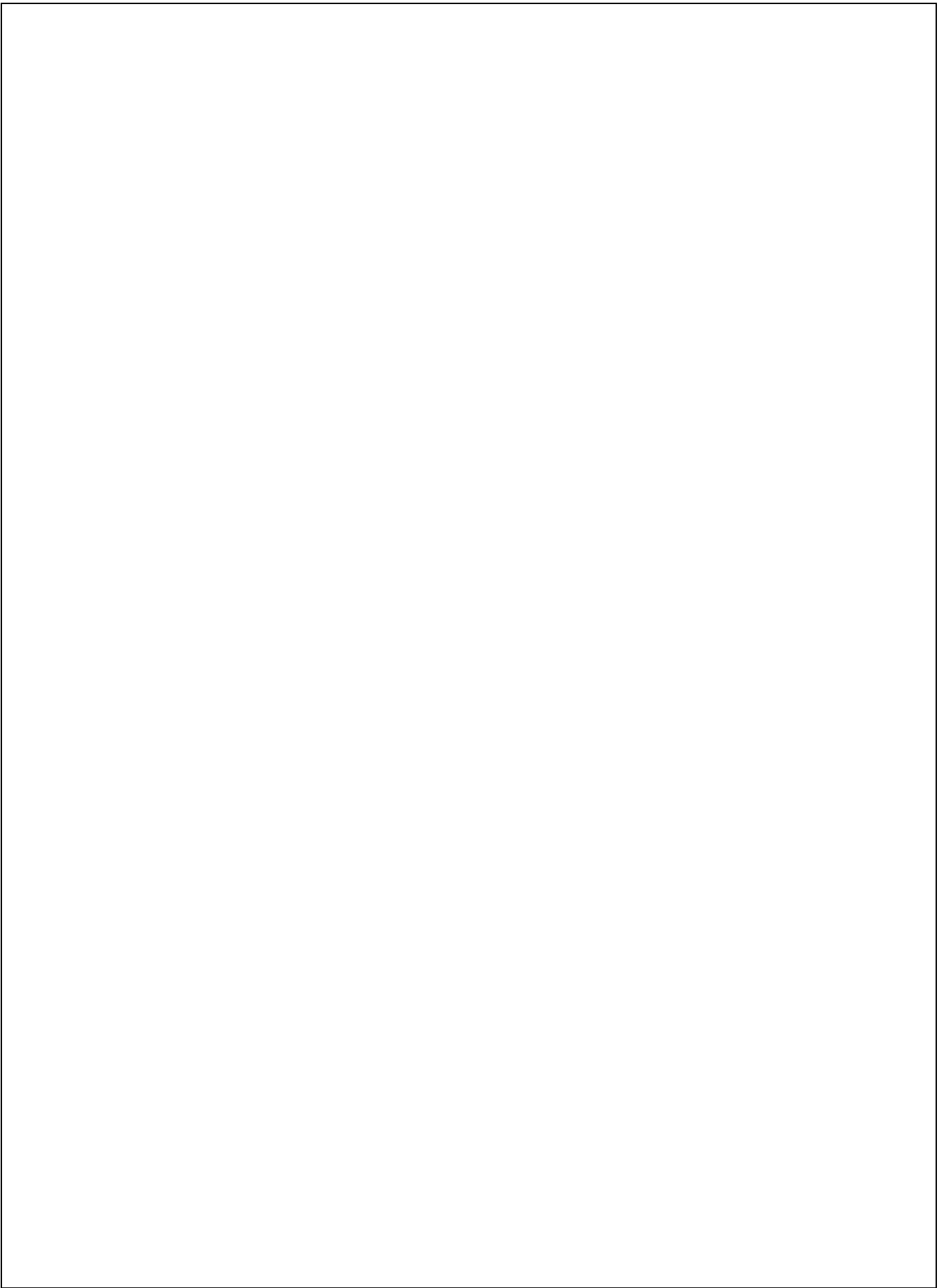
Based on the data obtained, it is known that the higher the concentration of the sample used, the higher the inhibition zone observed, although in overall, the positive controls have also been observed to inhibit much higher. The functional groups of compound 1 that play role on the antibacterial activities are hydroxyl group, carbonyl and isopropenyl. These groups are able to form hydrogen bond with protein from the bacteria

cell showing a specific interaction. According to Davis and Stout⁹, in the antibacterial activity, if the inhibition zone diameter observed is 5 mm or less, it is categorized as weak activity; 5-10 mm as medium activity, 10-19 as strong activity and 20 mm or more categorized as very strong activity. Based on the data obtained in this research, therefore artonin O is categorized as medium activity in the antibacterial activity test.

CONCLUSIONS

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From the root wood of *A. rigida* has successfully been isolated a xanthone compound, artonin O (1) showing medium antibacterial activity towards *B. subtilis*.



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