Fitoterapia 89 (2013) 126–130

Contents lists available at ScienceDirect

Fitoterapia

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

2-Methyl-L-erythritol glycosides from *Gardenia jasminoides*

Liguo Yang [a,b,1], Kaifeng Peng [a,b,1], Shizhe Zhao [a,b], Feng Zhao [c], Lixia Chen [a,b,*], Feng Qiu [a,b,**]

[a] Department of Natural Products Chemistry, School of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, Shenyang 110016, China
[b] Key Laboratory of Structure-Based Drug Design & Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, China
[c] School of Pharmacy, Yantai University, No. 32 Road QingQuan, Laishan District, Yantai 264005, China

ARTICLE INFO

Article history:
Received 21 August 2012
Accepted in revised form 22 May 2013
Available online 31 May 2013

Keywords:
Gardenia jasminoides
2-Methyl-L-erythritol glycosides
Triterpenoid
Quinic acid derivatives
Flavonoid
Anti-inflammatory activity

ABSTRACT

Two new glycosides, 2-methyl-L-erythritol-4-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside (**1**) and 2-methyl-L-erythritol-1-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside (**2**), along with two known triterpenoids (**3**–**4**), four quinic acid derivatives (**5**–**8**) and one flavonoid (**9**) were isolated from the fruit of *Gardenia jasminoides*. Their structures were elucidated through MS and 2D NMR experiments (HMQC and HMBC). Inhibitory effects of the isolated compounds on nitric oxide production in lipopolysaccharide-activated macrophages were evaluated. Though 2-methyl-D-erythritol and its glycosides have been reported in a few references, this is the first report about 2-methyl-L-erythritol glycosides. Based on this finding, we propose that 2-methyl-L-erythritol might be a new intermediate in the non-mevalonate biosynthesis of terpenoids.

1. Introduction

The dried ripe fruit of *Gardenia jasminoides*, an important traditional Chinese medicine (TCM), has been recorded as Fructus Gardeniae (Chinese herbal name is "zhi zi") in Chinese Pharmacopoeia and widely used for the treatment of diuretic, cholagogue, anti-inflammatory and antipyretic effects [1]. The phytochemical constituents of *G. jasminoides* have been extensively investigated and led to the isolation of iridoids and their glycosides [2,3], monocyclic monoterpenoids and their glycosides [4,5], flavonoids [6], crocetin and its glycosides [7,8], and quinic acid derivatives and vanillic acid glycosides [9]. Nitric oxide (NO) is derived from L-arginine by nitric oxide synthase (NOS) in numerous mammalian cells and tissues. As a well-known intracellular and intercellular signaling molecule, it plays an important role in the regulation of diverse physiological mechanisms in vivo, and a number of studies have shown that overproduction of NO by NOS is responsible for inflammation [10]. As a part of our program to investigate the anti-inflammatory constituents from this plant, chemical investigation of 60% EtOH extracts of fruit of *G. jasminoides* was undertaken. Though 2-methyl-D-erythritol glycosides have been found ten years ago [11], no reports have been published about 2-methyl-L-erythritol glycosides. In this study, two new 2-methyl-L-erythritol glycosides, 2-methyl-L-erythritol-4-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside (**1**) and 2-methyl-L-erythritol-1-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside (**2**), along with two known triterpenoids (**3**–**4**), four quinic acid derivatives (**5**–**8**) and one flavonoid (**9**) were isolated from the fruit of *G. jasminoides*. In the present research, we report the isolation and structural elucidation of the new compounds and the inhibitory effects of all compounds on NO production in LPS-activated macrophages.

2. Experimental

2.1. General

Optical rotations were measured with a Perkin-Elmer 241 polarimeter. UV spectra were recorded on a Shimadzu UV 2201

* Correspondence to: L. Chen, Department of Natural Products Chemistry, School of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, Shengyang 110016, China. Tel.: +86 24 23986515.
** Correspondence to: F. Qiu, Department of Natural Products Chemistry, school of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, Shengyang 110016, China. Tel.: +86 24 23986463; fax: +86 24 23993994.
E-mail addresses: syzyclx@163.com (L. Chen), fengqiu20070118@163.com (F. Qiu).
[1] Contributed equally to this work.

0367-326X/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.fitote.2013.05.018

spectrophotometer. IR spectra were conducted on a Bruker IFS 55 spectrometer. NMR experiments were performed on Bruker ARX-300 and AV-600 spectrometers. The chemical shifts are stated relative to TMS and expressed in δ values (ppm), with coupling constants reported in Hz. HRESIMS were obtained on a Bruker APEX-II mass spectrometer, and ESIMS were recorded on an Agilent 1100-LC/MSD TrapSL mass spectrometer. Silica gel GF_{254} (10–40 μm) prepared for TLC and silica gel (200–300 mesh) for column chromatography (CC) were obtained from Qingdao Marine Chemical Factory (Qingdao, People's Republic of China). Octadecyl silica gel was purchased from Merck Chemical Company Ltd. Macroporous resin D101 was a product of Chemical Plant of NanKai University (Tianjin, China). Preparative HPLC separations were conducted using a Shimadzu HPLC system equipped with a LC-6AD pump and a SPD-20A detector using a C_{18} column (250 mm × 20 mm, 5 μm; YMC Co. Ltd.). GC was carried out on an Agilent GC-series system and performed with an HP-5 column (30 m × 0.25 mm × 0.25 μm, Agilent, Santa Clara, CA). All the reagents were of HPLC grade or analytical grade and purchased from Tianjin Damao Chemical Company.

2.2. Plant material

The fruit of *G. jasminoides* was obtained from Jiangxi Province, China, and identified by Professor Qishi Sun, of the School of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University. A voucher specimen (GJ-20091016) has been deposited in the herbarium of the Department of Natural Products Chemistry, Shenyang Pharmaceutical University.

2.3. Extraction and isolation

Dried fruit (8.0 kg) of *G. jasminoides* was cut into pieces and extracted with 60% (v/v) EtOH (×3, 2 h each). The combined extract (1000 g) was suspended in 3.0 L water and partitioned with cyclohexane, EtOAc, and water-saturated n-butanol (×3, 3.0 L each), successively. The EtOAc extract (70 g) was subjected to silica gel column chromatography (CC) with a $CHCl_3$–MeOH gradient solvent system (100:0 to 0:100) to obtain 9 fractions (E1–E9), which were combined according to TLC analysis. Fraction E2 (10 g) was chromatographed on silica gel CC with a cyclohexane–EtOAc gradient solvent system (100:0 to 0:100) to obtain **3** (400 mg) and **4** (80 mg). Fraction E6 (5 g) was separated by preparative HPLC eluted with MeOH–H_2O (50:50) to afford **5** (12 mg, t_R 82.1 min), **6** (17 mg, t_R 109.4 min), **7** (15 mg, t_R 130.0 min) and **8** (16 mg, t_R 180.0 min). Fraction E7 (20 g) was chromatographed over silica gel eluted with $CHCl_3$–MeOH (100:10 to 0:100) and resolution of fraction E74 (1 g) by recrystallization with MeOH yielded **9** (200 mg).

The water extract (500 g) was chromatographed on D101 (100 mesh) eluted with a gradient of EtOH–H_2O (0:100 to 95:5) to obtain five fractions (W1–W5). Fraction W2 (2 g) was subjected to ODS open CC eluted with MeOH–H_2O (5:95 to 50:50) and resolution of fraction W22 (300 mg) by preparative HPLC (MeOH–H_2O, 40:60) afforded **1** (30 mg, t_R 56 min) and **2** (32 mg, t_R 69 min).

2-Methyl-L-erythritol-4-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside (**1**): yellow, amorphous powder; $[\alpha]^{18}_D$ −15.2 (c 0.50, CH_3OH); UV (CH_3OH) λ_{max} (log ε): 213 (4.20), 240 (3.82), 300 sh (4.10) nm; IR (KBr) V_{max}: 3396, 2934, 1702, 1633, 1604, 1516, 1457, 1427, 1383, 1285, 1157, 1114, 828 cm^{-1}; ^1H and ^{13}C NMR data: see Table 1; HRESIMS *m/z* 503.1769 $[M - H]^+$ (calcd. for $C_{22}H_{31}O_{13}$, 503.1770).

2-Methyl-L-erythritol-1-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside (**2**): yellow, amorphous powder; $[\alpha]^{18}_D$ −15.0 (c 0.50, CH_3OH); UV (CH_3OH) λ_{max} (log ε): 213 (4.22), 240 (3.80), 300 sh (4.12) nm; IR (KBr) V_{max}: 3398, 2936, 1700, 1635, 1602, 1515, 1458, 1424, 1382, 1283, 1154, 1118, 830 cm^{-1}; ^1H and ^{13}C NMR data: see Table 1; HRESIMS *m/z* 527.1725 $[M + Na]^-$ (calcd. for $C_{22}H_{32}O_{13}Na$, 527.1735).

2.4. Acid hydrolysis of 1–2 and determination of the absolute configuration of sugars

A solution of each compound (2.0 mg) in 2 M HCl (2 mL) was stirred at 90 °C in a stoppered vial for 2 h. The solution after cooling was evaporated under a stream of N_2. Anhydrous pyridine solutions (1.0 mL) of each residue and L-cysteine methyl ester hydrochloride (1.5 mg) were mixed and warmed at 60 °C for 2 h. After drying the solution, trimethylsilyl imidazole (150 μL) was added to the mixture, which was warmed at 60 °C for another 1 h and then partitioned between H_2O (500 μL) and cyclohexane (500 μL). The cyclohexane layer was concentrated and analyzed by GC using an HP-5 column. Temperatures of the injector and detector were 250 and 280 °C, respectively. A temperature gradient system was used for the oven, starting at 100 °C and increasing up to 140 °C at a rate of 4 °C/min, and then increasing up to 170 °C for 8 min at a rate of 13 °C/min, and finally, increasing up to 200 °C at a rate of 5 °C/min. The peaks of authentic samples of D-glucose and L-glucose after treatment in the same manner were detected at 21.47 and 21.87 min.

2.5. Acid hydrolysis of 1–2 and determination of the absolute configuration of the aglycones of 1–2

A solution of compound **1** (17.0 mg) in 2 M HCl (17 mL) was stirred at 90 °C in a stoppered vial for 2 h. The reaction mixture was evaporated to dryness and then applied to an open ODS column (2 × 5 cm, 50 μm). The column was eluted with 50 mL H_2O and 50 mL MeOH, successively. The H_2O eluate was concentrated and then purified by HPLC to obtain the aglycone (1.8 mg). HPLC conditions were as follows: Hypersil NH_2 column (4.6 × 250 mm, 10 μm); solvent, MeCN–H_2O (85: 15); flow rate, 1 mL/min; column temperature, 30 °C; detector, RID-10A. The aglycone was detected at a t_R of 6.5 min.

A solution of compound **2** (6.5 mg) in 2 M HCl (6.5 mL) was stirred at 90 °C in a stoppered vial for 2 h and then treated in the same manner as compound **1** to obtain the aglycone (0.8 mg). As we expected, these two aglycones from **1** and **2** have the same chromatographic behavior and spectral data.

2-Methyl-L-erythritol (the aglycone of **1** and **2**): white powder, $[\alpha]^{18}_D$ −10.6 (*c* 0.085, H_2O), $[\alpha]^{18}_D$ −27.1 (*c* 0.07, MeOH); ^1H NMR (D_2O, 600 MHz): δ 3.76 (1H, dd, J = 2.6, 11.6 Hz, H-4a), 3.59 (1H, dd, J = 2.6, 8.7 Hz, H-3), 3.53 (1H, dd, J = 8.7, 11.6 Hz, H-4b), 3.51 (1H, d, J = 11.7 Hz, H-1a), 3.40 (1H, d, J = 11.7 Hz, H-1b), 1.10 (3H, s, 2-CH_3). ^{13}C NMR (D_2O, 150 MHz): 76.6 (C-2), 75.7 (C-3), 67.9 (C-1), 63.6 (C-4), 19.9 (2-CH_3).

Table 1
^{1}H (300 MHz) and ^{13}C NMR (75 MHz) data of compounds **1** and **2** in CD_3OD.

No.	**1**		**2**	
1	68.6	3.59 (o), 3.50 (o)	76.4	4.04 (d, 10.2), 3.47 (o)
2	74.6		74.9	
3	74.9	3.88 (brd, J = 8.4)	75.4	3.78 (dd, J = 7.5, 3.0)
4	72.6	4.24 (brd, J = 8.4), 3.66 (o)	63.8	3.88 (dd, J = 11.1, 3.0) 3.64 (o)
5	19.9	1.18 (s)	19.4	1.16 (s)
1′	105.1	4.43 (d, J = 7.2)	105.2	4.41 (d, J = 7.5)
2′	75.4	3.34 (o)	75.2	3.35 (o)
3′	77.9	3.49 (o)	77.9	3.45 (o)
4′	71.8	3.47 (o)	71.8	3.47 (o)
5′	75.6	3.63 (o)	75.7	3.63 (o)
6′	64.8	4.58 (brd, J = 11.4) 4.40 (dd, J = 11.4, 6.0)	64.8	4.60 (brd, J = 11.4) 4.40 (dd, J = 11.4, 6.0)
1″	169.2		169.1	
2″	115.9	6.49 (d, J = 15.6)	115.8	6.49 (d, J = 15.9)
3″	147.4	7.70 (d, J = 15.6)	147.5	7.71 (d, J = 15.9)
4″	126.8		126.8	
5″, 9″	107.2	6.97 (s)	107.2	6.98 (s)
6″, 8″	149.6		149.6	
7″	139.8		139.9	
6″,8″-OCH_3	57.1	3.94 (s)	57.1	3.95 (s)

All the signals were assigned by 1D and 2D NMR spectra.

2.6. Cell culture and nitrite determination

Mouse monocyte–macrophage RAW 264.7 cells (ATCC TIB-71) were purchased from the Chinese Academy of Science. RPMI 1640 medium, penicillin, streptomycin, and fetal bovine serum were purchased from Invitrogen (New York). Lipopolysaccharide (LPS), dimethylsulfoxide (DMSO), 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyltetrazolium bromide (MTT), and hydrocortisone were obtained from Sigma Co. (St. Louis, MO). RAW 264.7 cells were suspended in RPMI 1640 medium supplemented with penicillin (100 U/mL), streptomycin (100 μg/mL), and 10% heat-inactivated fetal bovine serum. The cells were harvested with trypsin and diluted to a suspension in fresh medium. The cells were seeded in 96-well plates with 1×10^5 cells/well and allowed to adhere for 2 h at 37 °C in 5% CO_2 in air. Then, the cells were treated with 1 μg/mL of LPS for 24 h with or without various concentrations of test compounds. DMSO was used as a solvent for the test compounds, which were applied at a final concentration of 0.2% (v/v) in cell culture supernatants. NO production was determined by measuring the accumulation of nitrite in the culture supernatant using Griess reagent [12]. Briefly, 100 μL of the supernatant from incubates was mixed with an equal volume of Griess reagent (0.1% N-[1-naphthyl]ethylenediamine and 1% sulfanilamide in 5% H_3PO_4). Cytotoxicity was determined by the MTT colorimetric assay, after 24 h of incubation with test compounds. The concentration of NO_2^- was calculated by a working line from 0, 1, 2, 5, 10, 20, 50, and 100 μM sodium nitrite solutions, and the inhibitory rate on NO production induced by LPS was calculated by the NO_2^- levels as follows:

$$\text{Inhibitory rate } (\%) = 100 \times \frac{[NO_2^-]_{LPS} - [NO_2^-]_{LPS+sample}}{[NO_2^-]_{LPS} - [NO_2^-]_{untreated}}.$$

Experiments were performed in triplicate, and data are expressed as the mean ± SD of three independent experiments.

3. Results and discussion

Compound **1** was obtained as a yellow amorphous powder with a molecular formula of $C_{22}H_{32}O_{13}$ by analysis of its HRESIMS spectrum. The ^{1}H and ^{13}C NMR spectra of **1** (Table 1) showed typical signals of a *trans*-double bond [H-2″ (δ 6.49, 1H, d, J = 15.6 Hz), H-3″ (δ 7.70, 1H, d, J = 15.6 Hz), C-2″ (δ 115.9), C-3″ (δ 147.4)]. The presence of a symmetrical 1,3,4,5-tetrasubstituted phenyl group was deduced from the H-atom signals at δ 6.97 (2H, s, H-5″, 9″) and the C-atom signals at δ 107.2 (C-5″, 9″), 126.8 (C-4″), 139.8 (C-7″), 149.6 (C-6″, 8″). Two methoxy groups are located at C-6″ and C-8″ due to the HMBC correlations of δ 3.94 (6H, s)/C-6″, 8″. Furthermore, the HMBC correlations of H-3″/C-4″, C-5″, C-9″, C-1″, and H-2″/C-1″, C-4″ revealed the presence of a *trans*-sinapoyl moiety. The ^{13}C NMR spectrum showed 11 other carbon signals including one anomeric carbon signal at δ 105.1 and one methyl group at δ 19.9. The remaining nine carbon signals are in the range of δ 60–80 ppm, suggesting a possible sugar and a possible polyalcohol moiety in the molecule. Acid hydrolysis of **1** with 2 M HCl yielded D-glucose (see Experimental section) [13]. The β-configuration was established due to the coupling constant of the anomeric proton signal at δ 4.43 (1H, d, J = 7.2 Hz, H-1′) and the ^{13}C NMR data for the glucose were assigned as δ 105.1 (C-1′), 75.4 (C-2′), 77.9 (C-3′), 71.8 (C-4′), 75.6 (C-5′), 64.8 (C-6′) by analysis of its HMQC and HMBC experiments. The polyalcohol moiety was elucidated as 2-methyl-1,2,3,4-butanetetrol by studying the remaining ^{1}H and ^{13}C NMR signals and by the correlation from HMBC and HMQC spectra. Furthermore, the HMBC correlations of H-6′ (δ 4.58, 4.40)/C-1″ and H-1′ (δ 4.43)/C-4 (δ_C 72.6), H-4 (δ 4.24, 3.66)/C-1′, suggesting that

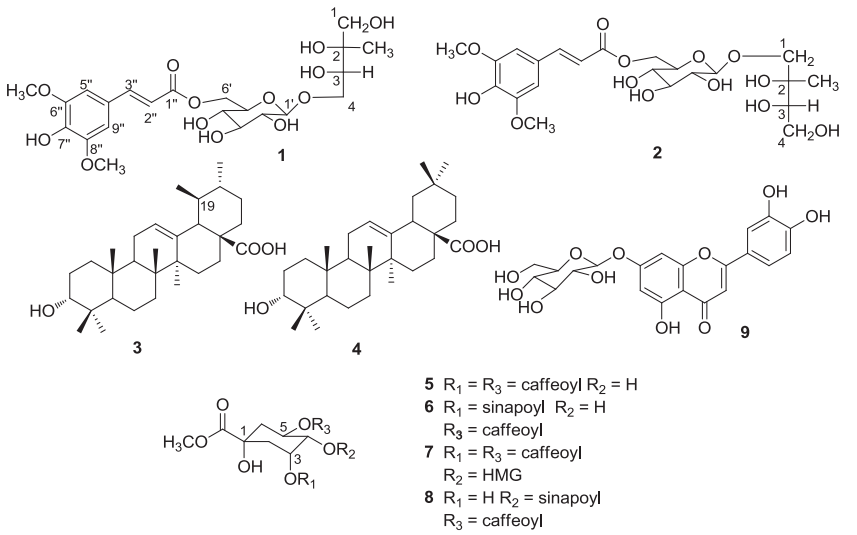

Fig. 1. Structures of compounds **1**–**9**.

the sinapoyl moiety was attached at C-6′ and the β-D-glucopyranose was established at C-4, respectively. The configuration of the aglycone was determined as (2*R*, 3*S*) by comparing its NMR data and optical rotation with those reported in the literature [14]. On the basis of the above evidence, the structure of **1** was elucidated as 2-methyl-L-erythritol-4-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside (Fig. 1).

Compound **2** was obtained as a yellow amorphous powder and had a molecular formula of $C_{22}H_{32}O_{13}$ established by HRESIMS. The ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1**, showing the presence of a *trans*-sinapoyl moiety, a 2-methyl-1,2,3,4-butanetetrol moiety and a glucosyl moiety, which was further elucidated as β-D-glucopyranose by the same method as described for compound **1**. In the HMBC spectrum, correlations of H-6′ (δ 4.60, 4.40)/C-1″ (δ 169.1), H-1 (δ 4.04, 3.47)/C-1′ (δ 105.2), H-1′ (δ 4.41)/C-1 (δ 76.4), suggesting the sinapoyl moiety was attached at C-6′ and the β-D-glucopyranose was established at C-1, respectively. The configuration of the aglycone of **2** was determined by using the same method as **1**. Thus, the structure of **2** was elucidated as 2-methyl-L-erythritol-1-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside.

2-Methyl-1,2,3,4-butanetetrol has two stereocenters and thus four stereoisomers: 2-methyl-D-erythritol, 2-methyl-L-erythritol, 2-methyl-D-threitol and 2-methyl-L-threitol (Fig. 2). These four stereoisomers, often being considered as SOA (secondary organic aerosol) components in the atmosphere, rarely exist in plants [15,16]. Only 2-methyl-D-erythritol and its glycosides were isolated in a few references [11,18]. 2-Methyl-D-erythritol, an important intermediate in the non-mevalonate biosynthesis of terpenoids [17], was isolated from *Torillis japonica* fruit [18], and its glycosides were obtained from *Pimpinella anisum* L.[11]. However, no reports have been published about 2-methyl-L-erythritol and its glycosides. In the present study, two 2-methyl-L-erythritol glycosides (**1** and **2**) were isolated from the fruit of *G. jasminoides*. This is the first report of 2-methyl-L-erythritol glycosides from plant. Based on this finding, we propose that 2-methyl-L-erythritol might be a new intermediate in the non-mevalonate biosynthesis of terpenoids.

In addition, the known compounds were identified as ursolic acid (**3**) [19,20], oleanolic acid (**4**) [21], methyl 3,4-di-*O*-caffeoylquinate (**5**) [9], methyl 5-*O*-caffeoyl-3-*O*-sinapoylquinate (**6**) [9], methyl 3,5-di-*O*-caffeoyl-4-*O*-(3-

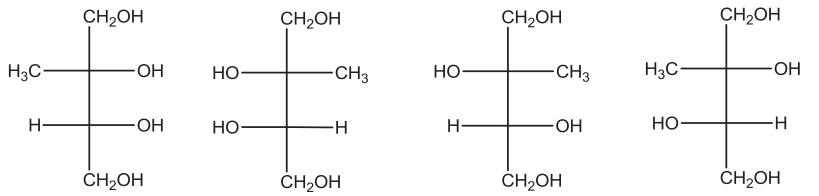

Fig. 2. The four stereoisomers of 2-methyl-1,2,3,4-butanetetrol.

Table 2
Inhibition of compounds **1**–**9** on the NO production in LPS-activated RAW 264.7 cells.

Compound	IC_{50} (mean ± SD)/μM
1	>100
2	>100
3	18.8 ± 1.1
4	>100
5	61.2 ± 7.8
6	>100
7	97.6 ± 8.8
8	52.1 ± 4.4
9	21.1 ± 1.5
Hydrocortisone[a]	64.3 ± 7.5

NO concentration of control group: 3.5 ± 0.2 μM. NO concentration of LPS-treated group: 34.0 ± 2.1 μM.
[a] Positive control.

hydroxy-3-methyl)glutaroylquinate (**7**) [9], methyl 5-*O*-caffeoyl-4-*O*-sinapoylquinate (**8**) [9], and luteolin-7-*O*-β-D-glucopyranoside (**9**) [22], by comparing their measured spectroscopic data with literature values.

All compounds isolated from the fruit of *G. jasminoides* were examined for their inhibitory effects on NO production induced by LPS in macrophages (Table 2). Cell viability was determined by the MTT method to find whether inhibition of NO production was due to cytotoxicity of the test compounds. As shown in Table 2, hydrocortisone (IC_{50} 64.3 ± 7.5 μM) was used as positive control. Compounds **3** and **9** showed significant inhibition effect with the IC_{50} values of 18.8 ± 1.1 μM and 21.1 ± 1.5 μM, respectively. Compounds **5** and **7** exhibited moderate activities, which were close to that of hydrocortisone. In comparison with IC_{50} values of ursolic acid (**3**) and oleanolic acid (**4**), we concluded compactly that the methyl group at position 19 is a determining factor in inhibiting NO production activity. Among the quinic acid derivatives with 5-*O*-caffeoyl functional group, the compounds with 3-*O*-caffeoyl (**5**) or 4-*O*-sinapoyl (**8**) had the best activities; when compound **6** was replaced by an additional *O*-HMG group at C-4 (**7**), the inhibitory activity was degraded. Furthermore, in comparison with IC_{50} values of **6** and **8**, it is found that the location of the sinapoyl moiety in the quinic acid plays an important role in defining the NO inhibitory effect.

In conclusion, the glycosides, triterpenoids, flavonoid and quinic acid derivatives isolated from the fruit of *G. jasminoides* were structurally diverse. In the NO production bioassay, compounds **3** and **9** showed significant inhibition effect, which provided candidates for the study of this medicinal plant.

Acknowledgments

The authors are grateful to Ms. Wen Li and Mr. Yi Sha of the Department of Instrumental Analysis, Shenyang Pharmaceutical University, for measuring the NMR and mass spectra.

References

[1] Ni HY, Zhang ZH, Fu HZ. Research and development of fructus Gardeniae. China J Chinese Materia Medica 2006;31:538–41.
[2] Chang WL, Wang HY, Shi LS, Lai JH, Lin HC. Immunosuppressive iridoids from the fruits of *Gardenia jasminoides*. J Nat Prod 2005;68:1683–5.
[3] Yu Y, Xie ZL, Gao H, Ma WW, Dai Y, Wang Y, et al. Bioactive iridoid glucosides from the fruit of *Gardenia jasminoides*. J Nat Prod 2009;72:1459–64.
[4] Chen QC, Youn UJ, Min BS, Bae KH. Pyronane monoterpenoids from the fruit of *Gardenia jasminoides*. J Nat Prod 2008;71:995–9.
[5] Yu Y, Gao H, Dai Y, Wang Y, Chen HR, Yao XS. Monoterpenoids from the fruit of *Gardenia jasminoides*. Helv Chim Acta 2010;93:763–71.
[6] Yu Y, Gao H, Dai Y, Yao XS. Advances in studies on chemical constituents in plants of Gardenia Ellis. Chin Tradit and Herbal Drugs 2010;41:148–53.
[7] Pfister S, Meyer P, Steck A, Pfander H. Isolation and structure elucidation of carotenoid-glycosyl esters in Gardenia fruits (*Gardenia jasminoides* Ellis) and Saffron (*Crocus sativus* Linne). J Agric Food Chem 1996;44:2612–5.
[8] Ichi T, LeBlanc JCY, Perreault D, Roewer I. Novel glycosidic constituents from Saffron. J Agric Food Chem 1997;45:1055–61.
[9] Kim HJ, Kim EJ, Seo SH, Shin CG, Jin C, Lee YS. Vanillic acid glycoside and quinic acid derivatives from Gardeniae fructus. J Nat Prod 2006;69:600–3.
[10] Mulligan MS, Hevel JM, Marletta MA, Ward PA. Tissue injury caused by deposition of immune complexes is L-arginine dependent. Proc Natl Acad Sci USA 1991;88:6338–42.
[11] Kitajima J, Ishikawa T, Fujimatu E, Kondho K, Takayanagi T. Glycosides of 2-C-methyl-D-erythritol from the fruits of anise, coriander and cumin. Phytochemistry 2003;62:115–20.
[12] Dirsch VM, Stuppner H, Vollmar AM. The Griess assay: suitable for a bio-guided fractionation of anti-inflammatory plant extracts? Planta Med 1998;64:423–6.
[13] Dai Y, Zhou GX, Kurihara H, Ye WC, Yao XS. Biphenyl glycosides from the fruit of *Pyracantha fortuneana*. J Nat Prod 2006;69:1022–4.
[14] Moen AR, Ruud K, Anthonsen T. Chemo-enzymatic synthesis of all isomers of 2-methylbutane-1,2,3,4-tetraol—important contributors to atmospheric aerosols. Eur J Org Chem 2007:1262–6.
[15] Claeys M, Graham B, Vas G, Wang W, Vermeylen R, Pashynska V, et al. Formation of secondary organic aerosols through photooxidation of isoprene. Science 2004;303:1173–6.
[16] Nozière B, González NJD, Karlson AKB, Pei YX, Redeby JP, Krejci R, et al. Atmospheric chemistry in stereo: a new look at secondary organic aerosols from isoprene.Geophys Res Lett 2011;38 L11807.
[17] Herz S, Wungsintaweekful J, Schuhr CA, Hecht S, Lüttgen H, Sagner S, et al. Biosynthesis of terpenoids: YgbB protein converts 4-diphosphocytidyl-2C-methyl-D-erythritol 2-phosphate to 2C-methyl-D-erythritol 2,4-cyclodiphosphate. Proc Natl Acad Sci USA 2000;97:2486–90.
[18] Kitajima J, Suzuki N, Ishikawa T, Tanaka Y. New hemiterpenoid pentol and monoterpenoid of *Torillis japonica* fruit, and consideration of the origin of apiose. Chem Pharm Bull 1998;46:1583–6.
[19] Huang PL, Wang LW, Lin CN. New triterpenoids of *Mallotus repandus*. J Nat Prod 1999;62:891–2.
[20] Jian Z, Cheng ZH, Yu BY, Geoffrey AC, Samuel XQ. Novel biotransformation of pentacyclic triterpenoid acids by *Nocardia* sp. NRRL 5646. Tetrahedron Lett 2005;46:2337–40.
[21] Jun H, Ruofan L, Jinrong L, Yong J. Synthesis and anion recognition of a novel oleanolic acid-based cyclic dimmer. Tetrahedron Lett 2011;52:4211–4.
[22] Lu Y, Foo LY. Flavonoid and phenolic glycosides from *Salvia officinalis*. Phytochemistry 2000;55:263–7.