Furofuran Lignans from *Cuscuta chinensis*

XIANG, Sheng-Xi(向胜习) **HE, Zhi-Sheng***(何直升) **YE, Yang***(叶阳)
State Key Laboratory of Drug Researech, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 200031, China

Three furofuran lignans named neocuscutosides A, B and C were obtained from the ethanolic extract of the dried seeds of *Cuscuta chinensis* and their structures were characterized by chemical and spectroscopic methods.

Keywords *Cuscuta chinensis*, lignans, glucoside

Introduction

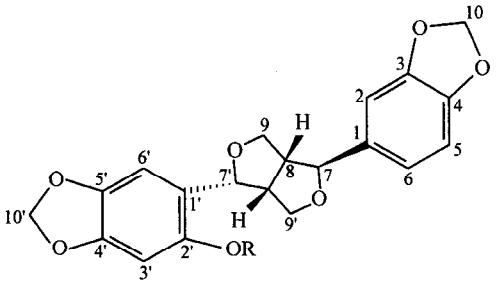
Cuscuta Semen, the dried seeds of *Cuscuta chinensis* Lam, is a traditional Chinese medicine used as a tonic for nourishing the liver and kidney.[1] Two related furofuran lignans cuscutosides A and B isolated from *Cuscuta chinensis* Lam. have been reported.[2] In our investigation, three new furofuran lignans named neocuscutosides A, B and C were obtained from the dried seeds of this plant. This paper describes the isolation and structure elucidation of these compounds.

Results and discussion

Neocuscutoside A (**1**), isolated as a white powder, $[\alpha]_D^{20}$ − 19.8°(*c* 0.103 in pyridine), showed the molecular formula $C_{37}H_{46}O_{21}$ as deduced from its ^{13}C NMR DEPT spectrum and FAB mass spectral data, which included quasi-molecular ion peaks at *m/z* 850 $[M + H + Na]^+$, 866 $[M + H + K]^+$ and a fragment ion peak at *m/z* 370[M − 2hexose − pentose]$^+$. The IR spectrum indicated the presence of hydroxyl groups, due to sugar moieties (ν_{max}: 3400, 1070 br. cm^{-1}). Acid hydrolysis of **1** yielded glucose and apiose identified by TLC comparison with authentic samples. The ^1H NMR spectrum of **1** (see Table 1) showed three anomeric protons at δ5.56 (d, *J* = 7.6 Hz, H-1″), 6.48 (d, *J* = 2.7 Hz, H-1‴) and δ5.13 (d, *J* = 7.7 Hz, H-1⁗); ABX-type aromatic protons at δ7.20 (d, *J* = 1.3 Hz, 1H, H-2), 7.06 (d, *J* = 8.0 Hz, 1H, H-5) and 7.12 (dd, *J* = 8.0, 1.3 Hz, 1H, H-6); two aromatic protons at 7.42 (s, 1H, H-3′) and 7.23 (s, 1H, H-6′); two methylenedioxy signals at δ6.17 (d, *J* = 3.9 Hz, 2H, H-10) and 6.09 (d, *J* = 19.0 Hz, 2H, H-10′). Thus, **1** was deduced to be an aromatic glycoside. The ^{13}C NMR spectrum of **1** exhibited 37 signals, which included two methylenedioxy functions (δ102.3, 102.5), two oxygenated methylenes at δ72.6 (C-9) and 74.2(C-9′), two methines at δ55.6 (C-8) and 55.7 (C-8′), two oxygenated benzylmethines at δ82.3 (C-7′) and 86.4 (C-7), a 1, 3, 4-trisubstituted benzene ring [δ137.2 (C-1), 107.9 (C-2), 148.3 (C-3), 148.1 (C-4), 109.3 (C-5), 120.8 (C-6)] and a 1′, 2′, 4′, 5′-tetrasubstituted benzene ring [δ125.1 (C-1′), 150.1 (C-2′), 99.5 (C-3′), 149.0 (C-4′), 143.5 (C-5′), 106.3 (C-6′)] in the aglycone moiety. The remaining 17 signals were due to the three sugar units (see Table 2). Thus the aglycone moiety of **1** was deduced to be a 2′- hydroxy asarinin type furofuran lignan by comparison of ^{13}C NMR data, especially, chemical shift values of C-2′and C-3′ of **1** with cuscutoside A[2](Table 2).

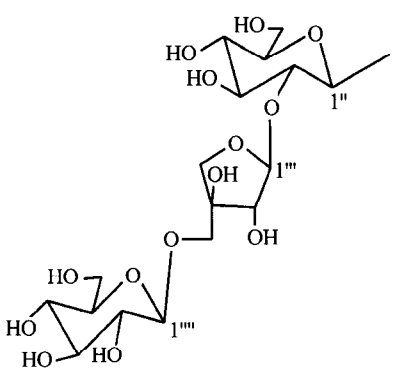
In the ^1H NMR spectrum, the chemical shifts of H-7 at δ5.08 (d, *J* = 4.5 Hz) and H-7′ at δ5.92 (overlapped) were not identical, which revealed that H-7 was α-axial bond and H-7′ was β-equatorial, because the ax-

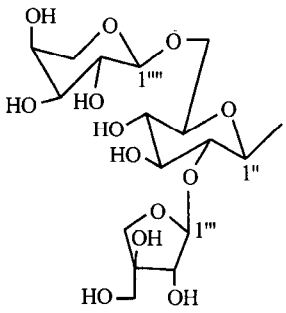
* E-mail: *zshe@mail.shcnc.ac.cn*
Received August 25, 2000; accepted November 1, 2000.
Project supported by the National Natural Science Foundation of China (No. 29632050).



R

1 2 3





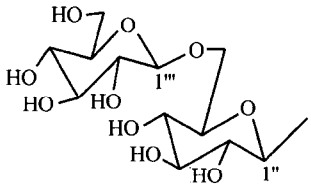


Table 1 ^{1}H NMR spectral data for the aglycones of **1**, **2** and **3**

H	1	2	3
1			
2	7.20 d(1.3)	7.20 d(1.4)	7.21br. s
3			
4			
5	7.06 d(8.0)	6.78 d(8.0)	7.03 d(7.6)
6	7.12 dd(8.0, 1.3)	7.03 dd(8.0, 1.4)	7.10 d(7.6)
7	5.08 d(4.5)	4.92 d(4.8)	4.95 d(4.6)
8	3.15—3.19 m	3.20—3.24 m	3.25—3.30 m
9	4.25—4.27 m	4.23—4.25 m	4.41—4.43 m
	4.45—4.47 m	4.35—4.37 m	4.52—4.54 m
OCH_2O	6.17 d(3.9)	6.04 d(1.2)	6.06 d(3.2)
1′			
2′			
3′	7.42 s	7.37 s	7.39 s
4′			
5′			
6′	7.23 s	7.22 s	7.22 s
7′	5.92 (overlap)	5.85 (overlap)	5.87 (overlap)
8′	3.30—3.35 m	3.25—3.30 m	3.20—3.25 m
9′	4.69—4.71 m	4.63—4.65 m	4.60—4.62 m
	4.77—4.79 m	4.70—4.72 m	4.84—4.86 m
OCH_2O	6.09 d(19.0)	5.94 d(8.3)	5.96 d(11.0)

ial proton (H-7) was held close to the α-axial aryl group at C-7′ and located in the shielding cone of the α-axial aryl group,[3] thus shifting H-7 upfield. The stereochemistry of H - 7 was further confirmed by analysis of the

Table 2 ^{13}C NMR spectral data for **1**, **2**, **3** and cuscutoside A*

C	1	2	3	*	DEPT	No.	1	2	3	*
1	137.2	136.8	136.7	136.6	C	1″	101.5	101.4	105.6	100.4
2	107.9	107.5	107.4	107.2	CH	2″	80.7	80.0	75.4	79.5
3	148.3	147.7	148.5	148.3	C	3″	79.0	78.8	79.0	78.9
4	148.1	147.5	147.7	147.4	C	4″	71.7	71.6	71.9	71.3
5	109.3	108.6	108.5	108.4	CH	5″	77.4	77.2	78.6	78.6
6	120.8	120.1	120.0	119.8	CH	6″	65.7	69.5	70.5	62.2
7	86.4	85.9	85.7	85.6	CH					
8	55.6	55.3	55.0	55.2	CH	1‴	111.7	111.3	104.2	111.2
9	72.6	71.9	72.0	71.8	CH2	2‴	78.8	78.4	75.0	78.2
OCH_2O	102.3	101.6	102.3	101.5	CH_2	3‴	80.9	80.5	78.5	80.3
1′	125.5	125.6	125.9	125.0	C	4‴	70.7	65.6	71.5	65.5
2′	150.1	150.0	151.1	149.4	C	5‴	75.6	75.4	77.5	75.2
3′	99.5	99.0	100.4	98.0	CH	6‴			62.9	
4′	149.0	149.1	149.3	150.1	C					
5′	143.5	143.0	143.2	142.6	C	1⁗	105.7	105.3		
6′	106.3	106.0	105.8	105.9	CH	2⁗	75.6	72.4		
7′	82.3	82.0	82.6	81.8	CH	3⁗	78.7	74.4		
8′	55.7	55.3	55.3	55.2	CH	4⁗	72.3	69.2		
9′	74.2	74.0	73.9	73.6	CH_2	5⁗	78.8	66.6		
OCH_2O	102.5	101.8	102.5	101.6	CH_2	6⁗	63.3			

* reference compound: cuscutoside A

^{13}C NMR spectrum, where the chemical shifts of C-1 (δ137.2) and C-1′ (δ125.5) are dependent on the configuration of the two aromatic rings, that is, when the C-1′ position of the aryl groups at C-7′ in the *epi*-series is moved from the equatorial position to axial, the chemical shift of C-1′ exhibits an upfield shift; otherwise, the signal of C-1 at the equatorial position should be relatively downfield.[4] Thus the aryl groups at C-1 should be β-equatorial, and H-7 was α-axial. The crosspeaks in the NOESY spectrum between H-7′ and H-8′, H-8 and H-8′ were observed, which proved that H-8 and H-8′ were also β-axial protons.

In the ^1H NMR spectrum, the J values of the anomeric signals indicated that the glucosyl and apiosyl moieties in **1** exhibited β-configuration.[5] The assignment of the corresponding protonated carbon shift of the sugar units was completed with the aid of 2D-NMR HMQC experiment. The position of attachment of the sugar chain to the aglycone and the sequence of sugar units in the sugar chain were revealed by analysis of the glycosidation shift values of the sugar carbon signals. The downfield shift of C-2″ (80.7) and C-4‴ (70.7) suggested the glycosidation site of the corresponding sugar units at C-2″ and C-4‴, respectively. The assignments were further confirmed by the presence of cross peaks between C-2′ and H-1″, C-2″ and H-1‴, C-4‴ and H-1⁗ in the HMBC spectrum. On the basis of the above evidence, the structure of **1** was elucidated to be 2′-hydroxy asarinin-2′-*O*-β-glucopyranosyl-(1→4)-β-apiofuranosyl-(1→2)-β-glucopyranoside, namely neocuscutoside A.

Neocuscutoside B (**2**), was isolated as a white powder, $[\alpha]_D^{20}$ −20.0° (*c* 0.501 in pyridine). The IR, ^1H NMR and ^{13}C NMR spectral data of **2** were similar to those of **1**, especially the ^{13}C NMR data which suggested that **2** have the same aglycone as **1** (Table 2). Acid hydrolysis of **2** afforded glucose, arabinose and apiose, which were identified by TLC comparison with authentic samples. Three anomeric signals were found at δ 5.50 (d, J = 7.2 Hz, H-1″), 6.56 (d, J = 2.4 Hz, H-1‴), and 4.83 (d, J = 6.7 Hz, H-1⁗) in the ^1H NMR spectrum and at δ101.4, 111.3, 105.3 in the ^{13}C NMR spectrum. The ^{13}C NMR spectrum exhibited a terminal β-arabinopyranosyl unit, a β-apiofuranosyl unit showing a glycosidation shift at C-1‴ (111.3) and a β-glucopyranosyl showing glycosidation shifts at C-2″ (80.0) and C-6″ (69.5). The assignments were confirmed by the presence of cross peaks between C-2′ and H-1″, C-2″ and H-1‴, C-6″ and H-1⁗ in the HMBC spectrum. Therefore the structure of **2** was elucidated to be 2′-hydroxy asarinin-2′-*O*-[β-arabinopyranosyl(1→6)]-β-api-

ofuranosyl-(1→2)-β-glucopyranoside, namely neocuscutoside B.

Neocuscutoside C (**3**) was isolated as a white powder, $[\alpha]_D^{20}$ - 12.5°(*c* 0.403 in pyridine). The IR, ^1H NMR and ^{13}C NMR spectral data of **3** were similar to those of **1** and **2**. Acid hydrolysis of **3** gave only glucose, but two anomeric signals were observed at δ5.91 (d, *J* = 7.0 Hz, H-1″) and 5.41 (d, *J* = 6.9 Hz, H-1‴) in the ^1H NMR spectrum and at δ105.6 (C-1″) and 104.2 (C-1‴) in the ^{13}C NMR spectrum. The ^{13}C NMR spectrum exhibited a terminal β-glucopyranosyl unit and a β-glucopyranosyl showing a glycosidation shift at C-6″ (70.5). The assignments were confirmed by the presence of the cross peaks between C-2′ and H-1″, and C-6″ and H-1‴ in the HMBC spectrum. Therefore the structure of **3** was elucidated to be 2′-hydroxy asarinin-2′-*O*-β-glucopyranosyl (1 → 6)-β-glucopyrano-side, namely neocuscutoside C.

Experimental

The NMR spectra of **1**—**3** were recorded on a Bruker AM-400 spectrometer, with TMS as internal standard in pyridine-d_5. The FABMS data were obtained using glycerol as the matrix on a MAT-95 double focusing mass spectrometer. The IR spectra were recorded on a Nicolet 750 instrument. The $[\alpha]_D^{20}$ values were obtained on a DIP-181 digital polarimeter.

Extraction and isolation

The seeds of *C. chinensis L.* were collected in Henan, China and authenticated by Xu-Lan at our institute. Avoucher specimen (No. 80) Crushed Cuscuta semen (10 kg) was extracted with ethanol and partitioned with petrol ether, $CHCl_3$, EtOAc and n-BuOH successively from a MeOH-H_2O solution. The *n*-butanolic fraction was further chomatographed on a polyamide column using H_2O as eluent. The H_2O fraction was further chromatographed on a Sephadex LH-20 column with MeOH, and then chromatographed on a silica gel column with $CHCl_3$: MeOH: H_2O (from 6:1:0.1 to 3:1:0.2 *V/V*), yielding **1** (70 mg), **2** (14 mg), and **3** (13 mg).

1 White powder, $[\alpha]_D^{20}$ - 19.8° (c 0.103 in pyridine). IR ν_{max}(KBr): 3386, 2860, 1633, 1483, 1247, 1078, 1039, 790 cm^{-1}. FABMS *m/z*: 850 [M + H + Na]$^+$, 866 [M + H + K]$^+$, 370 [M + H - 2hexose - pentose]$^+$, 289, 273. ^1H NMR spectral data (pyridine-d_5, 400 MHz): see Table 1; ^{13}C NMR spectral data (pyridine-d_5, 100 MHz): see Table 2.

2 White powder, $[\alpha]_D^{20}$ - 20.0° (*c* 0.501 in pyridine). IR ν_{max}(KBr): 3415, 2890, 1629, 1484, 1249, 1039, 931 cm^{-1}. FABMS *m/z*: 820 [M + H + Na]$^+$, 836 [M + H + K]$^+$, 370 [M + H - hexose - 2 pentose]$^+$. ^1H NMR spectral data (pyridine-d_5, 400 MHz): see Table 1; ^{13}C NMR spectral data (pyridine-d_5, 100 MHz): see Table 2.

3 White powder, $[\alpha]_D^{20}$ - 12.5°(*c* 0.403 in pyridine). IR ν_{max}(KBr): 3411, 2910, 1714, 1633.4, 1484, 1247, 1174, 1072, 1037, 931cm^{-1}. FABMS *m/z*: 718 [M + H + Na]$^+$, 734 [M + H + K]$^+$, 370 [M + H - 2hexose]$^+$. ^1H NMR spectral data (pyridine-d_5, 400 MHz): see Table 1; ^{13}C NMR spectral data (pyridine-d_5, 100 MHz): see Table 2.

Hydrolysis of **1**, **2** *and* **3**

MeOH solutions of **1**, **2** and **3** together with standard sugar samples were applied ca. 1 cm from the bottom of a precoated HPTLC silica gel plate and hydrolyzed with HCl vapor for 2 h at 50℃. The plate was then heated at 60℃ for 2 h to remove residual HCl, and developed using $CHCl_3$: MeOH: H_2O (7:3:0.1 *V/V*) as solvent. The plate was sprayed with 10% H_2SO_4(EtOH) and then heated to visualize spots.

References

1 Jiangsu New Medical Institute, *Dictionary of Chinese Medicine*, Shanghai Science and Technology Press, Shanghai, **1985**, pp. 2006—2008.

2 Yahara, S.; Domoto, H.; Sugimura, C.; Nohara, T.; Niiho, Y.; Nakajima, Y.; Ito, H. *Phytochemistry* **1994**, *37*, 1755.

3 Pelter, A.; Ward, R. S.; Rao, E. V.; Sastry, K. V. *Tetrahedron* **1976**, *32*, 2738.

4 Pelter, A.; Ward, R. S.; Nishino, C. *Tetrahedron Lett.* **1977**, *47*, 4137.

5 He, Z.-S.; Fang, S.-Y.; Wang, P.; Gao, J.-H. *Phytochemisty* **1996**, *42*, 1391.

(E20008169 JIANG, X.H.; DONG, L.J)