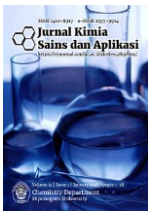
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Evaluation of the Antibacterial Activity of a Cycloartane-Type Triterpenoid from *Aglaia shawiana* Against Multidrug-Resistant Bacteria Type

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Abstract

Aglaia is the largest Genus in the Meliaceae family and is endemic to Indonesia. This study aims to isolate secondary metabolites from *Aglaia shawiana* that exhibit biological activity against multidrug-resistant pathogenic bacteria. Normal hexane extracts of *Aglaia shawiana* twigs were isolated and fractionated using various gravity column chromatography methods, resulting in a pure isolate. The structure of the pure isolate was determined by one-dimensional nuclear magnetic resonance spectroscopy and reference analysis. The pure isolate is a cycloartane-type tetracyclic triterpenoid compound named lagerenol. This study marks the first time that lagerenol has been successfully isolated as a pure, single compound. This is also the first time this compound has been discovered in the Meliaceae family. This study presents the first data on the biological activity of this compound. Previous research to determine the activity of compounds against bacteria has largely been conducted by evaluating them against standard bacterial strains; as a result, there remains a data gap regarding their efficacy against drug-resistant strains. Bioactivity of this compound was tested against four types of bacteria: two Gram-positive strains, *Bacillus subtilis* and *Pseudomonas aeruginosa*, and two Gram-negative strains, *Staphylococcus aureus* and *Escherichia coli*. However, lagerenol has not shown any activity at concentrations up to 100 ppm against any of the test bacteria. Tetracycline, which was used as a positive control, also showed no activity against the two types of Gram-negative bacteria tested. Therefore, it is also necessary to test their activity at higher concentration ranges to obtain more comprehensive data.

1. Introduction

Infectious diseases are one of the leading causes of high mortality rates in developing countries, including Indonesia. Infections can be caused by various pathogenic microorganisms, such as bacteria, viruses, parasites, or fungi [1]. One of the major challenges in treating bacterial infections today is the emergence of antibiotic resistance, known as multidrug resistance (MR). MR bacteria are a group of bacteria that exhibit resistance to at least one agent in three or more classes of antibiotics [2].

In Indonesia, there were 34,500 deaths directly caused by MR bacteria, as well as 133,800 deaths associated with MR infections in 2019. As microbial resistance to antibiotics increases and the side effects of conventional antibiotics become more apparent, the development of new antibacterial agents, particularly those derived from plants, has become crucial [3]. Prior research has mostly evaluated standard (non-MR) bacterial strains, leaving a gap in efficacy data against genuinely resistant strains.

Aglaia is the largest genus in the Meliaceae family, comprising approximately 150 species. These plants are endemic to tropical and subtropical regions, including Indonesia [4, 5]. The Aglaia genus has been studied for the isolation of its secondary metabolites since the 1960s. These secondary metabolites exhibit structural diversity, including triterpenoids, lignans, rocaglamida derivatives, sesquiterpenoids, tetraterpenoids, and steroids. Among these compounds, several have been found to possess interesting biological activities, such as anticancer, antifeedant, insecticidal, and antitumor activities [6, 7, 8, 9].

Given the highly promising potential of the compounds isolated from the genus Aglaia. We continue our efforts to isolate secondary metabolites from this genus, particularly those endemic to Indonesia. As part of ongoing research to identify compounds with biological activity that have the potential to be developed as starting materials for drug research from Indonesian Aglaia plants. We have successfully isolated several compounds, including those from the species *A. angustifolia* and *A. shawiana* [10, 11, 12, 13, 14]. While cycloartane-type triterpenoids from the genus Aglaia have demonstrated various biological activities, their specific efficacy against MR bacterial strains remains largely unexplored.

In this study, we report on the successful isolation and structural determination of a new cycloartane-type triterpenoid (compound **1**), which has been identified for the first time in the genus Aglaia or the family Meliaceae, and evaluate its antibacterial potential against four types of MR bacteria. The compound is named lagerenol (3β-hydroxycycloart-24-one). This is the first successful direct isolation of this compound without prior hydrolysis of lagerenyl acetate, as previously reported by Talapatra et al. [15] for its isolation from *Lagerstroemia lancasteri*. The results of this study can be used primarily to further develop the compound's structure and its activity against drug-resistant bacteria.

2. Experimental

2.1. Materials

Silica gel 60 (Merck Kieselgel 60 PF 253, Art. Nos. 7734.1000 and 9385.1000; particle sizes 0.063–0.200 mm and 0.040–0.063 mm) was used for normal-phase chromatography, while octadecylsilane (ODS; Fuji Silysia Chemical Ltd., Japan) was used for reversed-phase chromatography. Silica gel GF254 plates (Merck, 0.25 mm, Darmstadt, Germany) were used for thin-layer chromatography (TLC). A 10% H_2SO_4 solution in ethanol was used as the visualization reagent. $CDCl_3$ and tetramethylsilane (TMS) were used for NMR analysis. Technical-grade solvents (*n*-hexane, ethyl acetate, methanol, and dichloromethane) were distilled before use. High-purity solvents (Smart Lab, Indonesia, and Merck, Darmstadt, Germany) were used for final purification and spectroscopic measurements.

The pathogenic bacteria used in this study were four strains resistant to various antibiotics: *S. aureus*, *E. coli*, *B. subtilis*, and *P. aeruginosa*, which were obtained from the Microbiology Laboratory at the Research Center for Pharmaceutical Raw Materials and Traditional Medicine, National Research and Innovation Agency (BRIN), PUSPIPTEK Complex, Serpong. Media: Nutrient Agar (NA), Mueller Hinton Broth (MHB), Nutrient Broth (NB), and Tetracycline.

2.2. Plant Material Authentication

Aglaia shawiana twigs were collected from the Bogor Botanical Garden, Latitude: -6° 35' 30.59" S Longitude: 106° 47' 32.39" E, West Java, Indonesia, in July 2022. The taxonomy of this plant is: kingdom: Plantae, subkingdom: Tracheobionta, superdivision: Spermatophyta, division: Magnoliophyta, class: Magnoliopsida, subclass: Rosidae, order: Sapindales, family: Meliaceae, genus: Aglaia, species: *Aglaia shawiana* Merr. This plant was identified by the Plant Conservation Center at the Bogor Botanical Garden, Indonesia, and the voucher specimen (II.K.59) is housed in the Herbarium at the Bogor Botanical Garden, Bogor, West Java Province, Indonesia.

2.3. Instrumentation

The instruments and laboratory equipment used in this study included a CAMAG UV lamp operating at 254 and 365 nm; a Bruker Avance 700 NMR spectrometer (700 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) at the National Research and Innovation Agency (BRIN), Serpong; an IKA rotary evaporator; a vacuum liquid chromatography (VLC) system; a glass chromatography column; a multichannel micropipette; 50 mL centrifuge tubes; 96-well microplates; a Thermo Fisher Scientific ELISA reader; a laminar airflow cabinet; an incubator; an autoclave; a shaking incubator; and a reagent reservoir.

2.4. Isolation Procedure

A 1500 g sample of dried *A. shawiana* twigs was prepared as crude material and then macerated in *n*-hexane for 3 × 24 hours at room temperature. All filtrate from the maceration process was concentrated on a rotary evaporator at 50°C until a 20 g extract was obtained, yielding 0.13%.

The *n*-hexane extract of *A. shawiana* twigs obtained by maceration was subjected to further separation by VLC with silica gel G60 as the stationary phase and a gradient eluent of *n*-hexane, ethyl acetate, and methanol (10%), yielding 12 subfractions.

The combined fractions 3–5 (7 g), designated C2, were further separated using a KKG system with a 70–230 mesh silica gel stationary phase and an *n*-hexane-ethyl acetate gradient, yielding 20 subfractions. Fractions 3–4 (6 g) were then combined and designated as C2A; the TLC results with an *n*-hexane: ethyl acetate (8:2) eluent system showed a purple spot with an R_f value of 0.5. Fraction C2A was eluted using a TLC gradient eluent system of *n*-hexane: ethyl acetate at 5% and 10%. Subsequent repeated separations were performed using a polar silica (SiO_2) stationary phase with a combination of nonpolar and semipolar eluents, followed by a final stage with a nonpolar C18 silica stationary phase and methanol as the mobile phase, yielding a pure compound weighing 7.6 mg.

2.5. Structural Characterization

The pure isolate appeared as a single spot and was identified by TLC using an *n*-hexane: ethyl acetate eluent (9:1), with an R_f value of 0.3, as shown in Figure 1. The pure isolate was then analyzed using a Bruker 700 MHz NMR spectrometer, with $CDCl_3$ as the solvent and TMS as the internal standard, yielding 1D NMR data (^1H, ^{13}C, and DEPT-135°). The molecular formula and structure were determined based on 1D NMR data.

2.6. Antibacterial Protocol Assay

2.6.1. Media Preparation

NA medium was prepared by dissolving 1 g of NA medium powder in 50 mL of distilled water, while NB medium was prepared by dissolving 1.05 g of NB medium powder in 50 mL of distilled water. Both media were homogenized and then transferred into test tubes: 50 mL of NB medium and 50 mL of NA medium were transferred into Petri dishes. The medium used in this antibacterial test was MHB. MHB medium was prepared by dissolving 2.1 g of MHB medium powder in distilled water to a volume of 100 mL, then heating the medium until the powder was completely dissolved. Sterilization was then performed using an autoclave for 10 minutes at 1 atm pressure and 121°C.

2.6.2. Bacterial Inoculation and Dilution

Each bacterial culture was inoculated into 5 mL of NB already present in the test tubes. The test tubes containing the bacterial cultures were then incubated on a shaker at 37°C for 24 hours. After incubation, the turbidity of the medium (optical density/OD) was measured using an ELISA reader at a wavelength of 610 nm. The bacterial inoculum was standardized to 0.5 McFarland to prepare a stock solution, corresponding to 1-2 × 10^8 CFU/ml. A total of 10 µL of the suspension was mixed with 990 µL of 0.85% NaCl solution in a microtube, yielding a final concentration of 10^6 CFU/mL. Next, further dilution to a concentration of 10^4 CFU/mL was performed by pipetting 200 µL from the 10^6 dilution and mixing it with 19,800 µL of 0.85% NaCl solution, yielding a final volume of 20,000 µL (20 mL). Meanwhile, the concentration of the bacterial suspension after it was distributed into each well, following the addition of the sample solution in a 1:1 ratio, ultimately became 0.5 × 10^4 CFU/mL. Testing the activity of compound **1** against drug-resistant bacteria was based on the previous method and a slightly modified standard method [15, 16, 17].

2.6.3. Preparation of the Tetracycline Solution

A total of 2 mg of tetracycline was weighed and dissolved in 1,000 µL of methanol in a microtube, then homogenized using a vortex until the solution was homogeneous.

2.6.4. Minimum Inhibitory Concentration (MIC) Test

For the MIC test, 2 µL of methanol was added to wells A3 and A4 as negative controls. 4 µL of a 2000 ppm tetracycline solution was added to wells A5 and A6 as positive controls. A total of 100 µL of each solution in row A was transferred to row B using a multichannel micropipette. The same procedure was continued sequentially from row B to row H, with 100 µL transferred at each step. Subsequently, 100 µL of the MR bacterial suspension was added to all wells of the microplate. The microplate was then incubated in a shaking incubator at 37°C for 24 hours [18]. Biological replicates were performed four times, and technical replicates were performed twice.

3. Results and Discussion

3.1. Compound 1

Compound **1**, as shown in Figure 1, was successfully isolated and appears as a white precipitate with the molecular formula $C_{30}H_{50}O_2$. This molecular formula was determined from NMR data obtained for the isolated compound. Furthermore, the degree of unsaturation (Index of Hydrogen Deficiency; HD) for the isolate, calculated using the equation HD = ΣC − ΣH/2 + 1, is 6.

The ^1H NMR data ($CDCl_3$, 700 MHz, ppm) for compound **1** indicate the presence of four tertiary methyl groups at [δ_H 0.81 (3H, s, Me-18), 0.89 (3H, s, Me-28), 0.96 (3H, s, Me-30), and 0.97 (3H, s, Me-29)]. There are three secondary methyl groups at [δ_H 0.86 (3H, d, J = 6.6 Hz, Me-21), 1.10 (3H, d, J = 7.0 Hz, Me-26), and 1.10 (3H, d, J = 7.0 Hz, Me-27)]. An oxygenated methyl group is observed at δ_H 3.29 (1H, quint, J = 5.1 Hz, H-3), as shown in Figure 2.

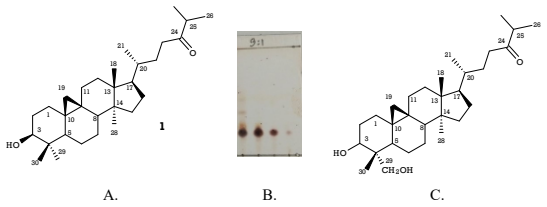


Figure 1. A) Compound **1**-lagarenol, B) TLC spot of **1**, and C) Cycloartan-3β,29-diol-24-one

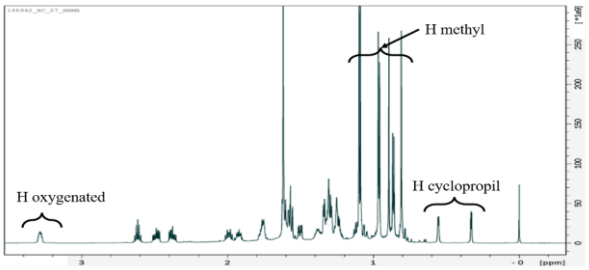


Figure 2. ^1H NMR spectrum of compound **1**

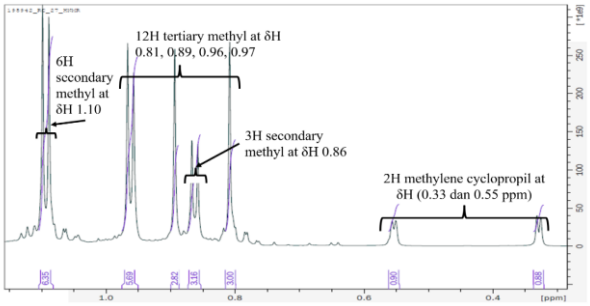


Figure 3. ^1H NMR spectrum of compound **1** at δ_H 0.3–1.2 ppm

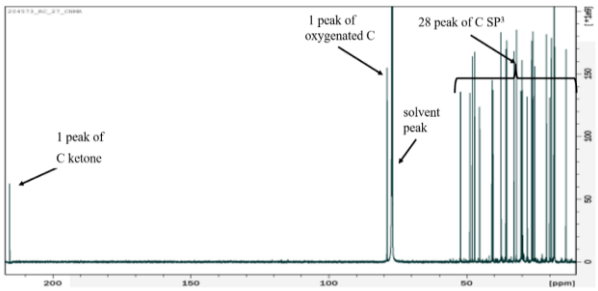


Figure 4. ^{13}C NMR spectrum of compound **1**

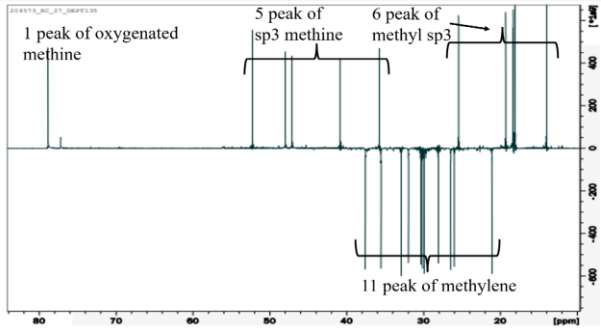


Figure 5. DEPT 135° spectrum of compound **1**

The signal (1–3 ppm), as shown in Figure 2, indicates the presence of a high-field sp^3 proton peak. Thus, it can be seen that most of the protons in this compound are of the sp^3 type, which can be in the form of methyl, methylene, or methine groups. A doublet spectrum is also observed at δ_H 0.33 (1H, d, H-19, J = 4.0 Hz) and 0.55 (1H, d, H-19, J = 4.0 Hz). This spectrum is characteristic of non-equivalent protons in a cyclopropyl methylene group, as shown in Figure 3.

Based on the ^{13}C NMR spectrum ($CDCl_3$, 175 MHz, ppm) and the DEPT 135° spectrum of compound **1**, there are 30 carbon peaks that can be classified by chemical shift and spectral patterns, as shown in Figure 4. There are 4 tertiary methyl groups at δ_C 14.1 (CH_3-30), 18.3 (CH_3-18), 19.3 (CH_3-28), and 25.4 (CH_3-29). The spectrum also shows 3 secondary methyl groups at δ_C 18.1 (CH_3-26), 18.1 (CH_3-26), and 18.4 (CH_3-21), bringing the total number of methyl peaks to 7.

Eleven methylene carbons were found at δ_C 29.9 (CH_2-1), 30.4 (CH_2-2), 21.1 (CH_2-6), 28.1 (CH_2-7), 26.1 (CH_2–11), 35.5 (CH_2–12), 32.9 (CH_2–15), 26.4 (CH_2–16), 30.1 (CH_2–19), 32.0 (CH_2–22), and 37.6 (CH_2–23). The sp^3 methine carbon spectrum showed 5 peaks at δ_C 47.1 (CH- 5), 48.0 (CH-8), 52.3 (CH-17), 35.8 (CH-20), 40.8 (CH-25), and one oxygenated methine group at δ_C 78.9 (CH-3), as shown in Figure 5. The sp^3 quaternary carbon spectrum was observed at δ_C 40.5 (C-4), 20.0 (C-9), 26.0 (C-10), 45.3 (C-13), 48.8 (C-14), and 1 quaternary carbon of the ketone functional group was found at δ_C 216.1 (C- 24).

The presence of this ketone functional group accounts for 1 of the 6 double-bond equivalents (hydrogen deficiency index), leaving 5 double-bond equivalents remaining, consistent with a tricyclic triterpenoid compound with an additional cyclopropyl group. Based on the ^1H, ^{13}C, and DEPT NMR spectral data, the presence of a cyclopropyl group is indicated at [δ_H 0.33 (1H, d, J = 4.0 Hz), 0.55 (1H, d, J = 4.0 Hz), δ_C 30.1], one hydroxyl group at δ_H 3.29 (1H, quint, J = 5.1 Hz); δ_C 78.9. The carbon and proton shifts of the basic structure of compound **1**, including rings A, B, C, and D, and the cyclopropyl groups (C-9, C-10, and C-19), are characteristic of the basic framework of a cycloartan-type triterpenoid molecule.

The chemical shifts in the NMR spectra of compound **1** are closely similar to those of the reference molecule, lagarenol, which has been successfully isolated from the leaves and twigs of *Lagerstroemia lancasteri*, as shown in Table 1. However, since the NMR data obtained from the reference journal for lagerenol is limited, the NMR shifts of compound **1** were also compared with those of cycloartan-3β,29-diol-24-one, which has a similar basic framework, which was first discovered by Inada *et al.* [19] in the leaves of *Aglaia harmsiana* Perkins (Meliaceae), and was subsequently discovered by Hutagaol *et al.* [11] in the leaves of *Aglaia shawiana*.

Based on the ^1H NMR spectrum (80 MHz, $CDCl_3$) of lagerenol, from literature, there are 5 protons from methyl singlets at δ_H (0.82, 0.90, and 0.97), 2 proton peaks from secondary methyl groups at δ_H 1.12 (CH_3-26) and CH_3-27, d, J = 7 Hz). Furthermore, there is a ^1H shift at δ_H 2.41 (2H-23, t, J = 4.8 Hz), δ_H 2.54 (H-25, sept, J = 7 Hz), and δ_H 3.30 (H-3, dd, J = 10 and 5 Hz). Furthermore, δ_H 0.35 and 0.59 (2H-19, d, J = 4.5 Hz) indicate non-equivalent cyclopropyl methylene. No additional data regarding the chemical shifts of the NMR spectrum of the legerenol compound were found in the reference journal. Based on a comparison of the ^1H NMR shifts of the lagerenol compound with those of compound **1**, there is a slight difference in the methyl-methyl shift values and their multiplicity patterns, which is suspected to be due to the NMR frequency used. However, based on the 1D NMR spectrum, which indicates high purity, compound **1** is believed to be identical to lagerenol.

Furthermore, based on the biogenesis approach, most natural triterpenoids and steroids contain a 3- hydroxyl group, which is an epoxide oxygen atom derived from oxidosqualene. The stereochemistry of the protosteryl cation, which is subsequently converted via enzymatic reactions to cycloartenol, features a -OH group at the C-3 position in the β configuration [20]. The hydroxyl group at C-3 in compound **1** is in the equatorial-β position based on the similarity of the ^1H shift values in compound **1** and lagerenol, namely δ_H 3.29 and δ_H 3.30.

Table 1. ^{1}H, ^{13}C, and DEPT-135° spectral data for compound **1** (700 MHz, in $CDCl_3$), lagerenol, and cycloartan-3β,29-diol-24-one

Carbon	Compound **1**			Lagerenol (80 MHz in $CDCl_3$ [21])		Cycloartan-3β,29-diol-24-one (400 MHz in $CDCl_3$ [19])	
	^{13}C [ppm]	^{1}H [ppm] (integ., mult., J = Hz)	DEPT-135°	*^{13}C [ppm]	^{1}H [ppm] (integ., mult., J = Hz)	^{13}C [ppm] (mult.)	^{1}H [ppm] (integ., mult., J = Hz)
C-1	29.9	-	CH_2		-	31.7	-
C-2	30.4	-	CH_2		-	30.2	-
C-3	78.9	3.29 (1H, quint, 5.1 Hz)	CHOH		3.30 (1H, dd, 10 and 5 Hz)	77.0	3.75 (1H, dd, 10.5, 4.5)
C-4	40.5	-	C			43.7	-
C-5	47.1	-	CH			42.5	-
C-6	21.1	-	CH_2			21.0	-
C-7	28.1	-	CH_2			28.1	-
C-8	48.0	-	CH			47.9	-
C-9	20.0	-	C		5 protons from the methyl singlet at δ_H (0.82, 0.90, and 0.97)	19.9	-
C-10	26.0	-	C			25.7	-
C-11	26.1	-	CH_2			25.4	-
C-12	35.5	-	CH_2			35.6	-
C-13	45.3	-	C			45.3	-
C-14	48.8	-	C			48.8	-
C-15	32.9	-	CH_2			32.9	-
C-16	26.4	-	CH_2			26.4	-
C-17	52.3	-	CH			52.3	-
C-18	18.3	0.81 (3H, s)	CH_3		-	18.0	0.94 (3H, s)
C-19	30.1	0.33 and 0.55 (2H-19, d, 4.0 Hz)	CH_2		0.35 and 0.59 (2H-19, d, 4.5)	30.0	0.38 (1H, d, 4.2), 0.58 (1H, d, 4.2)
C-20	35.8	-	CH		-	35.9	-
C-21	18.4	0.86 (3H, d, 6.6)	CH_3		-	18.4	0.86 (3H, d, 6.6)
C-22	32.0	-	CH_2		-	32.9	-
C-23	37.6	2.37 (1H, ddd, 4.0, 9.9, 16.0) and 2.49 (1H, ddd, 4.8, 10.2, 16.1)	CH_2		2.38 (2H, t, 4.8)	37.6	
C-24	216.1	-	C=O		-	215.5	-
C-25	40.8	2.61 (1H, sept, 7)	CH		2.54 (1H, sept, 7)	40.9	2.61 (1H, d, 6.8)
C-26	18.1	1.10 (3H, d, 7)	CH_3		1.12 (3H, d, 7)	18.3	1.09 (3H, d, 6.8)
C-27	18.1	1.10 (3H, d, 7)	CH_3		1.12 (3H, d, 7)	18.1	1.09 (3H, d, 6.8)
C-28	19.3	0.89 (3H, s)	CH_3		-	19.3	0.89 (3H, s)
C-29	25.4	0.97 (3H, s)	CH_3		-	71.1	3.73 (1H, dd, 10.5, 4.5), 3.52 (1H, d, 10.7)
C-30	14.1	0.96 (3H, s)	CH_3		-	10.1	0.96 (3H, s)

*^{13}C NMR chemical shift data were not reported in the referenced journal.

Table 2. OD value of MR*Pa*

[ppm]	MeOH		Tetracycline		Compound **1**	
100	0.640	0.590	0.128	0.197	0.630	0.634
50	0.475	0.512	0.069	0.036	0.549	0.548
25	0.744	0.494	0.070	0.018	0.535	0.446
12.5	0.714	0.407	0.132	0.066	0.612	0.576
6.25	0.552	0.440	0.135	0.096	0.610	0.556
3.125	0.439	0.359	0.158	0.083	0.518	0.479
1.5625	0.474	0.530	0.150	0.085	0.490	0.463
0.78125	0.503	0.497	0.206	0.173	0.598	0.493

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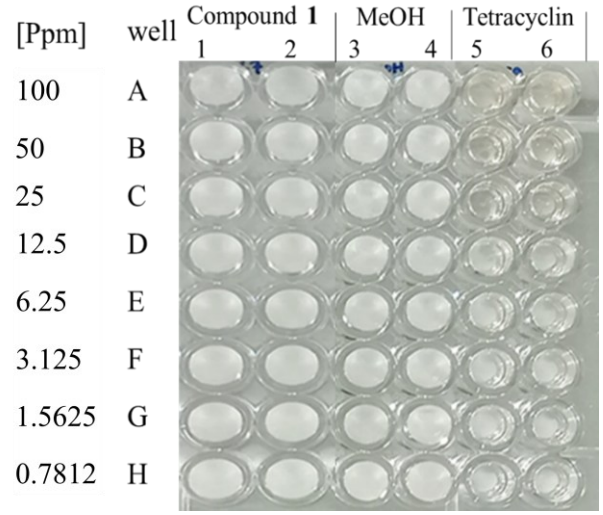


Figure 6. Well plate activity test of compound **1** against MR*Pa*

Based on optical density (OD) and visual turbidity measurements in the test wells. Compound **1**, at concentrations up to 100 ppm, did not exhibit any activity against the four MR bacterial species tested, as shown in the data in Supplementary Material (S1). Thus, the MIC value of compound **1** against all test bacteria was >100 ppm. The MIC of tetracycline, used as a positive control, was also >100 ppm against the MRSa and MREc test bacteria. Meanwhile, for MRPa bacteria, tetracycline had an MIC of 25 ppm, and for MRBs, it had an MIC of 3.125 ppm. The OD and turbidity data for the MRPa test bacteria are shown in Table 2 and Figure 6. Tetracycline was used in this study because it is commonly used as a positive control for antibacterial activity. Therefore, for future studies testing activity against MR bacteria, particularly MRSa and MREc, it is recommended to use another positive control in place of tetracycline.

Based on the literature review, compound 1 has not been reported previously from the genus Aglaia or even the family Meliaceae. This is the first successful direct isolation of lagerenol without prior hydrolysis of lagerenyl acetate, as previously reported by Talapatra *et al.* [21] for isolation from the *Lagerstroemia lancasteri* plant. However, the isolated compound showed no bioactivity against the four types of MR bacteria tested up to 100 ppm. This is thought to be due to the fact that the structure of this compound lacks more reactive or more polar functional groups, such as carboxylic acid or acetic acid groups, bound to its structure. Another possible reason is that the main backbone of compound **1** consists of a large cyclic structure, which may create steric hindrance that prevents the compound from forming bonds with the bacterial targets [22, 23].

The inactivity of compound **1** against the four types of MDR bacteria may also be due to several factors in the MDR bacteria that can inhibit the activity of compound **1**, such as bacterial efflux pump factors, changes in bacterial porin structure that reduce bacterial permeability to the entry of the compound, hydrolytic enzymes, and changes in the binding sites present in the bacteria [24]. During the bioactivity testing of compound **1**, several factors can reduce the compound's permeability and effectiveness during the test, such as its high lipophilicity due to a predominance of nonpolar groups, its molecular size, or its tendency to aggregate in aqueous solution.

4. Conclusion

A cycloartane-type triterpenoid, namely lagerenol (1), was successfully isolated from the n-hexane extract of *A. shawiana* twigs. To the best of our knowledge, this is the first reported isolation of pure lagerenol without prior hydrolysis of lagerenyl acetate, which was previously used for its isolation from *Lagerstroemia lancasteri*. Lagerenol did not exhibit antibacterial activity at the tested concentration of 100 µg/mL. This study provides a basis for further investigation of the structure–activity relationships of cycloartane-type triterpenoids. Future studies may focus on structural modification and evaluation of their antibacterial activity, synergistic effects with antibiotics, and other potential biological activities.

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