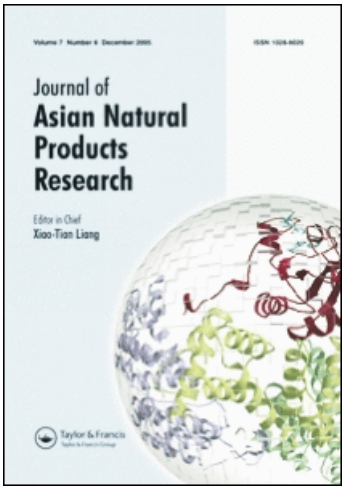

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Chemical constituents from *Mahkota dewa*

Yan-Bing Zhang[a]; Xiang-Jun Xu[a]; Hong-Min Liu[a]
[a] New Drug Research and Development Centre, Zhengzhou University, Zhengzhou, China

To cite this Article Zhang, Yan-Bing , Xu, Xiang-Jun and Liu, Hong-Min(2006) 'Chemical constituents from *Mahkota dewa*', Journal of Asian Natural Products Research, 8: 1, 119 — 123
To link to this Article: DOI: 10.1080/10286020500480472
URL: http://dx.doi.org/10.1080/10286020500480472

Journal of Asian Natural Products Research,
Vol. 8, No. 1–2, January–March 2006, 119–123

Chemical constituents from *Mahkota dewa*

YAN-BING ZHANG, XIANG-JUN XU and HONG-MIN LIU*

New Drug Research and Development Centre, Zhengzhou University, 75 Daxuebei Road, Zhengzhou 450052, China

(Received 27 June 2005; revised 6 September 2005; in final form 15 September 2005)

A new phenolic glycoside (**1**), mahkoside A, together with six known compounds including mangiferin (**2**), kaempferol-3-*O*-β-D-glucoside **(3)**, dodecanoic acid (**4**), palmitic acid (**5**) ethyl stearate (**6**) and sucrose (**7**), were isolated from the pit of *Mahkota dewa.* Their structures were identified on the basis of spectroscopic analysis. All the compounds were isolated from the title plant for the first time.

Keywords: 4,4′-Dihydroxy-2-methoxybenzophenone-6-*O*-α-D-glucopyranoside; Mangiferin; *Mahkota dewa*

1. Introduction

Mahkota dewa (*Phaleria macrocarpa* [Scheff.] Boerl) is widely distributed in Indonesia. The stems, leaves and fruits of *M. dewa* are used for medicinal treatment. Empirically, *M. dewa* has proved capable of controlling cancer, impotency, haemorrhoids, diabetes mellitus, allergies, liver and heart diseases, kidney disorders, blood diseases, rheumatism, high blood pressure, stroke, migraine, various skin diseases, acne and so forth [1]. The bioactivity results from antihistamine, antioxidant and anticancer substance in the plant [1]. Therefore there are many healthy teas and drinks made from *M. dewa* in Indonesia.

Despite the known bioactive effect, there are no reports on the chemical constituents of the plant. Our group is interested in the investigation of the constituents of the plant and have successfully isolated three glucosides and four other known compounds. Three glucosides, a new compound 4,4′-dihydroxy-2-methoxybenzo-phenone-6-*O*-β-D-gluco-pyranoside (**1**), mangiferin (**2**) and kaempferol-3-*O*-β-D-glucoside (**3**), and four known compounds were isolated for the first time from *M. dewa*. All of the compounds were identified by NMR, HR-MS, UV and IR spectral data. The present paper deals with the isolation and structural elucidation of the three glucosides.

*Corresponding author. E-mail: liuhm@zzu.edu.cn

Journal of Asian Natural Products Research
ISSN 1028-6020 print/ISSN 1477-2213 online © 2006 Taylor & Francis
http://www.tandf.co.uk/journals
DOI: 10.1080/10286020500480472

2. Results and discussion

Compound **1** was isolated as aurantium amorphous powder. The HRESI-MS gave a $[M + Na]^+$ ion peak at *m/z* 445.1096, indicating the molecular formula to be $C_{20}H_{22}O_{10}$. The $[M\text{-}162 + Na]^+$ ion peak at *m/z* 283.0589 in the secondary mass spectrum indicated that the compound may be a glycoside and the sugar moiety a hexose. The hexose was elucidated as glucose from the ^{1}H NMR and ^{13}C NMR spectra (see table 1) and GC analysis data. The ^{13}C NMR spectrum showed the presence of a glucose moiety at δ 100.8, 77.2, 76.9, 73.4, 70.0 and 61.0. By considering the coupling constant of the anomeric proton, the glucose moiety should be the β-anomor [2].

The IR and NMR spectra showed the presence of hydroxyl (3400 cm^{-1}) and conjugated ketone (1617 cm^{-1}, δ 192.7) functionality. In particular, the carbonyl absorption band at 1617 cm^{-1} indicated that the carbonyl group should be connected to a conjugative system. The UV spectrum of **1** exhibited characteristic absorption bands for benzene ring (207 and 249 nm) and carbonyl connection with a large conjugative system (290 nm).

The ^{1}H NMR spectrum revealed the presence of six aromatic proton signals due to two proton doublets at δ 6.12 ($J = 1.92$ Hz) and 6.30 ($J = 1.92$ Hz) and an AA′BB′ system at δ 6.80 and 7.57, and a methyl singlet at δ 3.73. The chemical shift and coupling constant of the aromatic protons indicated that there are two benzene rings, including a *meta*-substituted and a *para*-substituted benzene ring. The *meta*-substituted benzene ring can be assigned for H-3 and H-5 (δ 6.12 and 6.30, each 1H, d, $J = 1.92$ Hz) and the *p*-hydroxybenzoyl structure was confirmed by the two coupled doublets: 2H each at δ 6.80 and 7.57 ($J = 8.6$ Hz). After exchanging with D_2O, six proton signals (δ 10.29 (1H), 9.70 (1H), 5.00 (1H), 4.95 (1H) and 4.55 (2H)), disappeared in the ^{1}H NMR spectrum for compound **1**, revealing the presence of six hydroxyl groups in the molecule.

Table 1. ^{1}H NMR and ^{13}C NMR spectral data for compound **1**.

	δ_H (J_{Hz})	δ_C
1		110.8
2		156.5
3	6.12, d (1.92)	93.1
4		162.0
5	6.30, d (1.92)	95.3
6		156.3
7		192.7
1′		130.0
2′	7.57, d (8.64)	131.9
3′	6.80, d (8.68)	115.1
4′		161.2
5′	6.80, d (8.68)	115.1
6′	7.57, d (8.64)	131.9
1″	4.79, d (7.90)	100.8
2″	2.92, dd (7.90, 8.80)	73.4
3″	3.18, dd (8.80, 9.20)	76.9
4″	3.01, dd (9.20, 9.20)	70.0
5″	3.28, m	77.4
6″	3.69, m 3.39, m	61.0
$-OCH_3$	3.73, s	55.3

The ^{13}C NMR spectrum of **1** revealed the presence of twenty carbon signals. According to the chemical shifts, they are classified as four kinds of carbons: twelve benzene carbons, one carbonyl carbon, six sugar carbons and a methoxyl carbon. The DEPT spectrum confirmed the presence of one methyl, one methylene, 11 methenyl and seven quaternary carbons.

From analysis of the 2D NMR spectrum, the structure of compound **1** was deduced as 4,4′-dihydroxy-2-methoxybenzophenone-6-*O*-β-D-glucopyranoside, named as mahkoside A (figure 1). The HMBC correlations for compound **1** are shown in figure 2. The correlations between H-1″ and C-6, H-2′, H-6′ and C-7, as well as OCH_3 and C-2 revealed the glucosylation at C_6–OH functionality and the positions of carbonyl and methoxyl groups.

The occurrence of ^{13}C NMR shift value of anomeric carbon at δ 73.3 and the large coupling constant ($J = 9.8$ Hz) of the anomeric proton at δ 4.59 of glucosyl moiety indicated that the compound **2** is a C-β-glucoside. According to the data of literature [3–6], compound **2** was identified as mangiferin (**2**), a xanthone-C-glycoside. The UV spectrum of compound **3** exhibited characteristic absorption bands of a flavone moiety at 267 and 342 nm. Comparing with data of the literature [7–9], compound **3** was determined as kaempferol-3-*O*-β-D-glucoside (**3**) (shown in figure 1).

Compounds **4**–**7**, which are known but isolated for the first time from the title plant, are dodecanoic acid (**4**) [10], palmitic acid (**5**) [11], ethyl stearate (**6**) [12] and sucrose (**7**) [13]. Their structures were identified by spectral data and compared with authentic samples.

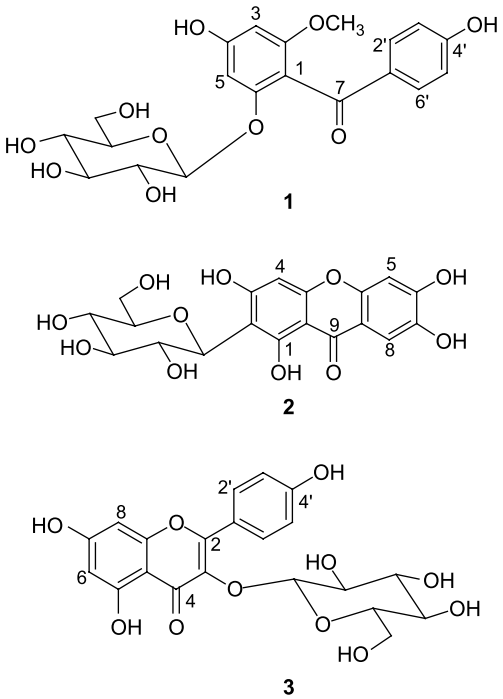

Figure 1. Structure of compounds **1**–**3**.

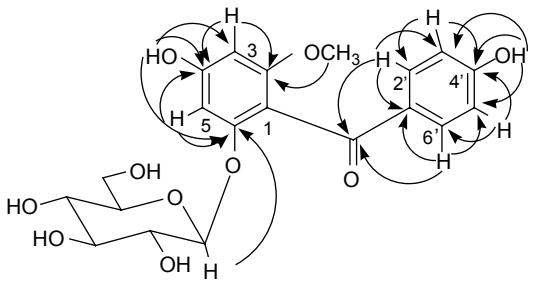

Figure 2. Key HMBC correlations of compound **1**.

3. Experimental

3.1 General experimental procedures

Melting points were determined on a (2F-2) apparatus and are uncorrected. IR spectra were recorded on a Thermo Nicolet (IR200) Spectrometer with KBr pellets. The mass spectrometry experiment was performed on a Waters Q-Tof micro hybrid quadrupole time-of-flight mass spectrometer equipped with an ESI interface. UV spectra were measured on a JASCO V-550 UV/VIS spectrophotometer in absolute MeOH. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, on a Brüker DPX-400 spectrometer with TMS as internal standard and DMSO-d_6 as solvent. Gas chromatography was carried out on an Agilent 6890N equipped with a ChemStation system.

For the chromatographic column, the silica gel (200–300 mesh) was purchased from the Qingdao Marine Chemical Company; the main chemical reagents, chloroform, ethyl acetate, ethanol, methanol and other reagents, were analytic grade or laboratory grade, being evaporated before used if necessary.

3.2 Plant material

Mahkota dewa plants were collected in Indonesia in October 2003, and identified by Professor Zhang Wenhui of the College of Forestry, Northwest Science-Technology, University of Agriculture and Forestry, China. A voucher specimen of the plant has been deposited in the New Drug Research and Development Centre, Zhengzhou University, Zhengzhou, China.

3.3 Extraction and isolation

The pit of *M. dewa* (3.2 kg), after being dried below 60°C by vacuum drier and finely powdered, was exhaustively extracted in 95% ethanol (industrial grade, 5 L) for two days; the supernatant was concentrated *in vacuo* to yield a crude paste (35 g). Water (500 ml) was added to the crude paste and then extracted with chloroform and ethyl acetate, respectively. The ethyl acetate extract was concentrated *in vacuo* to give a residue (6 g), which was chromatographed on a silica gel column and eluted gradiently by the component solvent of chloroform and ethanol. Compound **2** (35 mg) was eluted with 6:1 chloroform and ethanol; compound **3** (75 mg) eluted with 4:1, and compound **1** (3180 mg) eluted with 2:1 were

obtained, respectively. Compound **7** (21,000 mg) was obtained from the water fraction in fair crystal. Similarly, compounds **4–6** were isolated from the chloroform fraction by column chromatography of silica gel eluted with chloroform.

3.4 Structure identification

3.4.1 Compound 1. Aurantium amorphous powder. mp 103–105°C. HRESI-MS: *m/z* 445.1096 $[M + Na]^+$ (calcd for $C_{20}H_{22}O_{10}Na$, 445.1111). UV (MeOH) λ_{max}: 207, 221, 224, 246, 290 nm. IR (KBr) ν_{max} (cm^{-1}): 3400–3200, 1617, 1511, 1437. ^1H NMR (DMSO-d_6): δ 7.57 (2H, d, $J = 8.64$ Hz, H-2′, 6′), 6.80 (2H, dd, $J = 8.68$ Hz, H-3′,5′), 6.30 (1H, d, $J = 1.92$ Hz, H-5), 6.12 (1H, d, $J = 1.92$ Hz, H-3), 4.55–5.00 (5H, m, H-2″,6″). ^{13}C NMR (DMSO-d_6): δ 110.8 (C-1), 156.5 (C-2), 93.3 (C-3), 162.0 (C-4), 95.3 (C-5), 156.3 (C-6), 192.7 (C-7), 130.0 (C-1′), 131.9 (C-2′ or C-6′), 115.1 (C-3′ or C-5′), 161.2 (C-4′), 100.8 (C-1″), 73.4 (C-2″), 76.9 (C-3″), 70.0 (C-4″), 77.4 (C-5″), 61.0 (C-6″), 55.3 (OCH_3). GC analysis: R_t: 14.626, 14.799 min.

3.4.2 Compound 2. Faint yellow powder, mp 265°C (decomposed). HRESI-MS: *m/z* 423.0938 $[M + H]^+$ (calcd for $C_{18}H_{18}O_{11}$), 422.0849. UV (MeOH) λ_{max}: 205, 220, 241, 250, 258, 315, 369 nm. IR (KBr) ν_{max} (cm^{-1}): 3413 (OH), 1645 (C = O), 1618, 1595, 1505, 1320, 1083, 1040, 1025, 855.

3.4.3 Compound 3. Faint yellow powder, mp 264°C. HRESI-MS: *m/z* 447.0949 $[M-H]^-$ (calcd for $C_{21}H_{20}O_{11}$, 448.1006). UV (MeOH) λ_{max}: 204, 221, 226, 267, 342 nm. IR (KBr) ν_{max} (cm^{-1}): 3400–3200, 1658, 1603, 1493.

References

[1] N. Harmanto. *Conquering Disease in Unison with* Mahkota dewa, Ir. Harmantop (Ed.), p. 14, PT. Mahkotadewa Indonesia, North Jakarta (2003).
[2] V.H. Halbeek. *Methods Enzymol.*, **230**, 132 (1994).
[3] S. Catalano, S. Luschi, G. Flamini, P.L. Cioni, E.M. Nieri, I. Morelli. *Phytochemistry*, **42**, 1605 (1996).
[4] S. Rancom, A. Chaboud, N. Darbour, G. Comte, D. Barron, J. Raynaud, P. Cabalion. *Phytochemistry*, **52**, 1677 (1999).
[5] S. Alkhalil, H. Tosa, M. Iinuma. *Phytochemistry*, **36**, 729 (1995).
[6] X.D. Yang, N. An, L.Z. Xu, S.L. Yang. *J. Asian Nat. Prod. Res.*, **4**, 141 (2002).
[7] O.Y. Ma. *Chin. Trad. Herb. Drugs*, **34**, 196 (2003).
[8] H.B. Wang, H. Yao, G.H. Bao, H.P. Zhang, G.W. Qin. *Phytochemistry*, **65**, 969 (2003).
[9] Z.J. Ma, I. Fujii, Y. Ebizuka, X. Li. *J. Asian Nat. Prod. Res.*, **6**, 69 (2004).
[10] F.J. Gong, G.L. Wang, X. Yuan, J. Wu. *Nat. Prod. Res. Dev.*, **6**(3), 32 (1994).
[11] Y.H. Meng, Q.Y. Deng, G. Xu. *Nat. Prod. Res. Dev.*, **12**(3), 27 (2000).
[12] J.X. Xie, J.B. Chang, X.M. Wang. *IR Spectrum Application in Organic Chemistry and Pharmaceutical Chemistry*, pp. 96–97, Sciences Press (2001).
[13] W.M. Zhang, Z.H. Duan, F. Sun, G.X. Rao. *Nat. Prod. Res. Dev.*, **16**(3), 218 (2004).