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Phenylpropanoid glycosides from *Scrophularia ningpoensis*

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Abstract

Three phenylpropanoid glycosides named ningposides A (3-*O*-acetyl-2-*O*-feruloyl-α-L-rhamnopyranose), B (4-*O*-acetyl-2-*O*-feruloyl-α-L-rhamnopyranose) and C (3-*O*-acetyl-2-*O*-*p*-hydroxycinnamoyl-α-L-rhamnopyranose) along with the known compounds sibirioside A, cistanoside D, angoroside C, acteoside, decaffeoylacteoside and cistanoside F were obtained from the roots of *Scrophularia ningpoensis*. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: *Scrophularia ningpoensis*; Scrophulariaceae; Phenylpropanoid; Glycoside; Ningposides A, B, C

1. Introduction

Phenylpropanoid glycosides display quite interesting pharmacological properties including antioxidant, anti-viral, and inhibition of blood platelet aggregation and LTB_4 synthesis (Cano et al., 1990; Kimura et al., 1987; Li et al., 1997). Many phenylpropanoid glycosides have been isolated from plants of the genus *Scrophularia* (Scrophulariacaea). *Scrophularia ningpoensis* is used as a Chinese herb for the treatment of inflammation (Jiangsu New Medical College, 1977). In previous studies, two phenylpropanoid glycosides, angoroside C (Kajimoto et al., 1989) and 4-*O*-(*p*-methoxycinnamoyl)-α-L-rhamnopyranoside (Zhang et al., 1994), were isolated from *S. ningpoensis*. Here, we report the isolation and structural elucidation of three new phenylpropanoid glycosides **1**–**3** (Fig. 1), along with six known ones, from the roots of *S. ningpoensis*.

2. Results and discussion

Powdered roots of *S. ningpoensis* were extracted, as described (Li et al., 1999), to yield three new phenylpropanoid glycosides that were named ningposides A (**1**), B (**2**) and C (**3**), and six known ones: sibirioside A (**4**), cistanoside D (**5**), angoroside C (**6**), acteoside (**7**), decaffeoylacteoside (**8**) and cistanoside F (**9**). The structures of known compounds **4**–**9** were identified by comparison with published data (Lin et al., 1995; Calis et al., 1987, 1988; Kobayashi et al., 1985). The structures of new compounds **1**–**3** were established mainly by spectroscopic methods.

Ningposide A (**1**) was obtained as an oil. Its molecular formula was established as $C_{18}H_{22}O_9$ by EIMS and elemental analysis. In its ^{1}H NMR spectrum, a doublet at δ 5.20 ($J = 2.1$ Hz) and a doublet of a methyl group at δ 1.38 (3H, *d*, $J = 6.2$ Hz) showed an α-L-rhamnose residue. From the anomeric proton of rhamnose, we assigned every proton and carbon of the sugar by analysis of the ^{1}H–^{1}H COSY and HMQC spectra. In addition to rhamnose, **1** exhibited signals belonging to a feruloyl and an acetyl moiety, respectively: three protons of an aromatic ring [ABX, δ 7.03, (*d*, $J = 1.9$ Hz), 6.90 (*d*, $J = 8.0$ Hz), 7.07 (*dd*, $J = 8.0$, 1.9 Hz)], two *trans* olefinic protons [AB, δ 7.62, 6.33 (2 × 1H, *d*, $J =$

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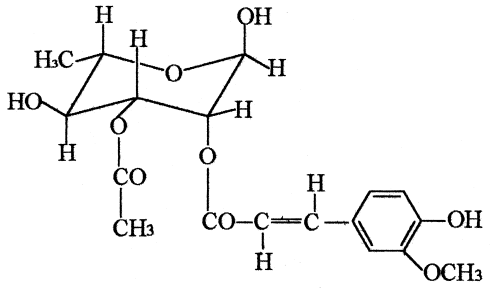
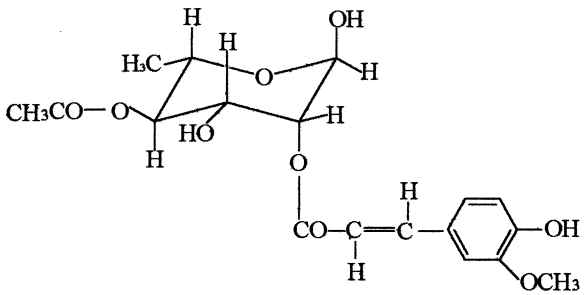
16.0 Hz)], three protons of an acetyl methyl group δ 2.06 (*s*). In the HMBC spectrum, the acyl carbon of the acetyl moiety was correlated with H-3 of the rhamnose; the acyl carbon of the feruloyl moiety was correlated with H-2 of the rhamnose. Acylation of hydroxyls at the second and third positions of the rhamnose were also deduced from the downfield shifts of H-2 (δ 5.38), H-3 (δ 5.25) of the rhamnose. Therefore, the structure of **1** was 3-*O*-acetyl-2-*O*-feruloyl-α-L-rhamnopyranose.

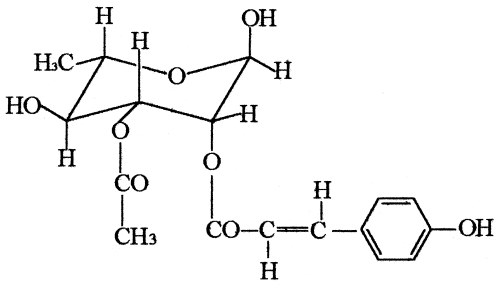
Ningposide B (**2**) was obtained as an oil. Its molecular formula was established as $C_{18}H_{22}O_9$ by EIMS and elemental analysis. Comparing the fragments of EIMS and the ^{1}H NMR spectrum of **2** with those of **1**, we could see that **2** also contained α-L-rhamnosyl, acetyl and feruloyl moieties. In the HMBC spectrum, the acyl carbon of the acetyl moiety of **2** was correlated with H-4 of the rhamnose; that of the feruloyl moiety of **2** was correlated with H-2 of the rhamnose. In the ^{1}H NMR spectrum, H-4 of the rhamnose was shifted downfield to δ 4.98. Therefore, the structure of **2** was 4-*O*-acetyl-2-*O*-feruloyl-α-L-rhamnopyranose.



(**1**)



(**2**)



(**3**)

Fig. 1. Chemical structures of ningposides A (**1**), B (**2**) and C (**3**).

Ningposide C (**3**) was obtained as an oil. Its molecular formula was established as $C_{17}H_{20}O_8$ by EIMS and elemental analysis. The ^{1}H NMR spectrum of **3** exhibited signals belonging to a *p*-hydroxycinnamoyl group: four protons of aromatic ring [AABB, δ 7.58 (2H, *m*), 6.91 (2H, *m*)], two *trans* olefinic protons [AB, δ 7.66, 6.40 (2 × 1H, *d*, $J = 16.0$ Hz)]. With the exception of the *p*-hydroxycinnamoyl group, the other ^{1}H NMR signals of **3** were in agreement with those of **1**. Therefore, **3** also contained a rhamnosyl and an acetyl moiety. In the HMBC spectrum, the acyl carbon of the acetyl moiety of **3** was correlated with H-3 of the rhamnose and that of the feruloyl moiety of **3** was correlated with H-2 of the rhamnose. In the ^{1}H NMR spectrum, H-2 and H-3 of the rhamnose were shifted downfield to δ 5.28 and 5.23, respectively. Therefore, the structure of **3** was 3-*O*-acetyl-2-*O*-*p*-hydroxycinnamoyl-α-L-rhamnopyranose.

3. Experimental

3.1. General

Instrumentation and plant materials were as previously described (Li et al., 1999).

3.2. Extraction and isolation

Eight kilograms of powdered roots of the plant was extracted with ethanol and concentrated as described (Li et al., 1999). The residue was suspended in H_2O and shaken successively with ether and *n*-BuOH, and the ether layer was subjected to CC column on silica gel with petrol–EtOAc (20:1–1:10). Six fractions (I–VI) were collected. Fraction V was subjected to further CC on silica gel with $CHCl_3$–MeOH (20:1) and PTLC (cyclohexane–acetone 1:1) to obtain **1** (42 mg), **2** (11 mg) and **3** (23 mg).

A portion of the *n*-BuOH layer residue (140 g) was subjected to a macro-porous resin DA-201 column eluted with H_2O and increasing amounts of EtOH. The 40% EtOH fraction was subjected to CC on silica gel with $CHCl_3$–MeOH–H_2O (9:1:0.1–7:3:0.3) to obtain four fractions (I–IV). Fraction I was subjected to CC on silica gel with EtOAc–MeOH–H_2O (10:2:0.1) to obtain **4** (63 mg). Fraction II was subjected to CC on silica gel with $CHCl_3$–MeOH–H_2O (4:1:0.1) to obtain **5** (57 mg). Fraction IV was subjected to CC on Sephadex LH-20 (30% EtOH) to yield two fractions (*a* and *b*). Fraction *a* was subjected to

CC on silica gel with $CHCl_3$–MeOH–H_2O (7:3:0.3) to obtain **6** (15.4 g). Fraction *b* was subjected to CC on silica gel with EtOAc–MeOH–H_2O (9:1:0.1–7:3:0.3) and ODS column (30% MeOH) to obtain **7** (97 mg). The 20% EtOH part was subjected to CC on silica gel with EtOAc–MeOH–H_2O (9:2:0.5) to yield two parts (1 and 2). Part 1 was subjected to CC on silica gel with EtOAc–MeOH–H_2O (200:15:15) and $CHCl_3$–MeOH–H_2O (9:3:0.3) to obtain **8** (32 mg). Part 2 was subjected to CC on silica gel with EtOAc–MeOH–H_2O (9:1.8:0.4) and $CHCl_3$–MeOH–H_2O (7:3:0.3) to obtain **9** (46 mg).

*3.2.1. Ningposide A (**1**)*

Oil; $[\alpha]_D^{20}$ +116.29° (*c* 0.630 acetone); EIMS *m/z*: 382 [M^+], 364, 304, 256, 194, 177. Analytically calculated for $C_{18}H_{22}O_9$: C 56.54, H 5.80; found: C 56.02, H 5.73; ^{1}H NMR spectral data ($CDCl_3$) δ ppm: 7.03 (1H, *d*, $J = 1.9$ Hz, H-2), 6.90 (1H, *d*, $J = 8.0$ Hz, H-5), 7.07 (1H, *dd*, $J = 8.0$, 1.9 Hz, H-6), 6.33 (1H, *d*, $J = 16.0$ Hz, H-α), 7.62 (1H, *d*, $J = 16.0$ Hz, H-β), 5.20 (1H, *d*, $J = 2.1$ Hz, rha-1), 5.38 (1H, *dd*, $J = 3.5$, 2.1 Hz, rha-2), 5.25 (1H, *dd*, $J = 10.1$, 3.5 Hz, rha-3), 3.71 (1H, *t*, $J = 10.1$ Hz, rha-4), 4.04 (1H, *m*, rha-5), 1.38 (3H, *d*, $J = 6.2$ Hz, rha-6), 3.92 (3H, *s*, OCH_3), 2.06 (3H, *s*, CH_3), ^{13}C NMR spectral data ($CDCl_3$) δ ppm: 126.7 (C-1), 109.4 (C-2), 146.8 (C-3), 148.2 (C-4), 114.8 (C-5), 123.4 (C-6), 114.5 (C-α), 146.0 (C-β), 166.3 (C═O), 92.4 (rha-1), 70.3 (rha-2), 72.1 (rha-3), 71.5 (rha-4), 68.6 (rha-5), 17.7 (rha-6), 21.0 (–CO–CH_3), 171.3 (–CO–CH_3), 56.0 (OCH_3).

*3.2.2. Ningposide B (**2**)*

Oil; $[\alpha]_D^{20}$ +87.23° (*c* 0.241 acetone); EIMS *m/z*: 382 [M^+], 364, 304, 256, 194, 177. Analytically calculated for $C_{18}H_{22}O_9$: C 56.54, H 5.80; found: C 56.87, H 5.65, ^{1}H NMR spectral data (CD_3COCD_3) δ ppm: 7.37 (1H, *d*, $J = 1.8$ Hz, H-2), 6.89 (1H, *d*, $J = 8.1$ Hz, H-5), 7.15 (1H, *dd*, $J = 8.1$, 1.8 Hz, H-6), 6.49 (1H, *d*, $J = 15.9$ Hz, H-α), 7.67 (1H, *d*, $J = 15.9$ Hz, H-β), 5.13 (1H, *d*, $J = 2.1$ Hz, rha-1), 5.16 (1H, *dd*, $J = 3.4$, 2.1 Hz, rha-2), 4.15 (1H, *dd*, $J = 9.9$, 3.4 Hz, rha-3), 4.98 (1H, *t*, $J = 9.9$ Hz, rha-4), 4.00 (1H, *m*, rha-5), 1.13 (3H, *d*, $J = 6.2$ Hz, rha-6), 3.93 (3H, *s*, OCH_3), 2.07 (3H, *s*, CH_3); ^{13}C NMR spectral data (CD_3COCD_3) δ ppm: 129.4 (C-1), 111.7 (C-2), 149.2 (C-3), 150.6 (C-4), 116.4 (C-5), 124.6 (C-6), 115.7 (C-α), 146.9 (C-β), 167.9 (C═O), 92.9 (rha-1), 74.8 (rha-2), 66.9 (rha-3), 75.8 (rha-4), 68.0 (rha-5), 18.3 (rha-6), 21.4 (–CO–CH_3), 171.6 (–CO–CH_3), 56.7 (OCH_3).

*3.2.3. Ningposide C (**3**)*

Oil; $[\alpha]_D^{20}$ +79.63° (*c* 0.383 acetone); EIMS *m/z*: 352 [M^+], 320, 274, 223, 205, 164, 147. Analytically calculated for $C_{17}H_{20}O_8$: C 57.95, H 5.72; found: C 57.31, H 5.69; ^{1}H NMR spectral data ($CDCl_3$) δ ppm: 7.58 (2 × 1H, *m*, H-2,6), 6.91 (2 × 1H, *m*, H-3,5), 6.40 (1H, *d*, $J = 16.0$ Hz, H-α), 7.66 (1H, *d*, $J = 16.0$ Hz, H-β), 5.11 (1H, *d*, $J = 1.8$ Hz, rha-1), 5.28 (1H, *m*, rha-2), 5.23 (1H, *dd*, $J = 10.0$, 3.4 Hz, rha-3), 3.63 (1H, *t*, $J = 10.0$ Hz, rha-4), 4.01 (1H, *m*, rha-5), 1.29 (3H, *d*, $J = 6.1$ Hz, rha-6), 1.96 (3H, *s*, CH_3); ^{13}C NMR spectral data ($CDCl_3$) δ ppm: 126.2 (C-1), 130.7 (C-2), 116.3 (C-3), 160.7 (C-4), 116.3 (C-5), 130.7 (C-6), 114.4 (C-α), 145.9 (C-β), 166.6 (C═O), 92.4 (rha-1), 70.9 (rha-2), 72.5 (rha-3), 71.3 (rha-4), 68.6 (rha-5), 17.9 (rha-6), 20.6 (–CO–CH_3), 170.5 (–CO–CH_3).

Acknowledgements

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