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Antimalarial tetranortriterpenoids from the seeds of *Lansium domesticum* Corr.

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Abstract

Five tetranortriterpenoids, domesticulide A–E (**1**–**5**), were isolated from seeds of *Lansium domesticum* Corr. together with 11 known triterpenoids (**6**–**16**). Their structures were elucidated by analysis of their spectroscopic data. Compounds **2**, **3**, **4**, **7**, **8**, **10**, **11**, and **15** showed antimalarial activity against *Plasmodium falciparum* with IC_{50}'s of 2.4–9.7 μg/ml.

Keywords: *Lansium domesticum* Corr.; Meliaceae; Tetranortriterpenoid; Antimalarial activity; *Plasmodium falciparum*

1. Introduction

Lansium domesticum Corr. is a genus of small trees from the family Meliaceae found both in the wild and cultivated in Thailand and surrounding countries in Southern Asia. The seeds of the fruit, traditionally, are said to be toxic to the malaria parasite (Leaman et al., 1995). The fruit is known locally, depending on variety, as *langsat*, *long*-*kong*, *duku*, *lang*-*sook*, and *langsat*-*khao* (in Thai). Previous phytochemical studies on *L. domesticum* Corr. have resulted in isolation of several types of triterpenoids (Kiang et al., 1967; Habaguchi et al., 1968; Nishizawa et al., 1982, 1983, 1984, 1985; Tanaka et al., 2002). As part of our search for bioactive constituents from Thai plants (Chantrapromma et al., 2000; Chumkaew et al., 2003; Laphookhieo et al., 2004), the CH_2Cl_2 extract of the seeds of a wild form of *L. domesticum* Corr., collected at Thumbon Nopitum, Nakhon Si Thammarat province (and commonly known as '*Langsat Khao*' in Thai) was found to significantly inhibit *Plasmodium falciparum* with an IC_{50} value of 9.9 μg/ml. Here we describe isolation and structure elucidation of five new tetranortriterpeniods (**1**–**5**), together with 11 known compounds. The structure elucidation of **1**–**5** and the biological evaluation of the isolates are described herein.

2. Results and discussion

The CH_2Cl_2 extract of the seeds of *L. domesticum* was separated by successive column and thin layer chromatography with various eluting systems to give five new tetranortriterpenoids (**1**–**5**), together with 11 known compounds: 6-hydroxymexicanolide (**6**), 6-acetoxymexicanolide (**7**), methyl angolensate (**8**), methyl 6-hydroxyangolensate (**9**), methyl 6-acetoxyangolensate (**10**), azadiradione (**11**), lansiolic acid (**12**), lansioside B (**13**), dukunolide B (**14**), dukunolide C (**15**), and dukunolide D (**16**). Spectroscopic data for compounds **6**–**16** were identical in all respects to those published (Okorie and Taylor, 1968; Connolly et al., 1967, 1968; Lee et al., 1988; Nishizawa et al., 1983, 1985b).

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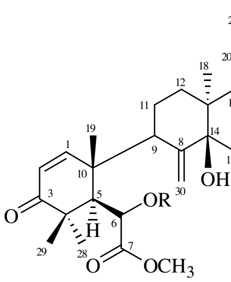

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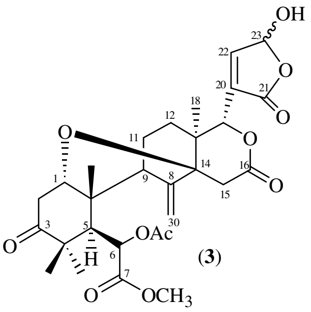

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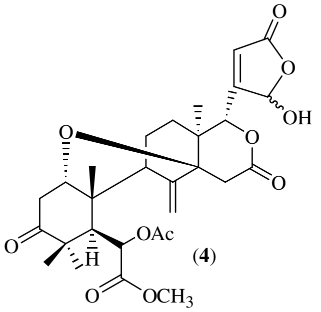

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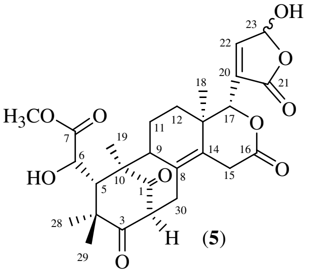

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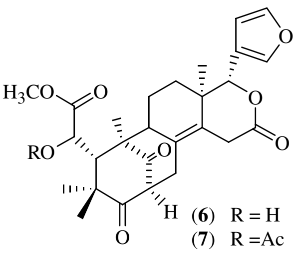

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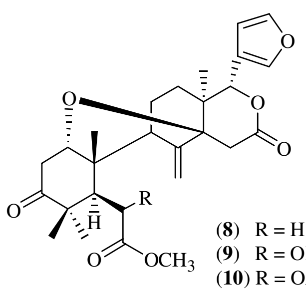

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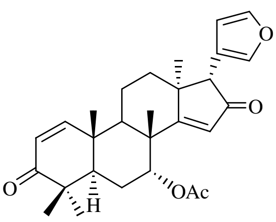

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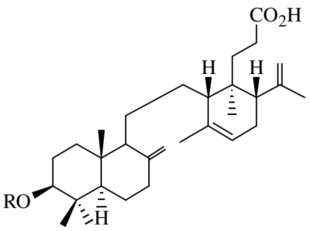

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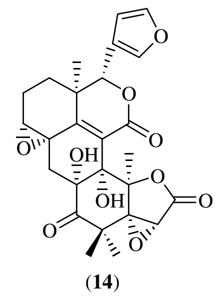

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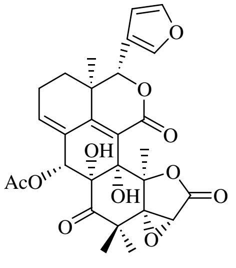

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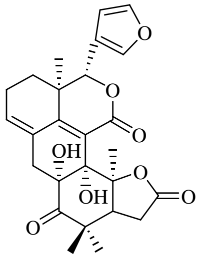

(16)

Domesticulide A (**1**) was isolated as a white solid, m.p. 175–176 °C. Its molecular formula was deduced as $C_{27}H_{34}O_8$ from the ESITOFMS (observed *m/z* 487.2331 $[M + H]^+$, calcd for $C_{27}H_{35}O_8$, 487.2323]. The IR spectrum showed hydroxyl (3460 cm^{-1}), carbonyl (1719, 1682 cm^{-1}), and furan (835 cm^{-1}) absorption band maxima. In the UV spectrum, the λ_{max} were at 216 nm (log ε 4.05) and 235 nm (log ε 4.05), respectively. The ^1H NMR spectrum (Table 1) of **1** showed a characteristic limonoid β-substituted furan ring at δ 7.41 (*s*), 7.04 (*s*), and 6.37 (*t*, $J = 1.5$ Hz). The presence of an α,β-unsaturated ketone in ring A was also indicated by a pair of *doublets* at δ 7.59 and 6.01 ($J = 10.5$ Hz) in the ^1H NMR spectrum, and by resonances at δ 154.2, 125.4, and 204.8 ascribable to C-1, C-2, and C-3, respectively, in the ^{13}C NMR spectrum (Table 2). Domesticulide A (**1**) was thus a ring B-opened limonoid. This was demonstrated by the presence of a carbomethoxy group at δ 3.81 (*s*), an exocyclic methylene group resonance at δ 5.27 (*s*) and 5.11 (*s*), and the fact that the compound contained four instead of the usual five tertiary methyl groups. The hydroxyl group at δ 3.02 also showed HMBC correlations (Table 3) with C-14 and C-15, indicating that the hydroxyl group was attached to C-14. The configuration at C-14 was supported by NOE experiments, which showed a correlation

Table 1
^{1}H NMR spectroscopic data for compounds **1**–**5**

H	**1**[a]	**2**[a]	**3**[b]	**4**[b]	**5**[b]
1	7.59 *d* (10.5)	7.56 *d* (10.5)	3.53 *m*	3.55 *dd* (5.0, 2.5)	
2	6.01 *d* (10.5)	6.01 *d* (10.5)	3.01 *dd* (15.0, 5.5)	3.06 *dd* (14.0, 5.0)	3.23 *dd* (11.0, 2.5)
			2.33 *dd* (14.0, 3.5)	2.37 *dd* (14.0, 2.5)	
5	2.34 *s*	2.54 *s*	3.02 *s*	2.93*/2.92 *s*	2.59/2.57 *d* (0.5)
6	4.55 *s*	5.67 *s*	4.94/4.91 *s*	5.46*/5.45 *s*	4.60 *s*
9	2.44 *d* (7.5)	2.55 *d* (6.0)	2.34 *m*	2.36 *m*	2.29 *br*
11α	1.55 *m*	1.53 *m*	1.61 *m*	1.67 *m*	1.87 *m*
11β	1.59 *m*	1.66 *m*	2.35 *m*	2.41 *m*	
12α	0.98 *td* (13.0, 4.5)	0.96 *m*	1.05 *dt* (12.5, 4.0)	1.25 *m*	1.25 *m*
12 β	1.69 *dt* (13.0, 4.5)	1.65 *m*	2.05 *m*	1.89 *dt* (13.5, 5.0)	1.79 *m*
15β	2.95 *d* (17.5)	2.91 *d* (17.5)	2.91 *d* (18.0)	2.88 *d* (18.0)	3.59/3.54 *m*
15α	3.09 *d* (17.5)	3.07 *d* (17.5)	2.55 *d* (18.0)	2.60*/2.59*d* (18.0)	3.45/3.41 *m*
17	5.74 *s*	5.72 *s*	5.55 *s*	5.58/5.57**s*	5.27/5.91 *s*
21	7.41 *s*	7.40 *t* (2.0)		6.14/6.10* *br*	
22	6.37 *dd* (1.5, 1.5)	6.35 *d* (2.0)	7.29/7.28 *t* (1.0)	6.28/6.22* *dd* (1.5, 0.5)	7.30 *m*
23	7.34 *s*	7.38 *s*	6.18/6.15 *s*		6.19/6.16 *s*
30	5.27 *s*	5.24 *s*	5.19 *s*	5.24*/5.23 *s*	3.22 *dd* (14.5, 1.5)
	5.11 *s*	5.17 *s*	4.94/4.91 *s*	4.93*/4.92 *s*	3.46 *m*
18-Me	0.87 *s*	0.86 *s*	0.93/0.91 *s*	0.93 *s*	1.00/0.97 *s*
19-Me	1.27 *s*	1.14 *s*	1.09/1.08 *s*	1.06 *s*	1.54/1.53 *s*
28-Me	1.42 *s*	1.38 *s*	1.13/1.13 *s*	1.09 *s*	1.15 *s*
29-Me	1.07 *s*	1.04 *s*	1.44/1.44 *s*	1.46 *s*	1.04 *s*
OCH_3	3.81 *s*	3.74 *s*	3.77/3.76 *s*	3.78 *s*	3.81/3.80 *s*
6-OAc		2.21 *s*	2.21 *s*	2.22 *s*	
6-OH	3.12 *s*				
14-OH	3.02 *s*	3.17 *s*			

[a] Recorded in $CDCl_3$, 500 MHz.
[b] Recorded in $CDCl_3 + CD_3OD$, 500 MHz.
[*] Data for major epimer.

of the signal of OH-14β (δ 3.02) with the H-17β (δ 5.74) resonance. In addition, the signal of H-15α (δ 3.09) showed interaction with the resonance of H_3-18 (δ 0.87), suggesting a spatial proximity of H-15α to H_3-18, which requires the hydroxyl group at C-14 to be anti (β) to H_3-18 (α). From these data, domesticulide A was deduced to be **1**.

Domesticulide B (**2**) was obtained as a white solid, m.p. 155–156 °C, with molecular formula $C_{29}H_{36}O_9$, 42 mass units greater than that of **1**, as indicated by the ion peak at *m/z* 529.2441 (calcd for $C_{29}H_{37}O_9$, 529.2428) $[M + H]^+$ in the ESITOFMS. The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) were similar to those of **1**, except that the H-6 (δ 5.67) of **2** resonated lower field than those of **1** (δ 4.55). In addition, **2** also showed an additional acetyl group resonance at δ 2.21. On the basis of these data, domesticulide B was identified as an acetate derivative of domesticulide A. The HMBC spectral data is summarized in Table 3.

Domesticulide C (**3**) was obtained as an amorphous solid, with a molecular formula of $C_{29}H_{36}O_{11}$ as determined from the molecular ion at *m/z* 583.2131 $[M + Na]^+$, (calcd for $C_{29}H_{36}O_{11}Na$, 583.2155). The ^{1}H NMR spectrum (Table 1) was that of a typical *seco* B,D-limonoid, with four singlet signals for four tertiary methyl groups at δ 0.91, 1.08, 1.13, and 1.44, a carbomethoxyl group at δ 3.76 (*s*), and an exocyclic methylene group resonance at δ 5.19 (*s*) and 4.91(*s*). The ^{1}H and ^{13}C NMR spectroscopic data for **3** (Tables 1 and 2) resembled closely that for methyl 6-acetoxyangolensate (**10**) (Connolly et al., 1967) except that compound **3** show the characteristic of 23-hydroxy-21,23-butenolide epimers (ratio 1:1 mixture) at δ_C 133.9 (C-20); δ_C 170.7 (C-21); δ_H 7.29 (*t*, $J = 1.0$ Hz, H-22)/δ_C 150.1 (C-22), and δ_H 6.18 (*s*, H-23)/δ_C 97.6 (C-23) instead of signal for the furan ring in **10**. Thus, domesticulide C was assigned as **3** (see Table 4).

Domesticulide D (**4**), molecular formula $C_{29}H_{36}O_{11}$ as determined from the molecular ion at *m/z* 583.2173 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{11}Na$, 583.2155), has spectroscopic characteristics similar to **3**, and also exhibited split signals suggesting both 21-hydroxy-21,23-butenolide epimers (ratio 4:1 mixture). In this case the major epimer showed two furan protons resonating at δ 6.22 (*dd*, $J = 1.5$ and 0.5 Hz, H-22) and 6.10 (*brs*, H-21) as well as scyned at δ 163.57, 98.26, 121.66, and 169.44 ascribed to C-20, C-21, C-22, and C-23, respectively. Therefore, domesticulide D was determined to be **4**.

Domesticulide E (**5**) was obtained as an amorphous solid, and its molecular formula was determined to be $C_{27}H_{32}O_{10}$ on the basis of the positive ion ESITOFMS (*m/z* 539.1893 $[M + Na]^+$, calcd for $C_{27}H_{32}O_{10}Na$, 539.1893) data. It showed IR absorption bands at 3446 and 1730 cm^{-1}, indicating the presence of hydroxyl and carbonyl functionalities. The ^{1}H NMR spectrum of compound **5** showed the presence for four singlet signals for four methyl groups at δ 0.97, 1.04, 1.15, and 1.53, and a carbomethoxyl group at δ 3.80 (*s*). The ^{13}C NMR spectrum

Table 2
^{13}C NMR spectroscopic data for compounds **1**–**5**

C	**1**[a]	**2**[a]	**3**[b]	**4**[b]	**5**[b]
1	154.2	153.9	77.8	78.2	214.1/214.0
2	125.4	125.5	39.1/39.0	38.9	57.1
3	204.8	203.9	211.6/210.9	211.6	210.4
4	46.7	46.5	48.8/48.7	48.7	49.5
5	47.9	47.6	46.3/46.2	46.6	43.6
6	71.4	71.1	72.4/72.3	72.2	72.4
7	177.0	171.3	170.7/170.5	170.8	175.6
8	145.5	145.6	145.2	144.7	125.7/125.5
9	47.7	47.3	50.5	50.4	52.9/52.7
10	44.9	44.5	44.2	44.4	53.4/53.4
11	19.9	19.9	24.1	24.0	18.9/18.9
12	27.5	27.5	28.4/28.2	28.7	29.6/29.4
13	39.6	39.6	41.8/41.7	41.8	38.3
14	72.8	72.7	80.2/80.2	80.3	132.6
15	39.7	39.5	33.7	33.4	33.1
16	170.6	170.8	170.1/170.1	169.0	170.0/169.7
17	79.4	79.5	78.2/78.1	79.9	78.4/78.1
18	15.5	15.5	13.6/13.5	14.2	18.2/17.8
19	20.5	19.4	22.8	22.6	17.2/17.2
20	120.6	120.6	133.9	163.5	132.5/132.2
21	140.9	140.3	170.7/170.5	98.2	169.5/169.1
22	109.9	109.9	150.1/149.3	121.6	150.6/150.1
23	142.9	142.9	97.6/96.6	169.4	97.9/97.3
28	25.1	25.1	23.6	23.8	20.4/20.3
29	21.3	21.3	24.7/24.7	24.7	20.5
30	118.2	118.6	112.0	112.5	36.7
OCH_3	53.3	53.0	53.0	53.2	53.1/53.1
6-OAc		169.9	170.0	170.5	
		20.9	21.1	21.1	

[a] Recorded in $CDCl_3$, 125 MHz.
[b] Recorded in $CDCl_3 + CD_3OD$, 125 MHz.

Table 4
Antimalarial activity of compounds **1**–**16**

Compounds	Antimalarial IC_{50} (μg/ml)
1	>20
2	3.2
3	2.4
4	6.9
5	>20
6	>20
7	9.7
8	5.9
9	>20
10	3.8
11	2.9
12	>20
13	>20
14	n.t.[a]
15	5.2
16	n.t.[a]
Artemisinin	0.001–0.003

Inactive at >20 μg/ml.
[a] Not tested.

(Table 2) showed the presence of two six membered ketones at δ 214.1, and 210.4, a γ-lactone at δ 170.0, an ester or lactone at δ 175.6, and a tetrasubstituted double bond at δ 125.7, and 132.6. A study of the ^{1}H NMR spectroscopic data (Table 1) for compound **5** indicated a mexicanolide skeleton (Daniewski et al., 1993). Additionally, the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) resembled closely that of 6-hydroxy mexicanolide (**6**) (Connolly

Table 3
Selective HMBC correlations data for domesticulide A–E (**1**–**5**)

Proton	HMBC correlations				
	1	**2**	**3**	**4**	**5**
1	19, 10, 5, 3	19, 10, 5, 3	19, 14, 5, 4, 2	19, 14, 5, 4, 2	
2	10, 4	10, 4	3, 1	3, 1	3
5	29, 28, 19, 10, 9, 7, 6, 3	29, 28, 19, 10, 9, 7, 6, 3	29, 10, 9, 7, 6	29, 10, 9, 7, 6	28, 19, 10, 9, 7, 6, 4, 3
6	10, 7, 5, 4	10, 7, 5, 4	10, 7, 5, 1	10, 7, 5, 1	10, 7, 5, 4
9	30, 14, 12, 11, 10, 8, 5, 1	30, 14, 12, 11, 10, 8, 5, 1			
11α	13, 10, 8	13, 10, 8			12, 10
11β	12, 10	12, 10			
12α	11	14, 13, 11, 9	14, 13, 9	14, 13, 9	13, 9
12β	18, 17,13, 11	18, 17,13, 11			
15β	16, 14	16, 14	16, 14	16, 14	14, 8
15α	16, 14, 13	16, 14, 13	16, 14, 13	16, 14, 13	14, 8
17	22, 21, 20, 18, 14, 13, 12	22, 21, 20, 18, 14, 13, 12	22, 21, 20, 18, 13	22, 21, 20, 18, 13	23, 22, 20, 18, 14, 13
18	17, 14, 13, 12	17, 14, 13, 12	14, 13, 12, 1	14, 13, 12, 1	17, 14, 13, 12
19	10, 5, 1	10, 5, 1	10, 9, 5, 1	10, 9, 5, 1	10, 9, 5, 1
21	23, 22, 20	23, 22, 20		23	
22	23, 21, 20	23, 20, 21	21, 17	21, 17	23, 21, 20
23	22, 21, 20	22, 21, 20	21		21, 20
28	29, 5, 4, 3	29, 5, 3			29, 5, 4, 3
29	28, 5, 4, 3	28, 5, 3			28, 5, 4, 3
30	14, 10, 9, 8	14, 10, 9, 8	14, 9	14, 9	14, 9, 8, 1
	14, 10, 9, 8	14, 10, 9, 8			14, 8, 3, 2
OMe	7	7			7
6-OH	7, 6				7, 6, 5
14-OH	14, 15	15			

et al., 1968; Okorie and Taylor, 1968), except with respect to the furan ring. The ^{1}H and ^{13}C resonances for the 23-hydroxy-21,23-butenolide protons of the epimers (ratio 1:1 mixture) were observed at δ 7.30 (H-22; δ 150.1, C-22) and 6.19 (H-23; δ 97.9, C-23) and for two quaternary carbons at δ 169.5 (C-21) and 132.5 (C-20). Thus, domesticulide E was assigned as **5**.

As summarized in Table 3, the isolates were evaluated for their antimalaria against *P. falciparum*. Compounds **2**, **3**, **4**, **7**, **8**, **10**, **11**, and **15** showed moderate antimalarial activity with IC_{50} values of 2.4–9.7 μg/ml. A comparison of activities of **8** and **9** suggests that the addition of a hydroxyl group at C-6 considerably decreases the antimalarial activity. The substitution of an acetoxyl group in the place of a hydroxyl group at C-6 resulted in higher activity in **2**, **7**, and **10**, as compared with **1**, **6**, and **9**, respectively. These results were similar to the observation from Bickii et al. (2000).

It is worth noting that the seeds extract of *L. domesticum* are a rich source of limonoids. In our present study, we isolated six classes of the limonoids, including andirobin derivatives (**1**–**2**), methyl angolensates (**3**, **4**, **8**, **9**, and **10**), mexicanolides (**5**–**7**), an azadiradione (**11**), onoceranoids (**12**–**13**), and dukunolides (**14**–**16**). In addition, the structures of **1**–**11** were isolated as the first time as metabolites of *L. domesticum*.

3. Experimental section

3.1. General methods

Melting points were determined on a Electrothermal melting point apparatus and are uncorrected. Specific rotations were obtained using an Autopol automatic II polarimeter, whereas UV spectra were measured with a UV SPECCORD S100. IR, ^{1}H and ^{13}C NMR were recorded on a Perkin–Elmer 1750 FTIR spectrophotometer and a Bruker Avance DPX-300 MHz and Varian Unity INOVA 500 MHz spectrometers with TMS as internal standard, respectively. The ESITOFMS were obtained using a Micromass LCT mass spectrometer, and the lock mass calibration was applied for the determination of accurate mass. Column chromatography was carried out on silica gel 60 GF_{254} (Merck). Silica gel 60 F_{254} precoated aluminum plates (0.2 mm, Merck) were used for TLC analysis, with detection performed by spraying with 1% vanillin in ethanol and heating at 100–110 °C for 5 min.

3.2. Plant material

Seeds of *L. domesticum* Corr. (2.0 kg), collected at Thumbon Nopitum, Nakhon Si Thammarat, Thailand, in August 2001 and identified by Dr. Chatchai Ngamriebsakul. A voucher specimen (number WU-0010) was deposited in the herbarium of the School of Science, Walailak University, Thasala, Nakhon Si Thammarat, Thailand.

3.3. Extraction and isolation

Air dried and powdered seeds of *L. domesticum* Corr. (2 kg) were extracted with CH_2Cl_2 at room temperature. The CH_2Cl_2 extract was evaporated to dryness under reduced pressure to give an extract that was separated by silica gel CC and eluted initially with hexane enriched with CH_2Cl_2, then with EtOAc followed by increasing amounts of MeOH in EtOAc and finally with MeOH. Each fraction was monitored by TLC, fractions that appeared similar on TLC were combined to yield 21 major fractions, F1–F21. Fraction F5 (30.1 g) was subjected to flash CC with CH_2Cl_2–EtOAc (4:1) to afford 5 fractions, which were further purified by preparative TLC with hexane–EtOAc (1:1) to give domesticulide A (**1**) (1.49 g), domesticulide E (**5**) (19.2 mg), 6-acetoxymexicanolide (**7**) (2.4 mg), methyl angolensate (**8**) (7.8 mg), methyl 6-hydroxyangolensate (**9**) (7.9 mg), and azadiradione (**11**) (5.7 mg). Fraction F6 (8.29 g) was further purified by flash CC with EtOAc–MeOH (9:1) and subsequently by preparative TLC with Et_2O–EtoAc (2:8) to give lansioside B (**13**) (354.1 mg), dukunolide B (**14**) (2.8 mg), dukunolide C (**15**) (5.0 mg), and dukunolide D (**16**) (2.8 mg). Fraction F7 (4.65 g) was applied to a silica gel flash column with CH_2Cl_2–EtOAc (3:2) to afford domesticulide B (**2**) (548.0 mg), 6-hydroxymexicanolide (**6**) (2.90 g), and lansiolic acid (**12**) (223.5 mg). Fraction F12 (5.47 g) was also further purified by flash CC with CH_2Cl_2–EtOAc (1:1) and subsequently by preparative TLC with Et_2O–EtOAc (1:1) to afford domesticulide C (**3**) (14.7 mg), domesticulide D (**4**) (7.1 mg), and methyl 6-acetoxyangolensate (**10**) (8.7 mg).

3.4. Domesticulide A (*1*)

White solid, m.p. 175–176 °C, $[\alpha]_D^{28} - 52.63$ (*c* 0.38, $CHCl_3$), UV (MeOH) λ_{max} ($\log\varepsilon$) 216 (4.05), 235 (4.05) nm, IR (KBr) λ_{max} 3460 (OH), 1719, 1682 (C=O), 835 (furyl) cm^{-1}, for ^{1}H and ^{13}C NMR spectra, see Tables 1 and 2, ESITOFMS *m/z* 487.2331 $[M + H]^+$ (calcd for $C_{27}H_{35}O_8$, 487.2323).

3.5. Domesticulide B (*2*)

White solid, m.p. 155–156 °C, $[\alpha]_D^{28} - 100$ (*c* 0.1, $CHCl_3$), UV (MeOH) λ_{max} ($\log\varepsilon$) 219 (3.62), 232 (3.60) nm, IR (KBr) λ_{max} 3464 (OH), 1734, 1682 (C=O), 875 (furyl) cm^{-1}, for ^{1}H and ^{13}C NMR spectra, see Tables 1 and 2, ESITOFMS *m/z* 529.2441 $[M + H]^+$ (calcd for $C_{29}H_{37}O_9$, 529.2428).

3.6. Domesticulide C (*3*)

Amorphous solid $[\alpha]_D^{28} - 47$ (*c* 0.18, $CHCl_3$), UV ($CHCl_3$) λ_{max} ($\log\varepsilon$) 240 (4.09) nm, IR (KBr) λ_{max} 3430 (OH), 1732, 1702 (C=O) cm^{-1}, for ^{1}H ^{13}C NMR spectra, see Tables 1 and 2, ESITOFMS *m/z* 583.2155 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{11}Na$, 583.2155).

3.7. Domesticulide D (**4**)

Amorphous solid, $[\alpha]_D^{28} - 39$ (c 0.12, $CHCl_3$), UV (MeOH) λ_{max} ($\log \varepsilon$) 239 (3.62) nm, IR (KBr) λ_{max} 3436 (OH), 1724, 1692 (C=O) cm^{-1}, for ^1H and ^{13}C NMR spectra, see Tables 1 and 2, ESITOFMS m/z 583.2173 $[M + Na]^+$(calcd for $C_{29}H_{36}O_{11}Na$, 583.2155).

3.8. Domesticulide E (**5**)

Amorphous solid, $[\alpha]_D^{28} + 185$ (c 0.13, $CHCl_3$), UV ($CDCl_3$) λ_{max} ($\log \varepsilon$) 219 (3.62) nm, IR (KBr) λ_{max} 3400 (OH), 1745 (C=O), cm^{-1}, for ^1H and ^{13}C NMR spectra, see Tables 1 and 2, ESITOFMS m/z 539.1893 $[M + Na]^+$ (calcd for $C_{27}H_{32}O_{10}Na$, 532.1893).

3.9. Antimalarial activity

The malarial parasite, *P. falciparum* (K1, multidrug resistant strain), was cultured according to the method of Trager and Jensen (1976). Quantitative assessment of malarial activity in vitro was determined by means of the microculture radioisotope technique based upon the method described by Desjardins et al. (1979). The inhibitory concentration (IC_{50}) represents the concentration that causes 50% reduction in parasite growth as indicated by the *in vitro* uptake of [^3H]-hypoxanthine by *P. falciparum*. An IC_{50} value of 0.001–0.003 μg/ml was observed for the standard compound, artemisinin, in this test system.

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