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Further Sesquiterpene Lactones from *Dugaldia hoopesii*

by M. Urbańska[1], G. Nowak[1] and W. Kisiel[2*]

[1]*Department of Medicinal Plants, University of Medical Sciences, Mazowiecka 33, Pl-60-623 Poznań, Poland*
[2]*Department of Phytochemistry, Institute of Pharmacology, Polish Academy of Sciences, Smętna 12, Pl-31-343 Kraków, Poland*

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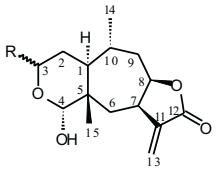
Orange sneezeweed (*Dugaldia hoopesii* (A. Gray) Rydb., Asteraceae), also known as *Helenium hoopesii* A. Gray, has been separated from the genus *Helenium* due to clear morphological differences [1]. The plant and several representatives of *Hymenoxys* species, *e.g. H. odorata* and *H. richardsonii*, are well-known livestock poisons of the American southwest [1,2]. The major toxic principle of the plants called hymenovin was found to be a mixture of the sesquiterpene lactone hymenoxon (**1**) and its C-3 and/or C-4 diastereoisomers [1,3,4]. In earlier work [5], *Dugaldia hoopesii* afforded the *seco*-pseudoguaianolide hymenoxon (**1**), the pseudoguaianolides hymenoratin (**5**), hymenograndin and its 4-O-acetyl derivative (**6**), first reported from *Hymenoxys* species [3], along with the guaianolide 2α-tigloyloxydugaldiolide (**8**) and some other secondary metabolites. More recently, compound **8** was found in *Hymenoxys lemmonii* [6], *H. richardsonii* and *H. subintegra* [7]. *Seco*-pseudoguaianolides (also known as *seco*-helenanolides) of the type exemplified by hymenoxon (**1**), which are particularly characteristic for plants of the genus *Hymenoxys*, were also isolated from *Dugaldia integrifolia* [8], previously placed in the genus *Helenium*. The compounds have not been reported from *Helenium* species. Therefore, the close relationship of *Dugaldia* and *Hymenoxys* species was suggested [7,8].

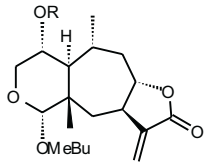
This paper deals with the isolation of further sesquiterpene lactone aglycones and glycosides from aerial parts of *Dugaldia hoopesii*, all of which are well known constituents of *Hymenoxys* species.

The aerial parts of the plant were extracted with methanol and the extract, after fractionation and repeated column chromatography on silica gel, yielded in order of increasing polarity acetylhymenograndin (**6**) [3], hymenoratin B (**3**) [9], a hymenovin mixture, 2α-tigloyloxydugaldiolide (**8**) [5], a mixture of hymenoratin (**5**) and neohymenoratin (**7**), pure neohymenoratin (**7**), hymenoratin B 2-O-β-D-(6'-O-acetyl)-glucopyranoside (**4**) and lemmonin A (**9**) [6] (Scheme). Of these, acetylhymenograndin was found to be the main constituent of the plant material. Compounds **3**–**9** were easily

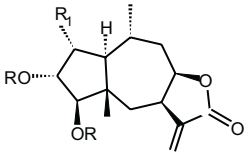
* Corresponding author, e-mail: kisielw@if-pan.krakow.pl



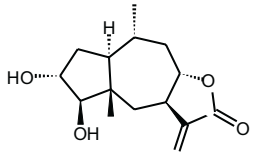
1 R=βOH
2 R=αOH



3 R=H
4 R=Glc(6'-Ac)



5 R=H, R_1=H
6 R=Ac, R_1=OAc



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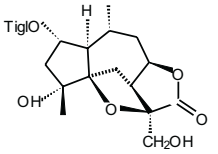

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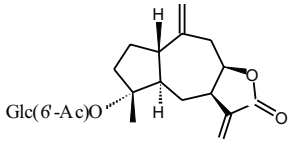

9

Glc(6'-Ac)=β-D-(6'-O-acetyl)-glucopyranosyl
MeBu=2-metylbutanoyl Tigl=tigloyl

identified by comparison of their spectral and physical properties with those in the literature. Analysis of the ^{1}H NMR spectrum of the hymenovin mixture which could not be separated by semi-preparative RP HPLC showed it to consist of various hymenoxon diastereoisomers. Two major constituents were identified as hymenoxon (**1**) and its C-3 epimer (**2**). This was evident on comparing their characteristic ^{1}H NMR signals with those reported [4]. The two epimers were present in significant quantities in a hymenovin mixture obtained from *Psilostrophe gnaphaloides* [4]. Compound **3** and compounds **4**, **7** and **9** were first isolated from *Hymenoxys odorata* [9] and *H. lemmonii* [6], respectively.

This is the first report on the presence of **2**, **3**, **4**, **7** and **9** in *Dugaldia* species. So far, sesquiterpene lactone glycosides have not been isolated from these plants. The chemical results described here and by earlier workers, in conjunction with a consideration of the morphological differences, further support the close relationship of the genus *Dugaldia* to *Hymenoxys* and its separation from *Helenium*.

Plant material: Aerial parts of *Dugaldia hoopesii* were collected in June 2001 from plants growing in the Garden of Medicinal Plants of the University of Medical Sciences in Poznań, Poland, where a voucher specimen (No. 74/92) is deposited.

Extraction and isolation: The dried plant material (730 g) was ground and exhaustively extracted with MeOH at room temperature providing a residue (10.0 g) which was suspended in H_2O (600 ml) and filtered. The filtrate was partitioned with $CHCl_3$ (3×150 ml) and the $CHCl_3$ layer was dried over anhydrous sodium sulphate and concentrated *in vacuo* to give 3.72 g of crude material. The material was chromatographed on a silica gel (Merck, Art. 7734) column eluted with a $CHCl_3$-acetone gradient solvent system affording 31 fractions. Fractions of the same compositions (by TLC) which contained sesquiterpene lactones were collected as follows: fractions 5, 6–7, 15–17 and 18–19 ($CHCl_3$-acetone, 5 : 1), fractions 20–21 ($CHCl_3$-acetone, 2 : 1), fractions 22–23 and 24–26 ($CHCl_3$-acetone, 1 : 2). The above fractions were further separated and purified by silica gel (Merck, Art. 7729) column chromatography. Rechromatography of fraction 5 and fractions 6–7 using hexane-EtOAc (4 : 1 and 2 : 1) mixtures gave **6** (41.0 mg) and **3** (10.0 mg), respectively. Fractions 15–17 on rechromatography ($CHCl_3$-acetone-hexane, 5 : 2 : 3) furnished a hymenovin mixture (40.8 mg). Part of the mixture was subjected to further purification by semi-preparative RP HPLC (H_2O-MeOH, 6 : 4) before spectral analysis. Purification of fractions 18–19 on silica gel columns using hexane-EtOAc-$CHCl_3$ (2 : 1 : 1 and 1 : 3 : 1) mixtures yielded **8** (2.9 mg). Rechromatography of fractions 20–21 (hexane-acetone, 2 : 1) gave a mixture (3.4 mg) of compounds **5** and **7** in the ratio *ca.* 1.0 : 6.8, indicated by ^{1}H NMR. Rechromatography of the material from fractions 22–23 ($CHCl_3$-EtOAc, 1 : 3, followed by EtOAc) gave pure **7** (3.1 mg) and subfractions containing impure **4** which were combined and further purified on a silica gel column eluted with $CHCl_3$ -acetone (2 : 1 and 1 : 1) mixtures to give **4** (4.1 mg). Fractions 24–26 on rechromatography using $CHCl_3$-EtOAc gradient solvent system and subsequent purification using hexane-acetone-$CHCl_3$ (2 : 2 : 1) furnished **9** (3.0 mg).

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