Pharmaceutical Biology
2006, Vol. 44, No. 9, pp. 643–645

informa
healthcare

Constituents of *Cynara syriaca* Leaves

A.H. Meriçli and G.V. Seyhan

Department of Pharmacognosy, Faculty of Pharmacy, Istanbul University, Istanbul, Turkey

Abstract

Six flavonoids (apigenin, chrysoeriol, luteolin, apigenin 7-*O*-glucoside, chrysoeriol 7-*O*-glucoside, luteolin 7-*O*-glucoside), four phenolic acids (caffeic acid, chlorogenic acid, 1,5-dicaffeoylquinic acid, cynarin), and three sesquiterpene lactones (11,13-dihydroxy-8-desoxygrosheimin, 11,13-dihydrodeacylcynaropicrin, solstitialin) were isolated from the leaves of *Cynara syriaca* Boiss (Asteraceae). Three of these compounds, chrysoeriol, chrysoeriol 7-*O*-glucoside, and 11,13-dihydrodeacylcynaropicrin, were isolated for the first time from *Cynara* species. 11,13-Dihydroxy-8-desoxygrosheimin was isolated for the second time from a plant.

Keywords: Asteraceae, *Cynara syriaca*, flavonoids, phenolic acids, sesquiterpene lactones.

Introduction

Many effects, such as hepatoprotective, lipid lowering, choleretic, diuretic, spasmolytic, cholesterol synthesis inhibiting, and anti-atherosclerotic effects, and uses of the leaves of *Cynara scolymus* L. (artichoke) and *C. cardunculus* have been shown by *in vivo*, *in vitro*, and controlled clinical studies. For this reason *Cynarae folium*, in particular for its hepatoprotective characteristics, has gained an important place in many phytopharmaca (Reynolds, 1989; Maros et al., 1996; Kraft, 1997; Pitler & Ernst, 1998; Neval et al., 2002). The artichoke, *Cynara scolymus*, is cultured to be used as a vegetable in Turkey. Another species, *C. cardunculus*, investigated by us previously (Mericli & Seyhan, 1998), grows naturalized in a narrow area around Sinop region. The only *Cynara* species growing wild in Turkey is *C. syriaca*, which also grows in a very narrow area in southern Turkey (Kupicha, 1975). There has been no chemical investigation on *Cynara syriaca* except for the lipid content of the seeds (Heidari et al., 1990).

Materials and Methods

General

NMR spectra were recorded on a Bruker DPX-400 MHz spectrometer. MS were determined on a Finnigan MAT 90 spectrometer. UV spectra were recorded on a Jasco 530 V UV-Vis spectrophotometer. IR spectra were recorded on a Perkin Elmer 1600 Series FTIR spectrometer. Vacuum-liquid chromatography (VLC) was carried out on SiO_2 60 G (7731). Thin-layer chromatograms were run on SiO_2 using the solvent system for flavonoids: $CHCl_3$:acetone:formic acid (9:2:1), toluene:EtOAc:formic acid (5:4:1), EtOAc: ethyl methyl ketone:formic acid:water (5:3:1:1); for phenolic acids: EtOAc:formic acid:glacial acetic acid:water (100:11:11:26), toluene:EtOAc:formic acid (5:4:1); for sesquiterpene lactones: ether:EtOAc:DEA (5:5:1), toluene:acetone (3:2).

The brine shrimp (*Artemia salina*) lethality bioassay method was used for determination of cytotoxic activity (Dey & Harborne, 1991).

Plant Material

Cynara syriaca Boiss. (Asteraceae) leaves were collected from the Ulas village Tarsus, Turkey, in June 1997. Voucher specimens have been deposited in the herbarium of the Faculty of Pharmacy, Istanbul University (ISTE: 75176). and were identified by Assoc. Prof. Dr. Emine Akalin.

Extraction and isolation

Air-dried and powdered leaves (3 kg) were used for extraction and isolation of flavonoids, phenolic acids, and sesquiterpene lactones.

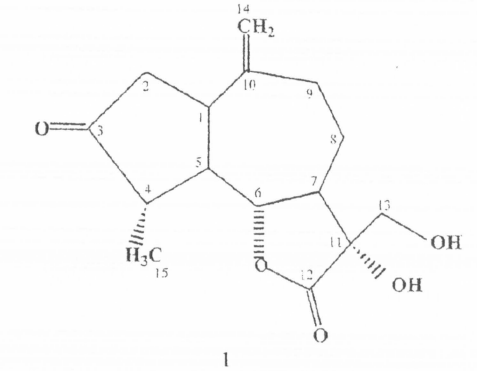
Accepted: June 21, 2006

Address correspondence to: Prof. Dr. Ali H. Meriçli, Department of Pharmacognosy, Faculty of Pharmacy, Istanbul University, 34116 Beyazıt, Istanbul, Turkey. E-mail: alimer@istanbul.edu.tr

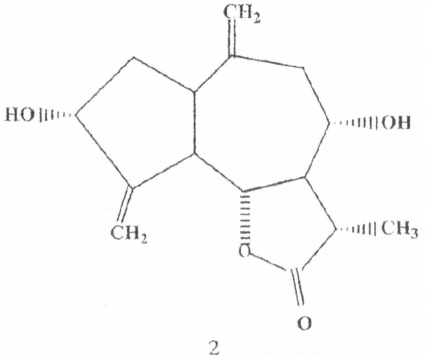
DOI: 10.1080/13880200601006830

Flavonoids

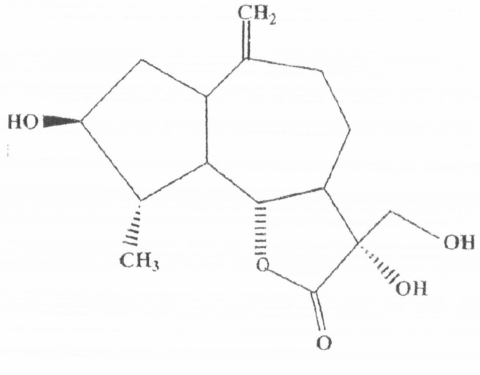
Leaves (1 kg) were extracted successively in a Soxhlet apparatus first with petroleum ether and then with ethanol. The ethanol part was concentrated, water was added and fractioned in a seperating funnel first with toluene, then with chloroform, and at last with ethyl acetate. The ethyl acetate extract (7.0 g) was fractioned using vacuum liquid chromatography (silica gel) with toluene:ethanol mixtures. Fractions 5 (32 mg), 6 (30 mg), and 8 (33 mg) were purified over Sephadex LH-20, and apigenin (3 mg), chrysoeriol (7 mg), and luteolin (8 mg) were obtained.



1



2



3

Figure 1. Structures of compounds **1**, **2**, and **3**.

Fraction 12 (1.5 g) was chromatographed over polyamide with water:ethanol mixtures, and apigenin 7-glucoside (12 mg), chrysoeriol 7-glucoside (6 mg), and luteolin 7-glucoside (25 mg) were obtained.

Phenolic acids

Leaves (1 kg) were extracted successively with methanol in a Soxhlet apparatus. The methanolic part was concentrated, diluted with water, and extracted in a separating funnel with petroleum ether. After removing the petroleum ether part, the pH of the aqueous part was adjusted to 2 with 0.1 N H_2SO_4 and extracted with ether. The ether extract (3.23 g) was chromatographed over silica gel using toluene:ether:methanol mixtures. Fractions 27 (19 mg), 52 (216 mg), and 54 (257 mg) were purified over Sephadex LH-20, and caffeic acid (18 mg), chlorogenic acid (10 mg), 1,5-dicaffeoylquinic acid (10 mg), and cynarin (10 mg) were obtained.

Sesquiterpene lactones

Leaves (1 kg) were percolated with petroleum ether:ether:methanol (1:1:1) mixture at room temperature, and the solvent was concentrated *in vacuo* up to 40°C. The extract (62.48 g) was chromatographed over silica gel with petroleum ether:ether:methanol mixtures. Fractions 7 (8.5 g) and 8 (7.2 g) were chromatographed using vacuum liquid chromatography (silica gel) with toluene:acetone:methanol mixtures, and 11,13-dihydrodesacylcynaropicrin (23 mg), 11,13-dihydroxy-8-desoxygrosheimin (6 mg), and solstitialin (34 mg) were obtained.

All isolated compounds were identified by comparing with authentic substances and with spectroscopic data (UV, IR, NMR, MS).

Table 1. ^{13}C NMR data of *Cynara syriaca* sesquiterpene lactones.

	Compound		
Position	1	2	3
1	39.63 d	45.61 d	43.02 d
2	43.89 d	38.68 t	38.47 t
3	212.73 s	73.18 d	73.50 d
4	47.08 d	152.72 s	52.68 d
5	49.06 d	49.45 d	50.09 d
6	87.23 d	78.29 d	82.12 d
7	51.36 d	51.53 d	52.16 d
8	24.70 t	73.73 d	26.63 t
9	38.67 t	43.93 t	35.87 t
10	148.86 s	143.45 s	148.65 s
11	77.22 s	39.78 d	77.71 s
12	178.34 s	175.64 s	179.92 s
13	67.23 t	14.12 q	63.08 t
14	112.65 t	115.87 t	113.71 t
15	13.98 q	112.74 t	11.68 q

The ^{13}C NMR data of 11,13-dihydroxy-8-desoxy-grosheimin (**1**; Fig. 1), which were not given fully in references (Barbetti et al., 1981), are shown together with the other isolated sesquiterpene lactones 11,13-dihydro-deacylcynaropicrin (**2**) and solstitialin (**3**) in Table 1.

Results and Discussion

As a result of this analysis, six flavonoids (apigenin, chrysoeriol, luteolin, apigenin 7-*O*-glucoside, chrysoeriol 7-*O*-glucoside, luteolin 7-*O*-glucoside), four phenolic acids (caffeic acid, chlorogenic acid, 1,5-dicaffeoylquinic acid, cynarin), and three sesquiterpene lactones [11,13-dihydroxy-8-desoxygrosheimin (**1**) 11,13-dihydrodeacylcynaropicrin (**2**) solstitialin (**3**)], were isolated from the leaves of *Cynara syriaca* and identified.

The flavonoids and the phenolic acids that are responsible for the hepatoprotective effect were similar to the compounds of *Cynara scolymus* and *Cynara cardunculus*. Only chrysoeriol and its 7-*O*-glucoside were isolated for the first time from *Cynara* species with this study. Sesquiterpene lactones are the compounds responsible for cytostatic activity. Cynaropicrin, the most known compound of *Cynara* species, could not be found in *Cynara syrica*, and, while sesquiterpene lactones of *Cynara syriaca* were inactive in brine shrimp assay, the authentic sample cynaropicrine was active. Among these compounds, 11,13-dihydrodeacylcynaropicrin was isolated for the first time from *Cynara* species. 11,13-Dihydroxy-8-desoxygrosheimin was found as a minor compound only in *Cynara scolymus* and is being reported again for the second time in a plant (Barbetti et al., 1981). Some isolated compounds were also tested for activity (Atasever et al., 2003).

References

Atasever B, Akgün-Dar K, Kuruca SE, Turan N, Seyhan GV, Meriçli AH (2003): *Cynara syriaca* 'dan elde edilen flavonoidlerin lösemi hücreleri üzerine Etkisi. *Ankara Ecz Fak Derg 32*: 143–150.

Barbetti P, Menghini A, Casinovi CG, Santurbano B (1981): Nuovi sesquiterpeni γ-lattonici da *Cynara scolymus* L. *3. Congresso Internazionale di studi sul. carciofo*. Bari, Industria Grafica Laterza, pp. 77–86.

Dey PM, Harborne JB (1991): *Methods in Plant Biochemistry*. New York, Academic Press, p. 8.

Heidari R, Siami A, Monazami CA (1990): Lipid content and fatty acid composition in some species of Compositae family. *Iran Agric Res 19*: 41–48.

Kraft K (1997): Artichoke leaf extract—Recent findings reflecting effects on lipid metabolism, liver and gastrointestinal tracs. *Phytomedicine 4*: 398–378.

Kupicha F (1975): *Cynara* L. In: Davis PH, ed., *Flora of Turkey and the East Aegean Islands*, Vol. 5. Edinburgh, University Press, pp. 327–329.

Maros T, Racz G, Katohai B, Kovács VV (1996): Wirkungen der *Cynara scolymus* Extrakte auf die Regeneration der Rattenleber. *Arzneim-Forsch (Drug Res) 16*: 127–129.

Meriçli AH, Seyhan GV (1998): Constituents of the leaves of *Cynara cardunculus* L. naturalized around Sinop. *Acta Pharm Turc 30*: 137–139.

Neval CA, Anderson LA, Phillipson JF (2002): *Herbal Medicines*. London, Pharamaceutical Press, pp. 36–37.

Pitler MH, Ernst E (1998): Artichoke leaf extracts for serum cholesterol reduction. *Perfusion 11*: 338–340.

Reynolds EJF (1998): *Martindale: The Extra Pharmacopeia*. London, Pharmaceutical Press, p. 1562.