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ScienceDirect
Phytochemistry 67 (2006) 2140–2145
PHYTOCHEMISTRY
www.elsevier.com/locate/phytochem

Bufadienolides from bulbs of *Urginea lydenburgensis* (Hyacinthaceae: Urgineoideae)

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Received 8 September 2005; received in revised form 3 May 2006
Available online 10 July 2006

Abstract

Bulbs of the ethnomedicinal hyacinthac *Urginea lydenburgensis* have yielded two bufadienolides, 16β-acetoxy-3β,14β-dihydroxy-19-formyl-bufa-4,20,22-trienolide (scillicyanosidin) and 4β,8β,11α,14β-tetrahydroxybufa-5,20,22-trienolide-12-one, 2α,3β-*O*-4,6-dideoxy-L-glucose (lydenburgenin).

Keywords: Amaryllidaceae; *Urginea lydenburgensis*; Bufadienolides; 16β-Acetoxy-3β,14β-dihydroxy-19-formyl-bufa-4,20,22-trienolide (scillicyanosidin); 4β,8β,11α,14β-Tetrahydroxybufa-5,20,22-trienolide-12-one, 2α,3β-*O*-4,6-dideoxy-L-glucose (lydenburgenin)

1. Introduction

Urginea lydenburgensis R.A. Dyer of the subfamily Urgineoideae (family Hyacinthaceae) occurs in the Mpumalanga Province of South Africa, particularly the Lydenburg District (Dyer, 1942). Although it is generally accepted that the genus *Urginea* Steinh. should be placed in synonymy under *Drimia* Jacq. (Jessop, 1977; Stedje, 1987; Manning and Goldblatt, 2003), there is presently little consensus on species boundaries in *Drimia* s.l., particularly in the summer-rainfall region of South Africa. *U. lydenburgensis* is one such taxon that has been variously accepted (Reid, 1993), or alternatively synonymised under *Drimia delagoensis* (Bak.) Jessop (Jessop, 1977). However, as *U. lydenburgensis* has not yet been formally transferred to *Drimia*, this current phytochemical report employs the basionym. *U. lydenburgensis* is a highly toxic species responsible for stock losses, which is how it first attracted the attention of toxicologists (Van der Walt and Steyn, 1939) and subsequently the taxonomist (the species' author) from whom a plant identification was requested (Dyer, 1942). Fresh bulbs in the pre-flowering state proved fatal when administered to sheep and rabbits; sheep exhibited tympanites, apathy, anorexy, diuresis and severe diarrhoea (Van der Walt and Steyn, 1939), symptoms consistent with cardiotoxicosis (Kellerman et al., 1988).

The subfamily Urgineoideae is phytochemically characterised by the presence of bufadienolides (Speta, 1998; Pohl et al., 2000). Although bufadienolides show typical digitalis-like activity, the therapeutic usefulness of these compounds is unfortunately impaired by side effects which include severe gastric irritation (Sapeika, 1951; Majinda et al., 1997). The sap of leaves and bulbs of *Drimia* (syn. *Urginea*) species are irritating to the skin; some species produce such marked topical stinging and itching effects that they are used by young Xhosa boys during pain-endurance games. Bufadienolide-containing plants are also used as anthelmintics, for bronchial asthma, heart conditions, fevers and during pregnancy

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doi:10.1016/j.phytochem.2006.05.009

(Hutchings and Terblanche, 1989). Ethnomedicinal plant traders in Nelspruit (Mpumalanga Province) sell *U. lydenburgensis* under the names *masi xabane* and *isiklenama*, for internal use in treating asthma and itching of the skin. Vendors also recommend that the plant be administered internally in conjunction with either *Drimia altissima* (L.f.) Ker Gawl. or *Urginea epigea* R.A. Dyer, to respectively relieve asthma, and "blood impurities". A Swazi traditional medical practitioner from Nelspruit reportedly alleviated "body pains" (possibly rheumatism) by washing the whole body with a solution prepared by soaking the finely chopped bulbs in water. Patients reported experiencing a bracing, stinging sensation (*J. Onderstall 381*, PRE), consistent with the presence of bufadienolides. This information represents the first published account of *U. lydenburgensis* as an ethnomedicinal subject. The Swazi practitioner further recognised the poisonous character of the bulb and recommended that it should not be eaten.

Two novel bufadienolides were isolated from *U. lydenburgensis*.

2. Results and discussion

Compounds **1** and **2** were isolated from the dichloromethane extract of *U. lydenburgensis*. Use was made of ^{1}H, ^{13}C, HSQC, HMBC, COSY, TOCSY and NOESY spectra to determine the structures of compounds **1** and **2** and to assign ^{1}H and ^{13}C NMR resonances (Tables 1 and 2). The molecular formula, $C_{26}H_{32}O_7$, was indicated by the positive-ion FAB-MS of compound **1** (*m*/*z* 457 $(M+H]^+$). Compound **1** was characterised as a bufadienolide by the proton and carbon resonances of the δ-pyrone ring. Two doublets at δ7.21 ($J = 2.5$ Hz) and δ6.17 ($J = 9.8$ Hz) were seen to be coupled to a double doublet at δ7.95 ($J = 2.5$, 9.8 Hz) in the COSY spectrum and were assigned as H-21, H-23 and H-22, respectively. The HMBC spectrum showed correlations between the H-21 and H-22 resonances and a resonance at δ56.8 (CH) ascribed to C-17. The singlet integrating to three protons at δ0.77 showed correlations to the C-17 resonance in the HMBC spectrum and was assigned to 3H-18. A quaternary carbon resonance in the δ80–85 region of the ^{13}C NMR spectrum

Table 1
^{1}H, ^{13}C, HMBC, NOESY and COSY NMR data for compound **1**

	^{1}H NMR data for compound **1**[a]	^{13}C NMR data for compound **1**[b]	HMBC correlations H → C	NOESY correlations	COSY Correlations
1	2.34	32.6 (CH$_2$)	5, 10, 19	19, 4	2α, 2β
2	2.08α	29.5 (CH$_2$)	3, 4, 10	–	1, 3
	1.33β		3, 19	3, 19	1, 3
3	4.15 *br s*	66.5 (CH)	–	2α	2α, 2β, 4
4	5.71 *s*	129.9 (CH)	2, 6, 10	1, 3	3, 6β
5	–	137.3 (C)	–	–	–
6	1.18α	27.72 (CH$_2$)	–	7α	7α, 7β
	2.20β		8	–	4, 7α, 7β
7	2.18α	28.8 (CH$_2$)	–	–	6α, 6β, 8
	1.12β			9α	6α, 6β, 8
8	1.82	43.3 (CH)	14	18, 19	7α, 7β, 9
9	1.22	49.4 (CH)	–	7α	8, 11a, 11b
10	–	53.1 (C)	–	–	–
11	1.50a	21.4 (CH$_2$)	–	–	9, 12α
	1.88b				9, 12α
12	1.24α	40.0 (CH$_2$)	–	17	11
	1.60β		13	18	11
13	–	49.2 (C)	–	–	–
14	–	83.8 (C)	–	–	–
15	2.46α	39.7 (CH$_2$)	–	16α	16
	1.80β		13, 14, 16, 17	18	16
16	5.47 *dt* (1.3, 8.8)	73.2 (CH)	14, 16-O*C*OCH$_3$	15α, 17	15α, 15β, 17
17	2.84 *d* (8.8)	56.8 (CH)	13, 14, 15, 16, 20, 21, 22	12α, 16α, 21	16
18	0.77 *s*	16.3 (CH$_3$)	12, 13, 14, 17	8, 21, 22	–
19	9.75 *s*	202.9 (CH)	10	1, 8, 2β	–
20	–	116.5 (C)	–	–	–
21	7.21 *d* (2.5)	151.0 (CH)	17, 23	17	22, 23
22	7.95 *dd* (2.5,9.8)	148.8 (CH)	17, 24	18, 23	21, 23
23	6.17 *d* (9.8)	113.2 (CH)	24	22	22
24	–	161.8 (C)	–	–	–
16-OCO*C*H$_3$	1.84 *s*	20.9 (CH$_3$)	16-O*C*OCH$_3$	18	–
16-O*C*OCH$_3$	–	169.9 (C)	–	–	–

[a] NMR data obtained in CDCl$_3$, 400 MHz.

[b] NMR data obtained in CDCl$_3$, 100 MHz.