文章编号:1001-6880(2011)06-0999-03

旋覆花的化学成分研究

覃江江[1],朱佳娴[1],朱　燕[1],严　岚[1],金慧子[1*],张卫东[1,2*]

[1]上海交通大学药学院,上海 200240;[2]第二军医大学药学院,上海 200433

摘　要:通过应用硅胶柱色谱,Sephadex LH-20 柱色谱,以及高效液相制备色谱等手段,从旋覆花地上部分分离纯化得到 10 个化合物,再通过光谱学方法,并结合化合物的理化性质鉴定为泽兰内酯(1)、7-羟基香豆素(2)、瑞香素(3)、东莨菪素(4)、蟛蜞菊内酯(5)、枸橼苦素(6)、杜仲树脂酚(7)、丁香酸(8)、香草酸(9)和异丁香酸(10)。化合物 1 ~ 10 均为首次从旋覆花属植物中分离得到。

关键词:旋覆花;化学成分;香豆素类化合物

中图分类号:R284.2;Q946.91　　**文献标识码**:A

Chemical Constituents from the Aerial Parts of *Inula japonica* Thunb.

QIN Jiang-jiang[1],ZHU Jia-xian[1],ZHU Yan[1],YAN Lan[1],JIN Hui-zi[1*],ZHANG Wei-dong[1,2*]

[1]*School of Pharmacy,Shanghai Jiao Tong University,Shanghai 200240,China*;

[2]*School of Pharmacy,Second Military Medical University,Shanghai 200433,China*

Abstract: Ten compounds were isolated and purified by column chromatography with silica gel,Sephadex LH-20 and preparative HPLC from the aerial parts of *Inula japonica* Thunb.. On the basis of physicochemical properties and spectroscopic data,their structures were identified as ayapin (**1**),7-hydroxycoumarin (**2**),daphnetin (**3**),scopoletin (**4**),wedelolactone (**5**),citrusin C (**6**),medioresinol (**7**),syringic acid (**8**),vanillic acid (**9**),and isovanillic acid (**10**). Compounds **1-10** were isolated from *I. japonica* for the first time.

Key words: *Inula japonica* Thunb.; chemical constituents; coumarin

Introduction

Inula japonica Thunb.,which belongs to Asteraceae,is widespread in Europe,Africa,Asia,and Mediterranean[1]. As one of the most important members in this genus,*I. japonica* has been reported to possess diverse biological activities,such as anti-tumor[2-4],anti-diabetic[5],and hypolipidemic[5] activities. During our search for bioactive compositions from this plant,anthranilic acid derivatives[6] and sesquiterpenes[7] have been reported by us before. In this paper,we described the isolation and structure elucidation of coumarins and other constituents which were isolated from this genus for the first time.

Received January 15,2010;Accepted April 21,2010

Foundation Item:This research project was supported by the Scientific Foundation of Shanghai China (08DZ1971302).

* Corresponding author Tel:86-21-34205989;E-mail:kimhz@sjtu.edu.cn;wdzhangy@hotmail.com

Experimental

General

^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 spectrometers at 500 and 125 MHz,respectively. ESIMS spectra were recorded on Varian MAT-212 mass spectrometer. A preparative column (Shimadzu PRC-ODS EV0233) was used for preparative HPLC (Shimadzu LC-6AD). All solvents used were of analytical grade (Shanghai Chemical Company,Ltd.). TLC analysis was run on $HSGF_{254}$ silica gel plates (10-40 μm,Yantai,China). Column chromatography was performed on silica gel (100-200,200-300 mesh,Yantai,China),silica gel H (10-40 μm,Qingdao,China) and Sephadex LH-20 (Pharmacia Co. Ltd.).

Plant material

The aerial parts of *I. japonica* were collected in Anhui province,PR China,in October,2006,and were authenticated by Professor Huang Baokang,Department of Pharmacognosy,School of Pharmacy,Second Military

Medical University. A voucher specimen (No. 2007XFH1) was deposited at School of Pharmacy, Shanghai Jiao Tong University.

Extraction and isolation

The dried aerial parts of *I. japonica* (20.0 kg) were powdered and extracted with 95% ethanol for three times at room temperature. The ethanolic extract was successively partitioned with petroleum ether (PE), CH_2Cl_2, EtOAc, and *n*-BuOH, respectively. The CH_2Cl_2 fraction (84.5 g) was chromatographed on a silica gel column eluting with a step gradient of CH_2Cl_2-MeOH (100:0, 50:1, 20:1, 10:1, 5:1, 2:1, 1:1) to give subfractions. Then subfractions were isolated and purified in a combination of sicila gel, Sephadex LH-20 and preparative HPLC to afford compounds **3** (6.0 mg), **4** (10.8 mg), **5** (6.6 mg), **6** (3.0 mg), **7** (3.0 mg), **8** (16.0 mg), **9** (4.0 mg), and **10** (26.0 mg). And from PE fraction (100.8 g), **1** (4.0 mg) and **2** (6.5 mg) were obtained.

Results and Discussion

Ayapin (1) White amorphous powder, ESI-MS *m/z* 213 $[M+Na]^+$, 189 $[M-H]^-$. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.58 (1H, d, J = 10.0 Hz, H-4), 6.83 (2H, s, H-5, 8), 6.28 (1H, d, J = 10.0 Hz, H-3), 6.07 (2H, s, H-11); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 161.2 (C-2), 113.5 (C-3), 143.4 (C-4), 105.0 (C-5), 144.9 (C-6), 151.3 (C-7), 98.4 (C-8), 143.4 (C-9), 112.7 (C-10), 102.4 (11-OCH_2O-). The MS and NMR data were consistent with those of ayapin [7].

7-Hydroxycoumarin (2) White amorphous powder, ESI-MS *m/z* 163 $[M+H]^+$, 161 $[M-H]^-$. ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 10.53 (1H, brs, 7-OH), 7.92 (1H, d, J = 9.0 Hz, H-4), 7.52 (1H, d, J = 8.0 Hz, H-5), 6.79 (1H, dd, J = 8.0, 2.0 Hz, H-6), 6.71 (1H, d, J = 2.0 Hz, H-8), 6.20 (1H, d, J = 9.0 Hz, H-3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 161.2 (C-2), 113.0 (C-3), 144.4 (C-4), 129.6 (C-5), 111.3 (C-6), 160.3 (C-7), 102.1 (C-8), 155.4 (C-9), 111.2 (C-10). The MS and NMR data were consistent with those of 7-hydroxycoumarin [8].

Daphnetin (3) White amorphous powder, ESI-MS *m/z* 201 $[M+Na]^+$, 177 $[M-H]^-$. ^{1}H NMR (CD_3OD, 500 MHz) δ: 7.85 (1H, d, J = 10.0 Hz, H-4), 7.01 (1H, d, J = 8.0 Hz, H-5), 6.84 (1H, d, J = 8.0 Hz, H-6), 6.20 (1H, d, J = 10.0 Hz, H-3); ^{13}C NMR (CD_3OD, 125 MHz) δ: 163.5 (C-2), 112.1 (C-3), 146.7 (C-4), 120.2 (C-5), 113.9 (C-6), 151.1 (C-7), 133.5 (C-8), 145.0 (C-9), 113.8 (C-10). The MS and NMR data were consistent with those of daphnetin [9].

Scopoletin (4) White amorphous powder, ESI-MS *m/z* 193 $[M+H]^+$, 215 $[M+Na]^+$. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.60 (1H, d, J = 10.0 Hz, H-4), 6.92 (1H, s, H-5), 6.85 (1H, s, H-8), 6.27 (1H, d, J = 10.0 Hz, H-3), 3.95 (3H, s, 6-OCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 161.4 (C-2), 113.4 (C-3), 143.3 (C-4), 107.5 (C-5), 150.3 (C-6), 149.7 (C-7), 103.2 (C-8), 144.0 (C-9), 111.5 (C-10), 56.4 (6-OCH_3). The MS and NMR data were consistent with those of scopoletin [10].

Wedelolactone (5) White amorphous powder, ESI-MS *m/z* 651 $[2M+Na]^+$, 313 $[M-H]^-$, 627 $[2M-H]^-$. ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 10.80 (1H, brs, 5-OH), 9.38 (2H, brs, 11, 12-OH), 7.25 (1H, s, H-10), 7.17 (1H, s, H-13), 6.63 (1H, s, H-6), 6.46 (1H, s, H-8), 3.82 (3H, s, 7-OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 158.8 (C-1), 101.6 (C-2), 155.2 (C-3), 96.7 (C-4), 154.8 (C-5), 93.2 (C-6), 162.2 (C-7), 98.1 (C-8), 157.7 (C-9), 104.5 (C-10), 145.4 (C-11), 144.3 (C-12), 98.8 (C-13), 148.8 (C-14), 113.7 (C-15), 55.7 (3H, s, 7-OCH_3). The MS and NMR data were consistent with those of wedelolactone [11].

Citrusin C (6) White amorphous powder, ESI-MS *m/z* 349 $[M+Na]^+$, 325 $[M-H]^-$. ^{1}H NMR (CD_3OD, 500 MHz) δ: 7.08 (1H, d, J = 8.2 Hz, H-6), 6.82 (1H, d, J = 1.8 Hz, H-3), 6.72 (1H, dd, J = 8.2, 1.8 Hz, H-5), 5.94 (1H, m, H-8), 5.03 (2H, m, H-9), 4.84 (1H, d, J = 7.5 Hz, H-1′), 3.86 (1H, dd, J = 12.2, 1.5 Hz, H-6′a), 3.83 (3H, s, 2-OCH_3), 3.68 (1H, dd, J = 12.0, 5.0 Hz, H-6′b), 3.48 (1H, m, H-2′), 3.45 (1H, m, H-5′), 3.38 (2H, m, H-3′, 4′), 3.33 (1H, m, H-7); ^{13}C NMR (CD_3OD, 125 MHz) δ: 146.7 (C-1), 151.1 (C-2), 114.5 (C-3), 136.8 (C-4), 122.4 (C-5), 118.6 (C-6), 41.1 (C-7), 139.3 (C-8), 116.1 (C-9), 103.4 (C-1′), 75.3 (C-2′), 78.5

(C-3′), 71.7(C-4′), 78.2(C-5′), 62.8(C-6′), 57.0 (2-OCH_3). The MS and NMR data were consistent with those of citrusin C [12].

Medioresinol (7) White amorphous powder, ESI-MS *m/z* 389 $[M+H]^+$, 387 $[M-H]^-$. ^1H NMR ($CDCl_3$, 500 MHz) δ: 6.90(1H, d, J = 8.0 Hz, H-5′), 6.88 (1H, d, J = 2.0 Hz, H-2′), 6.82(1H, dd, J = 8.0, 2.0 Hz, H-6′), 6.59(2H, s, H-2, 6), 5.59(1H, brs, 4′-OH), 5.48(1H, brs, 4-OH), 4.75(1H, d, J = 4.5 Hz, H-7′), 4.72(1H, d, J = 4.5 Hz, H-7), 4.26(2H, m, H-9), 3.91(9H, s, 3, 5, 3′-OCH_3), 3.90(2H, m, H-9′), 3.10(2H, m, H-8, 8′); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 134.3(C-1), 102.8(C-2, 6), 147.2(C-3, 5), 132.9(C-4), 86.2(C-7), 54.4(C-8), 71.9(C-9), 132.2(C-1′), 108.6(C-2′), 145.3(C-3′), 146.7 (C-4′), 114.3(C-5′), 119.0(C-6′), 85.8(C-7′), 54.1(C-8′), 71.6(C-9′), 56.4(3, 5-OCH_3), 56.0 (3′-OCH_3). The MS and NMR data were consistent with those of medioresinol [13].

Syringic acid (8) Yellow amorphous powder, ESI-MS *m/z* 221 $[M+Na]^+$, 197 $[M-H]^-$. ^1H NMR(DMSO-d_6, 500 MHz) δ: 12.58(1H, brs, 7-COOH), 9.18 (1H, brs, 4-OH), 7.21(2H, s, H-2, 6), 3.80(6H, s, 3, 5-OCH_3); ^{13}C NMR(DMSO-d_6, 125 MHz) δ: 120.4 (C-1), 106.9(C-2, 6), 147.4(C-3, 5), 140.2(C-4), 167.2(C-7), 56.0(3, 5-OCH_3). The MS and NMR data were consistent with those of syringic acid [14].

Vanillic acid (9) White amorphous powder, ESI-MS *m/z* 167 $[M-H]^-$. ^1H NMR (CD_3OD, 500 MHz) δ: 7.57(1H, brs, H-2), 7.52(1H, brd, J = 8.0 Hz, H-6), 6.80(1H, d, J = 8.0 Hz, H-5), 3.89(3H, s, 3-OCH_3); ^{13}C NMR(CD_3OD, 125 MHz) δ: 123.0(C-1), 114.0(C-2), 151.5(C-3), 148.4(C-4), 115.5 (C-5), 124.9(C-6), 170.0(C-7), 56.4(3-OCH_3). The MS and NMR data were consistent with those of vanillic acid [15].

Isovanillic acid (10) White amorphous powder, ESI-MS *m/z* 167 $[M-H]^-$. ^1H NMR(CD_3OD, 500 MHz) δ: 7.56(1H, dd, J = 8.0, 2.0 Hz, H-6), 7.55(1H, d, J = 2.0 Hz, H-2), 6.84(1H, d, J = 8.0 Hz, H-5), 3.89 (3H, s, 4-OCH_3); ^{13}C NMR(CD_3OD, 125 MHz) δ: 123.1(C-1), 115.8(C-2), 148.6(C-3), 152.6(C-4), 113.8(C-5), 125.3(C-6), 170.1(C-7), 56.4(4-OCH_3). The MS and NMR data were consistent with those of isovanillic acid [16].

References

1 Lin R, Yu DJ, Wu ZY. *Inula* L. In: Flora of China. Beijing: Science Press, 1989, 263-281.

2 Qin JJ, Jin HZ, Zhang WD, *et al*. Japonicones A-D, bioactive dimeric sesquiterpenes from *Inula japonica* Thunb.. *Bioorg Med Chem Lett*, 2009, 19: 710-713.

3 Wang CM, Jia ZJ, Zheng RL. The effects of 17 sesquiterpenes on cell viability and telomerase activity in the human ovarian cancer cell line HO-8910. *Planta Med*, 2007, 73: 180-184.

4 Yang C, Wang CM, Jia ZJ. Sesquiterpenes and other constituents from aerial parts of *Inula japonica*. *Planta Med*, 2003, 69: 662-666.

5 Shan JJ, Yang M, Ren JW. Anti-diabetic and hypolipidemic effects of aqueous-extract from the flower of *Inula japonica* in alloxan-induced diabetic mice. *Biol Pharm Bull*, 2006, 29: 455-459.

6 Qin JJ, Jin HZ, Zhang WD, *et al*. Anthranilic acid derivatives from *Inula japonica*. *Chin Chem Lett*, 2008, 19: 556-558.

7 Zhang GN, Zhang CF, Luo Y, *et al*. Chemical constituents of *Dendrobium thyrsiflorum* Rchb. f (II). *Chin J Nat Med*, 2005, 3: 287-290.

8 Hu XJ, Jin HZ, Su J, *et al*. Coumarins from *Daphne retusa*. *Chin J Nat Med*, 2009, 7: 34-36.

9 Zhang W, Zhang WD, Li TZ, *et al*. Studies on the chemical constituents in roots of *Daphne odora* var, atrocaulis. *China J Chin Mater Med*, 2005, 30: 513-515.

10 Luo JG, Kong LY. Lipophilic constituents from the leaves of *Ipomoea batatas* (CV. Simon). *Nat Prod Res Dev*, 2005, 17: 166-168.

11 Zhang JS, Guo QM. Studies on the chemical constituents of *Eclipta prostrata* (L). *Acta Pharm Sin*, 2001, 36: 34-37.

12 Yin YQ, Luo JG, Kong LY. Studies on the chemical constituents of *Ipanoea batatas* Lam. *Chin Tradit Herb Drugs*, 2007, 38: 508-510.

13 Li D, Liu MS, Li ZL, *et al*. Studies on chemical constituents of *Heliciopsis lobata* II. *China J Chin Mater Med*, 2008, 33: 409-411.

14 Dong Li, Li L, Liao ZH, *et al*. Chemical constituents in root of *Rhodiola bupleuroides*. *Acta Bot Boreal-Occident Sin*, 2007, 27: 2564-2567.

15 Ren DC, Qian SH, Yang NY, *et al*. Chemical constituents of *Changium smyrnioides*. *J Chin Med Mater*, 2008, 31: 47-49.

16 Li XH, Lin LD, Wu P, *et al*. Chemical constituents from barks of *Endospermum chinense* Benth. *J Trop Subtrop Bot*, 2007, 15: 35-39.