ORIGINAL ARTICLE

Four new phenolic glycosides from Baoyuan decoction

Xiaoli Ma, Xiaoyu Guo, Mingbo Zhao, Pengfei Tu, Yong Jiang*

State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing 100191, China

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KEY WORDS

Baoyuan decoction; Traditional Chinese medicine formula; Flavonoid glycosides; Lignan glycosides; Electronic circular dichroism; UPLC-Q-trap-MS

Abstract Four new phenolic glycosides, including two flavonoid glycosides (1 and 2) and two lignan glycosides (3 and 4), were isolated from the traditional Chinese medicine formula, Baoyuan decoction. Their structures were established by detailed analysis of the NMR and HR-ESI-MS spectroscopic data and their absolute configurations were determined by the experimental electronic circular dichroism data as well as chemical methods. Furthermore, the sources of the four new compounds were determined by the UPLC-Q-trap-MS method, which proved that 1 and 2 are originated from Glycyrrhiza uralensis, and 3 and 4 are from Cinnamomum cassia.

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*Corresponding author. Tel./fax: +86 10 82802719. E-mail address: yongjiang@bjmu.edu.cn (Yong Jiang).

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1. Introduction

Baoyuan decoction (BYD), a well-known traditional Chinese medicine (TCM) formula, has been used for the treatment of aplastic anemia, chronic renal failure, coronary heart disease, etc. It is comprised of four commonly used TCMs, i.e. Ginseng Radix et Rhizoma, Astragali Radix, Glycyrrhizae Radix et Rhizoma Praeparata Cum Melle, and Cinnamomum Cortex. In our previous studies, 31 flavonoids were isolated from the extract of BYD, and three of them are new compounds. As an ongoing search for bioactive constituents from BYD, four new phenolic glycosides, including two flavonoid glycosides, liquiritigenin-4’-O-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside (1) and liquiritigenin-4’-O-α-D-glucopyranosyl(1→6)-β-D-glucopyranosyl(2), and two lignan glycosides, (+)-(7S,8R,8R)-isolariciresinol-4’-O-β-D-apiofuranosyl(1→2)-β-D-glucopyranoside (3) and (+)-(7S,8R,8R)-isolariciresinol-3’-O-β-D-apiofuranosyl(1→2)-β-D-glucopyranoside (4), were obtained from the aqueous extract of BYD. Herein, the isolation and structure elucidation of these four new components and their inhibitory effects on lipopolysaccharide (LPS)-induced nitric oxide (NO) production in RAW 264.7 macrophages are reported, along with their source clarification.

2. Results and discussion

Compounds 1 and 2 were both obtained as a light yellow amorphous powder. Their molecular formulae were established as C_{27}H_{32}O_{14} from the 13C NMR and HR-ESI-MS data (m/z 579.1711 [M–H]− for 1 and m/z 579.1708 [M–H]− for 2, Calcd. for 579.1714) indicating that they were a pair of isomers with the same formula. Their IR spectra displayed identical absorption bands at 3402 cm−1 (hydroxy group), 1647 cm−1 (conjugated carbonyl group), 1598, 1502, and 1460 cm−1 (phenyl group). The 1H NMR data showed the presence of three characteristic aliphatic signals of flavanone [δH 3.12 (1 H, dd, J = 14.5, 13.0 Hz, H-3a), 2.66 (1 H, dd, J = 14.5, 3.0 Hz, H-3b), and 5.52 (1 H, dd, J = 13.0, 3.0 Hz, H-2) for 1; δH 3.10 (1 H, dd, J = 14.5, 13.0 Hz, H-3a), 2.64 (1 H, dd, J = 14.5, 3.0 Hz, H-3b), and 5.50 (1 H, dd, J = 13.0, 3.0 Hz, H-2) for 2], a group of ABX coupled phenyl proton signals [δH 7.65 (1 H, d, J = 8.7 Hz, H-5), 6.51 (1 H, dd, J = 8.7, 2.2 Hz, H-6), and 6.34 (1 H, d, J = 2.2 Hz, H-8) for 1; δH 7.66 (1 H, d, J = 8.7 Hz, H-5), 6.52 (1 H, dd, J = 8.7, 2.2 Hz, H-6), and 6.36 (1 H, d, J = 2.2 Hz, H-8) for 2], a group of AA’BB’ coupled aromatic signals [δH 7.43 (2 H, d, J = 8.7 Hz, H-2’, 6’) and 7.11 (2 H, d, J = 8.7 Hz, H-3’, 5’) for 1; δH 7.46 (2 H, d, J = 8.7 Hz, H-2’, 6’) and 7.13 (2 H, d, J = 8.7 Hz, H-3’, 5’) for 2], and two anomeric proton signals [δH 4.99 (1 H, d, J = 7.0 Hz, H-1’), 5.52 (1 H, d, J = 7.8 Hz, H-1’), 5.50 (1 H, d, J = 7.0 Hz, H-1’), 5.52 (1 H, d, J = 7.8 Hz, H-1’) for 1; δH 4.80 (1 H, d, J = 6.5 Hz, H-1’), 4.69 (1 H, d, J = 3.0 Hz, H-1’), 4.80 (1 H, d, J = 6.5 Hz, H-1’), 4.69 (1 H, d, J = 3.0 Hz, H-1’) for 2]. The 13C NMR data (Table 1) showed 27 carbon signals, including 12 phenyl carbons, two aliphatic carbons, one carbonyl carbon, and two groups of glucosyl carbons. The above data suggested that 1 and 2 are a pair of flavanone diglycosides with the same aglycone, and the aglycone was determined as liquiritigenin by comparison with the literature. In acid hydrolysis, both of them yielded two D-glucose after HPLC separation and optical rotation measurement. For compound 1, these two glucosyls were deduced to be both β- and α-configured, respectively, from their different J values of the anomeric protons [J = 6.5 Hz, H-1’; J = 3.0 Hz, H-1’] for 2]. An in-depth analysis of their 2D NMR data supported that 1 and 2 possess the different linkage position of the terminal glucosyl moiety (Fig. 1). For compound 1, the HMBC correlations of H-1’/C-4’ and H-1’/C-2’ suggested that the linkage positions of the two glucosyls are at C-4’ and C-2’, respectively. However, the HMBC correlations of H-1’/C-4’ and H-1’/C-6’ in 2 suggested that the linkage positions of the two glucosyls are at C-4’ and C-6’, respectively. The absolute configuration of the aglycone of 1 and 2 was determined as 2S from the negative Cotton effect at 300 nm in the experimental ECD spectra (see Supplementary Information Figs. S7 and S14), which is in accordance with that of other natural flavanone-7–9. Thus, compounds 1 and 2

| Position | δH (in ppm, J in Hz, in DMSO-d6) | δC (in ppm) |
|----------|---------------------------------|-------------|
| 2        | 5.52 dd (13.0, 3.0)             | 78.7        |
| 2        | 3.00 dd (7.8, 3.0)              | 78.9        |
| 2        | 2.66 dd (14.5, 3.0)             | 43.3        |
| 2        | 3.12 dd (14.5, 13.0)            | 189.9       |
| 2        | 6.51 dd (8.7, 2.2)              | 110.6       |
| 2        | 7.65 dd (8.7)                   | 190.0       |
| 2        | 6.34 dd (2.2)                   | 102.6       |
| 2        | 164.7                           | 102.6       |
| 2        | 163.0                           | 106.2       |
| 2        | 113.5                           | 124.5       |
| 2        | 132.5                           | 126.2       |
| 2        | 127.8                           | 132.5       |
| 2        | 127.8                           | 113.5       |
| 2        | 7.43 dd (8.7)                   | 115.5       |
| 2        | 6.54 dd (8.7, 2.2)              | 128.4       |

Table 1 The 1H NMR and 13C NMR data for compounds 1 and 2 (δ in ppm, J in Hz, in DMSO-d6).
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were determined as liquiritigenin-4′-O-β-D-glucopyranosyl (1→2)-β-D-glucopyranoside and liquiritigenin-4′-O-α-D-glucopyranosyl(1→6)-β-D-glucopyranoside, respectively.

Compounds 3 and 4 were both obtained as a light yellow amorphous powder. Their molecular formulae were established as C_{31}H_{32}O_{15} from the $^{13}$C NMR and HR-ESI-MS data (m/z 653.2444 [M−H]$^{-}$) for 3 and m/z 653.2449 [M−H]$^{-}$ for 4. Calculated for 653.2445. Their IR spectra displayed the absorption bands at 3396 cm$^{-1}$ (hydroxy group) and 1504 and 1463 cm$^{-1}$ (phenyl group). The $^1$H NMR data showed the presence of a 1,3,4-trisubstituted phenyl signals [δ$_H$ 6.68 (1 H, d, J=1.5 Hz, H-2), 6.69 (1 H, d, J=7.0 Hz, H-5), and 6.00 (1 H, dd, J=7.0, 1.5 Hz, H-6) for 3; δ$_H$ 6.73 (1 H, d, J=2.0 Hz, H-2), 6.59 (1 H, d, J=8.0 Hz, H-5), and 6.27 (1 H, dd, J=8.0, 2.0 Hz, H-6) for 4] and two singlet phenyl signals [δ$_H$ 6.67 (1 H, s, H-2′), and 6.33 (1 H, s, H-5′) for 3; δ$_H$ 6.58 (1 H, s, H-2′), and 6.71 (1 H, s, H-5′) for 4]. The $^{13}$C NMR data showed 31 signals, including 12 phenyl carbons, six aliphatic carbons, two methoxy carbons, and 11 sugar moiety carbons. Comparison of the $^1$H and $^{13}$C NMR spectroscopic data of 3 and 4 with those of isolariciresinol$^{10,11}$ indicated that they are both isolariciresinol diglycosides with the same sugar constitution. In acid hydrolysis, both of them yielded a D-glucose and a D-apiose after HPLC separation and optical rotation measurement, which were deduced to be both β-configured from the J value of the anomeric proton of glucosyl moiety [δ$_H$ 4.29 (1 H, d, J=8.0 Hz, H-1′) for 3; δ$_H$ 4.71 (1 H, d, J=7.0 Hz, H-1′) for 4] and the $^{13}$C NMR data of the apiosyl moiety$^{12}$. These two compounds were demonstrated to be different in the linkage site of the sugar chain moiety from the HMBC correlation (Fig. 2). The apiosyl moieties of 3 and 4 were both determined to be connected at the C-2″ of glucosyl according to the HMBC correlation of H-1′− to C-2″. Nevertheless, the glucosyl moiety of 3 was deduced to be linked at C-4 of isolariciresinol from the HMBC correlation of H-1′− to C-4, and the glucosyl moiety of 4 was linked at C-3′ of isolariciresinol from the HMBC correlation of H-1′− to C-3′. The aglycones of 3 and 4 were deduced to possess the same absolute configuration by examining their ECD spectra and NOE correlations. Their experimental ECD spectra both showed the negative Cotton effect at 291 nm and the positive Cotton effect at 276 nm, indicating the 7S configuration$^{13}$ (see Supplementary Information, Figs. S22 and S30). The NOE correlations between H-7/H-8/H-9α and H-7/a/H-8/H-9α were noted, while there were no NOE effects observed between H-7/a/H-8 and H-8/H-9, indicating that H-8'/H-8 and H-7/H-8 were trans-configurations (Fig. 3). Moreover, the large coupling constants (J=9.5 Hz for 3 and 10.6 Hz for 4) between H-7 and H-8 also supported the above assignment$^{10}$.

Thus, 8R and 8′R were configured and the structures of 3 and 4 were determined as (++)-(7S,8R,8′R)-isolariciresinol-4-O-β-D-apiofuranosyl(1→2)-β-D-glucopyranoside and (++)-(7S,8R,8′R)-isolariciresinol-3-O-β-D-apiofuranosyl(1→2)-β-D-glucopyranoside.

In order to clarify the sources of the new compounds, an UPLC-Qtrap-MS method was established to analyze the isolates in BYD and in each composition plant. Finally, the flavonoid glycosides, 1 and 2, were found to be originated from Glycyrrhiza uralensis, while the lignan glycosides, 3 and 4, were derived from Cinnamomum cassia (Fig. 4).

The inhibitory effects of the isolates on NO production in LPS-activated RAW 264.7 macrophage cells were screened, but unfortunately no obvious inhibitory effects (IC$_{50}$ > 100 μmol/L) were observed for compounds 1–4.

3. Conclusions

Four new compounds, including two flavonoid glycosides (1 and 2) and two lignan glycosides (3 and 4) were obtained from BYD. The structures of these four compounds were established by detailed spectroscopic analysis. Their absolute configurations were determined by using experimental ECD as well as chemical methods. Besides, 1 and 2 were found to be originated from G. uralensis, and 3 and 4 were derived from C. cassia. However, it is a regret to find that all these four new isolates were inactive against NO production in LPS-activated RAW 264.7 macrophage cells.

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4. Experimental

4.1. General experimental procedures

The NMR spectra were obtained on a Varian 500 spectrometer, with deuterated solvent as reference. The optical rotations were determined using an Autopol IV Automatic polarimeter. The FT-IR spectra were measured using a Nicolet NEXUS-470 infrared spectrometer. HR-ESI-MS spectra were recorded on a Xevo-G2 Q-TOF mass spectrometer with an electrospray ionization (ESI) interface (Waters, Milford, MA, USA) in the negative mode. Analytical HPLC was performed on an Agilent 1100 HPLC system, equipped with a diode array detector and an Agilent ZORBAX SB-Aq column (250 mm × 4.6 mm, 5 μm). Semi-preparative HPLC was carried out on an Agilent 1200 instrument, using an Agilent ZORBAX SB-Aq column (250 mm × 10 mm, 5 μm), detected at a UV wavelength of 230 nm. Column chromatography (CC) was performed on macroporous resin AB-8 (Cangzhou Bon Adsorber Technology Co.), silica gel (100–200 mesh or 200–300 mesh, Qingdao Haiyang Chemical Works, China), Sephadex LH-20 (Pharmacia Co.), and ODS (Merck). Analytical grade solvents were purchased from Beijing Chemical Factory.

4.2. Plant materials

The dried roots of Panax ginseng, the decoction pieces of G. uralensis and Astragalus membranaceus var. mongholicus, and the extracted ion chromatograms (EICs) at m/z 579 from BYD extract (B) and G. uralensis (D); EICs at m/z 653 from BYD extract (H) and G. uralensis (J); EICs of multiple reaction monitoring (MRM) transition (m/z 579/255) for compounds 1 and 2 (E, F); EICs of MRM transition (m/z 579/255) for compounds 3 and 4 (K, L).

Figure 4 UPLC-Qtrap-MS base peak chromatograms (BPCs) of Baoyuan decoction (BYD) extract (A, G), G. uralensis (C), and C. cassia (I); the extracted ion chromatograms (EICs) at m/z 579 from BYD extract (B) and G. uralensis (D); EICs at m/z 653 from BYD extract (H) and G. uralensis (J); EICs of multiple reaction monitoring (MRM) transition (m/z 579/255) for compounds 1 and 2 (E, F); EICs of MRM transition (m/z 579/255) for compounds 3 and 4 (K, L).
the barks of *C. cassia* were purchased from Anguo traditional Chinese medicine market (Hebei Province, China) and authenticated by Prof. Pengfei Tu. The voucher specimens (PG-AG-20130312, GU-AG-20130312, AM-AG-20130312, and CC-AG-20130312) were deposited at the herbarium of the Peking University Modern Research Center for Traditional Chinese Medicine.

### Table 2

| Position | \( \delta_3 \) | \( \delta_1 \) | \( \delta_3 \) | \( \delta_1 \) |
|----------|----------------|----------------|----------------|----------------|
| 1        | 136.9          | 137.3          | 133.7          | 144.5          |
| 2        | 6.68 d (1.5)   | 113.8          | 6.73 d (2.0)   | 114.7          |
| 3        | 147.7          | 145.0          | 146.5          | 144.5          |
| 4        | 6.69 d (7.0)   | 115.8          | 6.59 d (8.0)   | 114.6          |
| 5        | 6.00 dd (7.0)  | 121.8          | 6.27 dd (8.0, 2.0) | 122.4          |
| 6        | 7.37 d (9.5)   | 46.5           | 4.16 d (10.6)  | 44.1           |
| 7        | 1.88 m         | 38.5           | 1.86 m         | 33.8           |
| 8        | 3.44 m         | 60.4           | 3.37 m         | 59.9           |
| 9        | 130.4          | 131.4          |                 |                |
| 1'       | 6.67 s         | 112.3          | 6.58 s         | 117.2          |
| 2'       | 144.8          | 144.3          |                 |                |
| 3'       | 146.8          | 147.4          |                 |                |
| 4'       | 6.33 s         | 116.4          | 6.72 s         | 111.8          |
| 5'       | 133.1          | 129.8          |                 |                |
| 6'       | 2.76 m; 2.72 m | 32.5           | 2.87 m; 2.54 m | 31.6           |
| 7'       | 1.68 m         | 45.8           | 1.86 m         | 42.9           |
| 8'       | 3.31 m         | 64.1           | 3.41 m         | 63.3           |
| OCH3     | 3.71 s         | 56.0           | 3.74 s         | 55.5           |
| OCH3     | 3.69 s         | 56.0           | 3.68 s         | 55.6           |

Glc  

1"" | 4.29 d (8.0) | 99.6 | 4.71 d (7.0) | 99.4 |
2"" | 3.43 dd (7.5, 7.0) | 75.2 | 3.41 dd (7.0, 7.0) | 75.3 |
3"" | 3.26 m | 77.9 | 3.37 m | 77.2 |
4"" | 3.38 m | 69.8 | 3.18 m | 69.4 |
5"" | 2.76 m | 77.2 | 3.07 m | 76.8 |
6"" | 3.44 dd (10.5, 2.0) | 60.6 | 3.42 dd (11.0, 2.0) | 60.6 |
7"" | 3.16 dd (10.5, 5.5) | 56.0 | 3.02 dd (11.0, 5.5) | 55.5 |

Api  

1"""" | 5.36 s | 108.7 | 5.38 d (1.5) | 108.8 |
2"""" | 3.70 brs | 76.4 | 3.74 brs | 76.1 |
3"""" | 79.8 | 79.3 |
4"""" | 4.04 d (9.0); 3.56 d (9.0) | 74.3 | 3.99 d (9.0); 3.54 d (9.0) | 73.9 |
5"""" | 2.38 brs | 64.9 | 3.30 brs | 64.5 |

4.3. Extraction and isolation

The dried roots of *A. membranaceus* var. *mongolicus* (30 kg), *P. ginseng* (10 kg), *G. uralsensis* (10 kg), and the barks of *C. cassia* (5 kg) were powdered and mixed together according to the record in Pharmacology of Traditional Chinese Medical Formulae, and were extracted with the deionized water (550 L x 3), each for 2 h. The extract was filtered and concentrated in vacuo. The resulting residue was dissolved in H2O and subjected to AB-8 macroporous resin CC (30 L) eluted with aqueous EtOH solution (0%, 15%, 30%, 50%, and 95%) to give five fractions, respectively.

The 30% aqueous ethanol eluate (513.3 g) was subjected to silica gel CC (5 kg) eluting with the mixture of CH2Cl2–MeOH–H2O (95:5:0.5, 90:10:1, 85:15:1.5, 80:20:2 and 70:30:3) to give 11 fractions, F1s. A-K. Fr. H was first applied to Sephadex LH-20 CC using MeOH as eluent to yield six fractions, Frs. H1-H6. Fr. H2 (3.49 g) was applied to silica gel CC (60.0 g) eluting with CH2Cl2–MeOH–H2O (90:10:1, 85:15:1.5 and 70:30:3) to yield six fractions, Frs. H21-H26. Fr. H26 (17 mg) was further chromatographed on a semi-preparative HPLC using a mixed solvent (15% aqueous ACN) as mobile phase to yield 1 (3.0 mg, tR 19.0 min) and 2 (2.5 mg, tR 21.0 min). Fr. F was applied to Sephadex LH-20 CC using MeOH as eluent to yield five fractions, Frs. F1-F5. Fr. F3 (34 mg) was subjected to CC on silica gel, using CH2Cl2–MeOH–H2O (from 85:15:1 to 60:40:4) as eluent, and was then separated by HPLC, using the mixture of ACN-H2O (12:88) to yield 3 (3.0 mg, tR 12.0 min) and 4 (2.5 mg, tR 12.8 min).

4.3.1. Liquiritigenin-4′-O-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside

4.3.2. Liquiritigenin-4′-O-α-D-glucopyranosyl(1→6)-β-D-glucopyranoside

4.3.3. (±)-(75R,8R,8′R)-Isolariciresinol-4′-O-β-D-apiofuranosyl(1→2)-β-D-glucopyranoside

4.3.4. (±)-(75R,8R,8′R)-Isolariciresinol-3′-O-β-D-apiofuranosyl(1→2)-β-D-glucopyranoside

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Sample preparation: the decoction pieces of *A. membrane var. mongholicus* (100 g) were crushed into fine powders and extracted twice with 1 L of distilled water. The extract was concentrated and the supernatant was freeze-dried. An aliquot (500 mg) of the freeze-dried powder was dissolved into 10.0 mL of water by vortex mixing for 1 min. After centrifugation at 9600 rpm in a LXJ-II B centrifuge (Anke, Shanghai, China) for 10 min, the supernatant (5 mL) was concentrated to dryness under reduced pressure, and dissolved with 50% MeOH in water (v/v, 2 mL), and then filtered through a 0.22 μm membrane before LC–MS analysis. The sample preparation method was same for *P. ginseng* root, *L. mongholicus*, *P. ginseng* root, *L. mongholicus*, *S. scutellaris orientalis* (Rutaceae), *S. scutellaris orientalis* (Rutaceae), *G. uralensis* (Umbelliferae), *A. membrane var. mongholicus*, *S. scutellaris orientalis* (Rutaceae), *G. uralensis* (Umbelliferae), *A. membrane var. mongholicus*, *Scutellaria baicalense* (Lamiaceae), *G. uralensis* (Umbelliferae), *A. membrane var. mongholicus*, *Scutellaria baicalense* (Lamiaceae), *G. uralensis* (Umbelliferae), *A. membrane var. mongholicus*, *Scutellaria baicalense* (Lamiaceae), and *G. uralensis* (Umbelliferae).

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**Appendix A. Supplementary material**

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.apsb.2016.08.004.

**References**

1. Sun C, Han Y, Wu Q. Clinical efficacy of *Baoyuan Qingxue* particles containing different cinnamic aldehyde content on treatment of coronary heart disease in elderly. *Chin J Gerontol* 2013;33:4692–3.
2. Wang X, Gao G, Hu JG. Effect of Baoyuan decoction on cellular immune function after mending surgery for ventricular septal defect of infants and preventive effect on pulmonary infection. *J Hainan Med Coll Univ* 2012;18:235–7.
3. Wang JL. The experimental research of *Baoyuan jia jian fang* decoction treating coronary heart disease and angina pectoris. *J Mudanjiang Med Coll* 2005;26:8–12.
4. Sun JW, Zhao MB, Liang H, Tu PF. Isolation and identification of flavonoids from *Baoyuan Decoction*. *Chin Tradit Herb Drugs* 2010;41:696–700.
5. Ma X, Yu Q, Gao X, Zeng K, Zhao M, Tu P, et al. Nitric oxide inhibitory flavonoids from traditional Chinese medicine formula *Baoyuan Decoction*. *Fitoterapia* 2015;103:252–9.
6. Nakanishi T, Inada A, Kambayashi K, Yoneda K. Flavonoid glycosides of the roots of *Glycyrrhiza uralesis*, *P. ginseng*, and *C. cassia*, and the BYD water extract.
7. Slade D, Ferreira D, Marais JP. Circular dichroism, a powerful tool for the assessment of absolute configuration of flavonoids. *Phytochemistry* 2005;66:2177–2175.
8. Giorgio E, Parrinello N, Caccamese S, Rosini C. Non-empirical assignment of the absolute configuration of (–)-naringenin, by coupling the exciton analysis of the circular dichroism spectrum and the ab initio calculation of the optical rotatory power. *Org Biomol Chem* 2004;2:3602–7.
9. Tchendem MH, Douanla PD, Tabopa TK, Thcdina AT, Tamze V, Nkengfack AE, et al. Two new glycosides from *Duboscia macrocarpa* Bocq. *Phytochem Lett* 2014;10:1–4.
10. Jutiviboonsuk A, Zhang H, Tan GT, Ma C, Dan Hang N, Manh Cuong N, et al. Bioactive constituents from roots of *Bursera tonkinensis*. *Phytochemistry* 2005;66:2745–51.
11. Zhang Z, Guo D, Li C, Zheng J, Koike K, Jia Z, et al. Glauberthins A and B, two lignans from *Glauberthia yunnanensis*. *Phytochemistry* 1999;51:469–72.
12. Çalış İ, Saracoğlu İ, Başaran AA, Sticher O. Two phenethyl alcohol glycosides from *Scutellaria orientalis* subsp. *pinatifida*. *Phytochemistry* 1993;32:1621–3.
13. Ohashi K, Watanabe H, Okumura Y, Uji T, Kitagawa I. Indonesian medicinal plants. XII. Four isomeric lignan-glycosides from the bark of *Aegle marmelos* (Rutaceae). *Chem Pharm Bull* 1994;42:1924–6.
14. Deng ZJ. Pharmacology of traditional Chinese medical formulas. 2nd ed. Beijing: China Press of Traditional Chinese Medicine; 152–4.