Phytochemistry Letters 23 (2018) 132–136

Contents lists available at ScienceDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Three new chemical constituents of *Korthalsella japonica*

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ARTICLE INFO

Keyword:
Korthalsella japonica
Korthalin
6′,4″-dihydroxy-2′,3″-dimethoxychalcone-4′-*O*-*β*-D- glucopyranoside

ABSTRACT

The mistletoe *Korthalsella japonica* is used in traditional Chinese medicine to treat injury and to enhance blood circulation. Phytochemical constituents of this plant are not as well known as those of other species. In this study, three new compounds, korthalin (**1**), 6′,4″-dihydroxy-2′,3″-dimethoxy chalcone-4′-*O*-*β*-D-glucopyranoside (**2**) and viscolin 4′,4″-di-*O*-*β*-D-glucopyranoside (**3**), together with twenty-eight compounds (**4**-**31**) were isolated from *Korthalsella japonica*. The structures of all compounds were established on the basis of spectroscopic data analysis.

1. Introduction

Korthalsella japonica, which is distributed in tropical Asia, Australia to Polynesia, belongs to family of Loranthaceae. It is small parasitic subshrub that grows on the following species: *Ligustrum japonicum* Thunb., *Litsea mushaensis* (Hayata) Hayata, *Neolitsea acuminatissima* (Hayata) Kanehira & Sasaki, *Cinnamomum* sp., *Symplocos stellaris* Brand., *Symplocos morrisonicola* Hayata, *Osmantus matsumuranus* Hayata, *Pouteria obovate* (R. Brown) Baehni, *Syzygium buxifolium* Hook. & Am., and *Rhododendron kawakawii* Hayata (Chiu, 1996). The chemical constituents of this mistletoe have not yet been widely studied. Until now, only several constituents, such as chrysoeriol-4′-*O*-glucoside, luteolin 6,8-di-C-*β*-D-glucopyranoside, apigenin 6,8-di-C-*β*-D-glucopyranoside, chrysoeriol 6,8-di-C-*β*-D-glucopyranoside, phytosterol, oleanolic acid and fatty acids, have been reported (Fukunaga et al., 1989; Kim et al., 2016). As part of our continuing investigation on the chemical constituents from natural plants, we herein describe the detailed structures of three new compounds korthalin (**1**), 6′,4″-dihydroxy-2′,3″-dimethoxychalcone-4′-*O*-*β*-D-glucopyranoside (**2**) and viscolin 4′,4″-di-*O*-*β*-D-glucopyranoside (**3**), along with twenty-eight known compounds.

2. Results and discussion

Compound **1** was obtained as a yellowish oil. The HREI-MS of **1** exhibited a molecular ion peak at *m/z* 290.1155 (calcd 290.1154), consistent with the molecular formula $C_{16}H_{18}O_5$, which was supported by the presence of 16 carbon signals in its ^{13}C NMR spectrum. The UV spectrum of **1** showed absorption maxima at 278 and 227 nm. The IR spectrum showed strong absorption peaks for hydroxy (3421 cm^{-1}) and carbonyl groups (1730 cm^{-1}). The ^1H NMR spectrum showed three aromatic protons at δ 6.83 (1H, d, J = 8.0 Hz, H-13), 6.70 (1H, dd, J = 8.0, 1.2 Hz, H-14) and 6.67 (1H, d, J = 1.2 Hz, H-10), indicating a typical ABX moiety. In addition, two methoxy groups at δ 4.27 (3H, s,) and 3.90 (3H, s), four methylenes at δ 2.88 (2H, s, H-2), 2.60 (2H, t, J = 7.6 Hz, H-8), 2.44 (2H, t, J = 7.6 Hz, H-6) and 1.84 (2H, quint., J = 7.6 Hz, H-7) were observed in the ^1H NMR spectrum. The ^1H–^1H COSY spectrum showed the correlations between H-7 (δ 1.84) and H-6 (δ 2.44)/H-8 (δ 2.60) and revealed the $CH_2CH_2CH_2$ sequence in this molecule (Fig. 2). The ^{13}C NMR spectrum combined with the HMQC experiments indicated the presence of four methylenes (δ 42.6, 35.9, 29.5, 22.1), two methoxy groups (δ 60.0, 56.3), two conjugated ketones (δ 196.7, 195.9), two quaternary olefinic carbons (δ 166.5, 141.3) and six aromatic carbons (δ 146.7, 144.2, 133.9, 121.4, 114.6, 111.4). The HMBC spectrum showed ^2J and ^3J correlations between δ 2.88 (H-2) and δ 196.7 (C-1), δ 195.9 (C-3), δ 166.5 (C-4) and δ 141.3 (C-5), suggesting the 4-cyclopentene-1,3-dione moiety. The position of the trisubstituted aromatic ring at C-5 was elucidated using the HMBC correlations of δ 2.60 (H-8) to δ 133.9 (C-9), δ 121.4 (C-10) and δ 111.1 (C-14) and of δ 1.84 (H-7) to δ 133.9 (C-9) and δ 35.9 (C-8). Furthermore, the 4-cyclopentene-1,3-dione moiety was located at C-6 using the HMBC correlations of δ 2.44 (H-6) to δ 196.7 (C-1), δ 141.3 (C-5) and δ 166.5 (C-4) and of δ 1.84 (H-7) to δ 141.3 (C-5), δ 133.9 (C-9), δ 35.9 (C-8) and δ 22.1 (C-6). In addition, two methoxy groups at δ 4.27 and 3.90 showed ^3J HMBC correlations with δ 166.5 (C-4) and δ 146.7 (C-

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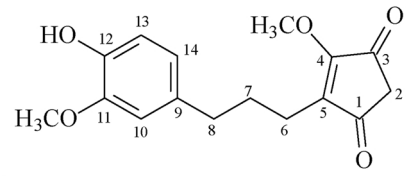
https://doi.org/10.1016/j.phytol.2017.12.003
Received 12 September 2017; Received in revised form 4 December 2017; Accepted 5 December 2017



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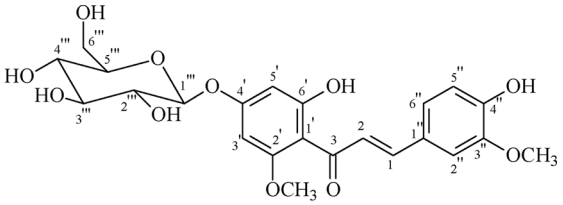

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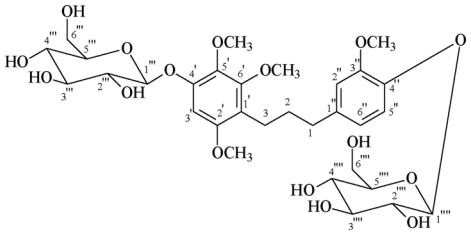

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Fig. 1. Structures of compounds 1–3.

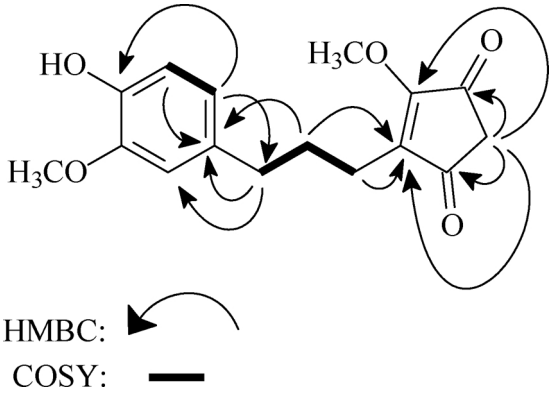

Fig. 2. Key HMBC and COSY correlations of compound 1.

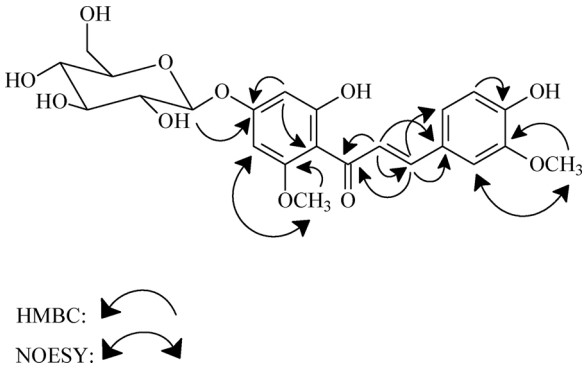

Fig. 3. Key HMBC and NOE correlations of compound 2.

11), respectively, indicating that C-4 and C-11 have OCH_3 substituents (Fig. 2). Based on the above structural evidence, compound **1** was identified as korthalin (Fig. 1).

Compound **2** was obtained as a yellowish powder with an elemental composition of $C_{23}H_{26}O_{11}$ as determined by its HRFAB-MS ($[M+H]^+$ *m/z* 479.1555; calcd 479.1553). The IR spectrum showed strong absorption bands at 3362 and 1624 cm^{-1}, and the UV spectrum exhibited bands at 376 and 258nm, suggesting the presence of a hydroxy group, an α,β-unsaturated ketone and a benzenoid moiety. The ^1H NMR spectrum of **2** displayed ABX-type aromatic proton signals at δ 7.36 (1H, d, J = 1.6 Hz, H-2″), 7.28 (1H, dd, J = 8.0, 1.6 Hz, H-6″) and 6.92 (1H, d, J = 8.0 Hz, H-5″), two doublet aromatic proton signals at δ 6.31 (1H, d, J = 2.4 Hz, H-5′) and 6.21 (1H, d, J = 2.4 Hz, H-3′), a pair of trans olefinic protons at δ 7.90 (1H, d, J = 15.6 Hz, H-2) and 7.77 (1H, d, J = 15.6 Hz, H-1), an anomeric proton signal at δ 5.13 (1H, d, J = 7.6 Hz, H-1‴), and two methoxy groups at δ 4.03 (3H, s) and 3.97 (3H, s). The ^{13}C NMR spectrum showed 23 signals, including two methoxy carbons (δ 56.1, 55.8), 12 aromatic carbons (δ 167.8, 164.5, 163.2, 149.8, 148.3, 127.9, 123.5, 115.2, 111.6, 108.4, 97.2, 92.3), an α,β-conjugated ketone system (δ 193.1, 143.8, 124.8), and a glucose moiety (δ 100.5, 77.6, 77.5, 74.1, 70.8, 62.1). The sugar moiety was identified by TLC analysis after acid hydrolysis. Moreover, the large coupling constant (7.6 Hz) of H-1‴ with H-2‴ indicated the presence of a β-configuration glucopyranoside. In the HMBC spectrum, the methoxy groups were located at C-2′ and C-3″ due to the ^3J correlations of δ 4.03 (3H, s) to δ 163.2 (C-2′) and of δ 3.97 (3H, s) to δ 148.3 (C-3″), respectively. Furthermore, δ 5.13 (H-1‴) was connected to δ 164.5 (C-4′), indicating a sugar substituent at C-4′ (Fig. 3). The NOESY signals showed correlations between δ 4.03 (OCH_3)/δ 6.31 (H-3′) and δ 3.97 (OCH_3)/δ 7.36 (H-2″), also confirming the locations of two methoxy groups (Fig. 3). Based on the above spectroscopic data and on comparison with chalcone glucopyranoside in the literature (Ninomiya et al., 2010), compound **2** was assigned as 6′,4″-dihydroxy-2′,3″-dimethoxychalcone-4′-*O*-β-D-glucopyranoside.

Compound **3** was obtained as a colorless powder. The molecular formula of **3** was determined to be $C_{31}H_{44}O_{16}$ based on its HRFAB-MS, which exhibited $[M+H]^+$ at *m/z* 673.2706 (calcd 673.2707). The IR spectrum of **3** showed absorption bands at 3367, 1595, 1512 and 1083 cm^{-1}, which are ascribable to hydroxy and benzene ring functions. The ^1H NMR spectrum of **3**, which showed aromatic signals at δ 6.98 (1H, d, J = 8.4 Hz, H-5″), 6.80 (1H, d, J = 1.4 Hz, H-2″), 6.68 (1H, dd, J = 8.4, 1.4 Hz, H-6″), 6.64 (1H, s, H-5′), combined with the ^{13}C NMR and HMBC spectrum, which showed resonances at δ 153.9, 152.4, 150.3, 137.1, 117.5, 97.3 (A ring) and δ 149.7, 145.5, 136.8, 120.9, 116.3, 113.7 (B ring), indicate the presence of one pentasubstituted and one trisubstituted aromatic moiety in compound **3**. In addition, signals for four methoxy groups at δ 3.75 (3H, s), 3.73 (3H, s), 3.72 (3H, s), and 3.71 (3H, s), three coupled methylene groups at δ 2.51 (2H, t, J = 6.8 Hz, H-1), 2.47 (2H, t, J = 6.8 Hz, H-3), and 1.69 (2H, quint., J = 6.8 Hz, H-2) and two β-glucosyl anomeric protons at δ 4.84 (2H, d, J = 6.8 Hz, H-1‴, H-1⁗) were evident in the ^1H NMR spectrum.