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Iridoid glucosides from *Kickxia abhaica* D.A. Sutton from Scrophulariaceae

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Abstract

Two iridoid glucosides namely; 6-acetylantirrinoside (**1**), 6′-*O*-*p*-hydroxybenzoylantirrinoside (**2**) were isolated from the aerial parts of *Kickxia abhaica*. Beside that, three known iridoid glucosides, antirrinoside (**3**), antirride (**4**) and mussaenosidic acid (**5**), one flavone glycoside (**6**) and a hexitol, D-mannitol (**7**) were isolated. The structures of the iridoid glucosides **1**–**2** were established by 1D and 2D NMR spectral data, including COSY, HMQC and HMBC experiments, as well as HRMS.

Keywords: *Kickxia abhaica*; Scrophulariaceae; Iridoid glucosides; 6-acetylantirrinoside; 6′-*O*-*p*-hydroxybenzoylantirrinoside

1. Introduction

The genus *Kickxia* is comprised of about 47 species worldwide (Mabberley, 1997). In Saudi Arabia, the genus is represented by 10 species (*Kickxia elatine*, *Kickxia aegyptiaca*, *Kickxia acerbiana*, *Kickxia collenetteana*, *Kickxia corallicola*, *Kickxia pseudoscoparia*, *Kickxia scalarum*, *Kickxia petiolata*, *Kickxia hastate* and *Kickxia abhaica*), which are distributed in different parts of the country (Chaudhary, 2001). Most of these species are distributed in the South and West regions including *K. abhaica*. Only seven *Kickxia* species world wide were chemically investigated and resulted in the isolation of mainly flavonoids and iridoid glycosides (Khan et al., 2001; Yuldashev et al., 1996; Handjieva et al., 1995; Amer, 1993; Kassem, 1992; Khan et al., 1991; Singh and Prakash, 1987; Nicoletti et al., 1987; Toth et al., 1978a,b,c; Pinar, 1973). Up to the present time nothing has been reported about the chemistry of *K. abhaica*. Therefore, the present paper reports on the isolation and characterization of the two new iridoid glucosides, 6-acetylantirrinoside (**1**), 6′-*O*-*p*-hydroxybenzoylantirrinoside (**2**) from the aerial parts of *K. abhaica*. In addition, the plant also yielded three known iridoid glucosides, antirrinoside (**3**) (Scarpati et al., 1968; Chaudhuri et al., 1980), antirride (**4**) (Handjieva et al., 1993) and mussaenosidic acid (**5**) (Damtoft et al., 1984), one flavone glycoside, hispidulin 7-neohesperidoside (**6**) (Lee et al., 1994; Park et al., 1995) and a hexitol, D-mannitol (**7**) (Khan and Aqil, 1993).

2. Results and discussion

Compound **1** was obtained as a gummy substance and its molecular formula $C_{17}H_{24}O_{11}$ was determined by HRFABMS. The 17 carbons were resolved in the ^{13}C NMR spectrum (Table 1). When compared to the spectrum of antirrhinoside (**3**), a very good correspondence could be seen for 15 of the signals, while the remaining two signals could be assigned to an acetyl moiety. Compound **1** was, therefore, a monoacetate of **3**, in agreement with the MS data. The point of attachment was evident from the ^1H NMR spectrum where the H-6 signal was seen at δ 4.86, 0.9 ppm downfield from that of **3**. The position of the acetate group at C-6 was further confirm by 2D NMR ^1H–^{13}C

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Table 1
^{1}H and ^{13}C NMR spectral data for compounds **1-2** in CD_3OD (δ values, J in parenthesis in Hz)[a]

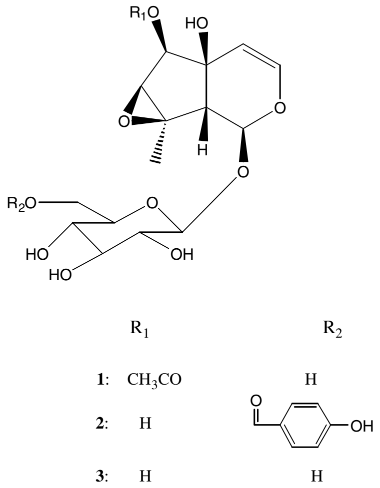
Proton	**1**		**2**	
	^{1}H	^{13}C	^{1}H	^{13}C
1	5.44 *d* (6.0)	94.6	4.99 *d* (8.0)	95.6
3	6.32 *d* (6.5)	143.4	6.24 *d* (6.0)	142.8
4	4.82 *d* (6.5)	107.5	4.77 *d* (6.0)	107.7
5	–	74.7	–	74.8
6	4.86 *d* (2.0)	79.4	3.69 *d* (1.0)	78.8
7	3.39 *d* (2.0)	64.2	3.15 *br.s*	66.0
8	–	64.5	–	63.0
9	2.36 *d* (6.0)	53.3	2.22 *d* (8.0)	53.3
10	1.39 *s*	17.4	1.24 *s*	17.6
1′	4.57 *d* (8.0)	99.8	4.62 *d* (8.0)	99.9
2′	3.14 *m*	74.7	3.16 *m*	74.8
3′	3.30 *m*	77.7	3.49 *m*	75.7
4′	3.15 *m*	71.8	3.32 *m*	71.8
5′	3.30 *m*	78.6	3.33 *m*	77.7
6′a	3.53 *dd* (11.75, 6.5)	63.0	4.40 *dd* (12.0, 7.0)	64.1
6′b	3.83 *dd* (11.75, 2.5)	63.0	4.52 *dd* (12.0, 2.5)	64.1
1″	–	172.0	–	167.8
2″	2.03 *s*	20.3	–	122.2
3″/7″			7.78 *d* (9.0)	132.9
4″/6″			6.73 *d* (9.0)	116.3
5″			–	163.7

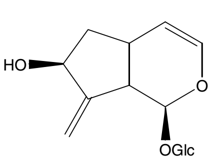
[a] Assignments made by combination of COSY, DEPT, HMQC, HMBC data and comparison with the literature.

HMBC experiments. The HMBC spectrum showed ^3J correlations between δ 4.82 (H-4), $\delta_{C\text{-}6}$ 79.4, $\delta_{C\text{-}9}$ 53.3, and between δ 4.86 (H-6) and $\delta_{C\text{-}1''}$ 172.0, confirming the placement of the acetate group at C-6. These findings unambiguously established the structure of **1** as 6-acetylantirrhinoside.

Compound **2**, analyzed for $C_{22}H_{26}O_{12}$ by HRFABMS, was isolated as amorphous powder and its UV spectrum exhibited absorption bands at λ_{max} 257 and 320 nm due to the presence of a conjugated system. The ^{1}H and ^{13}C NMR spectra of **2** (Table 1) were diagnostic for antirrhinsoide esterified with an aromatic acid (Fauvel et al., 1995). In the ^{1}H NMR of **2** the down field shift of H-6′ protons to δ 4.40 and 4.52, ca. 0.8 ppm from the usual position strongly support that C-6′is the site of esterification. Further confirmation was made by HMBC experiment. That showed ^3J correlations between δ 7.78($\delta_{C3''/7''}$132.9), $\delta_{C\text{-}1''}$ 167.8 and $\delta_{C\text{-}5''}$ 163.7, and between δ 4.40, 4.52 (H-6′a, H-6′b) and $\delta_{C\text{-}1''}$ 167.8, confirming the attachment of aromatic acid moiety at C-6′.The NMR spectra of **2** were found to be similar with those reported (Dawidar et al., 1989) for 6′-*O*-cinnamoylantirrhinoside but lacking the signals for the α and β positions of cinnamoyl moiety. Based on the foregoing data, the structure of **2** was established as 6′-*O*-*p*-hydroxybenzoylantirrinoside.

During the course of isolation of the above compounds, *K. abhaica* yielded three known iridoid glucosides **3–5**, one flavone glycoside (**6**) and one alditol (**7**). These compounds were identified by comparison of their physical and spectroscopic data with those reported in the literatures. This is the first time that the iridoid glucosides **1–2** appeared in the literature and the first report of **6** from the family scrophulariaceae. In addition, compounds **4** and **5** are reported for the second time from the genus *Kickxia* (Handjieva et al., 1995).





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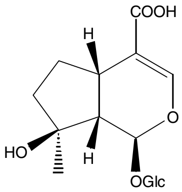

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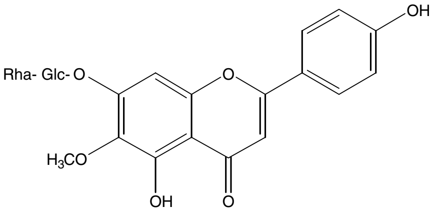

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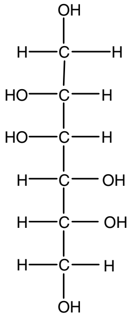

7

3. Experimental

3.1. General

Mp uncorr.; UV spectra were recorded on a Hewlett–Packard HP-845 UV–Vis spectrophotometer; FTIR spectra were obtained on a Nicolet Impact 410 spectrophotometer; Specific rotation measurements were recorded on a Perkin–Elmer 242 MC polarimeter; NMR spectra were acquired in CD_3OD or DMSO on a Bruker Avance DRX-500 instrument at 500 (^{1}H) and 125 (^{13}C) MHz using the residual solvent signal as internal standard. Standard Bruker pulse programs were used for APT, DEPT, 2D NMR COSY, HMQC and HMBC spectra. HRFABMS were obtained on a Bruker Bioapex-FTMS with electrospray ionization; EIMS were measured using an E.I. Finnigan model 4600 quadrupole system or a Shimadzu QP500 GC/mass spectrometer; TLC: silica gel 60 F254 (Merck) plates; solvents: different concentration of MeOH–$CHCl_3$ and H_2O–MeOH; CC: silica gel 60/230–400 mesh (EM