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Sesquiterpene lactones from *Centaurea helenioides* Boiss

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Grosheimin (**1**) and cynaropicrin (**3**) sesquiterpenes were isolated from the flowers of *Centaurea helenioides* Boiss., an endemic plant of Turkey. The products are known as they occur in another species, but they were isolated and identified for the first time from *C. helenioides* Boiss. In order to correlate spectral data of grosheimin, its acetyl derivative, 8α-acetyl grosheimin (**2**) was also prepared. Their structures were deduced by FT-IR, UV, 1D and 2D NMR, LC MS/MS, GC-mass spectra (EI), optical rotation, and chemical methods.

Key Words: *Centaurea helenioides* Boiss., Compositae, Sesquiterpene lactones, Grosheimin, Cynaropicrin.

Introduction

The genus *Centaurea* belongs to the family Compositae, which has 172 species in Turkey[1]. Most of them are endemic and have been used as folk medicines. Many of them show biological activities similar to *Centaurea cyanus* L. for antidiarrheic activity, *Centaurea behen* L. for stomach disorders, and *Centaurea calcitrapa* L. and *Centaurea jacea* L. for antipyretic activities[2]. One of the endemic species of the family, *Centaurea helenioides* Boiss. is distributed naturally in northern Turkey[1]. A literature survey revealed that there were no phytochemical studies on *C. helenioides* Boiss. In our chemical investigation of the chloroform extract of air-dried flowers of *C. helenioides* Boiss., grosheimin (1)[3] and cynaropicrin (3)[4−5] sesquiterpenes were isolated and characterized by spectral techniques for the first time.

In the literature, the genus *Centaurea* (Compositae) has been the subject of wide chemotaxonomic investigations for 40 years to study its different types of sesquiterpenes isolated from the aerial parts[6−18]. Cynaropicrin is a known natural compound found in many other species of *Centaurea* growing in various parts of Asia[6,7] and Europe[8,9]. However, grosheimin has not been reported in another species of *Centaurea*. This fact can probably be attributed to the different geographical origins of the plants.

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Grosheimin (1) and cynaropicrin (3) sesquiterpenes were isolated from various plants[19−24] and show many biological activities including anti-tumor, anti-inflammatory, anti-ulcer, cardiotonic, and neurocytotoxic[25−28].

Experimental

General and Instrumentation: NMR spectra were recorded on a Varian Mercury 200 MHz NMR instrument in $CDCl_3$. The mass spectral analyses were carried out on a Micromass Quattro LC-MS/MS spectrophotometer. Infrared spectra were obtained with a Perkin-Elmer 1600 FT-IR (4000-400 cm^{-1}) spectrometer. The optical rotation was measured with an Optical Activity Limited AA-5 series polarimeter. Melting point was measured on a Kofler hot-stage apparatus and was uncorrected. UV/VIS spectral analyses were carried out on a Unicam UV2-100, at 25 °C. Thin-layer chromatography (TLC) was carried out on Merck precoated 60 Kieselgel F_{254} analytical aluminum plates. PTLC was performed on Merck precoated 60 Kieselgel F_{254}(20 x 20, 0.5 mm) silica gel plates.

Plant material: *C. helenioides* Boiss. specimens were collected in July 2000 in the Maçka area of the Trabzon Hills (∼1600 m), Turkey. A specimen voucher was filed in the Department of Chemistry at Karadeniz Technical University. The identification of this species was carried out according to the Flora of Turkey[1].

Extraction and Isolation: Air-dried flowers of *C. helenioides* Boiss. (350 g) were extracted with $CHCl_3$ at room temperature (500 mL x 2). The extract was filtered and concentrated in vacuo at 30-35 °C until dry. The residue (12 g) was chromatographed over a silica gel column, eluted with n-hexane and a gradient of n-hexane-chloroform up to 100% chloroform, followed by MeOH up to 100%. The similar fractions were combined and further chromatographed on small columns, when necessary. Apolar fractions were mixtures of fatty acid esters and hydrocarbons. The latter fractions were further separated and cleaned by preparative TLC to yield compounds 1 and 3.

Acetylation of compound 1: Compound **1** (14.7 mg) in pyridine-Ac_2O (1:1) (2 ml) was kept at 40 °C for 3 h. The mixture was poured into ice-H_2O (5 mL) and the acetylated product was extracted with $CHCl_3$ (3 x 5 mL). Extracts were combined, evaporated, and then further purified by small column chromatography on silica gel using n-hexzane-$CHCl_3$ gradient to yield compound **2** (17 mg). ^{1}H NMR ($CDCl_3$, 200 MHz) and ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) see Tables 1 and 2.

Results and Discussion

The chloroform extract of *C. helenioides* Boiss. was repeatedly chromatographed on silica gel to yield compounds **1** and **3**. By comparing their FT-IR, UV, ^{1}H and ^{13}C NMR, LC MS/MS, GC-mass spectra (EI), and optical rotation with reported data[3−21], grosheimin (**1**) and cynaropicrin (**3**) sesquiterpenes were identified (Figure). Additionally, an acetyl derivative of compound **1** was prepared and its spectral data compared with known acetyl derivatives of grosheimin[3]. The ^{13}C NMR and ^{1}H NMR spectral data of compounds **1-3** are provided in Tables 1 and 2, respectively.

Based upon the spectral data and chemical methods, the structures of compounds **1** and **3** were grosheimin and cynaropicrin, respectively, which are natural products that were isolated for the first time from *C. helenioides* Boiss.

Table 1. ^{13}C NMR spectral data of compounds **1-3**[a,b] in $CDCl_3$.

C	**1,** δ (ppm)	**2,** δ (ppm)	**3,** δ (ppm)
1	40.09	40.00	45.28
2	43.19	43.17	39.02
3	219.12	218.56	73.74
4	46.94	46.90	152.14
5	51.03	50.93	51.35
6	82.30	82.40	78.42
7	49.08	46.21	47.52
8	73.09	74.26	74.29
9	47.91	43.45	36.97
10	143.14	142.20	137.20
11	136.32	135.60	139.11
12	169.93	169.75	169.27
13	125.80	125.03	122.77
14	115.61	116.76	118.26
15	14.87	14.79	113.64
-OAc	-	169.13	-
	-	21.12	-
1′			165.27
2′			141.65
3′			126.80
4′			62.30

[a]Chemical shifts (ppm) are relative to internal TMS in $CDCl_3$.

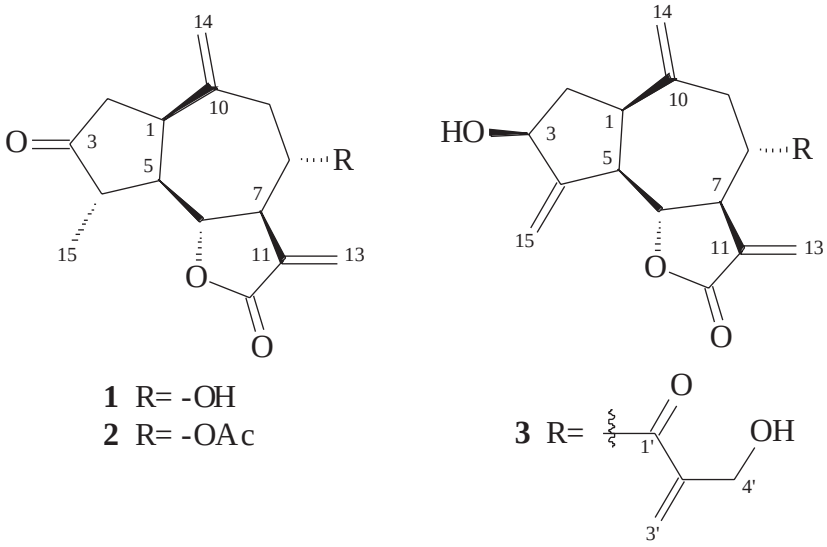
[b] Assignments based on ^{1}H, ^{13}C, APT, DEPT, 2D-COSY, HETCOR and NOESY spectra.

Table 2. ^{1}H NMR spectral data of compounds **1-3**[a,b] in $CDCl_3$.

H	**1,** δ (ppm)	**2,** δ (ppm)	**3,** δ (ppm)
1	3.15, m	3.16, m	2.96, m
2	2.52, m	2.50, m	2.24, m
			1.76, dt
3	-	-	4.56, dd, J= 7.4, 7.2 Hz
4	2.32, m	2.32, m	-
5	2.30, m	2.28, m	2.85, m
6	4.00, dd, J= 9.4, 8.9 Hz	4.06, dd, J= 9.4, 9.0 Hz	4.28, dd, J= 10, 9.2 Hz
7	3.09, dd, J= 9.2, 3.4 Hz	3.29, dd, J= 9.2, 3.4 Hz	3.20, m
8	3.92, ddd, J= 9.9, 5.8, 9.0 Hz	4.95, ddd, J= 10.0, 5.6, 9.0 Hz	5.13, m
9	2.87, dd, J= 5.8, 13.0 Hz	2.98, dd, J= 5.6, 13.0 Hz	2.42, m
	2.35, m	2.22, m	2.73, m
13	6.36, dd, J= 3.2, 1.0 Hz	6.35, d, J= 3.4 Hz	6.21, d, J= 3.4 Hz
	6.30, dd, J= 3.0, 1.2 Hz	5.84, d, J= 3.4 Hz	5.63, d, J= 3.4 Hz
14	5.09, bs	5.15, bs	5.15, bs
	4.83, bs	4.86, bs	4.93, bs
15	1.26, d, J= 7.0 Hz	1.27, d, J= 7.2 Hz	5.48, bs
			5.37, bs
-OAc	-	2.16, s	-
3′	-	-	6.34, bs
			5.97, bs
4′	-	-	4.38, bs

[a]Chemical shifts (ppm) are relative to internal TMS in $CDCl_3$.

[b]Assignments based on ^{1}H, ^{13}C, APT, DEPT, 2D-COSY, HETCOR and NOESY spectra.



Figure

Acknowledgments

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