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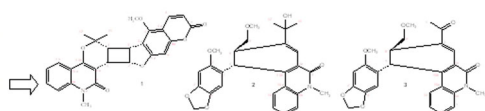
Three novel quinolinone alkaloids from the leaves of *Melicope denhamii*

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ABSTRACT

Three previously unreported quinolinone alkaloids: melicodenines J-L (**1-3**) and six known compounds (**4-9**), were isolated from the leaves of *Melicope denhamii* (Seem) T.G. Hartley. The structures of three quinolinone alkaloids were identified based on HRESIMS and NMR spectra. Compounds **1-9** were assayed in three cancer cells (MCF-7, HeLa, and P-388). Compounds **1** and **5** showed high cytotoxic activity against HeLa cells with IC₅₀ values of 1.8 and 0.8 μM, respectively.



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1. Introduction

M. denhamii (Seem) T.G. Hartley (Rutaceae) is one small tree indigenous to Java Islands, Indonesia. The *Melicope* genus produces alkaloids (Chen et al. 2003; Nakashima et al. 2011), flavonoids (Saputri et al. 2018), and phenylpropanoids (Nakashima et al. 2012), with terpenyl side chain in the aromatic ring. Many alkaloids from *Melicope* show biological activities as cytotoxic agents (Chen et al. 2003; Nakashima et al. 2012), and antimalaria (Rasamison et al. 2016). Recently studies on *Melicope* resulted in the hybrid compound by [2 + 2] cycloaddition and a Diels-Alder adduct from incorporated phenylpropanoid-phenylpropanoid, alkaloid-alkaloid, alkaloid-benzopyran, and alkaloid-phenylpropanoid derivatives (Nakashima et al. 2011, 2012; George et al. 2016; Saputri et al. 2021). Three new compounds, melicodenine J (**1**) is a [2 + 2] cycloaddition, melicodenines K (**2**), and L (**3**) are Diels-Alder adduct

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derivatives were isolated from *M. denhamii* leaves. The cytotoxic activities of their isolates (**1-9**) against MCF-7, HeLa, and P-388 cancer cell lines were reported in this study.

2. Result and discussion

Melicodenine **1** was isolated as a yellow amorphous solid and showed a positive ion peak $[M+H]^+$ at m/z 458.1613, consistent with the molecular composition $C_{27}H_{23}NO_6$. The UV exhibited maximum absorption (λ_{max} 219, 259, 292, 320, and 334 nm), indicating a typical quinolinone alkaloid-coumarin (Nakashima et al. 2012). The IR measurement showed absorption bands for conjugated carbonyl at 1627 cm^{-1} , aromatic ring at 1595 cm^{-1} , and ether at 1128 cm^{-1} . The ^1H NMR spectrum of **1** showed four protons [δ_{H} 5.41 (1H, *dd*, $J=6.7, 2.6$ Hz, H-2'), δ_{H} 4.75 (1H, *t*, $J=6.7$ Hz, H-3'), δ_{H} 4.08 (1H, *t*, $J=9.5$ Hz, H-4), δ_{H} 3.10 (1H, *dd*, $J=9.5, 6.7$ Hz, H-3)] were characteristics of a 1,2,3,4-tetrasubstituted cyclobutane ring. A signal at δ_{H} 5.41 indicates an oxymethine attached to the cyclobutane ring (Holla et al. 2012; Nakashima et al. 2012). Four signals of a 1,2-disubstituted benzene [δ_{H} 7.90 (1H, *dd*, $J=8.0, 1.2$ Hz, H-10), δ_{H} 7.43 (1H, *dt*, $J=8.5, 1.2$ Hz, H-8), δ_{H} 7.15 (1H, *t*, $J=8.0$ Hz, H-9), δ_{H} 7.08 (1H, *d*, $J=8.5$ Hz, H-7)], two methyls [δ_{H} 1.73 (3H, *s*, H-11), δ_{H} 1.20 (3H, *s*, H-12)] along with a N-methyl signal at δ_{H} 3.38 suggested that the partial structure of **1** as a N-methylflindersin moiety (Kamperdick et al. 1999). A signal of aromatic at δ_{H} 5.94 (1H, *s*, H-9'), two signals of *cis* vinylic [δ_{H} 7.85 (1H, *d*, $J=9.6$ Hz, H-5'), δ_{H} 5.95 (1H, *d*, $J=9.6$ Hz, H-6')], and a methoxyl at δ_{H} 4.25 (3H, *s*, 4'-OCH₃) recommended that the other partial structure of **1** as a bergapten moiety (Saputri et al. 2021). Based on the ^1H NMR data suggested that the structure of **1** is a [2 + 2] cycloaddition product between N-methylflindersin with bergapten (Nakashima et al. 2012). The ^{13}C NMR and HMQC spectra of **1** exhibited the signals of 27 carbons were completely separated, including four methyls [δ_{C} 25.4, 25.5, 29.0, 58.4], 11 methines [δ_{C} 35.5, 43.2, 45.0, 85.1, 90.5, 109.5, 113.5, 121.6, 123.1, 130.7, 139.5], five quaternary carbons [δ_{C} 104.4, 105.2, 107.3, 116.2, 138.5], one oxycarbon [δ_{C} 75.5], two carbonyls [δ_{C} 161.8, 162.2], and four oxyaryls [δ_{C} 152.6, 156.5, 156.6, 168.6]. The HMBC spectrum, an N-methyl signal at δ_{H} 3.38, showed a correlation with a carbonyl [δ_{C} 162.2 (C-5)] and a quaternary carbon [δ_{C} 138.5 (C-6a)]. An aromatic signal at δ_{H} 7.90 (H-10) correlated to C-6a and a methine carbon [δ_{C} 130.7 (C-8)]. Two methyl signals at δ_{H} 1.73 (H-11) and δ_{H} 1.20 (H-12) correlated to an oxycarbon [δ_{C} 75.5 (C-2)], and a methine carbon [δ_{C} 45.0 (C-3)] proved that a part of the structure of N-methylflindersin. A signal of vinylic at δ_{H} 7.85 (H-5') showed correlation with a lactone carbonyl [δ_{C} 161.8 (C-7')], two oxyaryls [(δ_{C} 152.6 (C-4'), and (δ_{C} 156.5, C-8á)]. A methoxyl at δ_{H} 4.25 (4'-OCH₃) correlated to C-4' verified the location of the methoxyl group at C-4'. One proton of aromatic at δ_{H} 5.94 (H-9') showed correlation with two oxyaryls [(δ_{C} 168.6, C-9á), C-8á)], two quaternary carbons [(δ_{C} 104.4, C-3á), and (δ_{C} 107.3, C-4á)] and carbonyl carbon (δ_{C} 161.8, C-7') reinforced the other partial structure of **1** as a bergapten (Saputri et al. 2021). An oxymethine proton at δ_{H} 5.41 (H-2') correlated to a methine carbon δ_{C} 35.5 (C-4). A signal at δ_{H} 4.75 (H-3') correlated to C-3á, C-4á, C-4', and C-9a' (a part of bergapten), C-3, and C-4 (a part of N-methylflindersin). A methine signal of a cyclobutane ring at δ_{H} 3.10 (H-3) correlated to

C-4, C-3á, and a methine, δ_C 85.1 (C-2'). A methine signal of a cyclobutane ring at δ_H 4.08 (H-4) correlated to C-4a and C-2'. In the NOESY spectrum, an oxymethine (H-2') correlated to H-3 and H-3', and a methine proton (H-3) correlated to H-4 and H-3' revealed the signal that a 1,2,3,4-tetrasubstituted cyclobutane ring is a *cis* orientation. Consequently, the structure of melicodenine J is shown in Figure 1.

Melicodenine K (**2**) was isolated as colorless oil in which showed an ion peak $[M + H]^+$ at m/z 464.2080 corresponding for a molecular composition $C_{27}H_{30}NO_6$ by the combination of HRESIMS spectra and NMR data. The IR spectrum showed bands of conjugated carbonyl (1639 cm^{-1}), aromatic (1502 and 1485 cm^{-1}), and ether (1112 cm^{-1}) groups. The ^1H NMR spectrum of **2**, showing four aromatic signals [δ_H 7.52 (1H, *dd*, $J = 8.6, 1.2\text{ Hz}$, H-10), δ_H 7.46 (1H, *t*, $J = 7.7\text{ Hz}$, H-8), δ_H 7.35 (1H, *d*, $J = 8.6\text{ Hz}$, H-7), δ_H 7.15 (1H, *t*, $J = 7.7\text{ Hz}$, H-9)], an N-methyl signal at δ_H 3.80, a vinylic at δ_H 6.97 (1H, *s*, H-4), and two methyls [δ_H 1.49 (3H, *s*, H-11), δ_H 0.88 (3H, *s*, H-12)] indicating for a 3-isoprenyl-1-methyl 2-quinolinone moiety (Chen et al. 2003). The ^1H NMR spectrum of **2** also exhibited two protons of aromatic [δ_H 6.57 (1H, *s*, H-3'), δ_H 6.13 (1H, *s*, H-6')], two methines [δ_H 4.82 (1H, *s*, H-7'), δ_H 3.19 (1H, *dd*, $J = 9.8, 6.0\text{ Hz}$, H-8')], splitting two signals of a methylene [δ_H 3.51 (1H, *dd*, $J = 8.3, 6.0\text{ Hz}$, H-9á, δ_H 3.38 (1H, *t*, $J = 9.8\text{ Hz}$, H-9b')], two methoxyls [δ_H 3.95 (3H, *s*, 2'-OCH₃), δ_H 3.30 (3H, *s*, 9'-OCH₃)], and splitting two signals of a methylenedioxy [δ_H 5.79 (1H, *d*, $J = 1.2\text{ Hz}$), δ_H 5.75 (1H, *d*, $J = 1.2\text{ Hz}$)] characteristics for a melicodin A moiety (Nakashima et al. 2012). Compound **2** indicated that 27 carbon signals were utterly separated in the ^{13}C NMR spectra, including five methyl carbons, two methylene carbons, nine methine carbons, one carbonyl carbon, and ten quaternary carbons. From the NMR (^1H , ^{13}C) NMR spectrum exhibited that the structure of **2** is a Diels-Alder adduct moiety and was confirmed by HMBC spectrum (Nakashima et al., 2012; George et al. 2016). The HMBC correlation, an N-methyl at δ_H 3.80, and an aromatic at δ_H 7.46 (H-8) very similar to **1**. A vinylic signal at δ_H 6.97 (H-4) correlated to δ_C 71.6 (C-2), δ_C 139.7 (C-3), δ_C 39.1 (C-8'), and δ_C 160.6 (C-5). Two methyls at δ_H 0.88 (H-12) and δ_H 1.49 (H-11) correlated to C-2, indicating the 3-isoprenyl 1-methyl 2-quinolinone moiety. Two signals of aromatic at δ_H 6.57 (H-3'), and δ_H 6.13 (H-6') correlated to δ_C 150.8 (C-2'), δ_C 147.0 (C-4'), and δ_C 140.7 (C-5'). A methylenedioxy signal [δ_H 5.79 and δ_H 5.75] correlated to C-4', C-5' indicated fused at C-4' and C-5', a methoxyl at δ_H 3.95 (2'-OCH₃) correlated to C-2'. A methoxyl signal at δ_H 3.30 (9'-OCH₃) correlated to δ_C 76.2 (C-9'). Two signals of an aromatic, a methylenedioxy, two methoxyls are the signal of a melicodin A moiety. A methine at δ_H 4.82 (H-7') correlated to δ_C 149.3 (C-10b), δ_C 124.9 (C-4a), δ_C 119.2 (C-1'), δ_C 108.5 (C-6'), C-8', and C-9'. A methine signal at δ_H 3.19 (H-8') correlated to C-3, δ_C 115.6 (C-4), C-10b, C-1', δ_C 34.7 (C-7'), and C-9'. The correlation of three methines [δ_H 4.82 (H-7'), δ_H 3.19 (H-8'), and δ_H 6.97 (H-4)], indicating the structure of **2** are Diels-Alder adduct. The NOE spectrum, the proton signal at H-3' correlated with H-8' and 2'-OCH₃ exhibited that the proton signal at H-7' and H-8' revealed *trans* orientation, and the relative configuration of **2** was similar to melicodenine H (Nakashima et al. 2012). The structure of melicodenine K (**2**) is shown in the Figure 1.

Melicodenine L (**3**) was obtained as a yellowish oil, showing an ion peak $[M + H]^+$ at m/z 448.1752, conforms for a molecular composition $C_{26}H_{25}NO_6$ through HRESIMS spectra. The UV (λ_{max} 226, 246, 259, 265, 309 nm), IR (1636, 1600, 1552, and 1119), and NMR (^1H and ^{13}C) of **3** had very identical with **2**. The significant difference in the 1D and 2D NMR, compound **3** showed an acetyl group at δ_H 2.45 (H-1), δ_C 25.8 (C-1), and δ_C 198.2 (C-2). The HMBC and HMQC experiments assigned the acetyl group at C-1

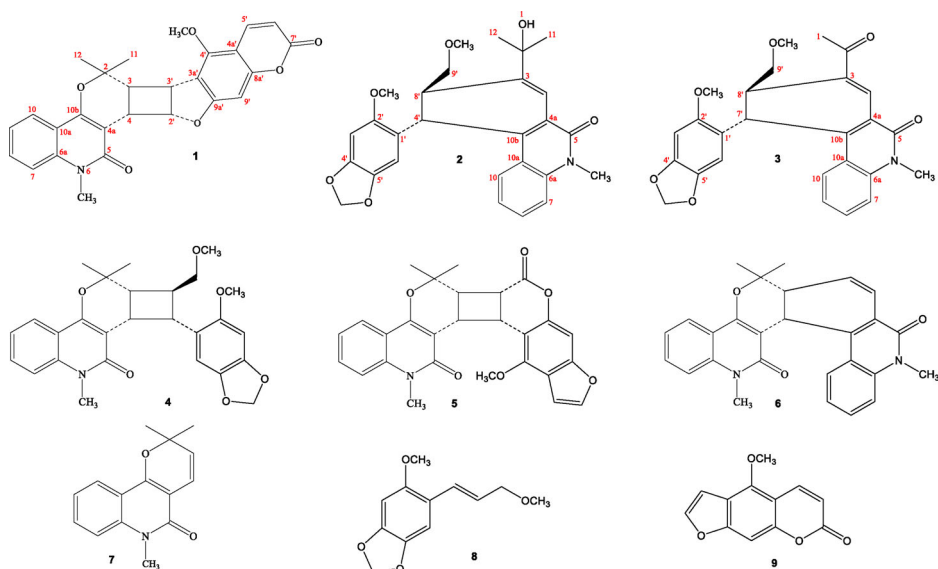


Figure 1. Structures of compounds 1-9 from *M. denhamii*.

Table 1. Cytotoxic activities of the isolated compounds from *M. denhamii*.

Compounds	μM		
	MCF-7	HeLa	P-388
Melicodenine J (1)	> 100	1.8 ± 0.02	> 100
Melicodenine K (2)	> 100	62.9 ± 1.45	29.1 ± 1.10
Melicodenine L (3)	> 100	40.9 ± 1.13	> 100
Melicodenine E (4)	> 100	> 100	11.9 ± 0.87
Melicodenine F (5)	> 100	0.8 ± 0.15	38.3 ± 1.42
Melicobisquinolinone B (6)	> 100	> 100	13.9 ± 0.65
N-methylflindersin (7)	> 100	> 100	87.2 ± 0.30
Melicodin A (8)	15.0 ± 0.15	> 100	> 100
Bergapten (9)	> 100	> 100	> 100
Doxorubicin	0.8 ± 0.02	0.9 ± 0.04	-
Artonin E	-	-	1.3 ± 0.07

and C-2. The methyl proton at δ_{H} 2.45 correlated with a carbonyl [δ_{C} 198.2 (C-2)] in the HMBC spectrum. A signal of α,β -unsaturated ketone at δ_{H} 8.09 (H-4) correlated to C-2, δ_{C} 146.2 (C-10b), δ_{C} 135.9 (C-3), δ_{C} 160.2 (C-5), and δ_{C} 37.3 (C-8'). The NOE spectrum of **3**, showing the relative configurations very similar to melicodenine K. Therefore, the structure of melicodenine L (**3**) in Figure 1. In conclusion, melicodenine L (**3**) is demethylation and is followed by an oxidation reaction of **2**.

Six known compounds, melicodenine E (**4**), F (**5**), melicobisquinolinone B (**6**), N-methylflindersin (**7**), melicodin A (**8**), and bergapten (**9**), elucidating by comparing their NMR spectra based on the chemical shift that reported (Johns et al. 1968; Kamperdick et al., 1999; Nakashima et al. 2011, 2012).

In vitro evaluation against MCF-7, HeLa, and P-388 for their activities in accord with the MTT method (Table 1) uses artonin E and doxorubicin as a positive control. The cells without active compound as a negative control (Tanjung et al. 2018; Tjahjandarie et al. 2021). Melicodenines J (**1**) and F (**5**) exhibited very high activity against HeLa. A

type Diels-Alder adduct (**2**, **3**, **6**), a type monomer, was inactive (**7-9**). However, compounds **1-9** were inactive on MCF-7 and P-388 cancer cells (Table 1). A type [2 + 2] cycloaddition adduct (**1**, **4**, **5**) plays a key role for the cytotoxic effect. The effect of the bond angle of the cyclobutane ring more than active the cyclohexene ring inhibiting the growth of HeLa cells.

3. Experimental

3.1. Plant material

The collecting of the fresh leaves of *M. denhamii* came from Tanah Merah, Bangkalan, Madura Island, East Java, Indonesia, in Feb 2016. The plant was identified by a senior botanist (I. Rachman) from the Bogoriense Herbarium, Indonesia. A specimen (MD 20171207) was deposited as a reference.

3.2. Extraction and isolation

The dried leaves of *M. denhamii* (3.1 kg), extracted with MeOH two times (10 L, each for three days) at room temperature, and the MeOH extract (100 g) treated with 5% aqueous H₂SO₄ (pH 3-4) and then partitioned with *n*-hexane (18 g), and EtOAc (15 g), respectively. The acid layer was treated with NH₄OH (pH 8-9) and extracted with EtOAc to give alkaloid extract (1 g). The alkaloid extract (4.8 g), fractionated by radial planar chromatography on silica gel, using a gradient of *n*-hexane-EtOAc (from 9:1 to 1:1 v/v) to afford two significant fractions, A (188 mg) and B (450 mg). Purification of fraction A by radial planar chromatography, eluted with *n*-hexane-acetone (from 9:1 to 4:1 v/v), gave compound **7** (88 mg). Fraction B (450 mg), further separated by CC chromatography on Sephadex LH-20, eluted with methanol, gave two subfractions, B₁ (253 mg) and B₂ (75 mg). Subfraction B₁ separated with radial planar chromatography, eluted with *n*-hexane-EtOAc (from 9:1 to 7:3 v/v), gave compounds **1** (9.8 mg), **6** (25 mg), and **2** (6.2 mg). Similarly, subfraction B₂ separated by the same method, eluted with *n*-hexane-CHCl₃ (from 7:3 to 3:7 v/v), afforded compound **3** (4.8 mg), compound **4** (5 mg), and compound **5** (6 mg). The EtOAc extract (14 g), fractionated by VLC on silica gel, using a gradient of *n*-hexane-EtOAc (from 9:1 to 3:7 v/v), gave four significant fractions, C-F. Fraction C (800 mg) further separated by radial planar chromatography on silica gel, eluted with *n*-hexane-CHCl₃ (4:1 to 1:1 v/v), afforded compound **8** (27 mg). Fraction E (205 mg) by the same method, eluted with *n*-hexane-diisopropyl ether (7:3 to 3:7 v/v), afforded compound **9** (16 mg).

3.3. Spectral data

Melicodenine J (**1**): yellow solid, m.p. 224-225°C, $[\alpha]_D^{20} = +6^\circ$ (c 0.0005, MeOH): UV (MeOH) λ_{\max} (log ϵ) 219 (4.48), 259 (3.83), 292 (3.83), 320 (4.06), and 334 nm (4.03). IR (KBr) ν_{\max} (cm⁻¹) 1627, 1595, 1461, and 1128. ¹H-NMR (CDCl₃, 4100 MHz), δ_H ppm: 7.90 (1H, *dd*, *J* = 8.0, 1.2 Hz, H-10), 7.85 (1H, *d*, *J* = 9.6 Hz, H-5'), 7.43 (1H, *dt*, *J* = 8.5, 1.2 Hz, H-8), 7.15 (1H, *t*, *J* = 8.0 Hz, H-9), 7.08 (1H, *d*, *J* = 8.5 Hz, H-7), 5.95 (1H, *d*, *J* = 9.6 Hz, H-6'), 5.94 (1H, *s*, H-9'), 5.41 (1H, *dd*, *J* = 6.7, 2.6 Hz, H-2'), 4.75 (1H, *t*,

$J=6.7$ Hz, H-3'), 4.25 (3H, *s*, 4'-OCH₃), 4.08 (1H, *t*, $J=9.5$ Hz, H-4), 3.38 (3H, *s*, N-CH₃), 3.10 (1H, *dd*, $J=9.5, 6.7$ Hz, H-3), 1.73 (3H, *s*, H-11), 1.20 (3H, *s*, H-12). ¹³C-NMR (CDCl₃, 100 MHz), δ_c ppm: 168.6 (C-9a), 162.2 (C-5), 161.8 (C-7'), 156.6 (C-10b), 156.5 (C-8a), 152.6 (C-4'), 139.5 (C-5'), 138.5 (C-6a), 130.7 (C-8), 123.1 (C-10), 121.6 (C-9), 116.2 (C-10a), 113.5 (C-7), 109.5 (C-6'), 107.3 (C-4a), 105.2 (C-4a), 104.4 (C-3a), 90.5 (C-9'), 85.1 (C-2'), 75.5 (C-2), 45.0 (C-3), 43.2 (C-3'), 35.5 (C-4), 29.0 (6-NCH₃), 25.5 (C-11), 25.4 (C-12). HRESIMS m/z 458.1613 [M + H]⁺ calculated for C₂₇H₂₃NO₆ m/z 458.1604.

Melicodenine K (**2**): colorless oil, $[\alpha]_D^{20} = +8^\circ$ (*c* 0.0005, MeOH): UV (MeOH) λ_{\max} (log ϵ) 229 (3.99), 259 (3.60), 308 (3.51), 325 (3.46), 359 (3.56) and 377 nm (4.41). IR (KBr) ν_{\max} (cm⁻¹) 1639, 1502, 1485, and 1112. ¹H-NMR (CDCl₃, 400 MHz), δ_H ppm: 7.52 (1H, *dd*, $J=8.6, 1.2$, H-10), 7.46 (1H, *t*, $J=7.7$ Hz, H-8), 7.35 (1H, *d*, $J=8.6$ Hz, H-7), 7.15 (1H, *t*, $J=7.7$ Hz, H-9), 6.97 (1H, *s*, H-4), 6.57 (1H, *s*, H-3'), 6.13 (1H, *s*, H-6'), 5.79 and 5.75 (2H, *d*, $J=1.2$ Hz, 4'-O-CH₂-O-5'), 4.82 (1H, *s*, H-7'), 3.95 (3H, *s*, 2'-OCH₃), 3.80 (3H, *s*, N-CH₃), 3.51 (1H, *dd*, $J=8.3, 6.0$ Hz, H-9'a), 3.38 (1H, *t*, $J=9.8$ Hz, H-9'b), 3.30 (3H, *s*, 9'-OCH₃), 3.19 (1H, *dd*, $J=9.8, 6.0$ Hz, H-8'), 1.49 (3H, *s*, H-11), 0.88 (3H, *s*, H-12). ¹³C-NMR (CDCl₃, 100 MHz), δ_c ppm: 160.6 (C-5), 150.8 (C-2'), 149.3 (C-10b), 147.0 (C-4'), 140.7 (C-5'), 139.7 (C-3), 139.3 (C-6a), 129.8 (C-8), 124.9 (C-4a/C-10), 122.5 (C-9), 120.2 (C-10a), 119.2 (C-1'), 115.6 (C-4), 114.5 (C-7), 108.5 (C-6'), 101.1 (4'-O-CH₂-O-5'), 94.4 (C-3'), 76.2 (C-9'), 71.6 (C-2), 59.0 (9'-OCH₃), 56.6 (2'-OCH₃), 39.1 (C-8'), 34.7 (C-7'), 30.0 (C-11), 29.9 (6-NCH₃), 29.2 (C-12), HRESIMS m/z 464.2080 [M + H]⁺ calculated for C₂₇H₃₀NO₆ m/z 464.2073.

Melicodenine K (**3**): yellowish oil, $[\alpha]_D^{20} = -8^\circ$ (*c* 0.0005, MeOH): UV (MeOH) λ_{\max} (log ϵ) 226 (4.38), 246 (4.20), 259 (4.07), 265 (3.65), and 309 nm (3.96). IR (KBr) ν_{\max} (cm⁻¹) 1636, 1600, 1552, and 1119. ¹H-NMR (CDCl₃, 400 MHz), δ_H ppm: 8.09 (1H, *s*, H-4), 7.68 (1H, *d*, $J=8.1$ Hz, H-10), 7.52 (1H, *t*, $J=7.8$ Hz, H-8), 7.36 (1H, *d*, $J=8.6$ Hz, H-7), 7.15 (1H, *t*, $J=7.8$ Hz, H-9), 6.56 (1H, *s*, H-3'), 6.10 (1H, *s*, H-6'), 5.79 and 5.75 (2H, *s*, 4'-O-CH₂-O-5'), 5.36 (1H, *s*, H-7'), 3.96 (3H, *s*, 2'-OCH₃), 3.81 (3H, *s*, 6-NCH₃), 3.51 (1H, *dd*, $J=9.7, 4.4$ Hz, H-8'), 3.38 (1H, *t*, $J=9.8$ Hz, H-9'b), 3.25 (1H, *dd*, $J=10.1, 4.4$ Hz, H-9'a), 3.16 (1H, *t*, $J=10.1$ Hz, H-9'b), 2.45 (3H, *s*, H-1). ¹³C-NMR (CDCl₃, 100 MHz), δ_c ppm: 198.2 (C-2), 160.2 (C-5), 150.6 (C-2'), 147.1 (C-4'), 146.2 (C-10b), 140.9 (C-5'), 140.4 (C-6a), 135.9 (C-3), 133.1 (C-4), 131.5 (C-8), 126.3 (C-10), 123.7 (C-4a), 123.0 (C-9), 120.5 (C-1'), 120.0 (C-10a), 114.7 (C-7), 107.8 (C-6'), 101.1 (4'-O-CH₂-O-5'), 95.0 (C-3'), 72.5 (C-9'), 58.2 (9'-OCH₃), 56.7 (2'-OCH₃), 37.3 (C-8'), 33.0 (C-7'), 30.0 (6-NCH₃), 25.8 (C-1). HRESIMS m/z 448.1752 [M + H]⁺ calculated for C₂₆H₂₅NO₆ m/z 448.1760.

4. Conclusions

In summary, three unreported quinolinone alkaloids: melicodenines J-L (**1-3**), along with six known compounds (**4-9**), were isolated from *Melicope denhamii* leaves. The cytotoxicity activity of compounds (**1-9**) was evaluated against MCF-7, HeLa, and P-388 cells. Compounds **1** and **5** showed high activity against HeLa cells.

Disclosure statement

No potential conflict of interest was reported by the authors.

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