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SESQUITERPENE LACTONES FROM *LACTUCA TATARICA*

WANDA KISIEL,* BARBARA BARSZCZ and EDWARD SZNELER†

Department of Phytochemistry, Institute of Pharmacology, Polish Academy of Sciences, PL-31-343 Kraków; †Department of Chemistry, Jagiellonian University, PL-30-060 Kraków, Poland

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Key Word Index—*Lactuca tatarica*; Asteraceae; Lactuceae; sesquiterpene lactones; guaianolides; germacrolides; glycosides.

Abstract—From the roots of *Lactuca tatarica*, one new and two known guaianolides were isolated together with five known guaianolide glycosides, three known germacrolide glycosides and benzyl-β-glucopyranoside. The structure of the new compound was elucidated as 11_{β}H, 13-dihydrolactucin-8-O-*p*-methoxyphenylacetate by spectral methods. © 1997 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Lactuca tatarica C. A. Meyer is widely distributed in central Asia. Chemically, the plant has received little attention apart from the work done on the aerial parts, from which α-amyrin and the two guaianolides, lactucin (**1**) and lactucopicrin (lactucin-8-O-*p*-hydroxyphenylacetate), have been isolated [1]. The guaianolides are known as biologically active constituents of *Lactuca virosa* [2]. We have examined sesquiterpene lactones present in the roots of *L. tatarica* and found the compounds to be accumulated mainly as glycosides. This paper deals with their isolation and characterization.

RESULTS AND DISCUSSION

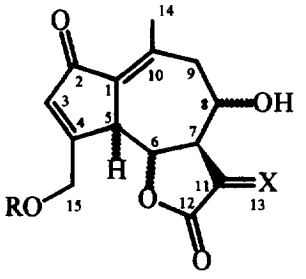
The ethanol extract of the fresh roots of *Lactuca tatarica* was chromatographed on a silica gel column and relevant fractions were further separated by preparative TLC or semipreparative HPLC to afford sesquiterpene lactone aglycones and glycosides.

Two of the aglycones were identified as lactucin (**1**) and jacquinelin (**3**) [3] by direct comparison with authentic samples. The third one appeared to be a new natural product and a minor component of the plant material. The structure **4** for the compound was readily assigned when its ^{1}H NMR and mass spectral data were compared with those reported for 11_{β}H, 13-dihydrolactucin-8-O-*p*-hydroxyphenylacetate, previously isolated from *Cichorium intybus* [4] and *Lactuca saligna* [5, 6]. In particular, the signals due to the skeleton part indicated that we were dealing with closely related analogues differing in the nature of the ester side chain at C-8. A molecular ion peak at *m/z* 426 analysing for $C_{24}H_{26}O_7$ and prominent peaks at *m/z* 166 $[A]^+$, *m/z* 149 $[A_1]^+$ and *m/z* 121 $[A_2]^+$ in the mass spectrum, together with an extra three-proton methoxy methyl singlet at δ 3.80 in the ^{1}H NMR spectrum, indicated that **4** was 11_{β}H,13-dihydrolactucin-8-O-*p*-methoxyphenylacetate.

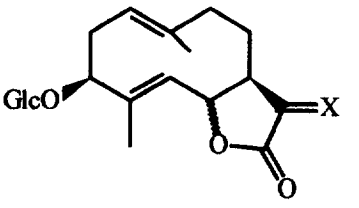
The sesquiterpene lactone glycosides contained guaianolide and germacrolide derivatives. The less polar compounds with very similar R_f values on TLC could be separated by semipreparative HPLC to give crepidiaside B (**5**) [7], picriside C (**9**) [8], sonchuside A (**10**) [9] and a mixture of 11_{β}H,13-dihydroglucozaluzanin C (**6**) [10] and picriside B (**11**) [8]. In addition, benzyl-β-glucopyranoside (**12**) was also isolated. Separation of the more polar glycosides afforded cichorioside B (**2**) [11] and a mixture of macrocliniside A (**7**) [12] and ixerin F (**8**) [13]. Compounds **5–8** and **12** were identified by direct comparison with authentic samples, while compounds **2** and **9–11** showed ^{1}H NMR and mass spectra identical to those published earlier. As the 89.55 MHz ^{1}H NMR data for **2** and **10** in the literature are not complete, they are listed in Table 1. The mixtures of **6** and **11** (*ca* 1:3), and **7** and **8** (*ca* 1:2.5) were not separated further, as the ^{1}H NMR signals could be assigned to the respective compounds by a careful analysis of the integrals. The sugar moiety in each glycoside was identified as β-glucopyranose by ^{1}H NMR.

Cichorioside B (**2**) and the germacrolide glycosides (**9–11**) have been isolated from *Lactuca* species for the

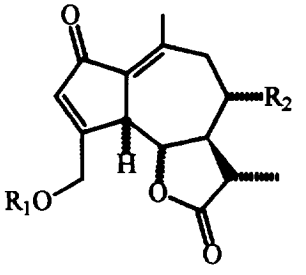
*Author to whom correspondence should be addressed.



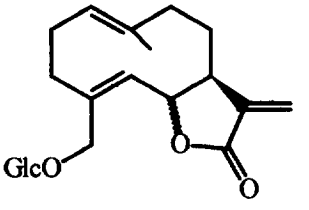
	R	X
1	H	CH_2
2	Glc	H,αMe



	X
9	CH_2
10	H,αMe



	R_1	R_2
3	H	H
4	H	OA_1
5	Glc	H



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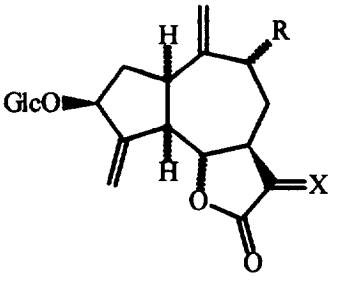
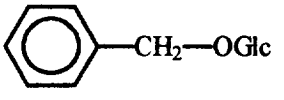


	R	X
6	H	H,αMe
7	OH	CH_2
8	OH	H,αMe



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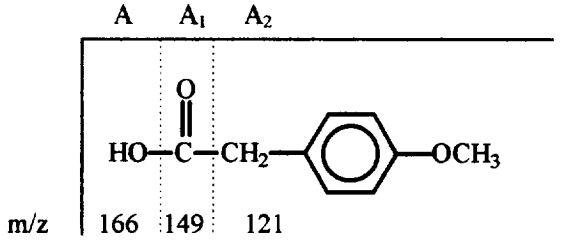

first time. The compounds are known as constituents of some other members of the Lactuceae tribe [8, 9, 11].

EXPERIMENTAL

General procedure. Merck silica gel was used for CC (Art. 7754) and TLC (Art. 5553). Semiprep. HPLC was performed on a Delta-Pak C 18 cartridge column (particle size 15 μm, 25 × 100 mm) coupled to a UV photodiode array detector. The column was eluted with MeOH–H_2O (1:1), flow rate 3 ml min^{-1}. Sesquiterpene lactone glycosides and aglycones isolated previously in this laboratory [6, 14] were used as authentic samples for comparing their physical and spectral data (500.13 MHz ^1H NMR, EIMS or LSIMS) with those of the known compounds.

Plant material. Roots of *L. tatarica* were collected in July 1994 from plants at the flowering stage, growing in the Garden of Medicinal Plants of the Institute of Pharmacology, Polish Academy of Sciences in Kraków, where a voucher specimen was deposited.

Table 1. ^{1}H NMR data of compounds **2**, **4** and **10** (500.13 MHz, TMS as internal standard, δ-values)

H	**2** (pyridine-d_5)	**4** ($CDCl_3$)	**10** (pyridine-d_5)
1			4.71 *dd*
2			2.50 *br ddd*
2′			2.45 *ddd*
3	6.94 *br d*	6.44 *br d*	4.73 *dd*
5	3.54 *br d*	3.59 *br d*	4.77 *br d*
6	3.59 *dd*	3.69 *dd*	4.67 *dd*
7	2.26 *ddd*	2.32 *ddd*	1.55 *br ddd**
8	3.82 *br ddd*	4.81 *ddd*	1.66 *br dd*
8′			1.47 *br ddd**
9	2.84 *dd*	2.69 *dd*	1.86 *br dd*
9′	2.53 *dd*	2.36 *dd*	2.19 *br dd*
11	2.77 *dq*	2.45 *dq*	2.30 *dq*
13	1.64 *d*	1.20 *d*	1.23 *d*
14	2.44 *s*	2.44 *s*	1.33 *s*
15	4.98 *br d*	4.54 *br d*	1.94 *s*
15′	5.22 *br dd*	4.85 *br dd*	
	Glucose moiety	Ester moiety	Glucose moiety
1	4.94 *d*		4.83 *d*
2	4.10 *dd*	3.57 *d* (H-2_a)	4.10 *dd*
		3.62 *d* (H-2_b)	
3	4.18–4.30 *m*		4.17–4.29 *m*
4	4.18–4.30 *m*	7.18 *d* (H-2′, H-6′)	4.17–4.29 *m*
5	3.90 *m*	6.88 *d* (H-3′, H-5′)	3.91 *m*
6	4.38 *dd*		4.40 *dd*
6′	4.52 *dd*		4.60 *dd*
OMe		3.80 *s*	

*Partially overlapped signals J (Hz): compound **2**: 3, 15′ = 1.4; 5, 6 = 10.0; 6, 7 = 7, 8 = 9.7; 7, 11 = 11.8; 8, 9 = 10.7; 8, 9′ = 1.7; 9, 9′ = 13.7; 11, 13 = 6.9; 15, 15′ = 17.4; compound **4**: 3, 15′ = 1.4; 5, 6 = 6, 7 = 10.1; 7, 8 = 8, 9 = 10.6; 7, 11 = 11.5; 8, 9′ = 1.9; 9, 9′ = 13.7, 11, 13 = 6.9; 15,15′ = 17.2; ester moiety: 2_a, 2_b = 15.7; 2′, 3′ = 5′, 6′ = 8.7; compound **10**: 1, 2 = 4.2; 1, 2′ = 11.9; 2, 2′ = 12.0; 2, 3 = 5.9; 2′, 3 = 10.7; 5, 6 = 9.0; 6, 7 = 9.8; 7, 8 = 8, 9 = 8′, 9′ = ca 1.0; 7, 8′ = 10.5; 7, 11 = 11.8; 8, 8′ = 13.9; 8, 9′ = 5.7; 8′, 9 = 11.0; 9, 9′ = 13.0; 11, 13 = 7.0. Glucose moieties: 1, 2 = 7.8; 2, 3 = 8.5; 5, 6 = 5.8; 5, 6′ = 2.1; 6, 6′ = 11.9.

Extraction and isolation of compounds. Fresh roots (490 g) were exhaustively extracted with EtOH at room temp. with shaking and the solvent was evapd under vacuum, giving 31 g of residue which was chromatographed on a silica gel column using hexane and a gradient of hexane–EtOAc (up to 50% EtOAc) followed by a gradient of $CHCl_3$–MeOH (up to 20% MeOH). Frs from hexane–EtOAc (1:1) were combined according to their content and compounds purified by repeated prep. TLC ($CHCl_3$–MeOH, 19:1) to give **4** (2.7 mg), **3** (47.9 mg) and **1** (10.6 mg), in that order. Initial frs from $CHCl_3$–MeOH (9:1) were further separated by HPLC to afford glycosides **5**, **6** and **9**–**12**. Yields and retention times as follows: **5** (8.9 mg, R_t = 20.08 min), **12** (7.5 mg, R_t = 25.64 min), **9** (10.5 mg, R_t = 38.30 min), **10** (43.6 mg, R_t = 45.97 min), **6** and **11** in a mixture (32 mg, R_t = 70.69 min). Further frs from $CHCl_3$–MeOH (9:1 and 17:3) gave a mixture of **7** and **8** (21.5 mg), and **2** (12.1 mg), after purification by prep. TLC using $CHCl_3$–MeOH (17:3 and 4:1) mixtures, respectively, as solvent systems.

11$_\beta$*H*,13-*dihydrolactucin*-8-O-p-*methoxyphenylacetate* (4). Colourless gum. EIMS *m/z* (rel. int.): 426 $[M]^+$ (1.6), 260 $[M-A]^+$ (2.5), 231 $[M-A-CHO]^-$ (2.5), 214 $[M-A-CO-H_2O]^+$ (4.7), 198 (21.7), 187 (30.2), 166 $[A]^+$ (28.1), 149 $[A_1]^+$ (10.8), 121 $[A_2]^+$ (64.7), 43 (100). ^{1}H NMR: Table 1.

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