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Flavonoids from the pods of *Millettia erythrocalyx*

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Abstract

From the pods of *Millettia erythrocalyx*, 2′-hydroxy-3,4-dimethoxy-[2″,3″:4′,3′]-furanochalcone, 2′,3-dihydroxy-4-methoxy-4′-γ,γ-dimethylallyloxychalcone, (−)-(2*S*)-6,3′,4′-trimethoxy-[2″,3″:7,8]-furanoflavanone, 3′,4′-methylenedioxy-[2″,3″:7,8]-furanoflavonol and 6,3′-dimethoxy-[2″,3″:7,8]-furanoflavone were isolated, along with six other known flavonoids. Their structures were elucidated through analysis of their spectroscopic data.
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Keywords: Millettia erythrocalyx; Leguminosae; Flavonols; Flavones; Chalcones; Flavanones

1. Introduction

Millettia erythrocalyx Gagnep., locally known in Thai as ''Chan'', is widely distributed in the central part of Thailand. In earlier reports, we described the isolation of several flavonoids from the stem bark, roots and leaves of this plant, some of which showed moderate activity against Herpes simplex virus. (Sritularak et al., 2002a,b; Likhitwitayawuid et al., 2005). In the present report, a chemical investigation of the pods of this plant led to the identification of five new flavonoids. In addition, six known compounds were identified by comparison of their spectroscopic properties with published data: derricidin (do Nascimento and Mors, 1972), 2′-hydroxy-3,4-methylenedioxy-4′-γ,γ-dimethylallyloxychalcone (Islam et al., 1994), ovalifolin (Tanaka et al., 1991), Pongol methyl ether (Sritularak et al., 2002a), 3′,4′-methylenedioxy-7-methoxyflavone (Mahmoud and Waterman, 1985) and millettocalyxin C (Sritularak et al., 2002a).

2. Results and discussion

Compound **1** was obtained as a yellow powder. The positive HRESITOFMS exhibited an $[M+H]^+$ ion at *m/z* 325.1077 (calcd. for $C_{19}H_{17}O_5$, 325.1076), suggesting the molecular formula $C_{19}H_{16}O_5$. The IR bands at 3423 (hydroxyl), 1635 (conjugated carbonyl) and 1564 (conjugated unsaturation) cm^{-1} and the UV absorptions at 246 and 372 nm were suggestive of a chalcone skeleton (Markham, 1982). The *trans*-olefinic proton signals at δ 7.53 (*d*, $J = 15.5$ Hz, H-α) and δ 7.89 (*d*, $J = 15.5$ Hz, H-β), a chelated hydroxyl proton at δ 14.07 (s) and the ^{13}C NMR signal at δ 193.3 (C-β′) (Table 1) suggested that compound **1** was a chalcone with a hydroxyl at C-2′. Compound **1** also showed characteristic ^1H and ^{13}C NMR resonances for a furan structure on ring A at δ 7.01 (1H, *dd*, $J = 2.1$, 0.9 Hz, H-4″)/δ 105.1 (C-4″) and δ 7.57 (1H, *d*, $J = 2.1$ Hz, H-5″)/δ 144.4 (C-5″) (Saxena et al., 1987). The AB splitting system at δ 7.08 (1H, *dd*, $J = 8.8$, 0.9 Hz, H-5′) and δ 7.85 (1H, *d*, $J = 8.8$ Hz, H-6′), along with the HMBC correlations of C-2′ (δ 160.2) with H-6′, and C-4′ (δ 159.7) with H-6′, H-4″ and H-5″ (Table 1), indicated the position of the furan ring at C-3′ and C-4′. The appearance of H-4″ as a double doublet was due to its long-range coupling with H-5′. In addition, the ^1H NMR spectrum of **1** revealed the presence of two methoxyls at δ 3.93 (3H, s, MeO-4) and δ 3.96 (3H, s, MeO-3), which should be located on ring B. The aromatic protons on ring B were observed as two doublets at δ 7.17 ($J = 2.1$ Hz, H-2) and δ 6.91 ($J = 8.2$ Hz, H-5) and a double doublet at δ 7.27 ($J = 8.2$, 2.1 Hz, H-6), suggesting the locations of the two methoxyls at C-3 and C-4. This was confirmed by the HMBC correlation of C-β with H-2 and

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Table 1
^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectroscopic data of compounds **1** and **2** (in $CDCl_3$)

Position	^{1}H[a]		^{13}C[b]		HMBC[c] (correlation with ^{1}H)	
	1	**2**	**1**	**2**	**1**	**2**
1	–	–	127.7 (*s*)	128.5 (*s*)	5 and α	5 and α
2	7.17 (*d*, 2.1)	7.27 (*d*, 2.1)	110.3 (*d*)	112.9 (*d*)	6 and β	6 and β
3	–	–	149.3 (*s*)	145.9 (*s*)	5, 2[d] and MeO-3	5 and 2[d]
4	–	–	151.7 (*s*)	148.9 (*s*)	2, 5[d], 6 and MeO-4	2, 6, 5[d] and MeO-4
5	6.91 (*d*, 8.2)	6.86 (*d*, 8.2)	111.2 (*d*)	110.6 (*d*)	–	–
6	7.27 (*dd*, 8.2,2.1)	7.13 (*dd*, 8.2, 2.1)	123.5 (*d*)	122.9 (*d*)	2 and β	2 and β
1′	–	–	114.5 (*s*)	114.0 (*s*)	5′	3′ and 5′
2′	–	–	160.2 (*s*)	166.6 (*s*)	6′ and HO-2′[d]	3′[d] and 6′
3′	–	6.45 (*d*, 2.4)	117.8 (*s*)	101.7 (*d*)	5′ and 5″	5′
4′	–	–	159.7 (*s*)	165.4 (*s*)	4″, 5″ and 6′	6′ and 1″
5′	7.08 (*dd*, 8.8, 0.9)	6.48 (*dd*, 8.8, 2.4)	103.6 (*d*)	108.2 (*d*)	–	3′
6′	7.85 (*d*, 8.8)	7.80 (*d*, 8.8)	125.9 (*d*)	131.1 (*d*)	–	–
α	7.53 (*d*, 15.5)	7.42 (*d*, 15.2)	118.3 (*d*)	118.5 (*d*)	–	–
β	7.89 (*d*, 15.5)	7.79 (*d*, 15.2)	145.1 (*d*)	144.2 (*d*)	2 and 6	2 and 6
β′	–	–	193.3 (*s*)	191.8 (*s*)	β, α[d] and 6′	β, α[d] and 6′
1″	–	4.55 (*d*, 6.7)	–	65.2 (*t*)	–	–
2″	–	5.47 (*dd*, 6.7, 6.7)	–	118.7 (*d*)	–	1″[d], 4″ and 5″
3″	–	–	–	139.1 (*s*)	–	1″, 4″[d] and 5″[d]
4″	7.01 (*dd*, 2.1, 0.9)	1.79 (*s*)	105.1 (*d*)	25.8 (*q*)	–	5″
5″	7.57 (*d*, 2.1)	1.74 (*s*)	144.4 (*d*)	18.2 (*q*)	–	4″
MeO-3	3.96 (*s*)	–	56.0 (*q*)	–	–	–
MeO-4	3.93 (*s*)	3.94 (*s*)	56.0 (*q*)	56.1 (*q*)	–	–
HO-2′	14.07 (*s*)	13.45 (*s*)	–	–	–	–

[a] Coupling constants (*J* in Hz) for ^{1}H.
[b] Multiplicities for ^{13}C are in parentheses.
[c] Protons correlating with carbon resonance (optimized J_{C-H} at 8 Hz).
[d] Two-bond coupling.

H-6, and the NOESY interactions of MeO-3 (δ 3.96, s) with H-2, and of MeO-4 (δ 3.93, s) with H-5. A ^{1}H–^{1}H COSY experiment was also used for identifying each pair of vicinally coupled protons, as follows: H-α/H-β, H-5′/H-6′, H-4″/H-5″ and H-5/H-6. Based on the above spectral evidence, compound **1** was identified as 2′-hydroxy-3,4-dimethoxy-[2″,3″:4′,3′]-furanochalcone.

Compound **2** possessed the molecular formula $C_{21}H_{22}O_5$, as suggested by its $[M+H]^+$ ion at *m*/*z* 355.1547 (calcd. for $C_{21}H_{23}O_5$, 355.1545) in the HRESITOFMS. The UV maxima at 260 and 380 nm and the IR absorptions at 3411 (hydroxyl), 1632 (conjugated carbonyl) and 1568 (conjugated unsaturation) cm^{-1} were indicative of a chalcone skeleton (Markham, 1982). In the ^{1}H NMR spectrum, a set of *trans*-olefinic protons at δ 7.42 and δ 7.79 (each *d*, *J* = 15.2 Hz, H-α and H-β) and a chelated phenolic proton at δ 13.45 (s) assignable to 2′-OH were observed. The ^{1}H NMR spectrum of **2** also exhibited signals for a prenyloxyl group at δ 4.55 (2H, *d*, *J* = 6.7 Hz, H-1″), δ 5.47 (1H, *dd*, *J* = 6.7, 6.7 Hz, H-2″), δ 1.79 (3H, s, H_3-4″) and δ 1.74 (3H, s, H_3-5″). This isoprene-related substituent should be located at C-4′ of ring A, as suggested by the signals of two doublets at δ 6.45 (1H, *J* = 2.4 Hz, H-3′) and δ 7.80 (1H, *J* = 8.8 Hz, H-6′), and a double doublet at δ 6.48 (1H, *J* = 8.8, 2.4 Hz, H-5′) (do Nascimento and Mors, 1972). This was confirmed by the HMBC correlations of H-6′ with C-β′ (δ 191.8) and H-1″ with C-4′ (δ 165.4), as well as the NOESY interactions of H-1″ with H-3′ and H-5′ (Table 1). Among the six aromatic carbons of ring B, two were oxygenated, resonating at δ 145.9 (C-3) and δ 148.9 (C-4). The ^{1}H–^{1}H COSY spectrum of **2**, showing ABM-type coupled aromatic protons of ring B at δ 6.86 (1H, *d*, *J* = 8.2 Hz, H-5), δ 7.13 (1H, *dd*, *J* = 8.2, 2.1 Hz, H-6) and δ 7.27 (1H, *d*, *J* = 2.1 Hz, H-2), suggested *ortho*-disubstitution at C-3 and C-4. The HMBC correlations of C-β (δ 144.2) with H-2 and H-6, together with the NOESY cross-peak between MeO-4 and H-5, placed the methoxyl at C-4 and hence the hydroxyl at C-3. Thus, compound **2** was identified as 2′,3-dihydroxy-4-methoxy-4′-γ,γ-dimethylallyloxychalcone.

Compound **3** gave an $[M+H]^+$ ion at *m*/*z* 355.1190 (calcd. for $C_{20}H_{19}O_6$, 355.1181) in the HRESITOFMS, indicating a molecular formula of $C_{20}H_{18}O_6$. The IR spectrum showed absorption bands for conjugated carbonyl (1678 cm^{-1}) and ether (1265 and 1217 cm^{-1}) functionalities. The UV spectrum exhibited absorptions at 233 and 348 nm, suggesting a flavanone moiety (Markham, 1982). The ^{1}H NMR spectrum of compound **3** disclosed the presence of three methoxyls at δ 3.90, δ 3.91 and δ 3.99 (each 3H, s), and a furan ring, as evidenced by two one-proton doublets (*J* = 2.1 Hz) at δ 6.92 (H-4″) and δ 7.61 (H-5″). Comparison of the ^{1}H and ^{13}C NMR signals of rings A and C of **3** with those of (−)-(2*S*)-6-methoxy-[2″,3″:7,8]-furanoflavanone (Sritularak et al., 2002b) revealed their close similarity. Thus, on ring A of **3**, a furan structure should be present, being fused in an angular position at C-7 and C-8, and this was corroborated by the HMBC connectivities from C-7 (δ 149.8) to H-5, H-4″ and H-5″.

A NOESY cross-peak between a methoxyl at δ 3.99 and H-5, which was assigned by three-bond HMBC coupling with C-4 (δ 191.4) (Table 2), placed this methoxyl at C-6 of ring A. For ring C, as expected, the methylene proton signals at δ 2.89 (*dd*, $J = 17.1$, 3.1 Hz, H-3_{eq}) and δ 3.16 (*dd*, $J = 17.1$, 13.4 Hz, H-3_{ax}) and the methine proton at δ 5.51 (*dd*, $J = 13.4$, 3.1 Hz, H-2) showed HMQC correlation to the carbons at δ 44.3 (C-3), and δ 80.5 (C-2), respectively. As for ring B, the presence of an ABM splitting pattern at δ 6.91 (1H, *d*, $J = 8.8$ Hz, H-5′), δ 7.03 (1H, *d*, $J = 2.1$ Hz, H-2′) and δ 7.04 (1H, *dd*, $J = 8.8$, 2.1 Hz, H-6′) and the HMBC correlation of C-2 (δ 80.5) with H-2′ and H-6′ suggested the locations of the two methoxyls at C-3′ and C-4′. This was supported by the NOESY interactions of MeO-3′ (δ 3.91, s) with H-2′, and MeO-4′ (δ 3.90, s) with H-5′, respectively. The absolute configuration at C-2 was proposed to be *S* because the compound showed a positive Cotton effect at 351 nm ($n \rightarrow \pi^*$) and a negative Cotton effect at 310 nm ($\pi \rightarrow \pi^*$) in the CD spectrum (Gaffield, 1970). Therefore, compound **3** was identified as (−)-(2*S*)-6,3′,4′-trimethoxy-[2″,3″:7,8]-furanoflavanone.

Table 2
^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectroscopic data of compound **3** (in $CDCl_3$)

Position	^{1}H[a]	^{13}C[b]	HMBC[c] (correlation with ^{1}H)
2	5.51 (*dd*, 13.4, 3.1)	80.5 (*d*)	2′, 6′ and 3[d]
3_{ax}	3.16 (*dd*, 17.1, 13.4)	44.3 (*t*)	–
3_{eq}	2.89 (*dd*, 17.1, 3.1)	–	–
4	–	191.4 (*s*)	2 and 5
5	7.28 (*s*)	102.1 (*d*)	–
6	–	141.5 (*s*)	5[d], MeO-6
7	–	149.8 (*s*)	5, 4″ and 5″
8	–	119.2 (*s*)	4″[d] and 5″
9	–	151.6 (*s*)	5
10	–	115.4 (*s*)	–
1′	–	131.2 (*s*)	2[d], 3, 2′[d], 5′ and 6′[d]
2′	7.03 (*d*, 2.1)	109.5 (*d*)	2 and 6′
3′	–	149.5 (s)	2′[d], 5′ and MeO-3′
4′	–	149.2 (*s*)	2′, 5′[d], 6′ and MeO-4′
5′	6.91 (*d*, 8.8)	111.1 (*d*)	6′[d]
6′	7.04 (*dd,* 8.8, 2.1)	118.9 (*d*)	2, 2′ and 5′[d]
4″	6.92 (*d*, 2.1)	105.3 (*d*)	5″[d]
5″	7.61 (*d*, 2.1)	145.3 (*d*)	4″[d]
MeO-6	3.99 (*s*)	56.3 (*q*)	–
MeO-3′	3.91 (*s*)	56.0 (*q*)	–
MeO-4′	3.90 (*s*)	56.0 (*q*)	–

[a] Coupling constants (*J* in Hz) for ^{1}H.
[b] Multiplicities for ^{13}C are in parentheses.
[c] Protons correlating with carbon resonance (optimized J_{C-H} at 8 Hz).
[d] Two-bond coupling.

Compound **4** was formulated as $C_{18}H_{10}O_6$ from its $[M+H]^+$ ion at *m/z* 323.0567 (calcd. for $C_{18}H_{11}O_6$, 323.0555) in the HRESITOFMS. The presence of flavonol skeleton was evident from the UV absorptions at 246 and 324 nm and the IR bands at 3401 (hydroxyl) and 1655 (conjugated carbonyl) cm^{-1} (Markham, 1982). In fact, the ^{1}H and ^{13}C NMR spectroscopic data of **4** were very close to those of the flavone pongaglabrone (Garcez et al., 1988), except for the absence of H-3 and the appearance of C-3 as an oxygenated olefinic carbon at δ 141.9. In **4**, ^{1}H and ^{13}C NMR signals (Table 3) for a furan ring were observed at δ 7.11 (1H, *dd*, $J = 2.4$, 0.9 Hz, H-4″)/δ104.2

Table 3
^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectroscopic data of compounds **4** and **5** (in $CDCl_3$)

Position	^{1}H[a]		^{13}C[b]		HMBC[c] (correlation with ^{1}H)	
	4	**5**	**4**	**5**	**4**	**5**
2	–	–	159.3 (*s*)	162.8 (*s*)	2′ and 6′	2′, 6′ and 3[e]
3	–	7.02 (*s*)	141.9 (*s*)	107.2 (*d*)	–	–
4	–	–	172.9 (*s*)	178.1 (*s*)	5	3[e] and 5
5	8.20 (*d*, 8.8)	7.52 (*s*)	122.3 (*d*)	99.8 (*d*)	–	–
6	7.58 (*dd*, 8.8, 0.9)	–	110.7 (*d*)	144.6 (*s*)	–	5[e] and MeO-6
7	–	–	158.4 (*s*)	148.5 (*s*)	5, 4″, 5″ and 6[e]	5, 4″ and 5″
8	–	–	116.9 (*s*)	118.9 (*s*)	6 and 5″	4″[e] and 5″
9	–	–	150.1[d] (*s*)	145.9 (*s*)	5	5 and 4″
10	–	–	117.7 (*s*)	119.6 (*s*)	6	3
1′	–	–	125.0 (*s*)	132.9 (*s*)	5′	3 and 5′
2′	7.43 (*d*, 1.8)	7.46 (*br d*, 2.4)	109.4 (*d*)	111.9 (*d*)	6′	4′ and 6′
3′	–	–	147.7 (*s*)	160.0 (*s*)	5′ and –OCH_2O–	5′ and MeO-3′
4′	–	7.08 (*dd*, 7.9, 2.4)	150.0[d] (*s*)	117.1 (*d*)	2′, 6′ and –OCH_2O–	2′ and 6′
5′	6.98 (*d*, 8.2)	7.45 (*dd*, 7.9, 7.9)	108.4 (*d*)	130.3 (*d*)	–	–
6′	7.53 (*dd*, 8.2, 1.8)	7.54 (*br d*, 7.9)	124.6 (*d*)	118.7 (*d*)	2′	2′ and 4′
–OCH_2O–	6.09 (*s*)	–	101.9 (*t*)	–	–	–
4″	7.11 (*dd*, 2.4, 0.9)	7.21 (*d*, 2.1)	104.2 (*d*)	104.7 (*d*)	–	–
5″	7.75 (*d*, 2.4)	7.78 (*d*, 2.1)	146.0 (*d*)	146.1 (*d*)	–	–
MeO-6	–	4.09 (*s*)	–	56.5 (*q*)	–	–
MeO-3′	–	3.89 (*s*)	–	55.5 (*q*)	–	–

[a] Coupling constants (*J* in Hz) for ^{1}H.
[b] Multiplicities for ^{13}C are in parentheses.
[c] Protons correlating with carbon resonance (optimized J_{C-H} at 8 Hz).
[d] Interchangeable.
[e] Two-bond coupling.

(C-4″) and δ 7.75 (1H, *d*, *J* = 2.4 Hz, H-5″)/δ 146.0 (C-5″). Similar to pongaglabrone, **4** had the furan ring fused in an angular position at C-7 and C-8 of ring A, as supported by the presence of aromatic protons at δ 8.20 (*d*, *J* = 8.8 Hz, H-5) and δ 7.58 (*dd*, *J* = 8.8, 0.9 Hz, H-6) and the HMBC correlation of H-5 with C-4 (δ 172.9). Furthermore, the HMBC couplings of C-7 (δ 158.4) with H-4″, H-5″ and H-5 were observed. The ^{1}H and ^{13}C NMR spectroscopic data of ring B of **4** were also similar to those of pongaglabrone, with signals for a methylenedioxy group at δ 6.09 (2H, s)/δ 101.9 (O$\underline{C}H_2$O). This substituent was placed at C-3′ and C-4′, as evident from the ABM spin system at δ 7.43 (*d*, *J* = 1.8 Hz, H-2′), δ 6.98 (*d*, *J* = 8.2 Hz, H-5′) and δ 7.53 (*dd*, *J* = 8.2, 1.8 Hz, H-6′). Thus, it was concluded that compound **4** was 3′,4′-methylenedioxy-[2″,3″:7,8]- furanoflavonol.

Compound **5** has a molecular formula of $C_{19}H_{14}O_5$, as indicated by the $[M+H]^+$ ion peak at *m*/*z* 323.0910 in the HRESITOFMS (calcd. for $C_{19}H_{15}O_5$, 323.0919). The IR bands at 1678 (conjugated carbonyl), 1608 (conjugated unsaturation) cm^{-1} and the UV absorptions at 270 and 309 nm were indicative of a furanoflavone (Mabfor et al., 1995), and this was supported by the ^{1}H and ^{13}C NMR signals (Table 3) for H-3/C-3 at δ 7.02 (1H, s)/δ 107.2 and for a furan ring at δ 7.21 (1H, d, *J* = 2.1 Hz, H-4″)/δ 104.7 (C-4″) and δ 7.78 (1H, *d*, *J* = 2.1 Hz, H-5″)/δ 146.1 (C-5″) (Sritularak et al., 2002a). Results from analysis of the DEPT and HMQC spectra revealed that **5** possessed two methoxyls. The first methoxyl [δ_H 4.09 (3H, s); δ_C 56.5 (q)] should be situated at C-6 of ring A, as shown by its NOESY interaction with H-5 (δ 7.52, 1H, s), which was assigned from its HMBC correlation with C-4 (δ 178.1) (Table 3). The second methoxyl [δ_H 3.89 (3H, s); δ_C 55.5 (q)] was situated at the *m*-position in relation to C-1′ on ring B, as evidenced by its NOESY interactions with protons at δ 7.46 (1H, *br d*, *J* = 2.4 Hz, H-2′) and δ 7.08 (1H, *dd*, *J* = 7.9, 2.4 Hz, H-4′). This was supported by HMBC three-bond correlations of C-2 with H-2′ and H-6′. On the basis of the above spectroscopic data, compound **5** was determined as 6,3′-dimethoxy-[2″,3″:7,8]-furanoflavone.

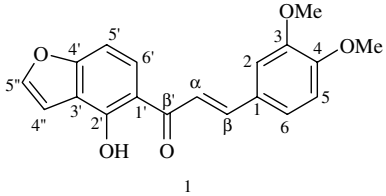
3. Conclusions

The genus *Millettia* of the family Leguminosae has been known to be rich in furanoflavonoids, with more than 20 structures being identified from six plant species (Maurya and Yadav, 2005). *Millettia* furanoflavonoids could be classified according to their basic skeleta as chalcones, flavones, flavonols, flavanones, and flavans. Almost all of the members in the last four categories have a furan structure located on ring A in an angular position, i.e., anellated at C-7 and C-8. This substitution pattern has also been observed for the flavonoids isolated in this study. So far, the only apparent exception to this generalization is the report of pinnatin from *M. pachycarpa* (Shao et al., 2001), a linear-furan bearing flavone which was first isolated from *Pongamia pinnata* (Pavanaram and Row, 1956). It should be noted that compound **5** has an unsual 3′-monooxygenated B-ring. Up to the present, furanoflavonoids with this rare oxygenation pattern have been found only in the genera *Millettia* and *Pongamia* (Maurya and Yadav, 2005).

4. Experimental

4.1. General experimental procedures

The optical rotation was measured on a Perkin-Elmer 341 polarimeter, and the CD spectrum was recorded on a JASCO J-715 spectropolarimeter. UV spectra were obtained on a Milton Roy Spectronic 3000 Array spectrophotometer, and IR spectra on a Perkin-Elmer FT-IR 1760X spectrophotometer. Mass spectra were recorded on a Micromass LCT mass spectrometer. NMR spectra were obtained with a Bruker Avance DPX-300 FT-NMR spectrometer (300 MHz) and a JEOL JMN-A 500 NMR spectrometer (500 MHz).



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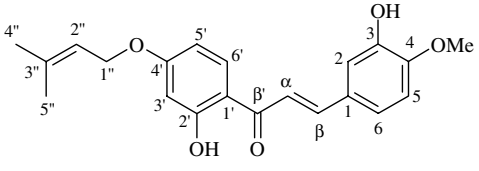

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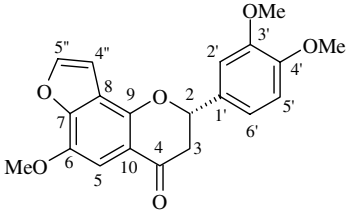

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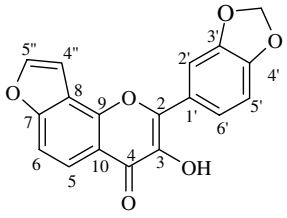

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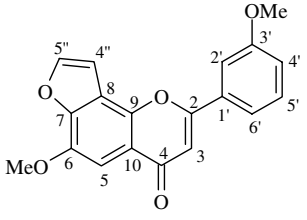

5

4.2. Plant material

The pods of *M. erythrocalyx* Gagnep. were collected from Tayang district, Petchaburi Province, Thailand, in April 2000. Authentication was performed by comparison with herbarium specimens at the Royal Forest Department, Ministry of Agriculture and Co-operatives, and a voucher specimen (KL-042543) is on deposit at the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Thailand.

4.3. Extraction and isolation

Dried powdered pods of *M. erythrocalyx* Gagnep. (1 kg) were extracted with MeOH at room temperature. The MeOH extract was filtered and evaporated under reduced pressure to give a viscous mass (30 g) of dried extract. This material was subjected to vacuum-liquid chromatography on silica gel (EtOAc–hexane gradient) to give fractions A-I. Fraction C (168 mg) was separated by CC (silica gel; CH_2Cl_2–hexane, 1:4) to give derricidin (5 mg; R_f 0.41, silica gel, CH_2Cl_2–hexane, 1:1). Separation of fraction *D* (398 mg) was performed by CC over silica gel, eluted with CH_2Cl_2–hexane (1:1) to give 55 fractions. 2′-Hydroxy-3,4-methylenedioxy-4′-γ,γ-dimethylallyloxychalcone (3 mg; R_f 0.53, silica gel, CH_2Cl_2–hexane, 4:1) and ovalifolin (12 mg; R_f 0.19, silica gel, CH_2Cl_2–hexane, 4:1) were obtained from fractions 10–13 and fraction 54, respectively. Fractions 25–30 (22 mg) were combined and then subjected to repeated CC over silica gel using EtOAc–hexane (1:9) to afford **1** (2 mg; R_f 0.31, silica gel, EtOAc–hexane, 1:2). Fraction F (723 mg) was separated by CC (silica gel; EtOAc–hexane 1:9) to give 6 fractions (I–VI). Fraction II (161 mg) was subjected to repeated CC (silica gel; MeOH–CH_2Cl_2, 1:99) to yield **2** (5 mg; R_f 0.46, silica gel, CH_2Cl_2) and pongol methyl ether (27 mg; R_f 0.23, silica gel, CH_2Cl_2). Fraction III (66 mg), after purification by CC on silica gel (MeOH–CH_2Cl_2 2:98) gave **3** (6 mg; R_f 0.31, silica gel, CH_2Cl_2). Fraction IV (259 mg) was separated by gel filtration chromatography (Sephadex LH-20, acetone) to give 19 fractions. Fractions 10–13 (176 mg) were combined and further purified by CC (silica gel) using EtOAc–CH_2Cl_2 (3:97) to furnish 3′,4′-methylenedioxy-7-methoxyflavone (3 mg; R_f 0.76, silica gel, EtOAc–hexane, 1:9) and milletocalyxin C (35 mg; R_f 0.50, silica gel, EtOAc–hexane, 1:9). Fraction 14 (13 mg) was purified by CC (silica gel; EtOAc–CH_2Cl_2, 3:97) to afford **4** (8 mg; R_f 0.51, silica gel, EtOAc–hexane, 1:9). Fraction V (67 mg) was separated by sephadex LH 20 (acetone) and then by CC (silica gel; EtOAc–CH_2Cl_2, 5:95) to yield **5** (16 mg, R_f 0.25, silica gel, EtOAc–hexane, 1:9).

4.4. 2′-Hydroxy-3,4-dimethoxy-[2″,3″:4′,3′]-furanochalcone (*1*)

Yellow powder; $C_{19}H_{16}O_5$; UV (MeOH) λ_{max} (log ε): 246 (3.72), 372 (3.75) nm; IR (film): 3423, 1635, 1564 cm^{-1}; For ^1H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectroscopic data, see Table 1; HRESITOFMS $[M+H]^+$ *m/z* 325.1077 (calcd. for $C_{19}H_{17}O_5$, 325.1076).

4.5. 2′,3-Dihydroxy-4-methoxy-4′-γ,γ-dimethylallyloxychalcone (*2*)

Yellow powder; $C_{21}H_{22}O_5$; UV (MeOH) λ_{max} (log ε): 260 (4.30), 380 (4.75) nm; IR (film): 3411, 1632, 1568 cm^{-1}; For ^1H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz) spectroscopic data, see Table 1; HRESITOFMS $[M+H]^+$ *m/z* 355.1547 (calcd. for $C_{21}H_{23}O_5$, 355.1545).

4.6. (−)-(2*S*)-6,3′,4′-trimethoxy-[2″,3″:7,8]-furanoflavanone (*3*)

White powder; $C_{20}H_{18}O_6$; $[\alpha]_D^{28}$ − 1.53° (MeOH; *c* 0.2); UV (MeOH) λ_{max} (log ε): 233 (4.46), 348 (2.78) nm; CD (MeOH; *c* 0.2): $[\theta]_{203}$ + 6563, $[\theta]_{210}$ + 8491, $[\theta]_{232}$ + 1876, $[\theta]_{245}$ + 1266, $[\theta]_{256}$ − 213, $[\theta]_{267}$ − 319, $[\theta]_{310}$ − 1443 $[\theta]_{351}$ + 1009; IR (film) 1678, 1265, 1217 cm^{-1}; for ^1H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectroscopic data, see Table 2; HRESITOFMS $[M+H]^+$ *m/z* 355.1190 (calcd. for $C_{20}H_{19}O_6$, 355.1181).

4.7. 3′,4′-Methylenedioxy-[2″,3″:7,8]-furanoflavonol (*4*)

Yellow powder; $C_{18}H_{10}O_6$; UV (MeOH) λ_{max} (log ε): 246 (3.58), 324 (3.29) nm; IR (film): 3401, 1655 cm^{-1}; For ^1H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectroscopic data, see Table 3; HRESITOFMS $[M+H]^+$ *m/z* 323.0567 (calcd. for $C_{18}H_{11}O_6$, 323.0555).

4.8. 6,3′-Dimethoxy-[2″,3″:7,8]-furanoflavone (*5*)

White powder; $C_{19}H_{14}O_5$; UV (MeOH) λ_{max} (log ε): 208 (4.23), 270 (3.84), 3.09 (3.74) nm; IR (film) 1678, 1608 cm^{-1}; For ^1H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectroscopic data, see Table 3; HRESITOFMS $[M+H]^+$ *m/z* 323.0910 (calcd. for $C_{19}H_{15}O_5$, 323.0919).

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