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长舟马先蒿化学成分研究

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摘　要:为了进一步研究玄参科长舟马先蒿的化学成分,我们从其全草的乙醇提取物中分离得到1个新环烯醚萜苷和12个已知化合物。根据波谱数据(1D,2D-NMR,HSQC,HMBC,ROESY,MS)分别鉴定为 gardoside methyl ester(**1**)、7-O-acetylgardoside methyl ester(**2**)、verbascoside(**3**)、leucosceptoside A(**4**)、jionoside D(**5**)、martynoside(**6**)、2″-O-acetylmartynoside(**7**)、uridine(**8**)、adenosine(**9**)、benzyl alcohol-O-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside(**10**)、2-phenylethyl O-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside(**11**)、apigenin(**12**)、lariciresinol-4′-O-β-D-glucopyranoside(**13**),其中7-O-acetylgardoside methyl ester(**2**)为一个新化合物。

关键词:玄参科;长舟马先蒿;环烯醚萜苷;山栀子苷甲基;7β-乙酰基山栀子苷甲基

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Chemical Constituents of *Pedicularis dolichocymba* Hand.-Mazz.

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Abstract: To study further the chemical constituents from the ethanol extract of the whole plants of *Pedicularis dolichocymba* Hand.-Mazz. (Scrophulariaceae), one new iridoid glycoside, 7-O-acetylgardoside methyl ester(**2**) was isolated, together with twelve known compounds, gardoside methyl ester(**1**), verbascoside(**3**), leucosceptoside A(**4**), jionoside D(**5**), martynoside(**6**), 2″-O-acetylmartynoside(**7**), uridine(**8**), adenosine(**9**), benzyl alcohol-O-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside(**10**), 2-phenylethyl O-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside(**11**), apigenin(**12**) and lariciresinol-4′-O-β-D-glucopyranoside(**13**). Structures of compounds **1-13** were elucidated mainly based on NMR (HSQC, HMBC and ROESY) and MS evidence.

Key words: Scrophulariaceae; *Pedicularis dolichocymba*; iridoid glycoside; gardoside methyl ester; 7-*O*-acetylgardoside methyl ester

Introduction

Pedicularis L. comprises about 329 species in China[1]. Some species of this genus are used to treat disease[2]. Many compounds were isolated from *Pedicularis*, including iridoids, phenylpropanoids and so on[3]. Among them, some compounds showed antioxidant and antitumour activities[4,5]. In the previous paper, we have reported four new iridoid glycosides dolichocymbosides A-D from P. *dolichocymba*[6]. Herein we report two iridoid glycosides from the plant, gardoside methyl ester(**1**), 7-O-acetylgardoside methyl ester(**2**), together with other eleven compounds(Fig. 1).

Results and Discussion

Compound **1** was obtained as a white powder solid. The IR spectrum (KBr) showed the presence of hydroxyl (3422 cm^{-1}), C=O(1693 cm^{-1}), double bond(1634 cm^{-1}) and C-O-C(1079 cm^{-1}). The FAB$^-$-MS spectrum gave quasi-molecular ion peak at *m/z* 387 $[M-H]^-$ and HR-TOF-MS provided the molecular formula of $C_{17}H_{24}O_{10}$.

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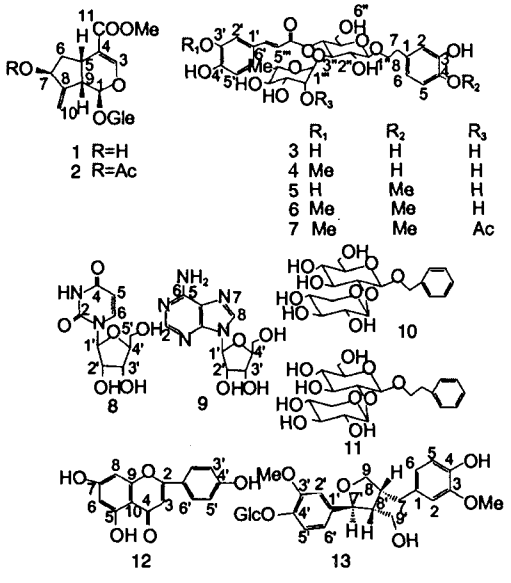

Fig. 1 Structures of compounds 1-13

The ^1H, ^{13}C NMR (DEPT) spectra (Table 1) of **1** revealed the presence of 1 CH_3, 3 CH_2, 10 CH and 3 quaternary C atoms. The ^1H NMR signal at 4.66 (1H, d, J = 7.9 Hz) suggested the presence of β-D-glucopyranosyl. HMBC correlations (Fig. 2) of δ_H 4.66 (1H, d, J = 7.9Hz, H-1′ of Glc) to δ_C 96.6 (CH, C-1), δ_H 3.70 (3H, s, -COOMe) to δ_C 169.1 (C, CO) suggested that β-D-glucose linked at C-1 and the methoxcarboyl located at C-4. Based on these evidence, compound **1** was shown to have an iridoid structure closely related to that of gardoside methyl ester[7,8].

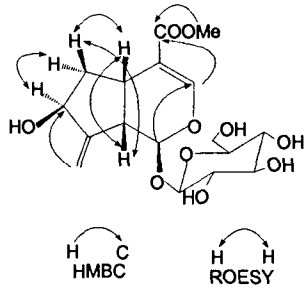

Fig. 2 Key correlations in HMBC and ROESY spectra of 1

Table 1 ^1H (1:500 MHz; 2:400 MHz) and ^{13}C NMR (100 MHz) data of 1 and 2 in CD_3OD

No.	1*		2	
	δ_C	δ_H (J, Hz)	δ_C	δ_H (J, Hz)
1	96.6(d)	5.44(d,1H,4.8)	96.0(d)	5.43(d,1H,6.0)
3	153.5(d)	7.44(s,1H)	153.6(d)	7.56(d,1H,1.1)
4	111.7(s)		110.8(s)	
5	31.8(d)	3.15(m,1H)	33.1(d)	3.26(m,1H)
6	40.6(t)	1.96(m,1H)	38.4(t)	2.09-2.25(m,2H)
		2.00(m,1H)		
7	73.8(d)	4.35(m,1H)	76.3(d)	5.49(m,1H)
8	152.7(s)		148.3(s)	
9	44.9(d)	2.99(m,1H)	44.4(d)	3.00(m,1H)
10	113.1(t)	5.36(br s,2H)	116.6(t)	5.55(br s,2H)
11	169.1(s)		168.8(s)	
-OMe	51.7(q)	3.70(s,3H)	51.6(q)	3.78(s,3H)
$-OCOCH_3$			172.3(s)	
$-OCOCH_3$			21.0(q)	2.11(s,3H)
Glucose				
1′	99.9(d)	4.66(d,1H,7.9)	99.6(d)	4.76(d,1H,7.9)
2′	74.7(d)	3.19(m,1H)	74.5(d)	3.28(m,1H)
3′	78.4(d)	3.29(m,1H)	78.3(d)	3.38(m,1H)
4′	71.6(d)	3.25(m,1H)	71.5(d)	3.30(m,1H)
5′	78.0(d)	3.35(m,1H)	77.8(d)	3.41(m,1H)
6′	62.8(t)	3.64(dd,1H,6.2,11.9)	62.7(t)	3.69(dd,1H,2.8,11.9)
		3.89(dd,1H,1.9,11.9)		3.96(dd,1H,2.0,11.9)

* Assignment from HSQC, HMBC experiments.

The relative configuration of **1** was determined from its ROESY experiment (Fig. 2). The correlations of δ 2.99 (H-9) with 3.15 (H-5), 3.15 (H-5) with 2.00 (H-6b), 1.96 (H-6a) with 4.35 (H-7), suggested that the H-5, H-9 and H-6b were in the same orientation. The chemical shift of C-1 will be less than 100 ppm if H-5

is β-oriented; whereas, the chemical shift of C-1 will be more than 100 ppm if the H-5 is α-oriented[9-13]. Hence, the H-5, H-9 and H-6b are β-oriented in view of the ^{13}C NMR signal at δ 96.6, but H-6a and H-7 are in α-orientation. From the above results, compound **1** was determined as gardoside methyl ester.

Compound **2** was obtained as a colorless sticky solid. The IR spectrum (KBr) showed the presence of hydroxyl (3428 cm^{-1}), C = O (1710 cm^{-1}), double bond (1635 cm^{-1}) and C-O-C (1076, 1021 cm^{-1}). The FAB$^-$-MS spectrum gave quasi-molecular ion peak at *m/z* 429 $[M-H]^-$ and HR-TOF-MS suggested the molecular formula of $C_{19}H_{26}O_{11}$. The spectra data of **2** (Table 1) are resemble closely related to that of **1**, but with an additional signal at δ_H 2.11, δ_C 21.0, 172.3 from an acetoxy group. Comparing with those of **1**, the signals of C-7 in **2** were shifted downfield by 2.5 ppm, and C-6 and C-8 upfield 1.8 and 4.4 ppm. Thus, the acetoxyl could be located at C-7. The ROESY experiment suggested the same relative configuration in **2** and **1**. Therefore, compound **2** was elucidated as 7-O-acetylgardoside methyl ester.

By MS, ^1H and ^{13}C NMR data, compounds **3-13** were identified as follows: verbascoside (**3**)[14], leucosceptoside A (**4**)[14], jionoside D (**5**)[14], martynoside (**6**)[15], 2″-O-acetyl-martynoside (**7**)[15], uridine (**8**)[16], adenosine (**9**)[17], benzyl alcohol-O-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside (**10**)[18], 2-phenylethyl O-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside (**11**)[19], apigenin (**12**)[20], and lariciresinol-4′-O-β-D-glucopyranoside (**13**)[21].

Experimental

General

Optical rotations were measured with a Horbia SEAP-300 polarimeter. IR spectrum was obtained on a Bio-Rad FTS-135 spectrophotometer (KBr discs). UV spectrum was recorded on a Shimadzu 2401PC spectrophotometer. EI, FAB-MS and HR-TOF-MS were carried out on a VG Auto Spec-3000 spectrometer. 1D and 2D-NMR spectra were recorded on a Bruker AM-400 and a DRX-500 spectrometer with TMS as internal standard. Column chromatography was performed over Silica gel (200-300 mesh, Qingdao Marine Chemical Inc., China), D_{101} resin (Tianjin Agriculture Chemical Co., Ltd., China) and Sephedax LH-20 (25-100 μm, Pharmacia Fine Chemical Co., Ltd., Sweden), respectively.

Plant material

The plant material was collected in Zhong Dian, Yunnan Province of China in August 2003 and identified by Prof. Wang Hong, Kunming Institute of Botany, Chinese Academy of Sciences. The voucher specimen (KUN 0556080) was deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and isolation

The dried whole plants (11 kg) of *P. dolichocymba* were extracted with 95% ethanol for three times (each a week) at room temperature. After concentration of the combined extracts under reduced pressure, the residue was dissolved with hot water and extracted successively with petroleum ether, EtOAc and *n*-BuOH. The EtOAc portion was divided into 5 fractions (Frs1-5) over silica gel column eluted with $CHCl_3$-MeOH (20: 1) followed by increasing concentrations of MeOH. Fr. 1 was separated over Sephedax LH-20 column to give **12** (6 mg). Compound **7** (8 mg) was isolated from Fr. 2 over silica gel column. Fr. 4 was separated further over silica gel and Sephedax LH-20 column to give **1** (34 mg), **2** (7 mg), **6** (300 mg), **8** (25 mg), **10** (16 mg) and **11** (5 mg). Fr. 5 was eluted with $CHCl_3$-MeOH (20: 1) over silica gel column to give compound **3** (17 mg) and a mixture, which was then purified by HPLC (Zorbax ODS-C18, MeOH-H_2O, 1: 4) to afford compound **4** (6 mg) and **5** (9 mg). The *n*-BuOH fraction was subjected to a silica gel column eluted with $CHCl_3$-MeOH (9: 1) followed by increasing concentrations of MeOH to give 2 fractions (Fr. A and B). Fr. B was separated over D_{101} resin eluted with MeOH-H_2O (3: 7, 7: 3, respectively), and the obtained residue was separated over silica gel and Sephedax LH-20 column successively to give compounds **9** (24 mg) and **13** (6 mg).

Gardoside methyl ester (**1**) White powder solid, $C_{17}H_{24}O_{10}$, $[\alpha]_D^{21}$ -44.6° (*c* 0.65, CH_3OH). UV λ_{max}^{MeOH} nm (log ε): 202 (4.08), 231 (4.07). IR ν_{max}^{KBr} cm^{-1}: 3422, 2924, 1693, 1634, 1440, 1297, 1079. ^1H NMR

(500 MHz, CD_3OD) and ^{13}C NMR (100 MHz, CD_3OD) data are shown in Table 1. FAB$^-$-MS *m/z*: 387 [M-H]$^-$ (53), 225 [M-Glc]$^-$ (91); HR-TOF-MS *m/z*: [M-H]$^-$ 387.1301 (for calcd. $C_{17}H_{23}O_{10}$, 387.1291).

7-Acetylgardoside methyl ester (2) Colorless sticky solid, $C_{19}H_{26}O_{11}$, $[\alpha]_D^{26}$ -65.8° (*c* 0.66, CH_3OH). UV λ_{max}^{MeOH} nm (log ε): 203 (3.77), 233 (4.01). IR ν_{max}^{KBr} cm^{-1}: 3428, 2927, 1734, 1710, 1635, 1440, 1374, 1286, 1247, 1157, 1076, 1021. ^1H NMR (400 MHz, CD_3OD) and ^{13}C NMR (100 MHz, CD_3OD) are given in Table 1. FAB$^-$-MS *m/z*: 429 [M-H]$^-$; HR-TOF-MS *m/z*: [M-H]$^-$ 429.1408 (for calcd. $C_{19}H_{25}O_{11}$, 429.1396).

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