Turk J Chem
27 (2003) , 765 – 772.

6-*O*-α-L-Rhamnopyranosylcatalpol Derivative Iridoids from *Verbascum cilicicum*

İ. İrem TATLI, Zeliha Ş. AKDEMİR
Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, TR-06100, Ankara-TURKEY
Erdal BEDİR, Ikhlas A. KHAN
The University of Mississippi, School of Pharmacy, National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, University MS 38677 USA

Received 26.03.2003

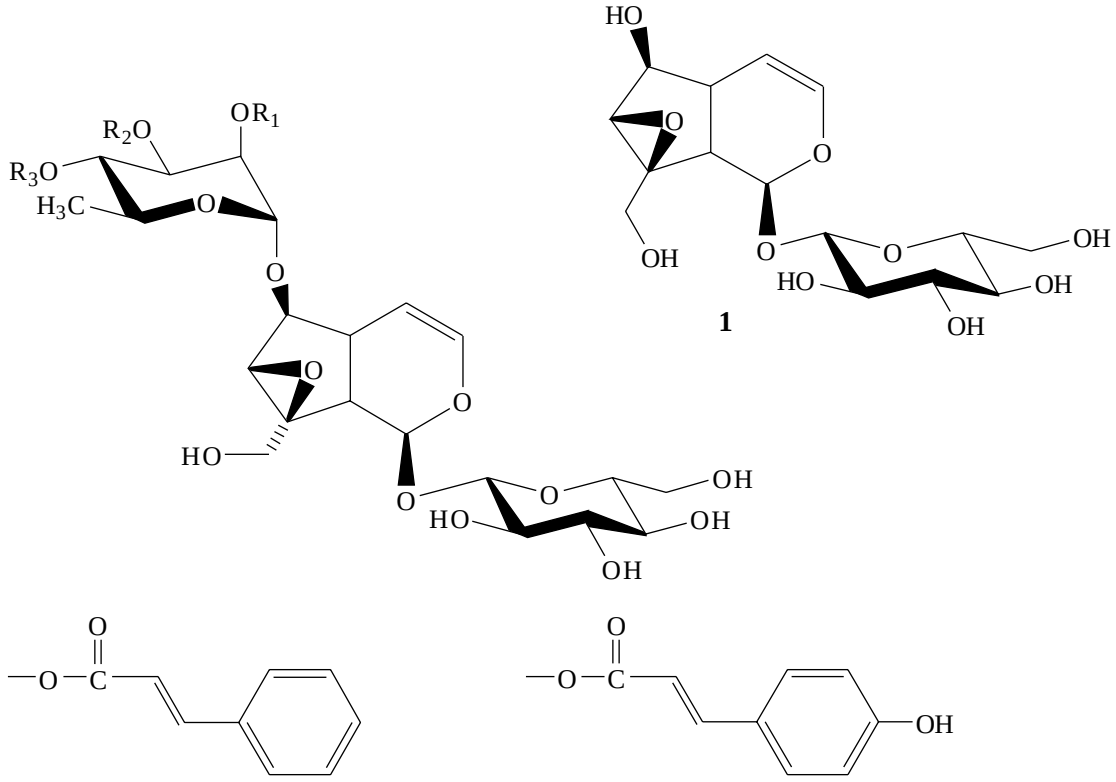
From the aerial parts of *Verbascum cilicicum* Boiss., 6 iridoid glycosides, namely catalpol (**1**), verbaspinoside [= 6-*O*-(2″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol] (**2**), 6-*O*-(3″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**3**), 6-*O*-(4″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**4**), saccatoside [= 6-*O*-(2″-*O*-*trans*-p-coumaroyl)-α-L-rhamnopyranosylcatalpol] (**5**), and 6-*O*-(3″-*O*-*trans*-p-coumaroyl)-α-L-rhamnopyranosylcatalpol (**6**), were isolated. The structures of the compounds were elucidated by means of 1 and 2 dimensional (DQF-COSY, HMQC and HMBC) NMR techniques and LC-ESIMS.

Key Words: *Verbascum cilicicum*, Scrophulariaceae, iridoid glycosides, catalpol (**1**), verbaspinoside (**2**), 6-*O*-(3″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**3**), 6-*O*-(4″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**4**), saccatoside (**5**), 6-*O*-(3″-*O*-*trans*-*p*-coumaroyl)-α-L-rhamnopyranosylcatalpol (**6**).

Introduction

In connection with a study on the constituents of the family Scrophulariaceae[1], we investigated a number of *Verbascum* species. These species are used in folk medicine as an expectorant, mucolytic, sudorific, sedative, diuretic and constipate[2]. They are consumed as tea to relieve abdominal pains and bronchitis[3]. *Verbascum* species are also used externally for desiccating wounds, anal fistula and pruritic conditions in the urogenital organs[3]. The genus *Verbascum* is represented by 228 species, 185 of which are endemic to Turkey[4]. Iridoid glycosides, especially catalpol esters of cinnamic acid derivatives[5], phenylethanoids[6] and flavonoids[7], have been reported from several *Verbascum* species. The presence of the iridoid glycosides is suggested to be of taxonomic importance[8].

The current study describes the isolation and structure elucidation of iridoid glycosides (**1-6**) from the aerial parts of *Verbascum cilicicum* Boiss., which is an endemic species distributed in South Anatolia[4].



trans-cinnamoyl *trans*-p-coumaroyl

	R_1	R_2	R_3
2	*trans*-cinnamoyl	H	H
3	H	*trans*-cinnamoyl	H
4	H	H	*trans*-cinnamoyl
5	trans-p-coumaroyl	H	H
6	H	*trans*-p-coumaroyl	H

Figure. Iridoid glycosides isolated from *Verbascum cilicicum.*

Experimental

General Experimental Procedures: The UV spectra (λ_{max}) were recorded on a Hitachi HP 8452 A spectrophotometer. The IR spectra (υ_{max}) were determined on an ATI Mattson Genesis Series FT-IR spectrophotometer. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance DRX 500 and 300 FT spectrometer operating at 500 and 300 MHz for^{1}H NMR, and 125 and 75 MHz for^{13}C NMR spectra. The chemical shift values are reported as parts per million (ppm) relative to tetramethylsilane (TMS), and the coupling constants are in hertz (Hz, in parentheses). For the ^{13}C NMR spectra, multiplicities were determined by a DEPT experiment. LC-ESIMS FT data were obtained using a Bruker BioApex FT-MS instrument in the ESI mode. Polyamide (ICN) and Si gel (230-400 mesh) (Merck) were used for column chromatography (CC), and reverse-phase material (C-18, Sepralyte 40μm) was used for vacuum liquid chromatography (VLC). Pre-coated silica gel 60 F_{254} aluminum sheets (Merck) were used for TLC

with a developing solvent-system, $CHCl_3$-MeOH-H_2O (61:32:7). Plates were examined by UV fluorescence and sprayed with 1% vanillin in conc. H_2SO_4, followed by heating at 105 °C for 1-2 min.

Plant Material *V. cilicicum* Boiss. was collected from the village of Alihoca, between the towns of Pozantı and Ulukışla in Adana province, in July 2000. A voucher specimen has been deposited in the Herbarium of the Pharmacognosy Department, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey (HUEF 00183).

Extraction and Isolation. Air-dried aerial parts of the plant (590.8 g) were extracted twice with MeOH (2 × 2.5 L) at 40 °C to give a crude MeOH extract (104.68 g). The MeOH extract was fractionated by polyamide CC (800 g) with H_2O and MeOH-H_2O mixtures (10-100%). This yielded 3 main fractions (frs. A-C). Fr. B (5.66 g) was subjected to silica gel CC (300 g) and eluted with $CHCl_3$ and $CHCl_3$-MeOH mixtures (95:5, 90:10, 85:15) to yield frs. B_1-B_4. Fr. B_3 (655.7 mg) was rechromatographed by VLC using reverse-phase material (Sepralyte 40μm, 150 g) eluted with MeOH-H_2O mixtures (20-100%) to afford catalpol (**1**) (109.7 mg), verbaspinoside [= 6-*O*-(2″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol] (**2**) (15.6 mg), 6-*O*-(3″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**3**) (7.2 mg), 6-*O*-(4″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**4**) (17.8 mg), saccatoside [= 6-*O*-(2″-*O*-*trans*-*p*-coumaroyl)-α-L-rhamnopyranosylcatalpol] (**5**) (28 mg), and 6-*O*-(3″-*O*-*trans*-*p*-coumaroyl)-α-L-rhamnopyranosylcatalpol (**6**) (26.9 mg).

Results

Catalpol (**1**): UV (MeOH) λ_{max} 210 nm, IR (KBr) υ_{max} 3470 (OH), 1642 (C=C) cm^{-1}, positive ion-LC-ESIMS m/z 385 $[M+Na]^+$ (calc. for $C_{15}H_{22}O_{10}$),^{1}H (300 MHz, DMSO-d_6) and ^{13}C (75 MHz, DMSO-d_6) NMR (see Tables 1 and 2) data superimposable with those reported in the literature[9].

Verbaspinoside [= 6-*O*-(2″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol] (**2**): UV (MeOH) λ_{max} 216, 242 (sh), 280 nm, IR (KBr) υ_{max} 3379 (OH), 1705 (C=O), 1643 (C=C), 1604, 1546, 1363 (aromatic ring) cm^{-1}, positive ion-LC-ESIMS m/z 661 $[M+Na]^+$, negative ion-LC-ESIMS m/z 637 $[M-H]^-$ (calc. for $C_{30}H_{38}O_{15}$).^{1}H (500 MHz, DMSO-d_6) and ^{13}C (125 MHz, DMSO-d_6) NMR (see Tables 1 and 2).

6-*O*-(3″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (3): UV (MeOH) λ_{max} 220, 244 (sh), 282 nm, IR (KBr) υ_{max} 3450 (OH), 1705 (C=O), 1643 (C=C), 1604, 1546, 1363 (aromatic ring) cm^{-1}, positive ion-LC-ESIMS m/z 661 $[M+Na]^+$, negative ion-LC-ESIMS m/z 637 $[M-H]^-$ (calc. for $C_{30}H_{38}O_{15}$).^{1}H (500 MHz, DMSO-d_6) and ^{13}C (125 MHz, DMSO-d_6) NMR (see Tables 1 and 2).

6-*O*-(4″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (4): UV (MeOH) λ_{max} 220, 240 (sh), 278 nm, IR (KBr) υ_{max} 3373 (OH), 1705 (C=O), 1635 (C=C), 1604, 1546, 1363 (aromatic ring) cm^{-1}, positive ion-LC-ESIMS m/z 661 $[M+Na]^+$, negative ion-LC-ESIMS m/z 637 $[M-H]^-$ (calc. for $C_{30}H_{38}O_{15}$).^{1}H (500 MHz, DMSO-d_6) and ^{13}C (125 MHz, DMSO-d_6) NMR (see Tables 1 and 2).

Saccatoside [= 6-*O*-(2″-*O*-*trans*-*p*-coumaroyl)-α-L-rhamnopyranosylcatalpol] (**5**): UV (MeOH) λ_{max} 216, 252 (sh), 314 nm, IR (KBr) υ_{max} 3430 (OH), 1706 (C=O), 1643 (C=C), 1604, 1546, 1363 (aromatic ring) cm^{-1}, positive ion-LC-ESIMS m/z 677 $[M+Na]^+$, negative ion-LC-ESIMS m/z 653 $[M-H]^-$ (calc. for $C_{30}H_{38}O_{16}$).^{1}H (500 MHz, DMSO-d_6) and ^{13}C (125 MHz, DMSO-d_6) NMR (see Tables 1 and 2).

Table 1. ^{1}H NMR (500 MHz, DMSO-d_6) data of compounds **1-6**.

	1*		**2**		**3**		**4**		**5**		**6**	
Position	δ (ppm)	J (Hz)	δ (ppm)	J (Hz)	δ (ppm)	J (Hz)	δ (ppm)	J (Hz)	δ	J (Hz)	δ (ppm)	J (Hz)
Aglycone												
1	4.86 d	9.6	5.08 †	-	5.12 †	-	5.11 †	-	5.09 d	8.0	5.06 †	-
3	6.30 d	5.2	6.39 dd	5.8/1.5	6.44 d	6.0	6.42 d	5.3	6.41 †	-	6.41 d	4.0
4	4.97 d	4.5	5.08 †	-	5.12 d	6.8	5.11 d	4.5	4.95 †	-	5.00 †	-
5	2.07 m	-	2.28 m	-	2.31 m	-	2.29 m	-	2.28 m	-	2.29 m	-
6	3.75 d	6.7	3.89 d	8.2	3.93 d	7.9	3.94 d	8.0	4.11 †	-	3.91 d	7.5
7	3.31 s	-	3.61 s	-	3.65 s	-	3.64 s	-	3.62 s	-	3.62 s	-
9	2.30 t	8.2	2.36 †	-	2.41 dd	9.4/7.7	2.39 t	9.1	2.38 dd	9.2/7.8	2.38 d	8.9
10a	4.15 †	-	4.24 †	-	4.28 †	-	4.27 †	-	4.13 †	-	4.13 †	-
10b	3.85 d	13.0	3.85 dd	13.5/4.1	3.90 d	13.2	3.89 †	-	3.80 †	-	3.85 †	-
β-D-Glucose												
1′	4.55 d	7.8	4.55 d	7.9	4.61 d	7.8	4.61 d	7.8	4.58 d	7.6	4.58 d	7.6
2′	3.03 †	-	3.00 †	-	3.05 †	-	3.05 †	-	3.00 †	-	3.02 †	-
3′	3.12 †	-	3.08-3.14 †	-	3.07-3.14 †	-	3.11 †	-	3.14 †	-	3.11 †	-
4′	3.09 †	-	3.08-3.14 †	-	3.07-3.14 †	-	3.05-3.12 †	-	3.00-3.14 †	-	3.05-3.13 †	-
5′	3.15 †	-	3.15 †	-	3.07-3.14 †	-	3.14 †	-	3.16 †	-	3.14 †	-
6′a	3.35 †	-	3.35 †	-	3.40 †	-	3.38 †	-	3.43 †	-	3.42 †	-
6′b	3.57 †	-	3.57 †	6.3	3.68 †	-	3.62 †	-	3.70 †	-	3.69 †	-
α-L-Rhamnose												
1″	-	-	4.92 d	1.5	4.86 brs	-	4.90 brs	-	4.94 brs	-	4.82 brs	-
2″	-	-	5.01 dd	3.2/1.7	3.93 †	-	3.76-3.79 †	-	5.05 †	-	3.91 †	-
3″	-	-	3.69 dd	9.1/4.6	5.02 †	-	3.76-3.79 †	-	3.69 †	-	4.98 †	-
4″	-	-	3.29 t	9.9	3.18 †	-	4.97 †	-	3.38 †	-	3.21 †	-
5″	-	-	3.57 dd	9.2/6.3	3.51 †	-	3.77 †	-	3.54 †	-	3.63 †	-
6″	-	-	1.18 d	6.2	1.20 d	6.1	1.08 d	6.2	1.18 d	5.8	1.17 d	5.6
Acyl moiety												
2‴/6‴	-	-	7.70 †	-	7.72 †	-	7.74 †	-	7.55 d	8.7	7.53 †	-
3‴/5‴	-	-	7.41 †	-	7.44 †	-	7.43 †	-	6.78 d	8.3	6.78 d	8.3
4‴	-	-	7.41 †	-	7.44†	-	7.43 †	-	-	-	-	-
α	-	-	6.62 d	16.0	6.66 d	16.1	6.67 d	16.0	6.40 d	16.1	6.39 d	15.7
β	-	-	7.63 d	16.0	7.70 d	16.1	7.69 d	16.0	7.56 d	16.0	7.58 d	15.5

†unclear due to overlapping

∗ 300 MHz

Table 2.^{13}C NMR (125 MHz, DMSO-d_6) data of compounds **1-6**.

Position	C_{Atom}	**1*** δ (ppm)	**2** δ (ppm)	**3** δ (ppm)	**4** δ (ppm)	**5** δ (ppm)	**6** δ (ppm)
Aglycone							
1	CH	94.1	93.9	94.0	94.0	93.9	93.9
3	CH	141.0	141.9	141.8	141.9	141.9	141.8
4	CH	104.1	103.1	103.2	103.1	103.1	103.2
5	CH	38.1	36.5	36.4	36.4	36.4	36.4
6	CH	77.1	82.4	82.6	82.9	82.4	82.5
7	CH	61.6	58.0	58.3	58.4	58.0	58.2
8	C	65.6	66.3	66.2	66.2	66.5	66.5
9	CH	43.0	42.7	42.8	42.8	42.7	42.7
10	CH_2	59.9	59.5	59.6	59.7	59.5	59.6
β− D-Glucose							
1′	CH	98.6	98.6	99.7	99.7	98.7	99.6
2′	CH	74.2	74.2	74.3	74.3	74.2	74.7
3′	CH	78.0	77.2	77.2	77.3	77.2	77.2
4′	CH	71.0	71.6	71.1	71.1	71.1	71.1
5′	CH	78.0	78.3	78.3	78.3	78.3	78.8
6′	CH_2	62.0	62.1	62.2	62.2	62.2	62.2
α- L-Rhamnose							
1″	CH	-	96.5	98.7	98.7	96.6	98.7
2″	CH	-	73.5	69.7	71.5	73.3	69.7
3″	CH	-	69.7	75.2	69.0	69.9	74.2
4″	CH	-	73.0	70.0	74.8	73.0	70.0
5″	CH	-	69.4	69.0	67.3	69.4	69.0
6″	CH_3	-	18.6	18.7	18.3	18.6	18.6
Acyl moiety							
1‴	C	-	134.9	131.2	134.9	127.0	128.1
2‴	CH	-	129.8	129.9	129.8	131.3	131.1
3‴	CH	-	129.3	129.1	129.2	116.7	116.7
4‴	CH(C)$^\xi$	-	131.4	135.0	131.3	161.0	161.0
5‴	CH	-	129.3	129.1	129.2	116.7	116.7
6‴	CH	-	129.8	129.9	129.8	131.3	131.1
α	CH	-	118.9	119.5	119.1	115.8	115.6
β	CH	-	145.9	145.2	145.5	146.1	145.4
C=O	C	-	167.0	166.9	166.8	168.0	168.0

ξ C for compounds 5 and 6

$*$ 75 MHz

6-*O*-(3″-*O*-*trans*-*p*-coumaroyl)-α-L-rhamnopyranosylcatalpol (**6**): UV (MeOH) λ_{max} 216, 250 (sh), 312 nm, IR (KBr) υ_{max} 3430 (OH), 1706 (C=O), 1642 (C=C), 1604, 1546, 1363 (aromatic ring) cm^{-1}, positive ion- LC-ESIMS *m/z* 677 $[M+Na]^+$, negative ion-LC-ESIMS *m/z* 653 $[M-H]^-$ (calc. for $C_{30}H_{38}O_{16}$). ^{1}H (500 MHz, DMSO-d_6) and ^{13}C (125 MHz, DMSO-d_6) NMR (*see* Tables 1 and 2).

Discussion

Compound **1** was obtained as an amorphous powder with the molecular formula $C_{15}H_{22}O_{10}$ (LC-ESIMS *m/z* $[M+Na]^+$ 385). Its UV spectrum suggested the presence of an iridoid enol ether system and its IR

spectrum showed typical absorption bands for olefinic double bonds (see the Results section). The ^{1}H and ^{13}C NMR spectra of **1** (see Tables 1 and 2) were consistent with a C-4 unsubstituted iridoid glucoside. By comparing its NMR data with those given in the literature, **1** was identified as catalpol[9].

The positive- and negative-ion ESIMS of compounds **2-6** exhibited pseudomolecular ions $[M+Na]^+$ at m/z 661 and $[M-H]^-$ at m/z 637 for **2-4**; similarly, $[M+Na]^+$ at m/z 677 and $[M-H]^-$ at m/z 653 molecular ion peaks were observed for **5** and **6**. These data are compatible with the molecular formula $C_{30}H_{38}O_{15}$ for **2-4** and $C_{30}H_{38}O_{16}$ for **5** and **6**. The UV spectra of all compounds (**2-6**) suggested the presence of an aromatic acyl moiety and an iridoid enol ether system. Similarly, the IR absorptions were in accordance with esterification and the presence of a non-conjugated enol ether system for **2-6** (see the Results section). In addition, the ^{1}H and ^{13}C NMR data of compounds **2-6** showed signals very similar to those of catalpol[9], with additional signals arising from an aromatic acid and rhamnopyranosyl moiety.

The anomeric proton of the second sugar unit (δ_H4.86- 4.92) in **2-4** indicated the presence of a rhamnosyl unit. A methyl signal at δ_H1.08-1.20 (d,J = 6.2 Hz) also supported this assumption. On the other hand, the acyl unit was identified as cinnamic acid in **2-4** on the basis of the following evidence: 2 *trans* olefinic protons (δ_H 6.62-6.67 and 7.63-7.70,d, AB system,J_{AB} = 16.0 Hz), and 5 aromatic protons (δ_H 7.41- 7.74).

The attachment of the rhamnose unit was determined to be the C-6 (OH) group of the aglycone for compounds **2-4** due to the downfield shift of the C-6 atom (δ_C 82.4-82.9) as well as an HMBC cross peak observed between C-6 (δ_C 82.4-82.9) and H-1$''$ (δ_H4.86-4.92,d,J = 1.5 Hz). The major difference in **2-4** was concluded to be an attachment site of the acyl unit (cinnamic acid) on the rhamnose moiety. The position of the acylation was determined by comparing the NMR data of **2-4** with those of 6-*O*-α-L-rhamnopyranosylcatalpol[5]. The downfield shift of H-2$''$ in rhamnose unit in **2** ($\Delta\delta$ = +1.10) in comparison with that of 6-*O*-α-L-rhamnopyranosylcatalpol[5] proved that the acylation was at the C-2$''$ position of the rhamnosyl unit. The ^{13}C downfield shift of the C-2$''$ signal (**2**, $\Delta\delta$ = +2.80) and the upfield shifts of the C-3$''$ (**2**, $\Delta\delta$ = -0.60) and the C-1$''$ signals (**2**, $\Delta\delta$ = -2.40) also supported this assumption. Likewise, the acylation in position C-3$''$ of the rhamnose unit of compound **3** was deduced from the downfield shift of the H-3$''$ signal ($\Delta\delta$ = +1.52) and the C-3$''$ signal ($\Delta\delta$ = +4.90), as well as the ^{13}C upfield shift of the C-4$''$ ($\Delta\delta$ = -1.90) and C-2$''$ signals ($\Delta\delta$ = -1.00) (see Tables 1 and 2). The site of esterification of the *trans*-cinnamoyl group was determined to be the C-4$''$ position of the rhamnopyranosyl moiety in **4** due to the downfield shift ($\Delta\delta$ = -1.71) of the H-4$''$ signal (δ_H 4.97) in comparison with that of 6-*O*-α-L-rhamnopyranosylcatalpol[5]. In the ^{13}C NMR spectrum, the C-3$''$, C-4$''$ and C-5$''$ resonances of the rhamnopyranosyl moiety were observed at δ_C 69.0 ($\Delta\delta$ = -1.30), δ_C 74.8 ($\Delta\delta$ = +2.90) and δ_C 67.3 ($\Delta\delta$ = -1.60), respectively, supporting the acylation at C-4$''$ in **4**. Finally, the site of esterification was confirmed by the HMBC spectrum on the basis of the correlation between the carbonyl carbon of the *trans*-cinnamoyl group (δ_C 166.8) and H-4$''$ (δ_H 4.97) of the rhamnose unit.

The structures of **2-4** were thus established as verbaspinoside [= 6-*O*-(2$''$-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol] (**2**)[10], 6-*O*-(3$''$-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**3**)[11] and 6-*O*-(4$''$-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**4**)[11], respectively.

The ^{1}H and ^{13}C NMR spectra of compounds **5** and **6** showed structural features similar to those of **2-4,** implying that **5** and **6** had the same subunits as in **2-4,** except for the acyl moiety. From the presence of 2

trans olefinic protons (δ_H 6.39-6.40 and 7.56-7.58,*d*, AB system, J_{AB} = 16.0 Hz) and 2 pairs of *ortho*-coupled aromatic protons (δ_H 6.78 and 7.54,*d*,J = 8.7 Hz) in the ^{1}H NMR spectrum, the acyl unit was identified as *trans-p*-coumaric acid in both **5** and **6**. The site of esterification in compound **5** was determined to be the C-2″ position of the rhamnose moiety, because of the up- and downfield shifts observed for C-1″, C-2″ and C-3″ ($\Delta\delta$ -2.30, +2.60 and -0.40, respectively). This was also supported by an HMBC correlation, where long-range coupling was observed between the carbonyl carbon of the *trans-p*-coumaroyl group at δ_C 168.0 and H-2″ of rhamnose unit at δ_H 5.05. To determine the esterification position in **6**, the ^{13}C NMR resonances of the rhamnose moiety were compared with those of unsubstituted rhamnose[5], and the C-3″ signal in **6** was observed significantly downfield (shifted ca. +3.90 ppm), while C-2″ and C-4″ signals were shifted upfield ca. -1.00 and -1.90 ppm, respectively. This established that the position of the *trans-p*-coumaroyl unit in compound **6** was C-3″ of the rhamnose unit. This was also confirmed by the HMBC correlation observed between δ_C 168.0 (carbonyl carbon of the *trans-p*-coumaroyl group) and δ_H 4.98 (H-3″ of rhamnose). In conclusion, the structures of **5** and **6** were established as saccatoside [= 6-*O*-(2″-*O*-*trans-p*-coumaroyl)-α-L-rhamnopyranosylcatalpol] (**5**)[12], and 6-*O*-(3″-*O*-*trans-p*-coumaroyl)-α-L-rhamnopyranosylcatalpol (**6**)[13], respectively.

Conclusion

To date, several acylated 6-*O*-α-L-rhamnopyranosylcatalpol derivatives have been reported from the family Scrophulariaceae[1], mainly from various *Verbascum* species[14]. Our investigation on *V. cilicicum* demonstrated that rhamnopyranosyl catalpol esters are the main iridoid constituents of this species. Thus, the significance of acyl rhamnopyranosylcatalpol derivatives as taxonomic markers is limited, as they obviously evolved several times independently in different families. However, at the genus and tribe levels the substitution pattern of these iridoids such as the 7, 8-oxido group and the 10-hydroxyl group as well as acylation of the iridoids with unsubstituted or substituted cinnamic acids might be useful characters[11].

To our knowledge, this is the first report of the isolation of 6-*O*-(3″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**3**) and 6-*O*-(4″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol (**4**) from *Verbascum* species. Verbaspinoside [= 6-*O*-(2″-*O*-*trans*-cinnamoyl)-α-L-rhamnopyranosylcatalpol] (**2**) has been isolated from *Verbascum* species for the second time. This compound has only been reported from *V. spinosum*[10], earlier. To date, saccatoside [= 6-*O*-(2″-*O*-*trans*-coumaroyl)-α-L-rhamnopyranosylcatalpol] (**5**) has been reported from *V. saccatum*[12] and *V. thapsus*[14], while 6-*O*-(3″-*O*-*trans*-coumaroyl)-α-L-rhamnopyranosylcatalpol (**6**) has previously been reported from *V. sinuatum*[13] and *V. thapsus*[14]. Additionally, this is the first report on the isolation and characterization of iridoid glycosides from *V. cilicicum* as well as a *Verbascum* species from Group F of the genus[4].

Acknowledgments

The authors are grateful to Prof. Dr. Hayri Duman (Gazi University, Faculty of Science, Etiler, Ankara, Turkey) for the authentification of the plant specimen. The authors are also grateful to Dr. Chuck Dunbar for conducting the LC-ESIMS analysis. We also thank Mr. Frank Wiggers for his assistance in obtaining the 2D NMR spectra of compounds **2-6**. This work was supported in part by the United States Department of Agriculture, ARS Specific Cooperative Research Agreement no. 58-6408-7-012.

References

1. T. Miyase and A. Mimatsu, **J. Nat. Prod.**, **62**, 1079-1084 (1999).
2. T. Baytop, "Therapy with Medicinal Plants in Turkey (Past and Present)", 2^{nd} ed. pp. 334-335, Nobel Tıp Kitabevleri Ltd., İstanbul (1999).
3. E. Sezik, E. Yeşilada, G. Honda, Y. Takaishi, Y. Takeda and T. Tanaka, **J. of Ethnopharm.**, **75**, 95-115 (2001).
4. A. Huber-Morath, "*Verbascum*" in: Flora of Turkey and the East Aegean Islands Vol. 6, ed. P.H. Davis, pp. 461-603, University Press, Edinburgh (1978).
5. Z.Ş. Akdemir, İ.İ. Tatlı, E. Bedir and I.A. Khan, **Turk. J. Chem.**, (2003). (*in press*).
6. P. Magiatis, S. Mitaku, E. Tsitsa, A.L. Skaltsounis and C. Harvala, **Nat. Prod. Lett.**, **2**, 111-115 (1998).
7. B. Klimek and M. Krolikowska, **Acta Pol. Pharm.**, **41**, 259-264 (1984).
8. C.A. Boros and F.R. Stermitz, **J. Nat. Prod.**, **53**, 1055-1147 (1990).
9. Z. Akdemir and İ. Çalış, **Doğa-Tr. J. of Pharmacy**, **1**, 67-75 (1991).
10. E. Kalpoutzakis, N. Aligiannis, S. Mitakou and A.L. Skaltsounis, **J. Nat. Prod.**, **62**, 342-344 (1999).
11. E. Helfrich and H. Rimpler, **Phytochemistry**, **50**, 619-627 (1999).
12. V.A. Mnatsakanyan, L.S. Arutyunyan and M.I. Eribekyan, **Khim. Prir. Soedin.**, (1), 38-41 (1983).
13. M.I. Eribekyan, L.S. Arutyunyan and V.A. Mnatsakanyan, **Khim. Prir. Soedin.**, (1), 146-147 (1987).
14. T. Warashina, T. Miyase and A. Ueno, **Chem. Pharm. Bull.**, **39**, 3261-3264 (1991).