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Antibacterial and cytotoxic xanthones from the roots of *Cratoxylum formosum*

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Abstract

Chemical investigation of the roots of *Cratoxylum formosum* has resulted in the isolation and characterization of xanthones: three new, named formoxanthone A–C and three known together with three known anthraquinones. Their structures were established on the basis of analysis of spectroscopic evidence. In addition, antibacterial and cytotoxic activities of the isolates were also evaluated.
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Keywords: *Cratoxylum formosum*; Formoxanthone; Guttiferae; Antibacterial activity; Cytotoxicity

1. Introduction

Cratoxylum formosum subsp. *formosum* (Jack) Dyer belongs to the Guttiferae family and is known locally as Tio Khao (Smitinand, 2001). This plant has been used by the local Thai people as folk medicine for the treatment of diarrhea, internal bleeding and food poisoning (Anderson, 1986). Xanthones (Iinuma et al., 1996; Kijjoa et al., 1998) and triterpenoids (Bennett et al., 1993) have been characterized from the genus *Cratoxylum*. The search for bioactive compounds from natural sources has been an ongoing project in our laboratory (Chumkaew et al., 2003; Laphookhieo et al., 2004). In this report, we describe the isolation and structure elucidation as well as antibacterial and cytotoxic activities of compounds from *C. formosum*.

2. Results and discussion

The crude hexane extract from the roots of *C. formosum* was subjected to a succession of chromatographic procedures, including silica gel column chromatography and preparative TLC to afford three new xanthones, named formoxanthone A–C (**1–3**) together with six known compounds: macluraxanthone (**4**) (Botta et al., 1986), xanthone V_1 (**5**) (Botta et al., 1986), gerontoxanthone I (**6**) (Chang et al., 1989), 3-geranyloxy-6-methyl-1,8-dihydroxyanthraquinone (Botta et al., 1983), vismiaquione (Goncalves and Mors, 1981) and madagascin (Camele et al., 1982). All structures were elucidated using 1D and 2D NMR spectroscopic data and by comparison with those reported in the literature (see Fig. 1).

Compound **1** was obtained as a yellow amorphous solid. The HREIMS spectrum showed a molecular ion peak at m/z 448.2224, corresponding to $C_{28}H_{32}O_5$. The IR spectrum of **1** exhibited strong vibration bands due to free hydroxyl (3373 cm^{-1}) and conjugated carbonyl (1650 cm^{-1}) groups. The UV absorption bands (245, 260 *sh*, 319 and 367 nm) were typical of a xanthone chromophore

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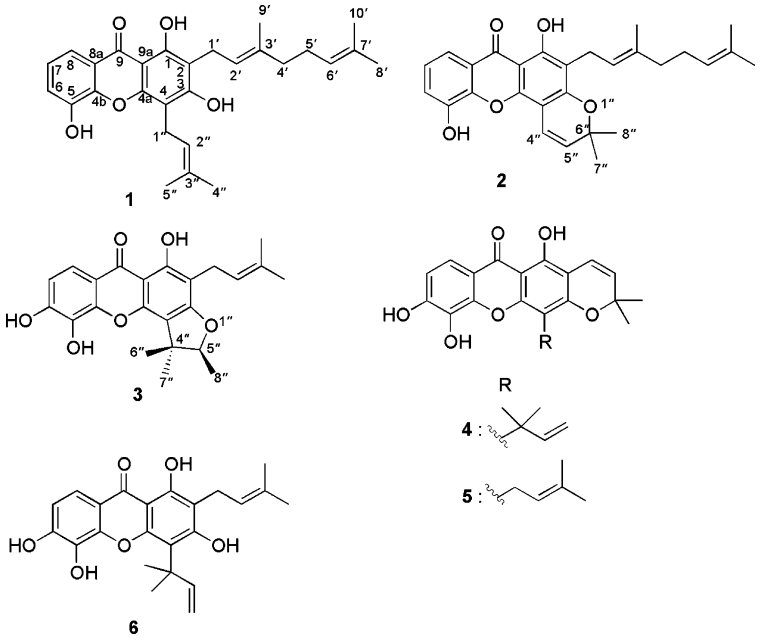

Fig. 1. Structures of compounds **1**–**6**.

(Seo et al., 2002; Ito et al., 2003). The ^{13}C NMR and DEPT spectroscopic data (Table 1) disclosed the presence of one carbonyl carbon (δ 181.1), twelve sp^2 quaternary carbons (five of which were oxygen-bearing) (δ 103.3, 105.7, 109.0, 120.9, 132.1, 133.1, 140.1, 144.3, 144.5, 152.5, 158.6, 161.0), six sp^2 methines (δ 116.9, 119.8, 121.1, 122.4, 123.7, 123.8), four sp^3 methylenes (δ 21.6, 22.0, 26.3, 39.7), and five methyl carbons (δ 16.3, 17.7, 17.9, 25.6, 25.7). The ^1H NMR spectrum of **1** (Table 1) contained resonances for one chelated [δ 13.18 (1H, *s*, 1-OH)] and two free hydroxyl groups [δ 6.59 (1H, *s*, 3-OH) and δ 5.84, (1H, *s*, 5-OH)]. A 1,2,3-trisubstituted benzene ring was revealed by resonances at δ 7.75 (1H, *dd*, $J = 7.8$, 1.5 Hz, H-8), 7.28 (1H, *dd*, $J = 7.8$, 1.5 Hz, H-6) and 7.21 (1H, *t*, $J = 7.8$ Hz, H-7). The lowest-field aromatic-proton (δ 7.75) was assigned to H-8 due to the anisotropic effect of the carbonyl group and this was supported by the HMBC correlations of H-8 to a carbonyl carbon at δ 181.1 (C-9), δ 119.8 (C-6) and δ 144.3 (C-4b), as well as those of H-7 to δ 144.5 (C-5) and δ 120.9 (C-8a) and of H-6 to δ 116.9 (C-8).

Furthermore, the ^1H NMR spectra displayed a geranyl moiety at δ 1.60 (3H, *s*, H-10′), 1.69 (3H, *s*, H-8′), 1.85 (3H, *s*, H-9′), 2.11 (4H, *m*, H-4′, H-5′), 3.49 (2H, *d*, $J = 7.2$ Hz, H-1′), 5.06 (1H, *m*, H-6′) and 5.30 (1H, *m*, H-2′), and a prenyl moiety at δ 1.74 (3H, *d*, $J = 1.2$ Hz, H-4″), 1.86 (3H, *s*, H-5″), 3.53 (2H, *d*, $J = 6.9$ Hz, H-1″) and 5.25 (1H, *m*, H-2″). In the HMBC spectrum, the chelated hydroxyl proton (δ 13.18) showed correlations with C-1 (δ 158.6), C-2 (δ 109.0) and C-9a (δ 103.3), the benzylic allylic methylene protons (δ 3.49, H-1′) of the geranyl group showed cross-peak with C-1 (δ 158.6), C-2 (δ 109.0) and C-3 (δ 161.0), and the allylic methylene protons of the prenyl group at δ 3.53 (H-1″) had correlations with C-3 (δ 161.0) and C-4a (δ 152.5), indicating that the geranyl and the prenyl moieties were located at C-2 and C-4, respectively. Therefore, compound **1** was identified as 1,3,5-trihydroxy-2-(3,7-dimethylocta-2,6-dienyl)-4-(3-methylbut-2-enyl)xanthone (formoxanthone A) which is the isomer of 2-geranyl-1,3,7-trihydroxy-4-(3,3-dimethylallyl)-xanthone previously isolated from *Cratoxylum cochinchinense* (Bennett et al., 1993).

Compound **2**, a yellow amorphous solid, gave a HREIMS molecular ion peak at *m/z* 446.2061 corresponding to a molecular formula $C_{28}H_{30}O_5$. The IR and UV spectra of **2** exhibited the same pattern as those of **1**. The ^1H NMR spectrum of **2** (Table 1) was similar to that of **1** except for the replacement of the prenyl group in **1** with the characteristic signals of a chromene ring, two vinylic protons at δ 6.79 and 5.64 (each, *d*, $J = 9.9$ Hz, H-4″, H-5″, respectively) and a methyl signal at δ 1.49 (6H, *s*, Me-7″, Me-8″) (Table 1). The dimethylchromene group was connected to ring A at C-3 and C-4 as evidenced by HMBC correlations of the vinylic proton at δ 6.79 (H-4″) with C-3 (δ 160.6), C-4 (δ 100.6) and C-4a (δ 149.2). Thus, compound **2** was characterized as 1,5-dihydroxy-2-(3,7-dimethylocta-2,6-dienyl)-6″,6″- dimethylpyrano(2″,3″:3,4)xanthone (formoxanthone B).

Compound **3** was obtained as a yellow amorphous solid and the HREIMS spectrum showed a molecular ion peak at *m/z* 396.1559 consistent with the molecular formula $C_{23}H_{24}O_6$. The UV and IR spectrum suggested that **3** was also a xanthone derivative (Seo et al., 2002; Ito et al., 2003). The ^1H NMR spectrocopic data of **3** (Table 2) consisted of one chelated hydroxyl signal at δ 13.40 and two *ortho*-coupled aromatic signals at δ 6.92 and 7.74 (1H each, *d*, $J = 7.7$ Hz, H-7, H-8, respectively). The presence of a prenyl group was evident from the two vinylic methyl signals at δ 1.69 (3H, *s*, Me-4′) and 1.79 (3H, *s*, Me-5′),

Table 1
^{1}H (300 MHz) and ^{13}C (75 MHz) NMR chemical shifts for compounds **1** and **2** in $CDCl_3$

Position	**1**		**2**	
	δ_H	δ_C	δ_H	δ_C
1		158.6		158.7
2		109.0		112.3
3		161.0		160.6
4		105.7		100.6
4a		152.5		149.2
4b		144.3		144.1
5		144.5		144.3
6	7.28, *dd* (7.8, 1.5)	119.8	7.30, *dd* (7.8, 1.5)	120.1
7	7.21, *t* (7.8)	123.8	7.23, *t* (7.8)	123.9
8	7.75, *dd* (7.8, 1.5)	116.9	7.78, *dd* (7.8, 1.5)	117.2
8a		120.9		121.2
9		181.1		180.8
9a		103.3		103.2
1′	3.49, *d* (7.2)	21.6	3.37, *d* (7.5)	21.1
2′	5.30, *m*	121.1	5.25, *m*	121.7
3′		140.1		135.2
4′	2.11, *m*	39.7	2.00, *m*	39.8
5′	2.11, *m*	26.3	2.05, *m*	26.7
6′	5.06, *m*	123.7	5.08, *m*	124.4
7′		132.1		131.3
8′	1.69, *s*	25.7	1.64, *brs*	25.7
9′	1.85, *s*	16.3	1.82, *s*	16.3
10′	1.60, *s*	17.7	1.57, *brs*	17.7
1″	3.53, *d* (6.9)	22.0		
2″	5.25, *m*	122.4		
3″		133.1		
4″	1.74, *d* (1.2)	25.6	6.79, *d* (9.9)	115.0
5″	1.86, *s*	17.9	5.64, *d* (9.9)	127.4
6″				78.1
7″			1.49, *s*	28.2
8″			1.49, *s*	28.2
1-OH	13.18, *s*		13.20, *s*	
3-OH	6.59, *s*			
5-OH	5.84, *s*		5.71, *s*	

Assignments were confirmed by COSY, HMQC, HMBC and DEPT experiments.

one methylene doublet at δ 3.31 (2H, *d*, $J = 6.9$ Hz, H-1′) and a vinylic proton signal at δ 5.29 (1H, *m*, H-2′). Furthermore, signals of an α,α,β-trimethylfuran ring which comprised of protons resonating at δ 1.32 (3H, *s*, Me-6″), 1.43 (3H, *d*, $J = 6.3$ Hz, Me-8″), 1.58 (3H, *s*, Me-7″) and 4.54 (1H, *q*, $J = 6.3$ Hz, H-5″) were observed. In the HMBC spectrum, the methylene signal at δ 3.31 (H-1′) showed cross-peaks with oxygenated aromatic carbons at δ 161.3 (C-1) and δ 164.3 (C-3), indicating that a prenyl group was connected to the C-2 position. In addition, the oxygenated methine proton signal at δ 4.54 (H-5″) showed a correlation with C-3 (δ 164.3) and the methyl groups at δ 1.32 and 1.58 were correlated with C-4 (δ 112.1). These observations suggested that the furan ring was fused at C-3 and C-4. The relative stereostructure of the trimethylfuran ring was postulated from NOESY cross-peaks of the oxygenated methine proton (δ 4.54, H-5″) with the methyl groups at δ 1.43 (Me-8″) and 1.58 (Me-7″) and the methyl doublet at δ 1.43 (Me-8″) with the methyl group at δ 1.32 (Me-6″). Therefore, compound **3** was identified as 4″,5″-dihydro-1,5,6-trihydroxy-2-(3-methylbut-2-enyl)-4″, 4″,5″-trimethylfurano(2″,3″:3,4)xanthone (formoxanthone C).

Table 2
^{1}H (300 MHz) and ^{13}C (75 MHz) NMR chemical shifts for compound **3** in $CDCl_3$

Position	δ_H	δ_C
1		161.3
2		107.3
3		164.3
4		112.1
4a		150.6
4b		145.1
5		130.6
6		149.2
7	6.92, *d* (7.7)	112.2
8	7.74, *d* (7.7)	118.3
8a		114.6
9		180.1
9a		103.0
1′	3.31, *d* (6.9)	21.8
2′	5.29, *m*	121.6
3′		132.2
4′	1.69, *s*	25.8
5′	1.79, *s*	17.8
4″		44.1
5″	4.54, *q* (6.3)	90.3
6″	1.32, *s*	21.7
7″	1.58, *s*	26.3
8″	1.43, *d*(6.3)	14.4
1-OH	13.40, *s*	

Assignments were confirmed by COSY, HMQC, HMBC and DEPT experiments.

The reported compounds were tested for their antibacterial activity against representative Gram-positive *Bacillus substilis*, *Staphylococcus aureus*, Gram-negative *Pseudomonas aeruginosa*, *Streptococcus faecalis*, and *Salmonella typhi* organisms and for their cytotoxicity against MCF-7, HeLa, HT-29 and KB cell lines. The results are summarized in Tables 3 and 4. The compounds tested for antibacterial

Table 3
Antibacterial activity of compounds isolated from the roots of *C. formosum*

Compound	Minimum inhibitive concentration (μg/ml)				
	P. aeruginosa	*B. substilis*	*S. aureus*	*S. faecalis*	*S. typhi*
1	–	18.7	37.5	–	–
3	–	4.6	2.3	18.7	4.6
4	–	4.6	4.6	2.3	9.3
5	9.3	1.1	1.1	1.1	1.1
6	–	2.3	1.1	4.6	1.1
Vancomycin	<0.078	<0.078	<0.078	<0.078	<0.078

–, inactive at >50 μg/ml.

Table 4
Cytotoxic activity of compounds isolated from the roots of *C. formosum*

Compounds	IC_{50} (μg/ml)			
	MCF-7	HeLa	HT-29	KB
3	4.9	3.7	5.3	3.3
5	>25.0	4.7	6.0	2.7
6	12.0	5.0	>25.0	4.7
Camptothecin	0.2–2.0	0.2–2.0	0.2–2.0	0.2–2.0

activity were xanthones (**1**, **3**–**6**) and anthraquinones (**7**–**9**), whereas compound **2** was not tested due to lack of material. Vancomycin was used as a positive control for growth inhibition and showed MIC value less than 0.078 μg/ml. The anthraquinones were found to be inactive. The order of the antibacterial active compounds were **5**, **6**, **3** and **4**. Compound **3** was the most cytotoxic against all four cancer cell lines (Table 4). Compound **5** and **6** showed the least activity against the MCF-7 and HT-29 cell lines, respectively, while compounds **1**, **2**, **4** and **7**–**9** were inactive. It is interesting to note that the catechol unit in the xanthone plays an important role in enhancing the activity. The anticancer drug used as a standard in our cytotoxic assay is camptothecin which has an IC_{50} in the range of 0.2–2.0 μg/ml.

3. Experimental

3.1. General experimental procedures

Melting points were determined on an Electrothermal 9100 melting point apparatus and are uncorrected. UV spectra were measured with a SPECORD S100 spectrophotometer (Analytikjena). The IR spectra were measured with a FTS 165 FT-IR Perkin–Elmer spectrophotometer. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using Bruker Avance 300 MHz spectrometers. Optical rotations were measured in MeOH solution at the sodium D line (589 nm) on JASCO D-1020 polarimeter. The EI-MS and HREIMS mass spectra were obtained using a Micromass LCT mass spectrometer. Quick column chromatography (QCC) and column chromatography (CC) were carried out on silica gel 60 F_{254} (Merck) and silica gel 100, respectively. Precoated plates of silica gel 60 GF_{254} were used for analytical purposes.

3.2. Plant material

The roots of *C. formosum* were collected from Nong Khai Province in the North Eastern part of Thailand in March 2004. The plant was identified by Prof. Puangpen Sirirugsa and a voucher specimen (No. PSU 0012676) has been deposited at the Herbarium of Department of Biology, Prince of Songkla University (PSU).

3.3. Extraction and isolation

Air-dried roots (5.2 kg) were chopped and extracted with hexane (3 × 15 L) at room temperature for three days. Evaporation of the solvent under reduced pressure furnished a crude hexane extract (47.6 g). This was subjected to quick CC on silica gel with solvent mixtures of increasing polarity [hexane to EtOAc–hexane (9:1)] to yield 16 fractions (1–16). Fraction 12 was subjected to silica gel, CC, the column being eluted with solvents of increasing polarity using hexane and EtOAc, to yield 16 subfractions (12A–12P). Crystallization of subfraction 12H from an acetone–hexane mixture (1:4) gave **4** (43.1 mg) as yellow needles. Subfraction 12K, upon standing overnight gave yellow needles of **5** (36.4 mg). Subfraction 16 L was further purified by prep. TLC on silica gel, eluting with acetone in CH_2Cl_2 (1:99), to yield **6** (10.6 mg) and **3** (5.7 mg). Fraction 4 was applied to silica gel column, eluting with solvent mixtures of increasing polarity, (3–10% EtOAc–hexane) to afford 12 subfractions (4A–4L). Subfractions 4A, 4E and 4H were further purified by crystallization from MeOH–CH_2Cl_2 (1:4) to give **7** (17.1 mg), **8** (9.6 mg) and **9** (6.2 mg), respectively. Fraction 10 was subjected to repeated CC over silica gel to afford **1** (31.7 mg) and **2** (4.6 mg).

3.3.1. Formoxanthone A (*1*)

Yellow solid. M.p. 111–113 °C. UV λ_{max}^{MeOH} nm (log ε): 367 (3.50), 319 (4.08), 260(*sh*) (4.29), 245 (4.39). IR (neat) ν_{max}: 3373, 2974, 1650 cm^{-1}. For ^1H and ^{13}C NMR ($CDCl_3$) spectra, see Table 1. MS *m/z* (rel. int.): 448 $[M]^+$ (7), 363 (40), 341 (46), 323 (87), 281 (86), 269 (100). HREIMS *m/z* 448.2224 $[M]^+$ (calcd. for $C_{28}H_{32}O_5$, 448.2250).

3.3.2. Formoxanthone B (*2*)

Yellow solid. M.p. 143–146 °C. UV λ_{max}^{MeOH} nm (log ε): 377 (3.18), 332 (3.71), 269 (4.11), 253 (4.15). IR (KBr) ν_{max}: 3426, 1646 cm^{-1}. For ^1H and ^{13}C NMR ($CDCl_3$) spectra, see Table 1. MS *m/z* (rel. int.): 446 $[M]^+$ (55), 431 (37), 377 (72), 323 (100), 309 (21), 295 (18). HREIMS *m/z* 446.2061 $[M]^+$ (calcd. for $C_{28}H_{30}O_5$, 446.2093).

3.3.3. Formoxanthone C (*3*)

Yellow solid. M.p. 152–154 °C. $[\alpha]_D^{29} = -44$ °C ($CHCl_3$, c0.05). UV λ_{max}^{MeOH} nm (log ε): 392 (3.85), 276 (4.44), 258 (4.51). IR (KBr) ν_{max}: 3440, 1646, 1624, 1598 cm^{-1}. For ^1H and ^{13}C NMR ($CDCl_3$) spectra, see Table 2. MS *m/z* (rel. int.): 396 $[M]^+$ (40), 381(43), 353 (30), 341 (100), 325 (26), 311 (15), 285 (14). HREIMS *m/z* 396.1559 $[M]^+$ (calcd. for $C_{23}H_{24}O_6$, 396.1573).

3.4. Bioassays

3.4.1. Antimicrobial assay

The isolated compounds from *C. formosum* were tested against the microorganisms, *B. substilis* (obtained from Department of Industrial Biotechnology, PSU), *Staphylococcus aureus* (TISTR517) (obtained from Microbial Resources Center (MIRCEN), Bangkok, Thailand), *P. aeruginosa*, *S. faecalis* and *S. typhi*. The last three microorganisms were obtained from Department of Pharmacognosy and Botany, PSU. The antimicrobial assay employed was the colorimetric microdilution broth technique using RPMI1640 medium and Alamar Blue as an indicator (Kanjana-Opas, 2002). Microbial inocula were prepared as suspension in RPMI1640 medium and mixed with 1% 100× Alamar Blue indicator. The cell suspension was then transferred into a 96-well microliter plate (100 μl/well except for first row which contained 190 μl/well). Crude extract (10 μl) dissolved in DMSO at a

concentration of 25 mg/ml was added to each well of the first row and mixed well with a micropipette. Half of the mixtures of cell suspension and extracts in the first rows were then transferred to the next well in the second row to perform a half-fold dilution. The dilution process was repeated as a sequence until the extracts were diluted 128 times in the last row. The excess 100 μl of the mixture in the last row was discarded. The plates were incubated at 37 °C for 8–12 h and 24 h for antibacterial and antifungal assays, respectively. The antimicrobial activity was determined as the MIC value which was the least concentration of the extract that could inhibit the change of Alamar Blue indicator from blue to red.

3.4.2. Cytotoxic assay

The procedure for the cytotoxic assay was performed by the sulphorhodamine B (SRB) assay as described by Skehan et al. (1990). In this study, four cancer cell lines obtained from National Cancer Institute, Bangkok, Thailand, were used: MCF-7 (breast adenocarcinoma), KB (human oral cancer), HeLa (human cervical cancer) and HT-29 (colon cancer).

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References

Anderson, E.F., 1986. Ethnobotanic of hill tribes of Northern of Thailand. II. Lahu medicinal plants. Econ. Bot. 40, 442–450.

Bennett, G.J., Harrison, L.J., Sia, G.-L., Sim, K.-Y., 1993. Triterpenoids, tocotrienols and xanthones from the bark of *Cratoxylum cochinchinense*. Phytochemistry 32, 1245–1251.

Botta, B., Delle Monache, F., Delle Monache, G., Marini Bettolo, G.B., Oguakwa, J.U., 1983. 3-Geranyloxy-6-methyl-1,8-dihydroxyanthraquinone and vismiones C, D and E from *Psorospermum febrifugum*. Phytochemistry 22, 539–542.

Botta, B., Delle Monache, G., Delle Monache, F., Marini Bettolo, G.B., Menichini, F., 1986. Vismione H and prenylated xanthones from *Vismia guineensis*. Phytochemistry 25, 1217–1219.

Camele, G., Delle Monache, F., Delle Monache, G., Marini Bettolo, G.B., Alves De Lima, R., 1982. 2-Isoprenylemodin and 5-5′-dimethoxysesamin from *Vismia Guaramirangae*. Phytochemistry 21, 417–419.

Chang, C.-H., Lin, C.-C., Kawata, Y., Hattori, M., Namba, T., 1989. Prenylated xanthones from *Cudrania cochinchinensis*. Phytochemistry 28, 2823–2826.

Chumkaew, P., Karalai, C., Ponglimanont, C., Chantrapromma, K., 2003. Antimycobacterial activity of phorbol esters from the fruits of *Sapium indicum*. J. Nat. Prod. 66, 540–543.

Goncalves, M.L.S., Mors, W.B., 1981. Vismiaquinone, a Δ^1-isopentenyl substituted anthraquinone from *Vismia reichardtiana*. Phytochemistry 20, 1947–1950.

Iinuma, M., Tosa, H., Ito, T., Tanaka, T., Madulid, D.A., 1996. Two xanthones from roots of *Cratoxylum formosanum*. Phytochemistry 42, 1195–1198.

Ito, C., Itoigawa, M., Takakura, T., Ruangrungsi, N., Enjo, F., Tokuda, H., Nishino, H., Furukawa, H., 2003. Chemical constituents of *Garcinia fusca*: structure elucidation of eight new xanthones and their cancer chemopreventive activity. J. Nat. Prod. 66, 200–205.

Kanjana-Opas, A., 2002. New antifungal compounds from marine Fungi. Ph.D. Thesis, University of California, San Diego.

Kijjoa, A., Jose, M., Gonzalez, T.G., Pinto, M.M.M., Damas, A.M., Mondranondra, I., Silva, A.M.S., Herz, W., 1998. Xanthones from *Cratoxylum maingayi*. Phytochemistry 49, 2159–2162.

Laphookhieo, S., Karalai, C., Ponglimanont, C., Chantrapromma, K., 2004. Pentacyclic triterpenoid esters from the fruits of *Bruguiera cylindrica*. J. Nat. Prod. 67, 886–888.

Seo, E.-K., Kim, N.-C., Wani, M.C., Wall, M.E., Navarro, H.A., Burgess, J.P., Kawanishi, K., Kardono, L.B.S., Riswan, S., Rose, W.C., Fairchild, C.R., Farnsworth, N.R., Kinghorn, A.D., 2002. Cytotoxic prenylated xanthones and the unusual compounds anthraquinobenzoquinones from *Cratoxylum sumatranum*. J. Nat. Prod. 65, 299–305.

Skehan, P., Storeng, R., Scudiero, D., Monks, A., McMahon, J., Vistica, D., Warren, J.T., Bokesch, H., Kenney, S., Boyd, M.R., 1990. New colorimetric cytotoxicity assay for anticancer drug screening. J. Natl. Cancer Inst. 82, 1107–1112.

Smitinand, T., 2001. Thai Plant Names. Prachachon Publisher, Bangkok, p. 152.