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Original article

Chemical Constituents with Antihyperlipidemic Activities from *Desmodium triquetrum*

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ABSTRACT

Objective To study the chemical constituents from *Desmodium triquetrum* and their antihyperlipidemic activities. **Methods** The constituents of *D. triquetrum* were isolated and purified using various column chromatographies. Their chemical structures were elucidated using extensive spectroscopic methods. The lipid-lowering effects of the isolates were evaluated in HepG2 cells. **Results** Nine compounds were obtained from the ethanol extract of *D. triquetrum* and determined to be 6′-*O*-*cis*-*p*-coumaroyl-3,5-dihydroxyphenyl-β-*D*-glucopyranoside (**1**), tadehaginoside (**2**), rutin (**3**), quercetin-3-*O*-β-*D*-glucopyranoside (**4**), quercetin-3-*O*-β-*D*-galactopyranoside (**5**), 6-*O*-(*E*)-*p*-hydroxy-cinnamoyl-β-glucose (**6**), 6-*O*-(*E*)-*p*-hydroxy-cinnamoyl-α-glucose (**7**), kaempferol-3-*O*-β-*D*-rutinoside (**8**), and 3-*O*-β-D-galacopyranosyl (6-1)-α-*L*-rhamnosyl quercetin (**9**). Compounds **1** and **2** significantly reduced the intracellular content of total cholesterols and triglycerides. **Conclusion** Compound **1** is a new phenolic compound and exhibits potent anti-hyperlipidemic activity. Additionally, compounds **6** and **7** are isolated from *D. triquetrum* for the first time.

Key words

antihyperlipidemic activities; 6′-*O*-*cis*-*p*-coumaroyl-3,5-dihydroxyphenyl-β-*D*-glucopyranoside; *Desmodium triquetrum*; 6-*O*-(*E*)-*p*-hydroxy-cinnamoyl-β-glucose; 6-*O*-(*E*)-*p*-hydroxy-cinnamoyl-α-glucose

1. Introduction

Desmodium triquetrum (L.) DC is widely distributed in sub-tropical and Pacific regions of the world. Its leaves have been traditionally used for the treatment of diabetes, obesity, flu fever, sore throat, nephritis, cholestatic hepatitis, enteritis, bacillary dysentery, pregnant vomiting, and prostatic hyperplasia worldwide (Wang et al, 2007). Previous chemical studies disclosed the presence of secondary metabolites belonging to terpenes, flavanoids, and phenolic compounds.

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For instance, ursolic acid, (+) catechin, ilexgenin A (Wen et al, 2000), and salicylic acid (Lv et al, 1995) were obtained from this plant, respectively. In addition, tadehaginoside, a unique phenolic compound, was isolated from this plant and exhibited interesting activities in heptoprotection (Tang et al, 2014). As part of an ongoing investigation on discovery of naturally occurring bioactive agents from the plants of genus *Desmodium* Desv., a new phenolic compound, analog of tadehaginoside, together with eight known compounds were obtained from *D. triquetrum*. Herein, this paper mainly deals with the isolation of the new compound as well as the lipid-lowering effects of the isolates.

2. Materials and methods

2.1 General

Optical rotations were obtained on a Perkin-Elmer 341 Digital Polarimeter (USA). UV and IR spectra were recorded on Shimadzu UV2550 and FTIR−8400S Spectrometer (Japan), respectively. NMR spectra were obtained with a Bruker AV 600 NMR Spectrometer (with TMS as internal standard) (German). HR-ESI-MS was performed on an LTQ-Obitrap XL Spectrometer (Thermo Fisher Scientific, USA). Silica gel (100−200 and 300−400 mesh, Qingdao Marine Chemical Inc., China) was used for column chromatography. Precoated silica gel GF_{254} plates (Zhifu Huangwu Pilot Plant of Silica Gel Development, China) were used for TLC analysis. Sephadex LH-20 was purchased from GE Healthcare Bio-Sciences Co., Ltd. (Swiss). All solvents used were of analytical grade (Beijing Chemical Works, China). HepG2 cells originally from the American Type Culture Collection (USA), were obtained from China Union Medical University.

2.2 Plant materials

The whole plants of *Desmodium triquetrum* (L.) DC were collected in July 2013 from Haikou, Hainan Province, China and identified by Prof. Jian-ping Tian, School of Pharmaceutical Science, Hainan Medical University. A voucher specimen has been deposited there (Voucher specimen No. DT20130810).

2.3 Extraction and isolation

The whole plants of *D. triquetrum* (5.0 kg) were extracted with 70% ethanol for three times. Removal of the solvent under reduced pressure yielded the ethanol extract (500 g). The extract was subjected to chromatography on silica gel (100−200 mesh) column eluted with petroleum ether, ethyl acetate, and *n*-butanol, respectively. The *n*-BuOH fraction (200 g) was subjected to silica gel column chromatography using $CHCl_3$-MeOH (1:0→2:1) as eluent to yield five fractions (Frs. A−E). Fr. B was purified using Sephadex LH-20 and eluted with MeOH. The subfractions were further purified with semi-preparative HPLC (35% MeOH-H_2O) to yield compounds **1** (7.5 mg) and **2** (14.0 mg), Fr. C was purified firstly with Sephadex LH-20 column followed by semi-preparative HPLC (40% MeOH-H_2O) to yield compounds **3** (4.5 mg), **4** (4.0 mg), and **5** (5.0 mg). Fr. D was purified by Sephadex LH-20 column and then further isolated with semi-preparative HPLC (45% MeOH-H_2O) to yield compounds **6** (4.0 mg) and **7** (5.0 mg). Fr. E was purified with preparative HPLC (35% MeOH-H_2O) to yield compounds **8** (10.5 mg) and **9** (10.0 mg).

2.4 Cell culture

HepG2 cells were grown to 70%−80% confluence and then incubated in 0.02% BSA (Sigma-Aldrich)/DMEM (Gibco-BRL, USA) for 12 h. Cells were then washed and incubated with 1 μmol/L compounds or 1 mmol/L AMPK activator AICAR (Sigma-Aldrich, China) in 0.02% BSA + 100 μmol/L oleic acid/DMEM or 0.02% BSA + 100 μmol/L oleic acid/DMEM alone for 6 h. Subsequently, the cells were subjected to oil-red O staining or TC and TG determination.

3. Results and discussion

Repeated chromatography of *n*-BuOH-soluble extract over silica gel and Sephadex LH-20 columns, followed by semi-preparative HPLC purification afforded compounds **1**−**9** finally.

Compound **1**: white powder, the molecular formula $C_{21}H_{22}O_{10}$, was deduced from quasimolecular ion peak at *m/z* 457.1101 $[M + Na]^+$ (Calcd. for 457.1111) in the positive HR-ESI-MS spectrum. The IR spectrum showed the presence of hydroxyl groups (3380 cm^{-1}), a conjugated carbonyl group (1690 cm^{-1}), and a benzene ring (1602, 1560 cm^{-1}). The ^{1}H-NMR (600 MHz, CD_3OD) spectrum displayed signals attributed to AA′BB′ type aromatic protons at δ_H 7.60 (2H, d, J = 7.2 Hz, H-2″, 6″), 6.72 (2H, d, J = 7.2 Hz, H-3″, 5″), and one glucose moiety. The anomeric proton was resonated at δ_H 4.86 (1H, d, J = 7.8 Hz) and the anomeric carbon was observed at δ 102.3. The large coupling constant of anomeric proton (J = 7.8 Hz) suggested a β-configured configuration (unit A). The ^{1}H-NMR spectrum also exhibited signals at δ_H 6.08 (2H, s, H-2, 6), 5.95 (1H, s, H-4) attributing to one phloroglucinol moiety (unit B). Additionally, two low-field doublets observed at δ_H 6.85 (1H, d, J = 12.0 Hz, H-7″), 5.84 (1H, d, J = 12.0 Hz, H-8″) are characteristic of α and β protons of a *cis*-double bond conjugated to a carbonyl group. The ^{13}C-APT (150 MHz, CD_3OD) exhibited signals which were clearly recognized as individual carbons by combination of HSQC and HMBC analyses as well as comparing with the reported data of tadehaginoside (Wen et al, 2000). These data were attributed to be δ 102.3 (C-1′), 74.9 (C-2′), 78.0 (C-3′), 71.7 (C-4′), 75.6 (C-5′), 64.3 (C-6′), 97.1 (C-2, 6), 160.2 (C-3, 5), 98.3 (C-4), 127.8 (C-1″), 133.8 (C-2″, 6″), 116.9 (C-3″, 5″), 160.2 (C-4″), 145.7 (C-7″), 116.0 (C-8″), 168.3 (C-9″). This elucidation unambiguously confirmed the presence of the three units of a glucosyl group, a phloroglucinol moiety, and a *cis p*-coumaroyl group. The above structural elucidation

was further confirmed by HSQC, ^{1}H-^{1}H COSY, and HMBC spectral analysis. The HMBC correlations between the olifenic protons and the carbonyl and benzene ring showed the presence of a *cis*-*p*-coumaroyl moiety (unit C). The linkages of units A, B, and C were successfully established by HMBC correlations between the anomeric proton (H-1′) at δ_H 4.86 and C-1 at δ_C 160.9. The correlations from H-6′ at δ_H 4.31, 4.45 to C-9″ at δ_C 168.3 are depicted in Figure 1. The spectroscopic data of compound **1** were superposable upon those of tadehaginoside (Wen et al, 2000), apart from the configuration of $\Delta^{7''(8'')}$ double bond. The observed NOE correlation from H-7″ and H-8″ further confirmed the *cis* configuration of the double bond. Based on these extensive analyses, the structure of compound **1** was fully established as 6′-*O*-*cis*-*p*-coumaroyl-3,5-dihydroxyphenyl β-*D*-glucopyranoside, and was characterized as a new phenolic compound as shown in Figure 2.

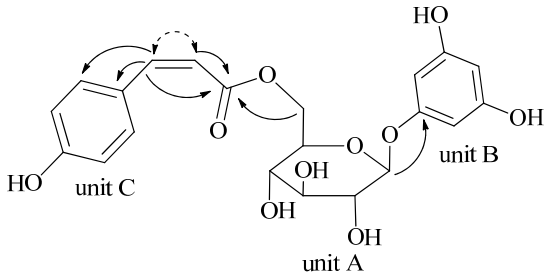

Figure 1 Key HMBC ( ) and NOE correlations ( ) of compound 1

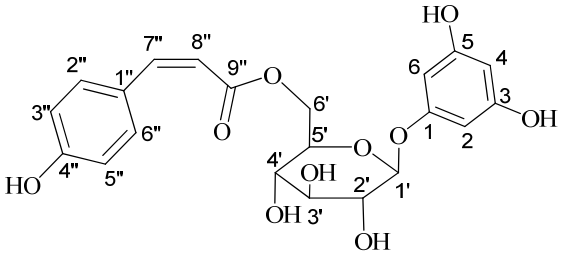

Figure 2 Chemical structure of compound 1

Compound **1**: white powder (MeOH); $[\alpha]_D^{25}$ −30° (*c* 0.1, MeOH). IR ν^{KBr}_{max} (cm^{-1}): 3380, 1693, 1604, 1560. ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 6.08 (2H, s, H-2, 6), 5.95 (1H, s, H-4), 7.60 (2H, d, *J* = 7.2 Hz, H-2″, 6″), 6.72 (2H, d, *J* = 7.2 Hz, H-3″, 5″), 6.85 (1H, d, *J* = 12.0 Hz, H-7″), 5.84 (1H, d, *J* = 12.0 Hz, H-8″), 4.86 (1H, d, *J* = 7.8 Hz, H-1′), 4.31 (1H, d, *J* = 10.8 Hz, H-6′a), 4.45 (1H, dd, *J* = 10.8, 2.0 Hz, H-6′b), 3.61 (1H, brs, H-5′), 3.40-3.44 (3H, m, H-2′, 3′, 4′). ^{13}C-NMR (150 MHz, CD_3OD) *δ*: 160.3 (C-1) 97.1 (C-2, 6), 160.2 (C-3, 5), 98.3 (C-4), 102.3 (C-1′), 74.9 (C-2′), 78.0 (C-3′), 71.7 (C-4′), 75.6 (C-5′), 64.3 (C-6′), 127.8 (C-1″), 133.8 (C-2″, 6″), 116.9 (C-3″, 5″), 160.2 (C-4″), 145.7 (C-7″), 116.0 (C-8″), 168.3 (C-9″).

Compound **2**: white powder (MeOH). HR-ESI-MS *m*/*z* 457.1104 $[M + Na]^+$. ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 6.10 (2H, s, H-2, 6), 5.97 (1H, s, H-4), 7.47 (2H, d, *J* = 7.2 Hz, H-2″, 6″), 6.80 (2H, d, *J* = 7.2 Hz, H-3″, 5″), 7.62 (1H, d, *J* = 16.2 Hz, H-7″), 6.40 (1H, d, *J* = 16.2 Hz, H-8″), 4.28 (1H, dd, *J* = 11.4, 6.6 Hz, H-6′a), 4.54 (1H, dd, *J* = 11.4, 2.0 Hz, H-6′b), 3.67 (1H, brs, H-5′), 3.41-3.48 (3H, m, H-2′, 3′, 4′). ^{13}C-NMR (150MHz, CD_3OD) *δ*: 160.9 (C-1), 97.0 (C-2, 6), 160.2 (C-3, 5), 98.2 (C-4), 102.2 (C-1′), 74.9 (C-2′), 78.1 (C-3′), 71.9 (C-4′), 75.6 (C-5′), 64.8 (C-6′), 127.4 (C-1″), 131.4 (C-2″, 6″), 116.9 (C-3″, 5″), 160.9 (C-4″), 147.0 (C-7″), 115.1 (C-8″), 169.4 (C-9″). Compound **2** was identified as tadehaginoside by comparison of the NMR data with the literature value (Wen et al, 2000).

Compound **3**: light yellow powder (MeOH). ^{1}H-NMR (600 MHz, DMSO-d_6) *δ*: 7.54 (1H, d, *J* = 2.0 Hz, H-2′), 7.52 (1H, dd, *J* = 8.4, 2.0 Hz, H-6′), 6.84 (1H, d, *J* = 8.4 Hz, H-5′), 6.38 (1H, d, *J* = 1.8 Hz, H-8), 6.19 (1H, d, *J* = 1.8 Hz, H-6), 5.33 (1H, d, *J* = 7.2 Hz, H-1″), 4.38 (1H, s, H-1‴), 3.05−3.70 (m, sugar protons), 0.98 (3H, d, *J* = 6.0 Hz, H-6‴). ^{13}C-NMR (150 MHz, DMSO-d_6) *δ*: 156.5 (C-2), 133.2 (C-3), 177.2 (C-4), 161.2 (C-5), 98.6 (C-6), 164.1 (C-7), 93.5 (C-8), 156.3 (C-9), 103.8 (C-10), 121.3 (C-1′), 115.1 (C-2′), 144.6 (C-3′), 148.3 (C-4′), 116.2 (C-5′), 121.0 (C-6′), 101.1 (C-1″), 74.0 (C-2″), 76.4 (C-3″), 69.9 (C-4″), 75.8 (C-5″), 66.9 (C-6″), 100.6 (C-1‴), 70.3 (C-2‴), 70.4 (C-3‴), 71.7 (C-4‴), 68.1 (C-5‴), 17.6 (C-6‴). Compound **3** was identified as rutin by comparison of the NMR data with the literature value (Tang et al, 2000).

Compound **4**: yellow powder (MeOH). ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 6.19 (1H, brs, H-6), 6.37 (1H, brs, H-8), 6.85 (1H, d, *J* = 7.2 Hz, H-5′), 7.56 (1H, d, *J* = 1.8 Hz, H-2′), 7.58 (1H, dd, *J* = 7.2, 1.8 Hz, H-6′), 5.23 (1H, d, *J* = 7.2 Hz, H-1″). ^{13}C-NMR (150 MHz, CD_3OD) *δ*: 158.2 (C-2), 135.7 (C-3), 179.2 (C-4), 162.6 (C-5), 100.0 (C-6), 165.8 (C-7), 94.8 (C-8), 159.2 (C-9), 105.5 (C-10), 122.6 (C-1′), 115.9 (C-2′), 145.5 (C-3′), 149.6 (C-4′), 117.8 (C-5′), 122.7 (C-6′), 101.2 (C-1″), 74.9 (C-2″), 77.8 (C-3″), 69.6 (C-4″), 76.7 (C-5″), 61.6 (C-6″). Compound **4** was identified as quercetin-3-*O*-β-*D*-glucopyranoside by comparison of the NMR data with the literature value (Li et al, 2010).

Compound **5**: brown yellow powder (MeOH). ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 7.71 (1H, dd, *J* = 7.2, 1.8 Hz, H-6′), 7.57 (1H, d, *J* = 1.8 Hz, H-2′), 6.85 (1H, d, *J* = 7.2 Hz, H-5′), 6.37 (1H, brs, H-8), 6.19 (1H, brs, H-6), 5.23 (1H, d, *J* = 7.2 Hz, glu-H-1). ^{13}C- NMR (150 MHz, CD_3OD) *δ*: 158.2 (C-2), 135.7 (C-3), 179.2 (C-4), 162.6 (C-5), 100.0 (C-6), 165.8 (C-7), 94.8 (C-8), 159.1 (C-9), 105.1 (C-10), 122.6 (C-1′), 115.5 (C-2′), 145.5 (C-3′), 149.6 (C-4′), 115.9 (C-5′), 122.7 (C-6′), 101.4 (C-1″), 75.3 (C-2″), 73.0 (C-3″), 70.8 (C-4″), 69.6 (C-5″), 61.6 (C-6″). Compound **5** was identified as quercetin-3-*O*-β-*D*-galactopyranoside by comparison of the NMR data with the literature value (Tang et al, 2008).

Compound **6**: white powder (MeOH). ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 7.61 (1H, d, *J* = 18.0 Hz, H-7), 7.44 (2H, d, *J* = 7.8 Hz, H-3, 5), 6.79 (2H, d, *J* = 7.8 Hz, H-2, 6), 6.30 (1H, d, *J* = 18.0 Hz, H-8), 4.43 (1H, d, *J* = 7.8 Hz, H-1′). ^{13}C-NMR (150MHz, CD_3OD) *δ*: 127.3 (C-1), 131.3 (C-2, 6), 117.0 (C-3, 5), 161.4 (C-4), 146.8 (C-7), 115.2 (C-8), 169.3 (C-9), 98.4 (C-1′), 73.9 (C-2′), 78.1 (C-3′), 71.9 (C-4′), 75.6 (C-5′), 65.1 (C-6′). Compound **6** was identified as 6-*O*-(*E*)-*p*-hydroxy-

cinnamoyl-β-glucose by comparison of the NMR data with the literature value (Wang et al, 2007).

Compound **7**: white powder (MeOH). ^{1}H-NMR (600 MHz, CD_3OD) δ: 7.61 (1H, d, J = 18.0 Hz, H-7), 7.45 (2H, d, J = 7.8 Hz, H-3, 5), 6.81 (2H, d, J = 7.8 Hz, H-2, 6), 6.34 (1H, d, J = 18.0 Hz, H-8), 5.10 (1H, d, J = 2.4 Hz, H-1′). ^{13}C-NMR (150 MHz, CD_3OD) δ: 127.3 (C-1), 131.3 (C-2, 6), 117.0 (C-3, 5), 161.4 (C-4), 146.9 (C-7), 115.1 (C-8), 169.4 (C-9), 94.2 (C-1′), 72.2 (C-2′), 76.4 (C-3′), 71.0 (C-4′), 74.9 (C-5′), 65.0 (C-6′). Compound **7** was identified as 6-*O*-(*E*)-*p*-hydroxy-cinnamoyl-α-glucose by comparison of the NMR data with the literature value (Wang et al, 2000).

Compound **8**: yellow powder (MeOH). ^{1}H-NMR (600MHz, DMSO-d_6) δ: 7.97 (2H, d, J = 7.8 Hz, H-2′, 6′), 6.87 (2H, d, J = 7.2 Hz, H-3′, 5′), 6.41 (1H, d, J = 1.8 Hz, H-8), 6.20 (1H, d, J = 1.8 Hz, H-6), 5.30 (1H, d, J = 7.2 Hz, H-1″), 4.37 (1H, d, J = 1.2 Hz, H-1‴), 3.05−3.70 (m, sugar protons), 0.99 (3H, d, J = 6.0 Hz, H-6‴). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 156.7 (C-2), 133.1 (C-3), 177.2 (C-4), 161.1 (C-5), 98.6 (C-6), 164.1 (C-7), 93.6 (C-8), 156.3 (C-9), 103.8 (C-10), 120.7 (C-1′), 130.7 (C-2′, 6′), 114.9 (C-3′, 5′), 159.7 (C-4′), 101.2 (C-1″), 74.1 (C-2″), 76.3 (C-3″), 69.8 (C-4″), 75.6 (C-5″), 66.8 (C-6″), 100.6 (C-1‴), 70.2 (C-2‴), 70.5 (C-3‴), 71.7 (C-4‴), 68.1 (C-5‴), 17.6 (C-6‴). Compound **8** was identified as kaempferol-3-*O*-β-*D*-rutinoside by comparison of the NMR data with the literature value of (Tang et al, 2000).

Compound **9**: yellow powder (MeOH). ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 1.06 (3H, d, J = 6.0 Hz, rha-CH_3), 4.40 (1H, d, J = 1.8 Hz, H-1‴), 5.34 (1H, d, J = 7.2 Hz, H-1″), 6.19 (1H, brs, H-6), 6.38 (1H, brs, H-8), 6.82 (1H, d, J = 7.8 Hz, H-5′), 7.53 (1H, brs, H-2′), 7.65 (1H, dd, J = 7.8, 1.8 Hz, H-6′), 12.59 (1H, s, 5-OH). ^{13}C-NMR (150MHz, DMSO-d_6) δ: 156.3 (C-2), 133.4 (C-3), 177.3 (C-4), 161.1 (C-5), 98.6 (C-6), 164.1 (C-7), 93.5 (C-8), 156.5 (C-9), 103.8 (C-10), 121.8 (C-1′), 115.1 (C-2′), 144.7 (C-3′), 148.4 (C-4′), 115.9 (C-5′), 120.9 (C-6′), 101.1(C-1″), 71.0 (C-2″), 73.5 (C-3″), 67.9 (C-4″), 73.0 (C-5″), 65.0 (C-6″), 99.9 (C-1‴), 70.2 (C-2‴), 70.5 (C-3‴), 71.8 (C-4‴), 68.2 (C-5‴), 17.6 (C-6‴). Compound **9** was identified as 3-*O*-β-*D*-galacopyranosyl (6-1)-α-*L*-rhamnosyl quercetin by comparison of the NMR data with the literature value (Zhang et al, 2001).

4. Conclusion

All the isolates are evaluated for their anti-hyperlipidemic activities. Among them, compounds **1** and **2** significantly reduce the oil-red O staining TC and TG (Figure 3) accumulation in HepG2 cells, suggesting that they play a vital role in the anti-hyperlipidemic activity of *D. triquetrum*. Considering their potent lipid-modulating activity and high concentration in *D. triquetrum*, phenolic compounds, particular tadehaginoside, are assigned as the main active components accounting for its anti-hyperlipidemic effect.

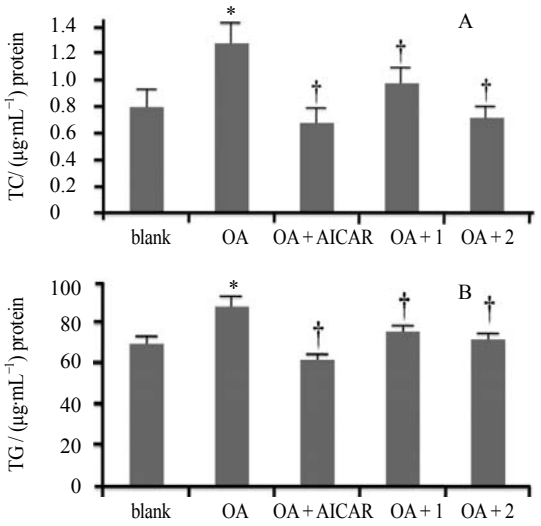

Figure 3 TC (A) and TG (B) accumulation in HepG2 cells

$^*P < 0.05$ *vs* normal group; $^\dagger P < 0.05$ *vs* OA group

References

Li CM, Wang T, Zhang W, Han LF, Liu EW, Gao XM, 2010. Isolation and identification of chemical constituents from the flowers of *Abelmoschus manihot* (L.) Medic. *J Shenyang Pharm Univ* 7 (10): 804-805.

Lv HC, He WX, Yang QW, Yuan HZ, 1995. Studies on the constituents of *Desmodium triquetrum* (L.) DC. *Chin Tradit Herb Drugs* 26(5): 180-182.

Tang AC, Chen XY, Lu QY, Zheng N, Wei YF, Wu XY, 2014. Antihepatotoxic effect of tadehaginoside, extracted from *Tadehagi triquetrum* (L.), against CCl_4-lesioned rats through activating the Nrf2 signaling pathway and attenuating the inflammatory response. *Inflammation* 37(4): 1006-1014.

Tang WZ, Su DM, Yu SS, Liu J, Qu J, Liu YB, 2008. Investigation on flavonoids from fruits of *Illicium oligandrum*. *Chin Tradit Herb Drugs* 39(10): 1452-1453.

Tang YP, Wang Y, Lou FC, Li YF, Wang JH, 2000. Flavonol glycosides from the leaves of *Ginkgo biloba*. *Acta Pharm Sin* 35(5): 363-366.

Wang YQ, Feng BM, Tang L, Shi LY, Shi HF, 2007. Research of *Desmodium triquetrum* (L.) DC. *Dalian Univ* 28(3): 49-51.

Wen XD, Lu MY, Tang RJ, Zheng XZ, Inoue K, 2000. Studies on the chemical constituents of *Desmodium triquetrum* (L.) DC. (II). *Chin Tradit Herb Drugs* 31(1): 3-5.

Wen XD, Zheng XZ, Shi JX, Inoue K, 1999. Studies on the chemical constituents of *Desmodium triquetrum* (L.) DC. (I). *Chin Tradit Herb Drugs* 30 (4): 252-253.

Xu QM, Shi F, Xu LZ, Yang SL, Li GQ, 2006. Studies on flavonoids in the leaves of *Uvaria kweichowensis*. *J Shenyang Pharm Univ* 23(5): 278-279.

Yang QW, Liang XH, Wang YP, 1981. Studies on the constituents of *Desmodium triquetrum* (L.) DC. *Acta Bot Sin* 31(2): 128-131.

Zhang PC, Xu SX. 2001. Chemical constituents from the leaves of *Grataegus pinnztifida* Bge. var. *major* N. E. Br. *Acta Pharm Sin* 36(10): 754-757.