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Chinese Journal of Natural Medicines 2016, **14**(11): 0876–0880
Chinese Journal of Natural Medicines

Identification of antioxidant activity of two new aromatic ring butyrolactone derivatives from *Dictamnus dasycarpus* Turcz.

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Available online 20 Nov., 2016

[ABSTRACT] The present study carried out a phytochemical investigation on the root barks of *Dictamnus dasycarpus* Turcz, leading to the isolation and characterization of two new aromatic ring butyrolactone derivatives, dasycarpusphenol acid A (**1**) and dasycarpusphenol acid B (**2**). Their structures were elucidated by using spectroscopic techniques and HR-FAB-MS. Compounds **1** and **2** exhibited antioxidant activity, with their IC_{50} values being 28.95 and 41.76 mg·mL^{-1}, respectively.

[KEY WORDS] Dasycarpusphenol acid A; Dasycarpusphenol acid B; *Dictamnus dasycarpus*; Antioxidant activity

[CLC Number] R284 **[Document code]** A **[Article ID]** 2095-6975(2016)11-0876-05

Introduction

Dictamnus, a genus of flowering plants in the family of Rutaceae, comprises of seven species, are widely distributed throughout Europe and North Asia. Two species, *Dictamnus dasycarpus* and *Dictamnus angustifolius*, are indigenous to China [1]. *D. dasycarpus* Turcz., a perennial herb, has been recorded in Chinese Pharmacopoeia. The root barks are used to treat rheumatism [2], bleeding [1], itching [3], jaundice [4], chronic hepatitis [5], and skin diseases, including eczema [6] and psoriasis [7]. The plant is reported to possess many activities, such as anti-cancer [8], anti-inflammatory [9], anti-microbial [10], and anti-insect activities [11]. Previous phytochemical reports have demonstrated the presence of quinolone alkaloids [12-14], limonoids [14-15], sesquiterpenes and its glycosides [16], flavones and coumarins [17], steroids and triterpenes [18], volatile oil, and other compounds [19-20]. To clarify the substances related to the biologicalactivities, we have done the phytochemical investigation of root barks of *D. dasycarpus* Turcz, resulting in the isolation and characterization of two new aromatic rings butyrolactone derivatives, as shown in Fig. 1. The relevant literatures showed that no biphenyl derivatives were reported in this plant, even in natural products. For example, no compounds have been reported in SciFinder with a similarity of above 85%. Herein, we reported the isolation and identified of the two compounds, named as dasycarpusphenol acid A (**1**) and dasycarpusphenol acid B (**2**). Our biological evaluation experiments showed that dasycarpusphenol acid A (**1**) and dasycarpusphenol acid B (**2**) exhibited antioxidant activity.

[Received on] 20-May-2016
[Research funding] This work was supported by the Natural Science Foundation of Heilongjiang (No. D201207).
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These authors have no conflict of interest to declare.

Results and Discussion

Chemistry and structure elucidation

Compound **1** was isolated as a yellowish powder with $[\alpha]_D^{20}$ +18.8 (*c* = 0.1, MeOH). The molecular formula $C_{22}H_{22}O_{13}$ was assigned according to the $[M + Na]^+$ ion peak at *m/z* 517.095 5 (Calcd. for $C_{22}H_{22}O_{13}Na$, 517.095 3) in the HR-FAB-MS, indicating 12 degrees of unsaturation. The IR spectrum revealed the presence of the hydroxyl, carbonyl, and aromatic moiety functions due to absorption at 3 451, 1 787, 1 702, 1 600, 1 514, and 1 465 cm^{-1}, respectively. The ^{1}H and ^{13}C NMR spectra (DMSO-d_6) showed 22 proton and 22 carbon signals, which were discerned as three methyl, two methylene, five methine and twelve quaternary carbons (three ester carbonyl at 165.1, 166.8, and 175.5) directed by HSQC spectrum. The ^{1}H and ^{13}C NMR spectra (DMSO-d_6) also displayed characteristic resonances for three methoxyl groups at δ_H/δ_c 3.87 (3H, s)/56.4 (9-OCH_3) and 3.77 (6H, s)/56.2 (3,

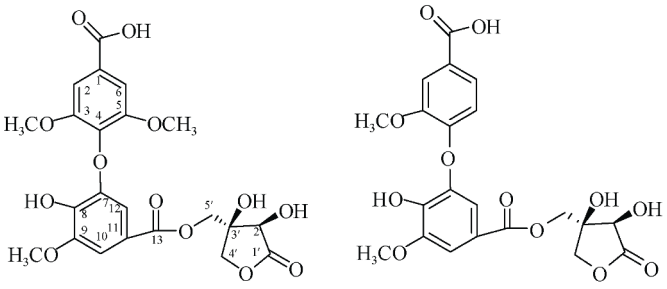

Fig. 1 Structures of compounds 1 and 2

5-OCH_3). Characteristic signals also included δ_H/δc 13.19 (1H, brs.)/166.8 (1-COOH), phenolic hydroxyl δ_H 9.75 (1H, s, 8-OH) and hydroxyl signals δ_H 5.54 (1H, s, 3′-OH), 6.02 (1H, d, *J* = 7.2 Hz, 2′-OH). The symmetrical structural of 1, 3, 4, 5-substituted aromatic ring can be deduced from the signals at δ_H/δ_c 7.36 (2H, s, H-2, 6)/106.6 (C-2, C-6). Another 1, 2, 3, and 5-substituted aromatic ring structure was gotten from the signals δ_H/δc 7.27 (1H, d, *J* = 1.8 Hz, H-10)/107.6 (C-10) and 6.62 (1H, d, *J* = 1.8 Hz, H-12)/108.0 (C-12). Two aromatic rings and the above three ester carbonyls indicated that there was another ring structure according to the 12 degrees of unsaturation. The ^{1}H and ^{13}C NMR exhibited methylene butyrolactone structure moiety by the following signals: δ_H/δc 4.39 (1H, d, *J* = 7.2, H-2′)/70.2 (C-2′), 4.03(1H, d, *J* = 9.6, H-4a′), 4.23 (1H, m, H-4b′)/72.1 (C-4′), 4.22 (2H, m, H-5′)/65.5 (C-5′), 75.4(C-3′), 175.5(C-1′) [21]. The ^{1}H and ^{13}C NMR data assignment as well as position of functional groups were confirmed by analysis of HMBC. The correlations in HMBC spectra of H-2 and H-6 (δ_H 7.36, 2H, s) with 1-COOH (δc 166.8), C-3 and 5 (δc 152.6) and C4 (δc 134.8), 3-OCH_3 or 5-OCH_3 (δ_H 3.77, 6H, s) with C-3 or C-5 (δc 152.6), correlation in NOESY spectrum between 3-OCH_3 or 5-OCH_3 (δ_H 3.77, 6H, s) with H-2 or H-6 (δ_H 7.36, 1H, s) revealed the first aromatic ring was 3, 5-OCH_3-4-oxygen-1-benzoic acid moiety. The correlations in HMBC spectraof 8-OH (δ_H 9.75, 1H, s) with C-7 (δc 145.7), C-8 (δc 140.7) and C-9 (δc 148.3), 9-OCH_3 (3.87, 3H, s) with C-9 (δc 148.3), H-12 (δ_H 6.62, 1H, d, *J* = 1.8 Hz) and H-10 (δ_H 7.27, 1H, d, *J* = 1.8 Hz) with C-11 (δc 118.6), C-8 (δc 140.7), C-13 (δc 165.1), and correlation in NOESY spectrum between 9-OCH_3 (δ_H 3.87, 3H, s) and H-10 (δ_H 7.27, 1H, d, *J* = 1.8 Hz) confirmed the second aromatic ring was 8-OH-9-OCH_3-11-benzoyl structural moiety. HMBC correlations of H-2′ (δ_H 4.39, 1H, d, *J* = 7.2 Hz) and H-4′ (δ_H 4.03, 1H, m) with C-1′ (δc 175.5), correlations of H-5′ (δ_H 4.22, 2H, m) with C-4′ (δc 72.1), C-3′ (δc 75.4), C-2′ (δc 70.2), correlations of H-2′ (δ_H 4.39, 1H, d, *J* = 7.2 Hz) with C-5′ (δc 65.5), 2′-OH (δ_H 6.02, 1H, s) with C-1′ (δc 175.5), C-2′ (δc 70.2) and C-3′ (δc 75.4), 3′-OH (5.54, 1H, s) with C-2′ (δc 70.2), C-3′ (δc 75.4) and C-4′ (δc 72.1), indicated that this was two hydroxyl *γ*-lactone connected with an oxydic methylene group moiety [21]. The structure could be attached by key correlations in the HMBC experiment (Fig. 2). The correlations of H-5′ (δ_H 4.22, 2H, m) with C-13 (δc 165.1) indicated that C-5′ connected with C-13 through oxygen atom. The molecular formula ($C_{22}H_{22}O_{13}$) and the ^{13}C NMR chemical shift at δ_C 134.8 (C-4) and 145.7 (C-7), indicted C-4 connected with C-7 also through oxygen atom (Fig. 2). The planar structure of Compound **1** was determined as 4-(5-(((3, 4-dihydroxy-5-oxotetrahydro-furan-3-yl) methoxy) carbonyl) -2-hydroxy-3-methoxy-phenoxy)-3, 5-dimethoxybenzoic acid. The relative configuration was deduced from the results of the NOESY experiment. The NOESY correlation between H-5′ (δ_H 4.19) and H-2′ (δ_H 4.39) and correlation of 3′-OH (δ_H 5.53) and 2′-OH (δ_H 6.03) were observed, revealing the same side of 3′-OH and 2′-OH.

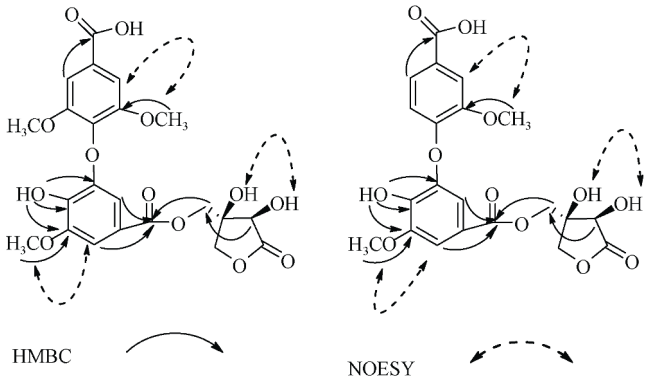

Fig. 2 Selective key HMBC and NOESY correlations of compounds 1 and 2