Phytochemistry 121 (2016) 58–64

Contents lists available at ScienceDirect

Phytochemistry

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

Phenylpropanoid and lignan glycosides from the aerial parts of *Lespedeza cuneata*

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ARTICLE INFO

Article history:
Received 15 May 2015
Received in revised form 30 September 2015
Accepted 7 October 2015
Available online 21 October 2015

Keywords:
Lespedeza cuneata
Leguminosae
Phenylpropanoid glucosides
Lignan glycosides
Inflammatory bowel disease
Xbp1 promoter

ABSTRACT

Four phenylpropanoid glucosides (**1**–**4**) and five lignan glycosides (**5**–**9**) were isolated from the aerial parts of *Lespedeza cuneata*, together with three known lignan glycosides (**10**–**12**). Their structures were elucidated on the basis of spectroscopic analyses, and the absolute configurations of compounds **5**–**9** were determined from the CD spectra. In addition, the compounds were tested for their ability to activate the transcription effect on *xbp1* promoter. Compounds **4**, **5**, **7**, **9**, **10**, and **12** could activate the transcription of *xbp1* to varying degrees, with EC_{50} values ranging from 0.18 to 0.64 μM.

1. Introduction

Inflammatory bowel disease (IBD), such as Crohn's disease and ulcerative colitis (UC), can be painful and debilitating and sometimes leads to life-threatening complications. Recent studies have indicated that the expression of *xbp1* (X-box binding protein 1) gene deletion or knock down would increase the body sensitivity on IBD induced by factors, promote IBD onset, and exacerbate IBD development. Consequently, it was previously speculated that *xbp1* may be a potential therapeutic for IBD (Kaser et al., 2008); the *Xbp1* gene promoter has thus been of interest with target molecules of natural product chemistry.

Lespedeza cuneata (Dum. Cour.) G. Don, a warm-season perennial legume, is widely distributed in East Asia, Northeast Australia, and North America, and has been extensively used as a traditional folk medicine to protect the function of kidneys, livers and lungs in China (Jiangsu New Medical College, 1986; Cai et al., 2011). Previous phytochemical investigations of this plant have led to the identification of flavonoids (Numata et al., 1979, 1980; Kwon and Bae, 2009; Kim et al., 2011), sterols and triterpenoids (Deng et al., 2007), as well as organic acid salts (Ueda et al., 1997; Shigemori et al., 1990) which showed diverse biological activities, such as hepatoprotective (Kim et al., 2011), nyctinastic leaf-movement (Ueda et al., 1997), and antioxidant (Kim and Kim, 2010) effects. As part of ongoing research to identify bioactive substances from traditional Chinese medicines, a 70% EtOH extract of the aerial parts of *L. cuneata* was investigated, resulting in identification of four new phenylpropanoid glucosides (**1**–**4**), five new lignan glycosides (**5**–**9**) and 3 known compounds (**10**–**12**). In addition, these two classes of compounds were isolated from the genus *Lespedeza* for the first time. In this paper, their isolation and structural elucidation, as well as an evaluation of their biological activities, are reported.

2. Results and discussion

The EtOAc-soluble part of the 70% EtOH extract of the aerial of *L. cuneata* was purified by column chromatography over silica gel, reversed-phase C18 silica gel, and preparative HPLC to afford 12 compounds, including 9 new (**1**–**9**) and three known compounds. The structures of the known compounds were identified as aviculin (**10**) (Kim et al., 1994), (+)-isolariciresinol-9′-*O*-*β*-D-glucopyranoside (**11**) (Achenbach et al., 1992), and (+)-5′-methoxyisolari-

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http://dx.doi.org/10.1016/j.phytochem.2015.10.002
0031-9422/

ciresinol-9′-*O*-α-L-rhamnoside (**12**) (Shen et al., 2012) by comparison of their spectroscopic data with published values.

Compound **1** was obtained as a white, amorphous, powder. Its IR spectrum indicated the presence of hydroxy (3379 cm^{-1}), carbonyl (1695 cm^{-1}), and aromatic functional groups (1604 and 1515 cm^{-1}). The molecular formula, $C_{35}H_{40}O_{13}$, was determined from positive-ion HRESIMS (669.2547 $[M+H]^+$, calcd 669.2542) and this was also supported by the NMR spectroscopic data (Tables 1 and 2). In the ^1H NMR spectrum (Table 1), the presence of two 1,4-disubstitued aromatic rings was deduced from the signals at δ_H [7.54 (2H, d, J = 8.5 Hz, H-2 and H-6), 6.78 (2H, d, J = 8.5 Hz, H-3 and H-5)], and [7.52 (2H, d, J = 8.5 Hz, H-2‴ and H-6‴), 6.77 (2H, d, J = 8.5 Hz, H-3‴ and H-5‴)]. The additional two *trans*-olefinic units were deduced from the resonances at δ_H [7.64 (1H, d, J = 16.0 Hz, H-7), 6.36 (1H, d, J = 16.0 Hz, H-8)] and [7.53 (1H, d, J = 16.0 Hz, H-7‴), 6.40 (1H, d, J = 16.0 Hz, H-8‴)], which were supported by corresponding signals at δ_C 145.2 (C-7), 144.8 (C-7‴), 113.9 (C-8‴) and 113.6 (C-8) in the HSQC spectrum. Two carbonyl carbons at δ_C 166.42 (C-9) and 166.45 (C-9‴) were also observed in the ^{13}C NMR spectrum (Table 2). The resonances at δ_H [4.41 (1H, d, J = 8.0 Hz, H-1′) and 4.16 (1H, d, J = 8.0 Hz, H-1″)], assignable to two anomeric protons of sugar units, were also observed in the ^1H NMR spectrum of **1**. In addition, the anomeric carbon signals at (δ_C 102.6 and 103.5), together with additional carbons (δ_C 72.9, 76.1, 70.0,

Table 1
^1H NMR spectroscopic data of compounds **1**–**9**.

No	**1**[a]	**2**[a]	**3**[b]	**4**[a]	**5**[a]	**6**[b]	**7**[a]	**8**[b]	**9**[a]
2	7.54 d (8.5)	7.69 d (8.5)	7.53 d (9.0)	7.56 d (8.5)					
3	6.78 d (8.5)	6.74 d (8.5)	6.76 d (9.0)	6.79 d (8.5)	6.08 s	6.08 s	6.08 s	6.10 s	6.26 s
5	6.78 d (8.5)	6.74 d (8.5)	6.76 d (9.0)	6.79 d (8.5)					
6	7.54 d (8.5)	7.69 d (8.5)	7.53 d (9.0)	7.56 d (8.5)	6.59 s	6.59 s	6.61 s	6.69 s	6.65 s
7	7.64 d (16.0)	6.85 d (13.0)	7.63 d (15.6)	7.58 d (16.0)	2.72[c] 2.70[c]	2.71[c] 2.70[c]	2.73[c] 2.72[c]	2.73[c] 2.72[c]	2.83 dd (16.0, 10.0) 2.56 dd (16.0, 5.5)
8	6.36 d (16.0)	5.76 d (13.0)	6.34 d (15.6)	6.45 d (16.0)	1.89 m	1.90 m	1.89 m	1.90 m	1.86 m
9					3.58 dd (10.0, 3.0) 3.46 dd (10.0, 6.0)	3.55 dd (10.8, 3.0) 3.44 dd (10.8, 6.0)	3.55 dd (10.0, 3.0) 3.41[c]	3.56[c] 3.40[c]	3.41[c] 3.33[c]
1′	4.41 d (8.0)	4.39 d (8.0)	4.38 d (7.8)	4.36 d (8.0)					
2′	3.06[c]	3.05[c]	3.05[c]	3.15[c]	6.78 d (2.0)	6.77 d (1.8)	6.63 br s	6.33 s	6.65 d (2.0)
3′	3.20[c]	3.20[c]	3.20[c]	3.39[c]					
4′	3.17[c]	3.13[c]	3.15[c]	3.45[c]					
5′	3.54[c]	3.52[c]	3.52[c]	3.64[c]	6.68 d (8.0)	6.67 d (8.4)	6.70 d (8.0)		6.62 d (8.0)
6′	4.54 dd (12.0, 1.5) 4.03 dd (12.0, 6.0)	4.43 dd (12.0, 2.0) 4.05 dd (12.0, 6.0)	4.53 dd (12.0, 1.8) 4.03 dd (12.0, 6.0)	4.53 d (10.5) 4.39[c]	6.49 dd (8.0, 1.5)	6.47 dd (7.8, 1.8)	6.49 dd (8.0, 1.5)	6.33 s	6.22 dd (8.0, 1.5)
7′					4.01 d (8.5)	4.00 m	3.75 d (10.5)	3.76 d (10.2)	4.09 d (5.0)
8′					1.73 m	1.71 m	1.80 m	1.84 m	2.03 m
9′					3.87 dd (10.0, 1.5) 3.04[c]	3.85 dd (10.8, 1.8) 3.01[c]	3.34[c] 3.15[c]	3.32[c] 3.32[c]	3.68[c] 2.78[c]
1″	4.16 d (8.0)	4.15 d (8.0)	4.14 d (7.8)	4.27 d (8.0)	4.01 d (8.5)	3.99 d (7.8)	4.44 br s	4.45 d (2.4)	4.44 br s
2″	3.09[c]	3.05[c]	3.08[c]	3.00[c]	3.03[c]	3.02[c]	3.60[c]	3.60[c]	3.77[c]
3″	3.43[c]	3.39[c]	3.41[c]	3.16[c]	3.17[c]	3.15[c]	3.49[c]	3.50[c]	3.52[c]
4″	3.49[c]	3.46[c]	3.42[c]	3.06[c]	3.14[c]	3.08[c]	3.17[c]	3.16[c]	3.20[c]
5″	3.65[c]	3.64[c]	3.62[c]	3.23[c]	3.34[c]	3.31[c]	3.48[c]	3.46[c]	3.44[c]
6″	4.50 dd (12.0, 1.5) 4.34 dd (12.0, 6.0)	4.49 dd (12.0, 2.0) 4.33 dd (12.0, 6.0)	4.48 dd (12.0, 1.8) 4.31 dd (12.0, 6.0)	3.71 d (10.0) 3.41[c]	4.36 dd (12.0, 1.5) 4.14 dd (12.0, 6.0)	4.29 dd (12.0, 1.8) 4.10 dd (12.0, 6.0)	1.06 d (6.0)	1.03 d (6.0)	1.11 d (6.0)
2‴, 6‴	7.52 d (8.5)	7.52 d (8.5)	7.65 d (8.4)	7.35[c]	7.52 d (8.5)	7.63 d (8.4)			
4‴				7.26[c]					
3‴, 5‴	6.77 d (8.5)	6.75 d (8.5)	6.74 d (9.0)	7.31[c]	6.77 d (8.5)	6.64 d (8.4)			
7‴	7.53 d (16.0)	7.53 d (16.0)	6.83 d (13.2)	4.75d (12.0) 4.39[c]	7.54 d (16.0)	6.77 d (13.2)			
8‴	6.40 d (16.0)	6.39 d (16.0)	5.77 d (13.2)		6.39 d (16.0)	5.64 d (13.2)			
5-OMe					3.69 s	3.70 s	3.70 s	3.70 s	3.68 s
3′-OMe					3.71 s	3.71 s	3.71 s	3.70 s	3.73 s
5′-OMe								3.70 s	
1″-OMe	3.34 s	3.35 s	3.35 s						

[a] Recorded in DMSO-d_6 at 500 MHz.
[b] Recorded in DMSO-d_6 at 600 MHz.
[c] Signals overlapped. Proton coupling constants (J) in Hz were given in parentheses. The assignments were based on ^1H–^1H COSY, HSQC, and HMBC experiments.