

ROOT CONSTITUENTS OF *LACTUCA SIBIRICA* AND A COMPARISON OF METABOLITE PROFILES OF *L. SIBIRICA* AND *L. TATARICA*

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(Received: June 5, 2008. Accepted: October 4, 2008)

ABSTRACT

Nine known sesquiterpene lactones, including four lactucin-type guaianolides, four costuslactone-type guaianolides and one germacranolide, were isolated from roots of *Lactuca sibirica* (Asteraceae), six of which were glycoside derivatives. The chemosystematic significance of the compounds is discussed in the context of sesquiterpenoids present in roots of the closely related species *Lactuca tatarica*. A comparison of sesquiterpene lactone profiles indicate that the species can be differentiated on the basis of their germacranolide glycoside compositions.

KEY WORDS: *Lactuca sibirica*, *L. tatarica*, Asteraceae, sesquiterpene lactones, chemotaxonomy.

INTRODUCTION

The genus *Lactuca* (Asteraceae, tribe Lactuceae), comprising approximately 100 species, is divided into seven sections and two (African and North American) geographical groups. The section *Mulgedium* (Cass.) C.B. Clarke is represented mainly by *Lactuca sibirica* (L.) Benth. ex Maxim. and *Lactuca tatarica* (L.) C.A. Mey., occurring in continental Europe and Asia. *Lactuca taraxacifolia* Schum. et Thonn. is a newly described species from the mountains of central Asia. Members of this section are herbaceous perennials with blue, lilac, rarely white florets (Doležalová et al. 2002; Koopman et al. 1998; Lebeda et al. 2004).

Chemically, plants of the genus *Lactuca* can be characterized by the accumulation of sesquiterpene lactones, consisting mainly of guaianolides and germacranolides, and phenolic compounds, among others (Kim et al. 2007; Kisiel and Barszcz 1997; Kisiel and Michalska 2008; Terencio et al., 1991 and references cited herein). *L. sibirica* has received little attention, apart from the work done recently in our laboratory, on its aerial parts from which four lactucin-type guaianolides and three furofuran lignans, including two new acylated glycosides of 4 α , 8 α -dihydroxypinoresinol, have been isolated (Kisiel and Michalska 2008). For *L. tatarica*, a previous chemical study has been carried out on the whole plant extract, resulting in the isolation of lactucin and its ester lactucopicrin (Akyev et al. 1990). Our investigation of the plant roots has led to the isolation of lactucin and its four derivatives, three costus lactone-type guaianolides and four germacranolides, accumulated mainly as glycosides (9 compounds) (Kisiel et al. 1997; Kisiel and Barszcz 1998). It should be pointed out that we could

find no sesquiterpene lactones in the aerial part extract. From the extract the flavonoid aglycones apigenin and luteolin have been isolated, in addition to apigenin-7-O- β -glucopyranoside, kaempferol- and quercetin-3-O- β -glucopyranosides (Kisiel 1998).

Phylogenetic relationships among *Lactuca* species inferred from ITS-1 DNA sequences and AFLP fingerprints were studied by Koopman et al. (1998 and 2001) and the close relationship between the section *Mulgedium* species, represented by *L. sibirica* and *L. tatarica*, was corroborated. Therefore, the purpose of the present study was to characterize the sesquiterpene lactone composition in roots of *L. sibirica* and to compare it with that found in *L. tatarica*. Below, we describe the isolation of compounds **1-9** (Fig. 1) from the hitherto not studied roots of *L. sibirica*.

MATERIAL AND METHODS

Plant material

Roots of *L. sibirica* were collected in August 2004 from plants growing in the Garden of Medicinal Plants, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland, where a voucher specimen (04/133) was deposited. Seeds of wild origin collected in Finland (Aavaranta, 62° 37' N, 29° 42' E) were obtained from the Botanical Garden in Joensuu.

Extraction and isolation

The dried and powdered plant material (29 g) was exhaustively extracted with EtOH at room temperature. After removing the solvent under reduced pressure, a resi-

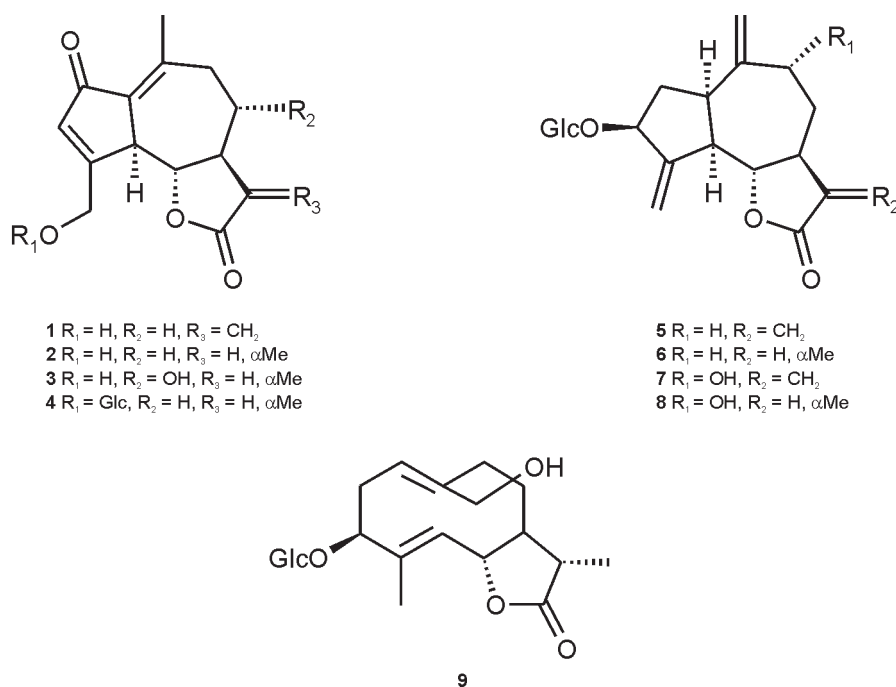


Fig. 1. Chemical structures of sesquiterpene lactones isolated from roots of *Lactuca sibirica* (Glc = β-glucopyranosyl).

due (4 g) was obtained, which was subjected to column chromatography on silica gel (Merck, Art. 7754), using hexane-EtOAc (up to 100 % EtOAc), followed by EtOAc-MeOH (up to 10% MeOH) gradient solvent systems. Fractions containing identical compounds were combined, after TLC analysis. The final step of purification was performed by preparative TLC (Merck, Art. 5553) and semipreparative HPLC on a Delta-Pak C-18 column (particle size 15 μm, 25×100 mm) coupled to a dual wavelength UV/Vis detector operating at 210 and 260 nm, using a H₂O-MeOH (7:3) mixture at a flow rate of 3.0 ml min⁻¹. Fractions eluted with hexane-EtOAc (1:1) gave a ca. 1:2 mixture of **1** and **2** (8.1 mg) and **3** (3.6 mg), after separation by preparative TLC (CHCl₃-MeOH, 9:1). Fractions from EtOAc elution contained sesquiterpene lactone glycosides. Initial fractions were separated by preparative TLC (CHCl₃-MeOH, 9:1) to give a ca. 3:0.5 mixture of **5** and **6** (24.4 mg). Further fractions were separated by preparative TLC (CHCl₃-MeOH, 17:3) and semipreparative HPLC to afford **4** (18.8 mg), **7** (4.4 mg), **8** (3.9 mg), and **9** (10.3 mg). The isolated compounds were identified as follows: 8-deoxylactucin (**1**), jacquinelin (**2**), 11β, 13-dihydroxylactucin (**3**), crepidiaside B (**4**), vernoflexuoside (glucozaluzanin C, **5**), 11β, 13-dihydroglucozaluzanin C (**6**), macroclinside A (**7**), ixerin F (**8**), and 3β, 14-dihydroxy-11β, 13-dihydrocostunolide-3-O-β-glucopyranoside (**9**) (Fig. 1). The compounds were readily characterized by direct comparison (HPLC, ¹H NMR, 300.18 MHz) with reference compounds from our collection isolated from *Lactuca* species (Kisiel and Barszcz 1997; Stojakowska et al. 1994).

RESULTS AND DISCUSSION

Our chemical study of the roots of *L. sibirica* has led to the isolation of four lactucin-type guaianolides (**1-4**), four costus lactone-type guaianolides (**5-8**), and one germacranolide (**9**), known as constituents of some other *Lactuca*

species, e.g. *L. virosa* (Kisiel and Barszcz 1997). Of these, the guaianolides **2**, **4**, **6-8** are common constituents of *L. sibirica* and *L. tatarica*. Both species can be differentiated based on their germacranolide glycoside compositions. The roots of *L. sibirica* yielded 3β, 14-dihydroxy-11β, 13-dihydrocostunolide-3-O-β-glucopyranoside (**9**), while the roots of *L. tatarica* afforded four different costunolide derivatives, including 3β, 11β, 14-trihydroxy-11,13-dihydrocostunolide-3-O-β-glucopyranoside (tataroside) (Kisiel and Barszcz 1998). Costunolide derivatives hydroxylated at C-3 and C-14 or C-3, C-11 and C-14 are rare natural products. Compound **9** and its aglycone have been found in *L. virosa* (Kisiel and Barszcz 1997) and *L. sativa* (Mahmoud et al. 1986), respectively, while tataroside has not been reported from other plant sources. The compounds seem to be restricted to the genus *Lactuca*. Moreover, *L. sibirica* can be differentiated by the accumulation of acylated glycosides of furofuran lignans in its aerial parts (Kisiel and Michalska 2008). The flavonoids isolated from the aerial parts of *L. tatarica* (Kisiel 1998) are quite common constituents in *Lactuca* species (Hou et al. 2003; Kim et al. 2007; Kisiel and Zielińska 2000; Terencio et al. 1991).

Conclusively, these results indicate that germacranolides and lignans are reliable taxonomic markers within the section *Mulgedium*.

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