Pergamon

0031-9422(95)00904-3

Phytochemistry, Vol. 42, No. 1, pp. 239–240, 1996

0031-9422/96 $15.00 + 0.00

AN IRIDOID GLUCOSIDE FROM *DIPSACUS ASPEROIDES*

HISAKO TOMITA* and YURI MOURI

Kobe Pharmaceutical University, 4-19-1, Motoyamakita-machi, Higashinada-ku, Kobe 658, Japan

(*Received in revised form* 23 *October* 1995)

Key Word Index—*Dipsacus asperoides*; Dipsacaceae; iridoid glucoside; sweroside; loganin; cantleyoside; loganic acid; loganic acid-6′-O-β-D-glucoside.

Abstract—A new iridoid glucoside, loganic acid-6′-*O*-β-D-glucoside, has been isolated from the defatted root of *Dipsacus asperoides*. Its structure has been elucidated by spectroscopic means as 1*S*-(1α,4aα,6α,7α,7aα)-1-[(6-*O*-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy]-1,4a,5,6,7,7a-hexahydro-6-hydroxy-7-methyl-cyclopenta[*c*]pyran-4-carboxylic acid.

INTRODUCTION

The root of *Dipsacus asperoides* C. Y. Cheng et T. M. Ai [1] is used as a Chinese medicine (crude drug, Xu-duan). It has been shown to contain sucrose, daucosterol and glycosides of hederagenin [2].

Many other species of the Dipsacaceae contain glucosides of iridoids and secoiridoids [3, 4]. Thus, from *D. sylvestris* Jensen *et al.* [5] isolated loganin, sweroside and several bis-iridoids.

In an investigation of the roots of *D. asperoids*, we have isolated sweroside (**1**) [6], loganin (**2**) [7], cantleyoside (**3**) [8], loganic acid (**4**) [9] and loganic acid-6′-*O*-β-D-glucoside (**5**), which is novel compound.

RESULTS AND DISCUSSION

Loganic acid-6′-*O*-β-D-glucoside (**5**), $C_{22}H_{34}O_{15}$, $[\alpha]_D^{25}$ −54.4° (H_2O, *c* 0.5) was obtained in the pure state by HPLC.

The ^{13}C NMR spectrum of **5** showed 23 signals of which 11 could be assigned to an aglucone and the remaining signals to two β-glucopyranosyl moieties of which one was substituted at C-6 as shown by the lowfield shift (δ 71.46) of this atom. The aglucone signals were almost superimposable on those of **4**, except for the C-3 and C-4 signals which showed differences attributable to the varying degree of protonation of those carbons.

The signals from the two sugar moieties were almost superimposable on those published [10] for the gentiobioside moiety in 6′-*O*-glucosyl-aucubin [11], and this indicated the structure shown. NMR connectivities between the central β-glucopyranosyl moiety and C-1 of the aglucone, as well as with the outer β-glucopyranosyl moiety were confirmed by HMBC (^1H detected heteronuclear multiple bond connectivity). Thus, H-1 showed long-range couplings to C-3, C-5 and C-1′, while the C-6′ protons were shown to be coupled to C-4′, C-5′ and C-1″.

It was determined that the structure of loganic acid-6′-*O*-β-D-glucoside (**5**) was 1*S*-(1α,4aα,6α,7α,7aα)-1-[(6-*O*-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy]-1,4a,5,6,7,7a-hexahydro-6-hydroxy-7-methyl-cyclopenta[c]pyran-4-carboxylic acid.

EXPERIMENTAL

General procedures. ^1H and ^{13}C NMR: 500 and 125 MHz, respectively; MS: positive SIMS (matrix: glycerol).

Isolation of iridoid glucosides. Root of *Dipsacus asperoides* obtained as the Chinese medicine, Xu-duan, from the market was identified anatomically by comparison with reference material [1].

Powdered root (879 g) after extractions with petroleum ether, n-hexane and benzene, respectively, was extracted (×3) with MeOH (2 l) for 3 hr with boiling.

One part of the extract (73.5 g of 316.9 g) obtained by removing the ppt. of sucrose from the concd MeOH soln was chromatographed on silica gel with the lower phase of $CHCl_3$–MeOH–H_2O (13:7:2) giving sweroside (**1**), (0.688 g), loganin (**2**), (0.220 g), and crude cantleyoside from which cantleyoside (**3**), (0.108 g), was obtained by chromatography on LiChroprep RP-8 with MeOH–H_2O (7:3). The spectral data of **1** were in agreement with reported values [12]. Compound **2** was identified by comparison with an authentic sample. Compound **3** was identified as its

chromatographed on Cosmosil 140C18-OPN with MeOH–H_2O (1:4). The iridoid fraction was chromatographed again on the same column material with MeOH–H_2O (1:9) and then on silica gel with $CHCl_3$–MeOH–H_2O (13:7:2) to yield crude loganic acid and a more hydrophilic iridoid fraction.

Loganic acid (**4**), (2.82 g) was purified by HPLC on CAPCELL PAK C_{18} AG120 with MeCN–H_2O (1:5).

Loganic acid-6′-*O*-β-D-glucoside (**5**) (0.0242 g) was isolated from the more hydrophilic iridoid fraction by HPLC on CAPCELL PAK C_{18} UG120 with MeCN–H_2O (1:8) and purified by HPLC on the same column with MeCN-H_2O (1:10).

Loganic acid (**4**). Powder. Dec. 168°; $[\alpha]_D^{26}$ −86.2° (H_2O, *c* 0.5); SIMS, *m/z*: 399 $[M + Na]^+$, 377 $[M + 1]^+$; HRMS: 399.1284 ($C_{16}H_{24}O_{10}Na$, calc. 399.1265), 377.1437 ($C_{16}H_{25}O_{10}$, calc. 377.1446); ^1H NMR (D_2O, is. TSP): δ 5.41 (1H, *d*, $J_{1,9}$ = 3.5 Hz, H-1), 7.31 (1H, *d*, $J_{3,5}$ = <1.0 Hz, H-3), 3.05 (1H, *dddd*, $J_{5,9}$ = 8 Hz, $J_{5,6\alpha}$ = 8 Hz, $J_{5,6\beta}$ = 6.0 Hz, H-5), 2.16 (1H, *ddd*, $J_{6\alpha,6\beta}$ = 14.5 Hz, $J_{6\alpha,7}$ = 1.5 Hz, H-6α), 1.77 (1H, *ddd*, $J_{6\beta,7}$ = 5.5 Hz, H-6β), 4.15 (1*H*, *ddd*, $J_{7,8}$ = 5.0 Hz, H-7), 1.91 (1H, *m*, H-8), 2.13 (1H, *ddd*, $J_{8,9}$ = 9 Hz, H-9), 1.06 (3H, *d*, $J_{8,10}$ = 7.0 Hz, H-10), 3.28 (1H, *dd*, $J_{1',2'}$ = 8.0 Hz, $J_{2',3'}$ = 9.5 Hz, H-2′), 3.50 (1H, *dd*, $J_{3',4'}$ = 9.5 Hz, H-3′), 3.40 (1H, *dd*, $J_{4',5'}$ = 9.5 Hz, H-4′), 3.49 (1H, *m*, H-5′), 3.92 (1H, *dd*, $J_{5',6'a}$ = 2.0 Hz, $J_{6'a,6'b}$ = 12.5 Hz, H-6′a), 3.72 (1H, *dd*, $J_{5',6'b}$ = 6.0 Hz, H-6′b); ^{13}C NMR (D_2O, is. TSP): δ 99.2 (C-1), 152.2 (C-3), 117.7 (C-4), 32.82 (C-5), 43.1 (C-6), 77.3 (C-7), 42.8 (C-8), 48.0 (C-9), 14.8 (C-10), 101.4 (C-1′), 75.6 (C-2′), 78.5 (C-3′), 72.5 (C-4′), 79.2 (C-5′), 63.6 (C-6′), identical with values of data of authentic sample.

Loganic acid-6′-O-β-D-glucopyranoside (**5**). Powder, Dec. 208–209°; $[\alpha]_D^{25}$ −54.4° (H_2O, *c* 0.5); SIMS, *m/z*: 577 $[M + K]^+$, 561 $[M + Na]^+$, 539 $[M + 1]^-$; HRMS: 577.1508 ($C_{22}H_{34}O_{15}K$, calc. 577.1532), 561.1778 ($C_{22}H_{34}O_{15}Na$, calc. 561.1793), 539.1962 ($C_{22}H_{35}O_{15}$, calc. 539.1973); IR ν_{max}^{nujol} cm^{-1}: 3350, 3170, 1640; ^1H NMR (D_2O, is. TSP): δ 5.38 (1H, *d*, $J_{1,9}$ = 2.5 Hz, H-1), 7.0 (1H, *d*, $J_{3,5}$ = <1.0 Hz, H-3), 3.05 (1H, *dddd*, $J_{5,9}$ = 9.0 Hz, $J_{5,6\alpha}$ = 9.0, $J_{5,6\beta}$ = 6.0, H-5), 2.12 (1H, *ddd*, $J_{6\alpha,6\beta}$ = 14.0 Hz, $J_{6\alpha,7}$ = 2.5 Hz, H-6α), 1.76 (1H, *ddd*, $J_{6\beta,7}$ = 6 Hz, H-6β), 4.17 (1H, *ddd*, $J_{7,8}$ = 5.0 Hz, H-7), 1.91 (1H, *ddq*, $J_{8,9}$ = 10.5, $J_{8,10}$ = 7.0, H-8), 2.11 (1H, *ddd*, H-9), 1.07 (3H, *d*, H-10), 4.8 (H-1′), 3.30 (1H, *dd*, $J_{1',2'}$ = 9.0 Hz, $J_{2',3'}$ = 9 Hz, H-2′), 3.51 (1H, *dd*, $J_{3',4'}$ = 9.0 Hz, H-3′), 3.48 (1H, *dd*, $J_{4',5'}$ = 9.0 Hz, H-4′), 3.67 (1H, *m*, H-5′), 4.23 (1H, *dd*, $J_{6'a,6'b}$ = 11.5 Hz, $J_{5',6'a}$ = 1.5 Hz, H-6′a), 3.88 (1H, *dd*, $J_{5',6'b}$ = 5.5 Hz, H-6′b), 4.52 (1H, *d*, $J_{1'',2''}$ = 8.0 Hz, H-1″), 3.33 (1H, *dd*, $J_{2'',3''}$ = 9.0 Hz, H-2″), 3.49 (1H, *dd*, $J_{3'',4''}$ = 9.5 Hz, H-3″), 3.40 (1H, *dd*, $J_{4'',5''}$ = 9.5 Hz, H-4″), 3.45 (1H, *m*, H-5″), 3.93 (1H, *dd*, $J_{6''a,6''b}$ = 12.0 Hz, $J_{5'',6''a}$ = 2.0 Hz, H-6″a), 3.73 (1H, *dd*, $J_{5'',6''b}$ = 5.5 Hz, H-6″b); ^{13}C NMR (D_2O, is. TSP): δ 98.59 (C-1), 147.68 (C-3), 121.78 (C-4), 33.35 (C-5), 43.64 (C-6), 77.29 (C-7), 42.64 (C-8), 48.18 (C-9), 14.86 (C-10), 178.57 (C-11), 101.16 (C-1′), 75.46 (C-2′), 78.33 (C-3′), 72.32 (C-4′), 78.11 (C-5′), 71.46 (C-6′), 105.83 (C-1″), 75.93 (C-2″), 78.56 (C-3″), 72.50 (C-4″), 78.80 (C-5″), 63.62 (C-8″).

Acknowledgements—We thank Dr M. Sugiura and Dr K. Saiki, Kobe Pharmaceutical University, Japan, for measurements of NMR spectra and mass spectra, respectively.

REFERENCES

1. Zhou, G. C., Komatsu, K., Yamaji, S. and Namba, T. (1994) *Nat. Medicines* **48**, 131.
2. Zhang, Y. W. and Xue, Z. (1992) *Acta Pharm. Sin.* **27**, 912.
3. Hegnauer, R. (1966) *Chemotaxonomic der Pflanzen* Vol. 4, p. 23. Birkhäuser, Basel.
4. Aliev, A. M. and Movsumov, I. S. (1981) *Ratit. Resur.* **17**, 602.
5. Jensen, S. R., Lyse-Petersen, S. E. and Nielsen, B. J. (1979) *Phytochemistry* **18**, 273.
6. Inouye, H., Ueda, S. and Nakamura, Y. (1966) *Tetrahedron Lett.* 5229.
7. Battersby, A. R., Hall, E. S. and Southgate, R. (1969) *J. Chem. Soc. C* 722.
8. Sévenet, T., Thal, C. and Potier, P. (1971) *Tetrahedron* **27**, 663.
9. Coscia, C. J. and Guarnaccia, R. (1968) *Chem. Commun.* 138.
10. Boros, C. A. and Stermitz, F. R. (1990) *J. Nat. Prod.* **53**, 1055.
11. Bianco, A., Bolli, D. and Passacantili, P. (1981) *Gazz. Chim. Ital.* **111**, 91.
12. Van Beek, T. A., Lankhorst, P. P., Verpoorte, R. and Baerheim Svendsen, A. (1982) *Planta Med.* **44**, 30.