A New Diarylheptanoid from Barks of *Mangifera indica*

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Abstract: **Objective** To study the chemical constituents from the barks of *Mangifera indica*. **Methods** The constituents were separated and purified by different methods of chromatography, and their structures were elucidated by IR, MS, 1D and 2D NMR techniques. **Results** Six compounds were isolated from the barks of *M. indica*. Their structures were identified as mangiferone (**1**), mangiferin (**2**), myricetin (**3**), myricitrin (**4**), rutin (**5**), and quercetin (**6**). **Conclusion** Mangiferone (**1**) is a new diarylheptanoid compound isolated from the barks of *M. indica*.

Key words: Anacardiaceae; *Mangifera indica*; mangiferin; mangiferone; myricitrin
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Introduction

Mangifera indica L., belonging to the family Anacardiaceae, is widely distributed in many tropical and sub-tropical regions of the world including south of China. *M. indica* is one of the most popular edible fruit trees in the world and its stem barks have been traditionally used for the treatment of menorrhagia, scabies, diarrhea, syphilis, diabetes, cutaneous infections, and anemia (Alberto *et al*, 2002). The chemical compositions in *M. indica* are mainly phenols such as xanthones and flavonoids (Ge *et al*, 2011). So far, mangiferin, isomangiferin, quercetin, kaempferol, (+)-catechin, and (−)-epicatechin etc have been isolated and reported from the stem barks of *M. indica* (Alberto *et al*, 2002; Andreas, Nicolai, and Reinhold, 2003). In a continuous search for bioactive compounds from the stem barks of *M. indica* collected in Guangzhou of Guangdong province, a new diarylheptanoid compound, named mangiferone (**1**) was isolated and identified. In the present paper, the isolation and the structural elucidation of the new compound and five known compounds (**2**—**6**) were described.

Compound **1** was obtained as red gum. The molecular formula $C_{21}H_{22}O_6$ was obtained from quasimolecular ion peak at *m/z* 393.1317 $[M + Na]^+$ (Calcd. for $C_{21}H_{22}O_6Na$: 393.1314) in the HR-ESI-MS spectrum. The IR spectrum showed the presence of a hydroxy group (3384), a conjugated carbonyl group (1651), an isolated carbonyl group (1710), and benzene ring (1610, 1560). The ^{1}H-NMR spectrum showed signals for one phenolic hydroxyl group (δ 5.93), two methoxyl groups (δ 3.98, 4.02), and 12 alkyl protons (δ 1.20—3.10). Besides, the signals for three aromatic protons (ABX system) at δ 6.67 (d, J = 1.8 Hz, H-19), 6.90 (d, J = 7.8 Hz, H-17), and 7.11 (dd, J = 1.8, 7.8 Hz, H-16) were also observed, suggested the presence of a 1, 2, 4-trisubstituted phenyl moiety in the molecule. A $-(CH_2)_2CO(CH_2)_4-$ moiety was established on the basis of ^{1}H-^{1}H COSY analysis combined with HMQC and HMBC experiments (Fig. 1). The remained ^{13}C-NMR spectrum showed 21 carbon signals, including those for a benzoquinone (with two carbonyls at δ 184.0, 184.1) derived moiety. The connections of C-8 to C-7, C-14 to C-15, and C-1 to C-2 were revealed by the HMBC correlations of H-8 with C-2, C-6 and C-7, H-14 with C-15, C-16, and C-19, and H-19 with C-2 and C-18. The aromatic hydroxyl group was assigned at C-18 according to the HMBC signals of 18-OH (δ 5.93) with C-1 (δ 121.1) and C-17 (δ 118.0). Two methoxyl groups were located at C-4 and C-5 on the basis of the HMBC cross signals of δ 3.98 (3H, s) with δ 144.4 and δ 4.02 (3H, s) with δ 144.9. No NOESY correlation between the

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methoxyl groups and 18-OH was observed, which supported the arrangement of the 1, 4-benzoquinone in the molecule. Therefore, the whole structure of compound **1**, trivially named mangiferone, was shown in Fig. 2.

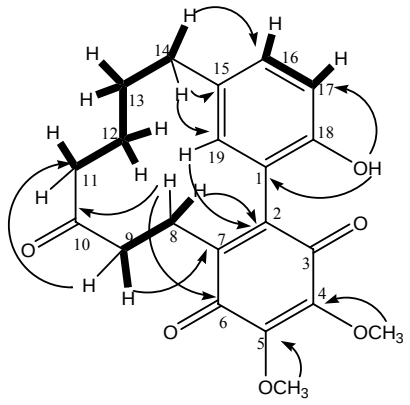

Fig. 1 HMBC and ^{1}H-^{1}H COSY correlation of compound 1

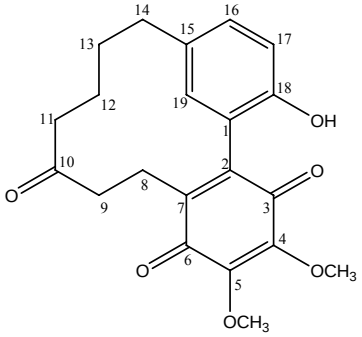

Fig. 2 Structure of compound 1

Materials and methods

Instruments and materials

Melting points were determined on XRC-1 Micromelting Point Apparatus. Optical rotations were measured on a Perkin Elmer 341 Automatic Polarimeter. NMR spectra were collected on a Bruker AM—600 Spectrometer. MS spectra were performed on Acquity UPLC-Q-T of Micro MS Mass Spectrometer equipped with electrospray ionization source (ESI) (Waters, USA). IR spectrum was recorded on Perkin-Elmer 599B Spectrometer. TLC was performed on silica gel GF_{254} and HRTLC on silica gel H (5 — 7 μm). Separation and purification were performed by column chromatography on silica gel (200 — 300 mesh, Qingdao Haiyang Chemical Co., Ltd.) or polyamide (100—200 meshes, Linjiang Chemical Co., Ltd.). All solvents were distilled prior to use.

The stem barks of *Mangifera indica* L. were collected from Guangzhou (Guangdong, China) in September 2006 and identified by Prof. WANG Ding-yong (School of Pharmacy, Guangdong Pharmaceutical University, China). A voucher specimen (No. 20060905) is deposited at the Herbarium of Guangdong Pharmaceutical University, China.

Extraction and isolation

Air-dried and powdered stem barks of *M. indica* (15 kg, 20—30 meshes) were soaked with 85% EtOH (50 L × three times, 7 d each) at room temperature. The EtOH solution was evaporated under reduced pressure to afford 750 g residue, which was suspended in water (2.0 L) and subsequently extracted with petroleum ether (2.0 L × four times), $CHCl_3$ (2.0 L × five times), and EtOAc (2.0 L × three times) to correspondingly give Frs. A (155.0 g), B (209.0 g), and C (568.0 g). Proper amount of Fr. B (105.0 g) was subjected to column chromatography on 200—300 mesh silica gel (1000 g, 1000 mm × 100 mm) to produce compound **1** (22.0 mg) (petroleum ether-EtOAc 50:1→20:1 as elute). Proper amount of Fr. C (150.0 g) was subjected to column chromatography on 100—200 mesh polyamide (1000 g, 1000 mm × 100 mm) to give compounds **6** (105.0 mg, $CHCl_3$-MeOH 20:1 as elute), **3** (51.0 mg, $CHCl_3$-MeOH 10:1 as elute), **4** (125.0 mg, $CHCl_3$-MeOH 1:1 as elute), **5** (125.0 mg, MeOH-H_2O 5:1 as elute), and **2** (385.0 mg, MeOH-H_2O 1:1 as elute), respectively.

Results and conclusion

Compound **1**: $C_{21}H_{22}O_6$, red gum; $[\alpha]_D^{20}$ −22.5° (*c* 0.35, MeOH); IR ν_{max}^{KBr} (cm^{-1}): 3384, 3012, 2937, 2856, 1710, 1651, 1610, 1560, 1453, 1288, 1202, 1145, 1109, 1070, 1015,1006, 758; ^{1}H-NMR (600 MHz, $CDCl_3$) *δ*: 6.67 (1H, d, *J* = 1.8 Hz, H-19), 6.90 (1H, d, *J* = 7.8 Hz, H-17), 7.11 (1H, dd, *J* = 1.8, 7.8 Hz, H-16), 5.93 (1H, brs, 18-OH), 4.02 (3H, s, 4-OCH_3), 3.98 (5-OCH_3), 3.02 (1H, dt, *J* = 13.2, 3.0 Hz, H-8a), 2.73 (1H, dt, *J* = 13.2, 4.2 Hz, H-8b), 2.38 (1H, m, H-9a), 2.54 (1H, m, H-9b), 2.20 (1H, m, H-11a), 2.10 (1H, m, H-11b), 1.98 (1H, m, H-12a), 1.12 (1H, m, H-12b), 1.92 (1H, m, H-13a), 1.38 (1H, m, H-13b), 2.32 (1H, m, H-14a), 1.67 (1H, m, H-14b); ^{13}C-NMR (150 MHz, $CDCl_3$) *δ*: 121.1 (C-1), 140.3 (C-2), 184.0 (C-3), 144.9 (C-4), 144.4 (C-5), 184.1 (C-6), 146.3 (C-7), 32.9 (C-8), 44.2 (C-9), 213.2 (C-10), 44.2 (C-11), 25.8 (C-12), 21.2 (C-13), 27.0 (C-14), 132.9

(C-15), 130.5 (C-16), 118.0 (C-17), 151.5 (C-18), 130.2 (C-19), 61.3 (4-OCH_3), 61.2 (5-OCH_3). ESI-MS *m/z*: 393.2 $[M + Na]^+$ (positive mode), 369.1 $[M - H]^-$ (negative mode), HR-ESI-MS *m/z*: 393.1317 $[M + Na]^+$ (Calcd. for $C_{21}H_{22}O_6Na$: 393.1314).

Compound **2**: light yellow needle (MeOH), mp 271.5—272.5 ℃. ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 13.76 (1H, s, 1-OH), 10.59 (3H, brs, 3, 6, 7-OH), 7.38 (1H, s, H-8), 6.87 (1H, s, H-5), 6.37 (1H, s, H-4), 4.59 (1H, d, J = 9.6 Hz, H-1′). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 179.6 (C-9), 164.3 (C-3), 162.2 (C-1), 156.7 (C-4a), 154.5 (C-9a), 151.3 (C-6), 144.2 (C-7), 12.2 (C-8a), 108.5 (C-8), 108.1 (C-2), 103.1 (C-5), 101.8 (C-10a), 93.8 (C-4), 82.0 (C-5′), 79.5 (C-3’), 73.5 (C-1′), 71.4 (C-4′), 70.8 (C-2′), 62.0 (C-6′). ESI-MS *m/z*: 421.1 $[M - H]^-$ (negative mode). These data accorded with the literature value of mangiferin (Rancon *et al*, 1999).

Compound **3**: brown yellow needle (MeOH), mp 324.0—325.50 ℃. ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 12.50 (1H, s, 5-OH), 6.37 (1H, d, J = 2.0 Hz, H-6), 6.18 (1H, d, J = 2.0 Hz, H-8), 7.25 (2H, s, H-2′, 6′). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 147.3 (C-2), 136.3 (C-3), 176.2 (C-4), 161.2 (C-5), 98.6 (C-6), 164.4 (C-7), 93.7 (C-8), 156.6 (C-8a), 103.4 (C-4a), 121.3 (C-1′), 107.7 (C-2′), 146.2 (C-3′), 136.3 (C-4′), 146.2 (C-5′), 107.7 (C-6′). ESI-MS *m/z*: 319.3 $[M + H]^+$ (positive mode), 317.1 $[M - H]^-$ (negative mode). These data accorded with the literature value of myricetin (Liao, Liu, and Wang, 2006).

Compound **4**: light yellow needle (MeOH), mp 183.5—185.0 ℃. ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 12.69 (1H, s, 5-OH), 6.37 (1H, d, J = 2.1 Hz, H-6), 6.20 (1H, d, J = 2.1 Hz, H-8), 6.89 (2H, s, H-2′, 6′), 5.20 (1H, brs, rha-1-H), 0.84(3H, d, J = 6.2 Hz, rha-6-H), 3.78 (1H, brs, rha-2-H), 3.55 (1H, dd, J = 9.4, 2.9 Hz, rha-3-H), 3.16 (1H, t, J = 9.4 Hz, rha-4-H), 3.99 (1H, brs, rha-5-H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 156.9 (C-2), 134.7 (C-3), 178.2 (C-4), 161.8 (C-5), 99.1 (C-6), 164.6 (C-7), 94.0(C-8), 158.0 (C-8a), 104.5 (C-4a), 121.1 (C-1′), 108.3 (C-2′), 146.2 (C-3′), 136.9 (C-4′), 146.2 (C-5′), 108.3 (C-6′), 102.4 (rha-1-C), 70.8 (rha-2-C), 71.0 (rha-3-C), 71.7 (rha-4-C), 70.5 (rha-5-C), 18.0 (rha-6-C). ESI-MS *m/z*: 465.3 $[M + H]^+$ (positive mode), 463.1 $[M - H]^-$ (negative mode). These data accorded with the literature value of myricitrin (Liao, Liu, and Wang, 2006).

Compound **5**: yellow needle (MeOH), mp 190.5—192.0 ℃. ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 12.59 (1H, s, 5-OH), 6.18 (1H, d, J = 1.5 Hz, H-8), 6.38 (1H, d, J = 1.5 Hz, H-6), 6.84 (1H, d, J = 8.0 Hz, H-5′), 7.53 (1H, d, J = 1.5 Hz, H-2′), 7.55 (1H, dd, J = 8.0, 1.5 Hz, H-6′), 5.34 (1H, d, J = 7.0 Hz, glc-1-H), 4.38 (1H, brs, rha-1-H), 0.99 (3H, d, J = 6.5 Hz, rha-6-H), 3.00—3.80 (10H, m, other sugar proton). These data accorded with the literature value of rutin (Vasaenge, Liu, and Welch, 1997).

Compound **6**: yellow needle (MeOH), mp 312.0—313.5 ℃. ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 12.48 (1H, s, 5-OH), 6.19 (1H, d, J = 1.5 Hz, H-6), 6.42 (1H, d, J = 1.5 Hz, H-8), 6.91 (1H, d, J = 8.0 Hz, H-5′), 7.67 (1H, d, J = 1.5 Hz, H-2′), 7.54 (1H, dd, J = 8.0, 1.5 Hz, H-6′), 10.79 (1H, brs, OH), 9.59 (1H, brs, OH), 9.33 (2H, brs, 2OH). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 156.6 (C-2), 136.2 (C-3), 176.3 (C-4), 161.2 (C-5), 98.7 (C-6), 164.4 (C-7), 93.9 (C-8), 156.8 (C-8a), 103.9 (C-4a), 122.5 (C-1′), 115.6 (C-2′), 145.5 (C-3′), 147.3 (C-4′), 116.0 (C-5′), 120.5 (C-6′). These data accorded with the literature value of quercetin (Ding *et al*, 1990).

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