Polyanxanthone A, B and C, three xanthones from the wood trunk of *Garcinia polyantha* Oliv.

Gabin Nselapi Louh [a], Alain Meli Lannang [a,*], Celine Djama Mbazoa [a],
Jean Gustave Tangmouo [a], Justin Komguem [a], Paula Castilho [b],
Fernande Ngounou Ngninzeko [a], Naz Qamar [c], David Lontsi [a,*],
Muhammad Iqbal Choudhary [c], Beiban Luc Sondengam [a]

[a] *Department of Organic Chemistry, Faculty of Science, University of Yaoundé I, P.O. Box 812, Yaoundé, Cameroon*
[b] *Centro de Quimica da Madeira, Departamento de Quimica, Universidade da Madeira, Campus Universitario da Penteada, 9000-390 Funchal, Portugal*
[c] *International Center for Chemical and Biological Sciences, H.E.J. Research Institute of Chemistry, University of Karachi, Karachi 75270, Pakistan*

Abstract

Three xanthones, polyanxanthone A (**1**), B (**2**) and C (**3**) have been isolated from the methanol extract of the wood trunk of *Garcinia polyantha*, along with five known xanthones: 1,3,5-trihydroxyxanthone (**4**); 1,5-dihydroxyxanthone (**5**); 1,3,6,7-tetrahydroxyxanthone (**6**); 1,6-dihydroxy-5-methoxyxanthone (**7**) and 1,3,5,6-tetrahydroxyxanthone (**8**). Their structures were determined by means of 1D- and 2D-NMR techniques. Some of the above compounds were screened for their anticholinesterase activity on acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes.
© 2007 Elsevier Ltd. All rights reserved.

Keywords: *Garcinia polyantha*; Polyanxanthone A; Polyanxanthone B; Polyanxanthone C; Prenyloxyxanthones; Anticholinesterase

1. Introduction

The genus *Garcinia* of the Guttiferae family is well known to be a rich source of bioactive isoprenylated xanthones (Kanda et al., 2006; Deachathai et al., 2006; Komguem et al., 2005) and benzophenones (Nilar et al., 2005; Williams et al., 2003). In continuation of our search for bioactive substances from *Garcinia* species, we have investigated the methanol extract of the wood trunk of *Garcinia Polyantha* Oliv, a tree distributed in the lowland tropical rainforest of west, east and central Africa (Ampofo and Waterman, 1986; Brehaut, 1975). This investigation led to the isolation of three new xanthones (**1–3**) and five

known xanthones (**4–8**). We report herein, the structure elucidation of the above compounds along with their anticholinesterase activities.

2. Results and discussion

The methanol extract of powder wood trunk of *G. polyantha* was separated by silica gel column chromatography to give three new xanthone derivatives named polyanxanthone A (**1**), B (**2**) and C (**3**) along with five known xanthones: 1,3,5-trihydroxyxanthone (**4**) (Zhang et al., 2002); 1,5-dihydroxyxanthone (**5**) (Nkengfack et al., 2002); 1,3,6,7-tetrahydroxyxanthone (**6**) (Carpenter et al., 1969); 1,6-dihydroxy-5-methoxyxanthone (**7**) (Zhang et al., 2002) and 1,3,5,6-tetrahydroxyxanthone (**8**) (Frahm and Chandhuri, 1979).

The following spectral data showed that all the new xanthones have a prenyloxy groups at C-1 and C-5. UV

absorption of these compounds showed two strong bands at λ_{max} 240–248 and 254–266 nm, a medium bands at λ_{max} 302–312 nm, and weak broad bands at λ_{max} 352–390 nm indicated the conjugated chromophore systems (Ito et al., 2003). The IR spectra showed evenly bands at ν_{max} 1656–1665 and 1560–1601 cm^{-1} (Meli et al., 2005) suggesting a carbonyl and an aromatic double bonds, respectively.

Polyanxanthone A (1) was isolated as a whitish crystal, mp: 135–137 °C. The HREIMS spectroscopy of this compound gave the molecular ion peak at m/z 448.2277 (Calc. 448.2212) corresponding to $C_{28}H_{32}O_5$ formula. The ^1H NMR spectrum showed signals due to three prenyloxy groups, respectively at [δ_H 4.63(2H, d, $J = 6.3$ Hz, H-1′), 5.57 (1H, t, $J = 6.3$ Hz, H-2′), 1.76 (3H, s, H-5′), 1.80 (3H, s, H-4′)]; [δ_H 4.57 (2H, d, $J = 6.8$ Hz, H-1″), 5.52 (1H, t, $J = 6.8$ Hz, H-2″), 1.72 (3H, s, H-5″), 1.77 (3H, s, H-4″)] and [δ_H 4.70 (2H, d, $J = 6.6$ Hz, H-1‴), 5.62 (1H, t, $J = 6.6$ Hz, H-2‴), 1.75 (3H, s, H-5‴), 1.80 (3H, s, H-4‴)], as three substituents of xanthone nucleus. Furthermore, an ABX type signals, a lower field signal at δ_H 7.84 (1H, dd, $J = 7.8$ and 1.4 Hz) was assignable to H-8, which was affected by deshielding due to 9-C=O, and two others signals at δ_H 7.19 (1H, t, $J = 7.8$) and δ_H 7.14 (1H, dd, $J = 7.8$ and 1.4 Hz) attributed to H-7 and H-6, respectively. The remaining signals observed as meta-coupled aromatic proton at δ_H 6.60 (1H, d, $J = 2.2$ Hz) and δ_H 6.34 (1H, d, $J = 2.2$ Hz) were assignable to H-2 and H-4, respectively. HMBC correlations (Table 1) from 9-C=O, C-6, C-10a to H-8, from C-8, C-5, C-10a to H-6, from C-5, C-8a to H-7, from C-9a, C-4 to H-2 and from C-9a, C-2 to H-4 firmly confirm the location of different aromatic protons. As far as, C–H long range correlations in the HMBC spectrum (Table 1) from oxygenated quaternary carbon C-1 to H-1′, from C-3 to H-1″ and from C-5 to H-1‴ indicated the assignment of the location of the three prenyl groups. On the basis of these data, the structure of polyanxanthone. A was determined to be (1), identified as 1,3,5-triprenyloxyxanthone.

Polyanxanthone B (2) was obtained as a white crystal, mp: 139.9–140 °C. The molecular formula was determined as $C_{23}H_{24}O_5$ from the HREIMS, m/z 364.168 (Calc. 364.1675). It is ^1H NMR spectrum was shown to be quite similar to that of (1), with characteristic resonances which again could be associated with two prenyloxy moieties, respectively at [δ_H 4.68 (2H, d, $J = 5.7$ Hz, H-1′), 5.57 (1H, t, $J = 5.7$ Hz, H-2′), 1.80 (3H, s, H-4′), 1.78 (3H, s, H-5′)] and [δ_H 4.70 (2H, d, $J = 4.2$ Hz, H-1″), 5.62 (1H, t, $J = 4.2$ Hz, H-2″), 1.78 (3H, s, H-4″), 1.74 (3H, s, H-5″)], and three aromatic protons [δ_H 7.17 (1H, dd, $J = 7.8$ and 1.6 Hz, H-6), 7.21 (1H, t, $J = 7.8$ Hz, H-7) and 7.85 (1H, dd, $J = 7.8$ and 1.6 Hz, H-8)]. These were observed except for the appearance of new aromatic proton ABX system on ring C at δ_H 6.77 (1H, dd, $J = 8.4$ and 1.2 Hz, H-2), 7.14 (1H, dd, $J = 8.4$ and 1.2 Hz, H-4) and 7.56 (1H, t, $J = 8.4$ Hz, H-3), and the lack of a typical prenyloxy moiety aforementioned in compound (1). Examination of the contour plot of an HMBC experiment (Table 1) then revealed that the ring A of (2) was identical to that of polyanxanthone A and characterized with one prenyloxy group at C-5. Therefore, polyanxanthone B (2) was identified as 1,5-diprenyloxyxanthone.

Polyanxanthone C (3) was isolated as yellow oil. This compound was showed to have the molecular formula $C_{28}H_{32}O_4$ by HREIMS which showed the [M+] ion peak at m/z 432.1683 (Calc. 432.1679). The ^1H NMR features were similar to those of (2), except for the appearance of prenyl group at δ_H 3.45 (2H, d, $J = 7.2$ Hz), 5.30 (1H, t, $J = 7.2$ Hz), 1.71 (3H, s) and 1.74 (3 H, s) instead of an aromatic proton appearing at δ_H 6.77 in ring C of (2). The lack of ABX system aforenamed on (2) and the presence of two aromatic protons *ortho*-coupled firmly indicated that H-2 was substituted by a new prenyl moiety. This hypothesis was confirmed after recording of HMBC and NOESY experiments showing on one side the expected long range correlation between H-1″ of prenyl group and C-1, C-2 and C-3 (Table 1) together with the strong nuclear overhauser effects between H-1′/H-1″,and in the other side the strong nuclear overhauser between H-3/H-4, H-3/H-2″ and H-1‴/H-6 (Fig. 1). These results indicated the structure of polyanxanthone C (3), identified as 1,5-prenyloxy-2-(3-methylbut-2-enyl)xanthone.

2.1. Anticholinesterase activity

Compounds 1, 2, 4, 5 and 7 were screened for their cholinesterase inhibitory potential. The compounds 4, 5 and 7 showed significant inhibition against BChE with an IC$_{50}$ value of 93.0, 2.54 and 74.4 μM, respectively, while compound 2 showed significant inhibition against both AChE (IC$_{50}$ = 46.3 μM) and BChE (IC$_{50}$ = 25.5 μM) compared to the standard, galantamine (IC$_{50}$ = 0.5 μM and 8.5 μM, respectively). Compound 1 showed 41.8% and 7.0% inhibition against AChE and BChE, respectively, at the concentration of 0.2 mM.

3. Experimental

3.1. General procedure

The melting points were determined on a micro melting point apparatus (Yanaco MP-S3 apparatus) and are uncorrected. Infrared spectra were obtained on a JASCO A-302 spectrophotometer using KBr pellets. Ultraviolet spectra were recorded on a Shimadzu UV 240 spectrophotometer in methanol. Mass spectra (EI and HREIMS) were measured in an electron impact mode on Varian MAT 312 spectrometers. The ^1H NMR spectra were registered on a Bruker Avance AMX 500 NMR spectrometer with tetramethylsilane (TMS) as an internal standard; while ^{13}C NMR spectra were recorded on a Bruker Avance AMX 500 NMR spectrometer operating at 125 MHz using CDCl$_3$ as solvent. Methyl, methylene and methine carbons were distinguished by DEPT experiments. Homonuclear

Table 1
^{1}H and ^{13}C NMR data of polyanxanthone A (**1**), B (**2**) and C (**3**) (500, 125 MHz) in CDCl$_3$

Position	1			2			3		
	^{1}H(m, J (Hz))	^{13}C	HMBC	^{1}H(m, J (Hz))	^{13}C	HMBC	^{1}H(m, J (Hz))	^{13}C	HMBC
1		161.1			159.6			156.2	
2	6.60 (d, 2.2)	93.6	C-3, C-9a, C-4, C-1	6.77 (dd, 8.4 and 1.2)	106.7	C-1, C-9a, C-4		131.1	
3		163.9		7.56 (t, 8.5)	134.5	C-1, C-4a	7.50 (d, 8.7)	135.4	C-1, C-4, C-2
4	6.34 (d, 2.2)	96.9	C-3, C-9a, C-4a, C-2	7.14 (dd, 8.4 and 1.2)	110.2	C-2, C-9a, C-4a	7.31 (d, 8.7)	113.9	C-9a, C-4a, C-3
4a		159.6			157.9			155.9	
10a		145.6			145.7			145.9	
5		147.1			147.3			147.4	
6	7.14 (dd, 7.8 and 1.4)	116.3	C-10a, C-8, C-5	7.17 (dd, 7.8 and 1.6)	116.6	C-8, C-5, C-10a	7.18 (dd, 7.1 and 1.9)	116.7	C-10a, C-8
7	7.19 (t, 7.9)	123.1	C-5, C-8a	7.21 (t, 7.9)	123.1	C-5, C-8a	7.21 (t, 7.1)	123.0	C-5, C-8a
8	7.84 (dd, 7.8 and 1.4)	117.9	C-9, C-10a, C-6	7.85 (dd, 7.8 and 1.6)	117.8	C-9, C-10a, C-6	7.89 (dd, 7.1 and 1.9)	117.8	C-6, C-9
8a		124.2			124.0			123.7	
9a		107.4			112.7			116.1	
9		175.2			176.4			176.3	
1′	4.63 (d, 6.3)	66.3	C-1, C-2′, C-3′	4.68 (d, 5.7)	66.4	C-2′, C-3′, C-1	4.56 (d, 7.1)	71.5	C-1, C-2′, C-3′
2′	5.57 (t, 6.3)	119.4		5.57 (t, 5.7)	119.3		5.71 (t, 7.1)	120.5	
3′		137.5			137.6			137.8	
4′	1.80 (s)	25.8	C-5′, C-3′, C-2′	1.80 (s)	25.8	C-5′, C-3′, C-2′	1.80 (s)	25.8	C-5′, C-3′, C-2′
5′	1.76 (s)	18.4	C-4′, C-3′, C-2′	1.75 (s)	18.3	C-4′, C-3′, C-2′	1.77 (s)	18.1	C-4′, C-3′, C-2′
1″	4.58 (d, 6.8)	66.3	C-3, C-2″, C-3″	4.70 (d, 4.2)	66.4	C-5, C-2″, C-3″	3.45 (d, 7.2)	27.7	C-1, C-2, C-3, C-2″, C-3″
2″	5.52 (t, 6.8)	118.4		5.62 (t, 4.2)	119.4		5.30 (t, 7.2)	122.5	
3″		139.4			138.6			133.1	
4″	1.76 (s)	25.8	C-5″, C-2″, C-3″	1.78 (s)	25.9	C-5″, C-2″, C-3″	1.74 (s)	25.9	C-5″, C-2″, C-3″
5″	1.72 (s)	18.3	C-4″, C-2″, C-3″	1.74 (s)	18.4	C-4″, C-2″, C-3″	1.71 (s)	17.8	C-4″, C-2″, C-3″
1‴	4.70 (d, 6.6)	66.4	C-5, C-2‴, C-3‴				4.71 (d, 6.5)	66.4	C-5, C-2‴, C-3‴
2‴	5.62 (t, 6.6)	119.4					5.59 (t, 6.5)	119.2	
3‴		138.4						138.6	
4‴	1.80 (s)	25.8	C-5‴, C-2‴, C-3‴				1.69 (s)	25.9	C-5‴, C-2‴, C-3‴
5‴	1.75 (s)	18.4	C-4‴, C-2‴, C-3‴				1.62 (s)	18.4	C-4‴, C-2‴, C-3‴

^{1}H connectivities were determined by using the COSY experiment. One-bond ^{1}H–^{13}C connectivities were determined with HMQC gradient pulse factor selection. Two and three bond ^{1}H-^{13}C connectivities were determined by HMBC experiment. Chemical shifts were reported in δ(ppm) and coupling constants (J) were measured in Hz. TLC was performed on precoated silica gel cards (E. Merck), spots were viewed under ultraviolet light at 254 nm for fluorescence quenching spots and at 366 nm for fluorescent spots and stained by spraying with a solution of ceric sulphate (0.2%) in H$_2$SO$_4$ (5%). For column chromatography, silica gel (E. Merck, 230–400 mesh) were used. All reagents used were of analytical grades.

3.2. Plant material

The wood trunk of *G. polyantha* was collected from Mt Kala, central-province Cameroon in August 2003, and identified by Dr. Tchiengue Bathelemy of the Cameroon Nation Herbarium (Yaoundé), where a voucher specimen (21337/SRF/Cam/Mt Kala) was deposited.

3.3. Extraction and isolation

Air dried and ground wood trunk of *G. polyantha* (3.5 kg) was macerated in methanol for three days at room temperature and the fractions were concentrated under reduce pressure to yield 83 g of methanol extract. The methanol extract was subjected to column chromatography eluting with hexane, hexane-CH$_2$Cl$_2$, CH$_2$Cl$_2$-MeOH in increasing order of polarity to afford fractions A-D. The mixture of fraction A and B (4.2 g) obtained with Hexane-CH$_2$Cl$_2$ (9.5:0.5 and 8.5:1.5, respectively) was purified by column chromatography over silica gel (5 × 80 cm) eluted with a mixture of hexane-CH$_2$Cl$_2$ in increasing order of polarity to yield compounds **1** (16 mg), **4** (122 mg) and
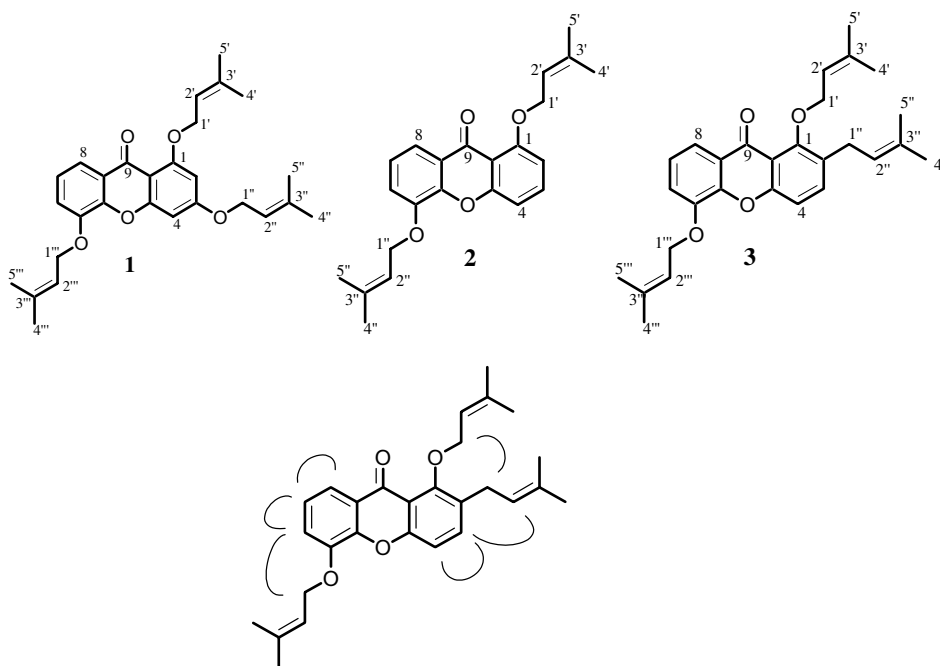
Fig. 1. NOESY correlations of **3**.

three sub fractions (B$_1$–B$_3$). The sub fraction B$_2$ (1.4 g) obtained with hexane-CH$_2$Cl$_2$ (9.0:1.0) was further purified by silica gel column chromatography (3 × 50 cm) with hexane-CH$_2$Cl$_2$ (9.3:0.7) to give compound **2** (15 mg) and **5** (47 mg), and the sub fraction B$_1$ was purified by preparative TLC (hexane-CH$_2$Cl$_2$ (9.5:0.5) to give compound **3** (14 mg). Fraction C (1.6 g) obtained with hexane-CH$_2$Cl$_2$ (8.0:2.0) was purified by column chromatography over silica gel (3 × 50 cm) eluted with a mixture of hexane-CH$_2$Cl$_2$ in increasing order of polarity to yield compounds **6** (14 mg), **8** (14 mg) and **7** (37 mg). Finally, fraction D was found to contain mainly very polar compounds.

3.3.1. Polyanxanthone A (1)

Whitish crystal, m.p.: 135–137 °C. UV (MeOH) λ max (log$^\varepsilon$): 303 (2.5), 247 (3.04), 202 (3.03), 275 (2.35), 225 (2.75). IR (KBr) v_{max} cm^{-1} 3626, 2914, 1656, 1601, 1289, 1159, 1101, 956, 670. EIMS: m/z 448 [M$^+$] (6.86), 379 (4), 312 (16), 244 (69), 228 (4), 69 (100). HR-EIMS: m/z 448.2277 (calc. 448.2250 for C$_{28}$H$_{32}$O$_5$). ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR, see Table 1.

3.3.2. Polyanxanthone B (2)

White crystal; m.p.: 139.9–140 °C. UV (MeOH) λ max (log$^\varepsilon$): 353 (2.53), 303 (2.6), 246 (3.24), 202 (3.09). IR (KBr) v_{max} cm^{-1} 3629, 2972, 1601, 1490, 1379, 821, 767. EIMS: m/z 364 [M$^+$] (2.1), 296 (6), 228 (100), 119 (37). HR-EIMS: m/z 364.1686 (calc. 364.1675 for C$_{23}$H$_{24}$O$_4$). ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR, see Table 1.

3.3.3. Polyanxanthone C (3)

Yellow oil. UV (MeOH) λ max (log$^\varepsilon$): 389 (2.05) 340 (1.70), 297 (2.08), 255 (2.86), 203 (3.05). IR (KBr)

v_{max} cm^{-1} 3566, 2972, 1656, 1566, 1432, 1268, 1227, 1101, 956, 767. EIMS: m/z 432 [M$^+$] (2.07) 364 (10), 296 (34), 253 (25), 241(77), 69 (100). HR-EIMS: m/z 432.1234 (calc. 432.1237 for C$_{28}$H$_{32}$O$_4$). ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR, see Table 1.

3.4. Anticholinesterase assays

Electric-eel AChE (EC 3.1.1.7), horse-serum BChE (EC 3.1.1.8), acetythiocholine iodide, butyrylthiocholine chloride, 5,5′-dithio-bis-nitrobenzoic acid (DTNB) and galanthamine were purchased from the Sigma (St. Louis, MO, USA). All other chemicals were of analytical grade. AChE and BChE inhibiting activities were measured by the spectrophotometric method developed by Ellman (Ellman et al., 1961). Acetylthiocholine iodide and butyrylthiocholine chloride were used as substrates to assay AChE and BChE, respectively. The reaction mixture contained 130 µl (100 mM) sodium phosphate buffer (pH 8.0), 20 µl of DTNB, 10 µl of test compound solution and 20 µl of AChE or BChE solution, which were mixed and incubated for 15 min at 25 °C. The reaction was then initiated by the addition of 20 µl acetylthiocholine or butyrythiocholine, respectively. The hydrolysis of acetylthiocholine and butyrylthiocholine were monitored by the formation of yellow 5-thio-2-nitrobenzoate anion as a result of the reaction of DTNB with thiocholine, released by the enzymatic hydrolysis of acetylthiocholine and butyrylthiocholine, respectively at a wavelength of 412 nm (15 min). Test compounds and the positive control (galanthamine) were dissolved in EtOH. All the reactions were performed in triplicate in 96-well micro-plates in SpectraMax 340 (molecular Devices, USA). The concentrations of test

compounds that inhibited the hydrolysis of substrates (acetylthiocholine and butyrylthiocholine) by 50% (IC_{50}) were determined by monitoring the effect of increasing concentrations of these compounds in the assays on the inhibition values. The IC_{50} values were then calculated using the EZ-Fit Enzyme Kinetics program (*Perrella Scientific Inc.*, *Amherst*, USA.).

Acknowledgements

References

Ampofo, A.S., Waterman, G.P., 1986. Xanthones from three *Garcinia* species. Phytochemistry 25, 2351–2355.

Brehaut, J., 1975. Flore illustrée du Sénégal. Gouvernement du Sénégal, ministère du développement rural et de l'hydraulique, direction des eaux et forêt, Dakar, pp. 89–90.

Carpenter, I., Locksley, H.D., Scheinmann, F., 1969. Xanthones in higher plants: biogenetic proposals and a chemotaxonomic survey. Phytochemistry 8, 2013–2015.

Deachathai, S., Mahabubarakam, W., Phongpaichit, S., Taylor, W.C., Zhang, Y.-J., Yang, C.-R., 2006. Phenolic Compounds from the flowers of *Garcinia dulcis*. Phytochemistry 67, 464–469.

Ellman, G.L., Courtney, D., Andres, V., Featherstone, R.M., 1961. A new and rapid colorimetric determination of acetylcholinesterase activity. Blochem. Pharmacol. 7, 88–95.

Frahm, A.W., Chandhuri, R.K., 1979. Carbon-13 NMR spectroscopy of substituted xanthones II. Carbon-13 NMR spectral study of polyhydroxyxanthones. Tetrahedron 35, 2035–2038.

Ito, C., Itoigawa, M.C., 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.

Kanda, P., Pongcharoen, W., Phongpaichit, S., Walter, C.T., 2006. Tetraoxygenated xanthones from the fruits of *Garcinia Cowa*. Phytochemistry 67, 999–1004.

Komguem, J., Meli, A.L., Manfouo, R.N., Lontsi, D., Ngounou, F.N., Kuete, V., Kamdem, W.H., Tane, P., Ngadjui, B.T., Sondengam, B.L., Connelly, J.D., 2005. Xanthones from *Garcinia smeathmannii* (Oliver) and their antimicrobial activity. Phytochemistry 66, 1713–1717.

Meli, A.L., Komguem, J., Ngounou, F.N., Tangmouo, J.G., Lontsi, D., Ajaz, A., Iqbal, M.C., Ranjit, R., Devkota, K.P., Sondengam, B.L., 2005. Bangangxanthone A and B, two xanthones from the stem bark of *Garcinia polyantha* Oliv. Phytochemistry 66, 2351–2355.

Nilar, L.-H., Nguyen, D., Ganpathi, V., Sim, k.-Y., Harrison, L.J., 2005. Xanthones and benzophenones from *Garcinia griffithii* and *Garcinia mangostana*. Phytochemistry 66, 1718–1723.

Nkengfack, E.A., Mkounga, P., Fomum, T.Z., Meyer, M., Bodo, B., 2002. Globulixanthones A and B, two new cytotoxic xanthones with isoprenoid groups from the root bark of *Symphonia globulifera*. J. Nat. Prod. 65, 734–736.

Williams, R.B., Hoch, J., Glass, T.E., Evans, R., Miller, J.S., Wisse, J.H., Kingstone, D.G.I., 2003. A novel cytotoxic guttiferone analogue from *Garcinia macrophylla* from the Surinam rainforest. Planta Med. 69, 864–866.

Zhang, Z., Elsohly, H.N., Jacob, M.R., Pasco, D.S., Walter, L.A., Clark, A.M., 2002. Natural products inhibiting Candida albicans secreted aspartic proteases from *Tovomita krukovii*. Planta Med. 68, 49–50.