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Sesquiterpenoids from *Aglaia cucullata* Peel Fruit and Their Cytotoxic Activities Against B16-F10 and HeLa Cancer Cell Lines

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ABSTRACT. Sesquiterpenoids are terpenoid derivative compounds that have a diverse chemical structure and pharmacological effects. Sesquiterpenoids can be found in many plants of *Aglaia* which is the large source of natural compounds in the Meliaceae family. This investigation was intended to elucidate the structure of sesquiterpenoids from *Aglaia cucullata* peel fruit and their cytotoxicity against two human cancer cell lines. *n*-hexane extracts were separated by various chromatographic methods to yield three sesquiterpenoids. These sesquiterpenoids were identified by spectroscopy analysis (HR-TOFMS, IR, ^{1}H, ^{13}C-NMR, DEPT-135) as well as compared with spectral data which reported previously. The sesquiterpenoid compounds **1-3** were identified as spathulenol (**1**), alismol (**2**), and 10-oxoisodauc-3-en-15-al (**3**). The cytotoxic activity of three sesquiterpenoid compounds were tested against B16-F10 skin cancer cell and HeLa cervical cancer cell using the PrestoBlue method. Compound **2** exhibited the highest activity against both HeLa and B16-F10 cancer cell lines with IC_{50} 218.33 µM and 258.90 µM, respectively.

Keyword: *Aglaia cucullata*, sesquiterpenoid, cytotoxic activity, HeLa, B16-F10

INTRODUCTION

Sesquiterpenoids are terpenoid derivative compounds that consisted of fifteen carbon atoms and formed by three isoprene units (C_5). Sesquiterpenoids have a diverse chemical structure and exists in a several skeletal forms based on the total of its rings. Sesquiterpenoids in general are a scented oil and usually considered as major component of essential oil. The biological activities of sesquiterpenoids have been widely reported such as antimalarial (Wu et al., 2020), cytotoxic activities (Izdihar et al., 2021), antitumor (Liu et al., 2014), and antifungal (Dharmayani et al., 2020). Sesquiterpenoids can be found in plants of the Meliaceae, Cactaceae, Solanaceae, Araceae, and Euphorbiaceae family (Mbaveng et al., 2014).

Aglaia is the large source of natural compounds in the Meliaceae family which has a total of 150 species distributed in subtropical and tropical rainforests in the south-eastern and southern Asia and Pacific (Pan et al., 2014; Harneti & Supratman, 2021) and the northern Australia (Peng et al., 2015). In Asia, plants of the *Aglaia* genus are distributed in India, Malaysia, Thailand, Indonesia, and Vietnam (Joycharat et al., 2008) and eight species of them spread in the south of China (Xie et al., 2007). Around 65 species of *Aglaia* plants grow in Indonesia and spread in the island of Java, Sumatra, Bali, Sulawesi, and Kalimantan (Heyne, 1987). Plants from *Aglaia* genus is widely used as indigenous medicine for treatment of cough, diarrhea, fever (An et al., 2016), skin diseases (Hutagaol et al., 2020), heart disease (Yodsaoue et al., 2012), and bruises (Harneti et al., 2014). In addition, the biological activities of this plants have been investigated such as antioxidant, antibacterial (Pervin et al., 2016), insecticidal (Schneider et al., 2000), antiviral (Esimone et al., 2010), antitumor (Awang et al., 2012), antifungal (Joycharat et al., 2010), and cytotoxic activities (Farabi et al., 2017; Hidayat et al., 2017a, 2017b, 2018) . In the *Aglaia* genus, twenty-six sesquiterpenoid compounds have been reported, there were the type of cadinene (Huang et al., 2022), aromadendrane, isodaucane, and eudesmane (Harneti et al., 2022), guaiane (Liu et al., 2014), clovane, caryolane (Izdihar et al., 2021), and caryophyllene-type (Benosman et al., 1995).

Aglaia cucullata is a mangrove plant that grow in tobacco swamps and is the only species from the *Aglaia* genus that has pneumatophores roots (Heads, 2019). *A. cucullata* is distributed in the rainforests of

Southeast Asia, India, Bangladesh, Nepal, Pakistan, Myanmar, Malaysia, Thailand, Vietnam, Solomon Islands, and Indonesia in the islands of Borneo and Sumatra (Pervin et al., 2016). Twenty-two compounds from *A. cucullata* have been reported such as diterpenoids, triterpenoids (Ahmed et al., 2010), alkaloids (Chumkaew et al., 2019), bisamides (Abdelfattah et al., 2010; Ahmed et al., 2010), rocaglamides (Chumkaew et al., 2006), and flavonoids (Abdelfattah et al., 2010). Amocurin C isolated from the root of *A. cucullata* showed the cytotoxicity against KB cells and MCF-7 breast cancer cells (IC_{50} 4.2 and 3.5 μM, respectively) (Chumkaew et al., 2019). In addition, rocaglamide derivatives from the fruit of *A. cucullata* showed the strong cytotoxicity against KB, BC, and NCI-H187 cells (Chumkaew et al., 2006). Based on literatures, sesquiterpenoids have not been reported from this species. This paper described the isolation, structure elucidation and cytotoxic evaluation against HeLa and B16-F10 cancer cell lines of three type of aromadendrane, guaiane, and isodaucane sesquiterpenoids from *A. cucullata*.

EXPERIMENTAL SECTION

General Experimental Procedures

Perkin Elmer spectrum 100 FTIR in plate of KBr (Waltham, Massachusetts, USA) was used to obtain IR spectra. Waters QTOF-HRTOFMS-XEV^{otm} mass spectrometer was used to obtain high-resolution mass spectra. Meanwhile, NMR spectras of **1** and **2** were also recorded by Bruker Av-500 spectrometer (Bruker, Karlsruhe, Germany) at 500 MHz for ^{1}H and 125 MHz for ^{13}C, whereas **3** was recorded by JEOL JNM-ECZ500R/S1, $CDCl_3$ as a solvent and tetramethyl silane (TMS) as an internal standard. ODS 100–200 mesh (Fuji Sylisia Chemical LTD.) and silica gel 60 70-230 and 230-400 mesh (Merck) were used for column chromatography. Silica gel 60 GF_{254} and RP-18 F_{254}s plates (Merck) were used for thin-layer chromatography. Detection of TLC plate was monitored under UV-Vis light and sprayed with H_2SO_4 (10%) in ethanol.

Plant Materials

A. cucullata (Roxb.) Pellegr. peel fruit was collected from the Manggar River, Balikpapan, East Kalimantan, Indonesia in December 2020. The plant was examined at the Herbarium Wanariset (WAN), Balikapapan (collection No. FF7.20), and stored at the Faculty of Forestry, Mulawarman University.

Extraction and Isolation

Dried *A. cucullata* peel fruit (1 kg) was macerated using ethanol 70% repeatedly, filtered, and evaporated to give concentrated orangish ethanol extract. This orangish extract was fractionated consecutively with *n*-hexane, EtOAc, and *n*-butanol. Furthermore, all organic fractions were evaporated with rotary evaporator at temperature 37°C to produce a concentrated extracts of *n*-hexane (250.7 g, 25.1%), EtOAc (40.9 g, 4.1%), and *n*-butanol (5.9 g, 0.6%). All extracts were tested their cytotoxicities against two human cancer cells and showed respectively an IC_{50} values 7.85, 85.03, 120.22 μg/mL against B16-F10 cancer cells, and 23.77, 166.40, 243.30 μg/mL against HeLa cancer cells. *n*-hexane extracts demonstrated the highest cytotoxicity and according to the analysis of TLC, this extracts showed the content of terpenoid compounds.

The extract of *n*-hexane was separated by VLC using 10% gradient eluent system of *n*-hexane-EtOAc (100:0 – 0:100) on silica gel to gained five fractions (A-E). B Fraction (9.4 g) was performed by column chromatography/CC silica gel (70-230 mesh) with gradient solvent of *n*-hexane and EtOAc (100:0 – 90:10) to obtained seven combined fractions (B1-B7). Then, separation of B4 fraction (952.0 mg) was performed by CC silica gel (230-400 mesh) using *n*-hexane:EtOAc (100:1) to give five fractions (B4A-B4E). Purification of the subfraction B4D (34.7 mg) and subfraction B4E (29.7 mg) on silica gel (230-400 mesh) CC using *n*-hexane:EtOAc (70:1) yield compound **1** (8.5 mg) from B4D subfraction meanwhile compound **2** (5.2 mg) from B4E subfraction.

Separation of the B5 fraction (2.71 g) performed by CC silica gel (70-230 mesh) with *n*-hexane:dichloromethane:EtOAc (25:25:1) eluent to obtained nine combined fraction (B5A-B5I). Furthermore, fraction B5B (269.0 mg) was eluted using *n*-hexane:EtOAc (15:1) to give five subfraction (B5B1-B5B5) by CC silica gel (230-400 mesh). Then, the subfraction B5B2 (154.0 mg) was purificated with ODS CC and eluted with 7:3 of MeOH:H_2O to yield compound **3** (28.5 mg).

Spathulenol (**1**). Colourless oil; IR (KBr) ν_{max} cm^{-1}: 3396, 2926, 2856, 1636, 1457, 1376, 1096 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 1.31 (1H, m, H-1), 1.88 (1H, dd, *J*= 6.0, 12.0 Hz, H-2a), 1.64 (1H, dd, *J*= 6.0, 12.0 Hz, H-2b), 1.76 (1H, m, H-3a), 1.54 (1H, m, H-3b), 1.31 (1H, m, H-5), 0.46 (1H, dd, *J*= 9.0, 10.8 Hz, H-6), 0.70 (1H, m, H-7), 1.96 (2H, m, H-8), 2.41 (1H, dd, *J*= 6.0, 13.8 Hz, H-9a), 2.04 (1H, dd, *J*= 6.0, 13.8 Hz, H-9b), 1.04 (3H, s, CH_3-12), 1.06 (3H, s, CH_3-13), 4.66 (1H, br.s, H-14a), 4.69 (1H, br.s, H-14b), 1.28 (3H, s, CH_3-15); ^{13}C-NMR in Table 1; HR-TOF MS $[M+K]^+$ ion peak at *m/z* 259.1453 (calculated for $C_{15}H_{24}OK$, *m/z* 259.1464).

Alismol (**2**). Yellowish oil; IR (KBr) ν_{max} cm^{-1}: 3399, 2958, 2871, 1640, 1462, 1382, 1080; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 5.54 (1H, s, H-6), 1.23 (3H, s, CH_3-12), 0.98 (3H, d, *J*= 6.4 Hz, CH_3-13), 0.96 (3H, d, *J*= 6.4 Hz, CH_3-14), 4.75 (1H, s, H-15), 4.69 (1H, s, H-15); ^{13}C-NMR in Table 1; HR-TOF MS $[M+K]^+$ ion peak at *m/z* 259.1453 (calculated for $C_{15}H_{24}OK$, *m/z* 259.1464).

10-oxo-isodauc-3-en-15-al (**3**) Yellowish oil; IR (KBr) ν_{max} cm^{-1}: 3350, 2961, 1720, 1711, 1636, 1465, 1377; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 6.60 (1H, d, *J*= 5.4 Hz, H-4), 0.91 (3H, d, *J*= 7.1 Hz, CH_3-13),

0.92 (3H, d, *J*= 7.1 Hz, CH_3-12), 1.30 (3H, s, CH_3-14), 9.30 (1H, s, H-15); ^{13}C-NMR in Table 1; HR-TOF MS $[M+Na]^+$ ion peak at *m/z* 257.1520 (calculated for $C_{15}H_{22}O_2Na$, *m/z* 257.1517).

Determination of Cytotoxic Activity

PrestoBlue® method with resazurin reagent was used to obtain the cytotoxic activities of compound **1-3** towards melanoma skin cancer cells (B16-F10) and HeLa cancer cells. The first stage of this method was seeding cells. HeLa and B16-F10 cells were seeded into 96 well plates on Rosewell Park Memorial Institute (RPMI) medium and incubated for 24 hours for B16-F10 cell and 48 hours for HeLa cell (temperature 37°C and 5% CO_2 gas) until density of 1.7×10^4 cell/well reached. The second stage was cell treatment with samples, positive, and negative control. In this stage, the RPMI medium on the plates were discarded and added the medium containing sample (DMSO as solvent) with various concentration (250.00, 125.00, 62.50, 31.25, 15.63, 7.81, 3.91, and 1.95 μg/mL) and also cisplatin as positive control. The cells which were treated with sample and positive control were incubated for two days. The last was adding the PrestoBlue® reagents and measurement of absorbances. The medium containing sample on the plates were discarded, then added the PrestoBlue® reagent and incubated for 2 hours until the color changes. Subsequently, the absorbance of each sample was recorded by multimode reader (wavelength 570 nm). Absorbances were converted into percent cell viability to obtain the IC_{50} value.

RESULTS AND DISCUSSION

Three known sesquiterpenoid compounds namely spathulenol (**1**), alismol (**2**), and 10-oxoisodauc-3-en-15-al (**3**) (**Figure 1**) have been isolated from the peel fruit of *A. cucullata*. These compounds were reported for the first time from *A. cucullata,* and **2** was first reported from genus *Aglaia*.

Compound **1** was isolated as a colorless oil. Its molecular formula is $C_{15}H_{24}O$ according to the HR-TOFMS *m/z* 259.1453 $[M+K]^+$ (calcd. 259.1464), with four unsaturated degrees. The IR spectrum demonstrated the existence of hydroxyl (3396 cm^{-1}), aliphatic (2926 and 2856 cm^{-1}), olefinic (1636 cm^{-1}), *gem*-dimethyl (1457, 1376 cm^{-1}), and ether bond (C-O) (1096 cm^{-1}). Meanwhile, ^{1}H-NMR showed the existence of three proton singlets resonance at δ_H 1.04 (3H, s, CH_3-12), 1.06 (3H, s, CH_3-13), and 1.28 (3H, s, CH_3-15) for tertiary methyl groups. Then, the existence of one methylene sp^2 group which has the chemical shift of geminal proton at δ_H 4.66 (1H, br.s, H-14a), and 4.69 (1H, br.s, H-14b). Furthermore, the ^{13}C-NMR spectra detailed with DEPT 135º of **1** demonstrated signals for 15 carbons, including three methyls sp^3, four methylenes sp^3 resonance at δ_C 16.3 (C-12), 28.7 (C-13), 26.1 (C-15), 26.7 (C-2), 41.7 (C-3), 24.8 (C-8), 38.9 (C-9), respectively. One olefinic methylene at δ_C 106.3 (C-14), four methines at δ_C 53.4 (C-1), 54.3 (C-5), 29.9 (C-6), 27.5 (C-7), and three quaternary carbons at δ_C 20.3 (C-11), including oxygenated quaternary carbon at δ_C 81.0 (C-4), and quaternary olefinic carbon at δ_C 153.5 (C-10). Based on ^{13}C-NMR spectral data, the disubstituted double bond has been identified as terminal olefinic group ($C=CH_2$) which calculated for one unsaturated degree. Therefore, three remaining unsaturated degrees indicated the tricyclic sesquiterpenoid skeleton. All NMR spectral data show the characteristic of aromadendrane-type sesquiterpenoid (Roux et al., 1998). It is supported by presence of upfield quaternary carbons at δ_C 20.3 (C-11) which prove the cyclopropane ring in aromadendrane skeleton. The upfield quaternary carbon is due to the presence of isopropyl group bound to the cyclopropane ring to give shielding effect (Feliciano et al., 1989). In addition, the presence of two tertiary methyls at δ_C 16.3 (C-12) and 28.7 (C-13) supported the existence of isopropyl group. Moreover, presence of downfield proton of tertiary methyl at δ_H 1.28 (3H, s, H-15) showed the existence of methyl that bound to the quaternary oxygenated carbon at δ_C 81.0 (C-4). Then, the terminal olefinic group ($C=CH_2$) was suggest at position C-10/C-14 based on biosynthetic approached (Dewick, 2009). The structure determination was carried out by the approach of aromadendrane-type sesquiterpenoids in *Aglaia* genus. These compounds were spathulenol, 4β, 10α-dihydroxyaromadendrane (Harneti et al., 2022; Izdihar et al., 2021), 4α,10α-dihydroxyaromadendrane (Milawati et al., 2020), T-cadinol, ledol (Roux et al., 1998), and viridilflorol (Pointinger et al., 2008). Spathulenol has a similarity

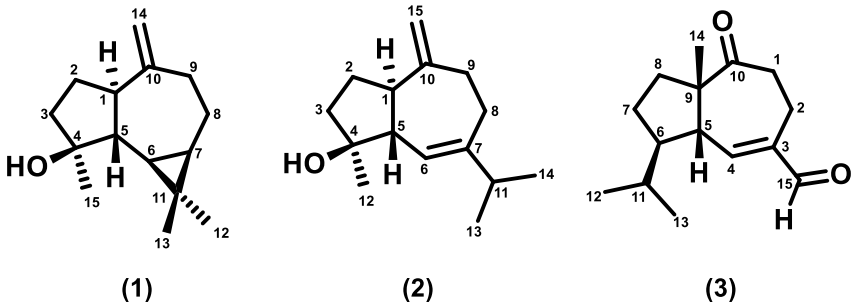

Figure 1. Structure of compound **1-3**

functional group with compound **1**, so the spectral data of compound **1** and spathulenol (Milawati et al., 2020) were comprised. The result showed the NMR spectral data of both were similar (**Table 1**). Therefore, compound **1** was identified as known compounds, namely spathulenol.

Compound **2** was purified as a yellowish oil, having the molecular formula of $C_{15}H_{24}O$ based on the HR-TOFMS *m/z* 259.1453 $[M+K]^+$ (calcd. 259.1464), with four unsaturated degrees. The IR spectra demonstrated the absorption bands of hydroxyl (3399 cm^{-1}), C-H sp^3 (2958 and 2871 cm^{-1}), olefinic (1640 cm^{-1}), *gem*-dimethyl (1462 and 1382 cm^{-1}), and ether group (C-O) (1080 cm^{-1}). Subsequently, ^{1}H-NMR spectrum gave the signals for one methyl singlet resonance at δ_H 1.23 (3H, s, CH_3-12), two secondary methyls resonance at δ_H 0.98 (3H, d, *J*= 6.4 Hz, CH_3-13), 0.96 (3H, d, *J*= 6.4 Hz, CH_3-14), one olefinic methylene at δ_H 4.75 (1H, s, H-15), 4.69 (1H, s, H-15), and one olefinic methine at δ_H 5.54 (1H, s, H-6). Moreover, the ^{13}C-NMR spectra detailed with DEPT 135º of **2** exhibited the presence of 15 carbons, including three methyls sp^3, four methylenes sp^3 resonance at δ_C 21.5 (C-13), 21.3 (C-12), 24.0 (C-14), 24.7 (C-2), 30.0 (C-8), 37.0 (C-9), 41.2 (C-3), respectively. One olefinic methylene resonance at δ_C 106.5 (C-15), four methines at δ_C 37.4 (C-11), 47.2 (C-5), 55.0 (C-1), and one of them is methine sp^2 at δ_C 121.2 (C-6), then three of quaternary carbon including oxygenated quaternary carbon at δ_C 80.7 (C-4) and two quaternary olefinic carbons at δ_C 149.8 (C-7) and 153.9 (C-10). Based on ^{1}H, ^{13}C-NMR, and DEPT 135° compound **2** have two of double bond such as terminal olefinic group (C=CH_2) and methine olefinic group (C=CH). These olefinic groups were calculated for two unsaturated degrees. The remaining hydrogen deficiency indexes were indicating the existence of bicyclic sesquiterpenoid structure. The absence of quaternary aliphatic carbon and the number of methyls, methylenes, and methines carbons indicates the characteristic of guaiane-type sesquiterpenoid (Ellithey et al., 2013). All NMR data of **1** and **2** have a similarity chemical shift. Therefore, the determination of the structure of **2** was carried out with the same approach as compound **1**. The position of terminal olefinic group (C=CH_2) was suggest in the position C-10/C-11 and the hydroxyl group in the position C-4 with β-orientation which have the similarity chemical shift with compound **1**. However, the cyclopropane ring in the **1** was thought to have undergone ring opening and formed the isopropyl group that indicated a guaiane-type. It is supported by presence of two methyl doublets which have the same *J* value at δ_H 0.98 (*J*= 6.4 Hz, CH_3-13) and 0.96 (*J*= 6.4 Hz, CH_3-14) which proved the isopropyl in guaiane-type (El-kassem et al., 2018). Then, the position of methine olefinic group (C=CH) suggested in C-6/C-7 based on biosynthetic approached (Dewick, 2009). NMR spectral data of compound **2** was comprised with the data of alismol (Ellithey et al., 2013), including its stereochemistry. The result showed the high similarity (**Table 1**). Consequently, **2** was obtained as alismol.

Compound **3** was purified as a yellowish oil. Possessed a molecular formula of $C_{15}H_{22}O_2$ based on HR-TOFMS *m/z* 257.1520 $[M+Na]^+$ (calcd. 257.1517), indicated five unsaturation degrees. Subsequently, IR spectrum demonstrated the absorption bands of hydroxyl (3350 cm^{-1}), aliphatic (2961 cm^{-1}), ketone (1720 cm^{-1}), aldehyde (1711 cm^{-1}), olefinic (1636 cm^{-1}), and *gem*-dimethyl (1465 and 1377 cm^{-1}). Furthermore, the ^{1}H-NMR spectra of **3** presented one methyl singlet resonance at δ_H 1.30 (3H, s, CH_3-14), methyls doublet resonance at δ_H 0.91 (3H, d, CH_3-13), 0.92 (3H, d, CH_3-12). These methyls have same *J* value 7.1 Hz. One methine sp^2 at δ_H 6.60 (1H, d, *J*=5.4 Hz, H-4), aldehyde proton resonance at δ_H 9.30 (1H, s, H-15). The ^{13}C-NMR spectrum detailed with DEPT 135º of **3** showed the presence of 15 carbons, namely three methyls resonance at δ_C 19.5 (C-13), 22.0 (C-12), and 25.0 (C-14), four methylenes resonance at δ_C 39.0 (C-1), 19.7 (C-2), 26.8 (C-7), 35.1 (C-8), four methines at δ_C 53.2 (C-5), 55.4 (C-6), 32.4 (C-11) and one of them is olefinic methine at δ_C 158.9 (C-4), three of quaternary carbon resonance at δ_C 59.7 (C-9), including olefinic quaternary carbon resonance at δ_C 143.8 (C-3) and carbonyl ketone at δ_C 212.4 (C-10), then one of carbonyl aldehyde at δ_C 192.9 (C-15). Based on ^{1}H-NMR, ^{13}C-NMR, and DEPT 135°, compound **3** have three of double bond such as methine olefinic group (C=CH), carbonyl of ketone and aldehyde. Therefore, compound **3** is bicyclic sesquiterpenoid. The presence of one quaternary aliphatic carbon, one tertiary methyl carbon, and two secondary methyl carbons indicates the characteristic of isodaucane-type sesquiterpenoid (Jares et al., 1989). Two secondary methyl carbons which have the same *J* coupling constant value at δ_H 0.92 (*J*= 7.1 Hz, CH_3-12) and 0.91 (*J*= 7.1 Hz, CH_3-13) showed the existence of isopropyl group on the position C-6 which is the characteristic of isodaucane-type (Jares et al., 1989). The isopropyl group is β-orientation. It supported by the presence of isopropyl bonded methine at δ_C 55,4 (C-6), whereas α-orientation at δ_C 49,4 (Qin et al., 2018). Subsequently, the position of aldehyde group was suggested on the C-15 and near the olefinic methine (C=CH) on the C-4/C-3, formed the conjugated double bond which caused the compound to absorb a wavelength at 254 nm. While the position of ketone was suggested on C-10 which made the quaternary aliphatic at δ_C 59.7 (C-9) more deshielded. The structure determination of **3** was also carried out by the approach of isodaucane-type sesquiterpenoids in *Aglaia* genus. Only two isodaucanes, 10-oxoisodauc-3-en-15-al (Pan et al., 2013) and aphanamol I (Harneti et al., 2022)

Table 1. ^{13}C-NMR data of **1-3** ($CDCl_3$, 125 MHz) and literatures.

Carbon Position	Compound **1**	Spathulenol*	Compound **2**	Alismol**	Compound **3**	10-oxo-isodauc-3-en-15-al***
	δ_C (mult.)	δ_C (mult.)	δ_C (mult.)	δ_C (mult.)	δ_C (mult.)	δ_C (mult.)
1	53.4 (d)	53.5 (d)	55.0 (d)	54.6 (d)	39.0 (t)	38.8 (t)
2	26.7 (t)	26.8 (t)	24.7 (t)	24.6 (t)	19.7 (t)	19.6 (t)
3	41.7 (t)	41.8 (t)	41.2 (t)	40.0 (t)	143.8 (s)	143.6 (s)
4	81.0 (s)	81.1 (s)	80.7 (s)	80.4 (s)	158.9 (d)	158.3 (d)
5	54.3 (d)	54.5 (d)	47.2 (d)	47.0 (d)	53.2 (d)	53.1 (d)
6	29.9 (d)	29.9 (d)	121.2 (d)	121.4 (d)	55.4 (d)	55.3 (d)
7	27.5 (d)	27.5 (d)	149.8 (s)	149.3 (s)	26.8 (t)	26.7 (t)
8	24.8 (t)	24.8 (t)	30.0 (t)	29.8 (t)	35.1 (t)	35.0 (t)
9	38.9 (t)	38.9 (t)	37.0 (t)	36.9 (t)	59.7 (s)	59.0 (s)
10	153.5 (s)	153.5 (s)	153.9 (s)	153.9 (s)	212.4 (s)	211.9 (s)
11	20.3 (s)	20.4 (s)	37.4 (d)	37.3 (d)	32.4 (d)	32.3 (d)
12	16.3 (q)	16.4 (q)	21.3 (q)	21.1 (q)	22.0 (q)	21.9 (q)
13	28.7 (q)	28.7 (q)	21.5 (q)	21.3 (q)	19.5 (q)	19.4 (q)
14	106.3 (t)	106.4 (t)	24.0 (q)	23.8 (q)	25.0 (q)	24.9 (q)
15	26.1 (q)	26.2 (q)	106.5 (t)	106.4 (t)	192.9 (d)	192.4 (d)

*($CDCl_3$, 125 MHz); **($CDCl_3$, 50 MHz); ***($CDCl_3$, 25.1 MHz).

Table 2. Cytotoxicity of **1-3** against HeLa and B16-F10 cancer cells

Compounds	IC_{50} (μM)	
	HeLa	B16-F10
1	443.56	303.24
2	218.33	258.90
3	412.40	339.89
Cisplatin	9.00	43.00

have been reported. Compound 3 has a similarity functional group with 10-oxoisodauc-3-en-15-al, so the spectral data of compound **3** and these isodaucanes (Jares et al., 1989) were comprised. The result showed the NMR spectral data were similar (**Table 1**). Compound **3** was obtained as 10-oxo-isodauc-3-en-15-al

Cytotoxicity of all sesquiterpenoids **1-3** were evaluated against B16-F10 and HeLa cells corresponded to a method explained previously with cisplatin as positive control. Among all sesquiterpenoid compounds, alismol (**2**) displayed the highest cytotoxic activity against both of HeLa and B16-F10 cancer cells with IC_{50} values 218.33 and 258.90 μM, respectively while spathulenol (**1**) and 10-oxoisodauc-3-en-15-al (**3**) showed the weak activity (**Table 2**). Comparison of IC_{50} values of compound **1** and **2** showed that the cytotoxicity of **2** is more active than **1** of both cancer cells, indicating that opening cyclopropane ring can increase the cytotoxic activity. Subsequently, cytotoxicity of **3** against HeLa cell showed more active than **1**, but the activity of **1** against B16-F10 cell more active than **3**. This indicated that each compound has its own potential for certain cancer cell. The cytotoxicity of compound **1-3** against B16-F10 cells and compound **1** and **3** against HeLa cells were reported for the first time while the cytotoxicity of **2** against HeLa cells was reported by Ellithey et al., (2013).

CONCLUSIONS

Three sesquiterpenoids namely, one aromadendrane-type, spathulenol (**1**), one guaiane-type, alismol (**2**), and one isodaucane-type, 10-oxoisodauc-3-en-15-al (**3**) were isolated from the peel fruit of *Aglaia cucullata*. Compound **2** was first isolated from *Aglaia* genus, and compounds **1-3** were isolated for the first time from *A. cucullata*. Compound **2** showed the highest cytotoxicity against HeLa cervical and B16-F10 melanoma skin cancer cell lines with IC_{50} value 218.33 μM and 258.90 μM, indicating that the opening of cyclopropane ring influenced the cytotoxicity.

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