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朝鲜蓟叶中一个新的倍半萜内酯

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摘要: 从朝鲜蓟 (*Cynara scolymus*) 叶中分离得到 2 个倍半萜内酯, 其中一个是新化合物, 通过波谱学方法确定其结构为 3β, 8α, 11α, 13-四羟基-10 (14)-愈创木烯-1α, 4β, 5α, 6β氢-6α, 12-内酯 (1)。

关键词: 朝鲜蓟; 菊科; 倍半萜内酯

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A New Sesquiterpene Lactone from the Leaves of *Cynara scolymus* (Compositae)

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Abstract: A new guaiane-type sesquiterpene lactone, named 3β, 8α, 11α, 13-tetrahydroxy-10 (14)-guaien-1α, 4β, 5α, 6βH-6α, 12-olide (1), together with a known sesquiterpene lactone, cynarinin A (2), were isolated from the leaves of *Cynara scolymus* (Artichoke). The structure of 1 was elucidated on the basis of MS, IR, 1D, and 2D NMR.

Key words: *Cynara scolymus*; Compositae; Sesquiterpene lactone

Cynara scolymus (Artichoke) is a traditional herbaceous plant belonging to the family Compositae and originating from Mediterranean area. Today, artichoke is widely distributed all over the world and its sprout is edible as vegetable. The leaves of artichoke have been used as choleretic and diuretic in traditional medicine (Kirchhoff *et al.*, 1994). Various chemical constituents (Wang *et al.*, 2003; Shimoda *et al.*, 2003; Zhu *et al.*, 2004; Schütz *et al.*, 2004) including polyphenols such as cynarin, caffeoylquinic acids, chlorogenic acids, sesquiterpenes, and sesquiterpene glycosides which were found from artichoke, show pharmacological activities (Dranik *et al.*, 1996; Kraft, 1997; Brown and Rice-Evans, 1998) such as antibacterial, antioxidative, antihyperlipidemic, choleretic, bileexpelling, and hepatoprotective activities. Therefore, we carried out a further chemical investigation on the leaves of artichoke cultivated in Vietnam. A new guaiane-type sesquiterpene lactone, 3β, 8α, 11β, 13-tetrahydroxy-10 (14)-guaien-1α, 4β, 5α, 6βH-6α, 12-olide (1) and a known sesquiterpene lactone, cynarinin A (2) (Li *et al.*, 2005) were obtained. This paper reports the isolation and structural elucidation of compound 1.

Results and Discussion

Compound 1 was obtained as a colorless oil. The negative-ion FABMS showed a quasi-molecular ion peak $[M-H]^-$ at *m z* 297. The molecular formula,

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$C_{15}H_{22}O_6$, was established by HRESIMS (*m z* 297.1336 [M-H]$^-$; calcd 297.1338), indicating five degrees of unsaturation. The IR spectrum of 1 exhibited absorption at 3418, 1769 and 1639 cm^{-1} ascribable to hydroxyl, γ-lactone and C = C functional groups. The ^{1}H NMR spectrum (Table 1) displayed one secondary methyl at δ_H 1.21 (3H, d, J = 6.5 Hz, H-15). The ^{13}C NMR and DEPT spectra (Table 1) revealed 15 carbon resonances including one methyl, four methylenes, seven methines and three quaternary carbons. The lactone carbonyl resonances were located at δ_C 82.0 (d, C-6), 180.4 (s, C-12), four oxygenated carbon resonances were observed at δ_C 78.6 (d, C-3), 71.2 (d, C-8), 79.4 (s, C-11) and 64.3 (t, C-13), and exocyclic methylene resonances at δ_C 145.4 (s, C-10) and 114.7 (t, C-14), respectively.

Table 1 ^{1}H and ^{13}C NMR data of 1 (500 and 125 MHz, resp.) and 2 (400 and 125 MHz, resp.)

No.	1 (CD_3OD)		2 (C_5D_5N)	
	δ_C	δ_H	δ_C	δ_H
1	43.1	2.85 (m)	40.2	3.50 (m)
2	39.1	2.04 (m); 1.69 (m)	43.7	2.48 (m); 2.09 (m)
3	78.6	3.63 (m)	218.6	
4	47.8	1.77 (m)	47.5	2.33 (m)
5	52.6	1.96 (m)	52.2	2.18 (m)
6	82.0	4.16 (dd, 10.4, 10.1)	82.4	4.63 (dd, 10.2, 9.8)
7	61.7	2.29 (dd, 10.4, 10.0)	57.4	3.21 (dd, 10.2, 9.8)
8	71.2	4.04 (m)	70.5	4.84 (m)
9	47.7	2.77 (dd, 12.0, 4.2); 2.09 (brd, 12.0)	49.6	3.13 (m); 2.56 (brd, 11.4)
10	145.4		145.9	
11	79.4		79.8	
12	180.4		179.8	
13	64.3	4.00 (d, 10.4); 3.76 (d, 10.4)	65.0	5.03 (d, 10.1); 4.56 (d, 10.0)
14	114.7	5.01 (s); 4.99 (s)	113.7	4.98 (s); 4.69 (s)
15	18.9	1.21 (d, 6.5)	15.0	1.24 (d, 7.1)

Chemical shift values δ in ppm, coupling constants J in Hz (in parentheses)

The comparison of the ^{13}C NMR data of 1 with those of 2 implied that they shared the same planar structure except for a hydroxyl at C-3 in 1 instead of the ketone carbonyl group at C-3 in 2 (Li *et al.*, 2005), causing the upfield shifts of C-3 from δ_C 218.6 in 2 to δ_C 78.6 in 1. The partial structural unit C-1 to C-9 was deduced from the analysis of the HSQC and ^{1}H-^{1}H COSY spectra of 1. The HMBC correlations between the AB system signals at δ_H 4.00 (1H, d, J = 10.4 Hz, Ha-13) and δ_H 3.76 (1H, d, J = 10.4 Hz, Hb-13) and C-12 and the oxygenated quaternary carbon signal at δ_C 79.4 (s, C-11) confirmed two hydroxyl groups attached to C-11 and C-13, respectively. The HMBC showed the cross-peaks of H-15 [δ_H 1.21 (d, J = 6.5 Hz)] to C-3, C-4 and C-5, H-6 [δ_H 4.16 (dd, J = 10.4, 10.1 Hz)] to C-12 (δ_C 180.4), H-14 [δ_H 5.01 (s), 4.99 (s)] to C-1, C-9 and C-10, and H-9 [δ_H 2.77 (dd, J = 12.0, 4.2 Hz), 2.09 (brd, J = 12.0 Hz)] to C-1, C-10 and C-14, respectively. These information confirmed the planar structure of 1. The relative configuration of 1 was determined by comparison with 2 and confirmed by a ROESY experiment. The ROESY correlations (Fig.2) of H_α-1 with H-3, and H_α-5 with H-3, H-7 and Me-15 indicated that H-3, H-7 and Me-15 possessed α-orientations, respectively. The ROESY correlations of H-6 with H_β-4 and H-8 suggested that H-6 and H-8 possessed β-orientations, respectively. On the basis of the evidence mentioned above, the structure of 1 was elucidated as 3β, 8α, 11α, 13-tetrahydroxy-10 (14)-guaien-1α, 4β, 5α, 6βH-6α, 12-olide.

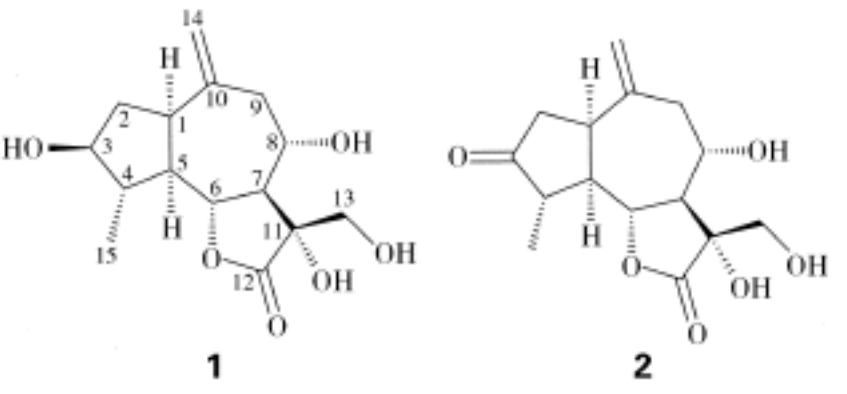

Fig. 1 The structures of compounds 1 and 2

Experimental

General experimental procedures Fractions were monitored by TLC, and spots were visualized by heating silica gel plates sprayed with 10% H_2SO_4 in ethanol. Silica gel (200-300 mesh, Qingdao Marine Chemical Inc., China) and Sephadex LH-20 (Amersham Biosciences, Sweden) were used for column chromatography. Optical rotation was measured on a Horbia SEPA-300 polarimeter. IR spectrum was obtained on a Bruker Tensor 27 instrument with KBr pellets. NMR spectra were recorded on Bruker AM-400 and Bruker DRX-500 spectrometers in CD_3OD with TMS as an internal standard. FAB-MS was taken on

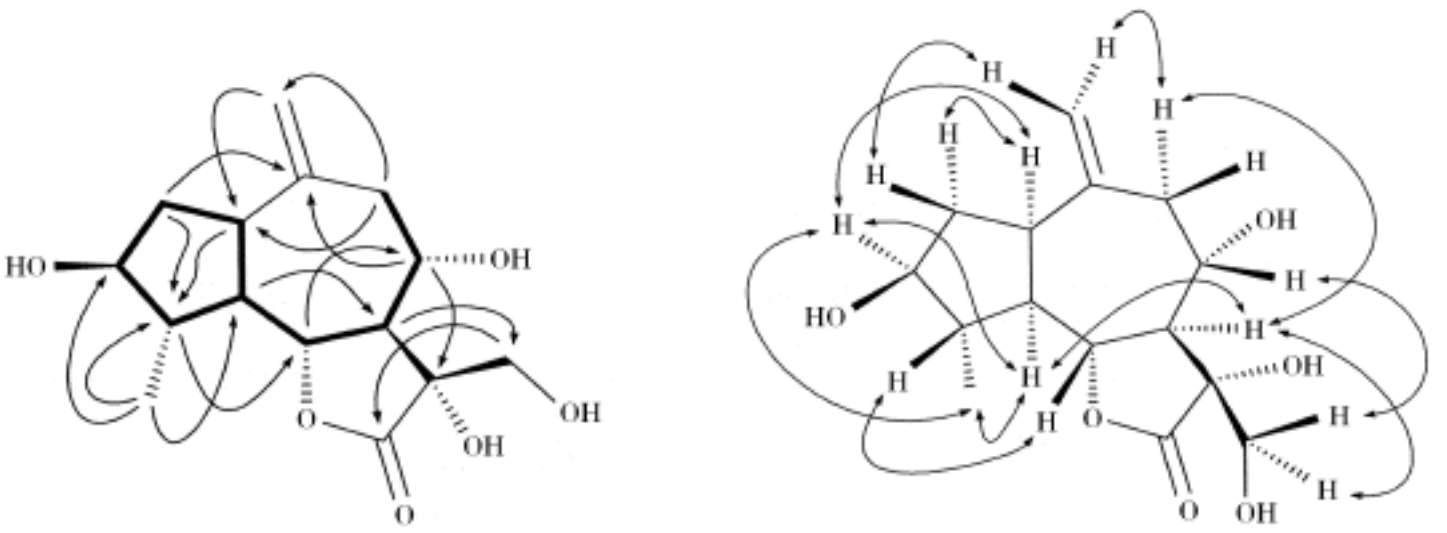

Fig. 2 Key HMBC and ROESY correlations of compounds 1

a VG Auto Spec-3000 spectrometer, and HRESI-MS was recorded with an API QSTAR Pulsar 1 spectrometer.

Plant material The leaves of *Cynara scolymus* were collected from Ho Chi Minh City, Vietnam, in February, 2007. The voucher specimen (20070208-Tony-01) was deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences (CAS).

Extraction and isolation The dried leaves of Artichoke (*Cynara scolymus*) (5 kg) were mashed and extracted with 75% ethanol at room temperature for 3×48 h. The extracts were combined and concentrated to dryness under reduced pressure to give the residue (380 g), which was suspended in H_2O and partitioned sequentially with petroleum ether, EtOAc, and *n*-BuOH. The EtOAc extract (50 g) was separated into eleven fractions (F_1-F_{11}) by silica gel column chromatography using a $CHCl_3$ MeOH gradient. The fraction F_9 (100 mg) was further subjected to Sephadex LH-20 column chromatography using $CHCl_3$ MeOH (1∶1, v v) as eluent, and repeated silica gel column chromatography eluted with chlroform acetone form 10∶1 (v v) to 4∶1 (v v) to afforded the compounds 1 (20 mg) and 2 (7 mg).

3β, 8α, 11α, 13-Tetrahydroxy-10 (14)-guaien-1α, 4β, 5α, 6βH-6α, 12-olide (1) $C_{15}H_{22}O_6$, colorless oil. $[\alpha]_D^{23}$ +32.1° (*c* = 0.78, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3418, 2928, 1769, 1639, 1139, 1071, 980. ^1H and ^{13}C NMR: see Table 1. Negative FABMS *m z* 297 [M-H]$^-$; HRESIMS *m z* 297.1336 [M-H]$^-$ (calcd for $C_{15}H_{21}O_6$ 297.1338).

Cynarinin A (2) $C_{15}H_{20}O_6$, white power. $[\alpha]_D^{22}$ +90.5° (*c* = 1.59, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3479, 3423, 1771, 1749, 1134, 977. ^1H and ^{13}C NMR: see Table 1.

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References:

Brown JE, Rice-Evans CA, 1998. Luteolin-rich artichoke extract protects low density lipoprotein from oxidation in vitro [J]. *Free Radical Research*, 29: 247—255

Dranik LI, Dolganenko LG, Slapke J *et al.*, 1996. Chemical composition and medical usage of *Cynara scolymus* L. [J]. *Rastit Resur*, 32: 98—104

Kraft K, 1997. Artichoke leaf extract-recent findings reflecting effects on lipid metabolism, liver, and gastrointestinal tracts [J]. *Phytomedicine*, 4: 369—378

Kirchhoff R, Beckers C, Kirchhoff GM *et al.*, 1994. Increase in choleresis by means of artichoke extract. Results of a randomized placebo-controlled double-blind study [J]. *Phytomedicine*, 1: 107—115

Li XL, Qian PL, Liu ZY *et al.*, 2005. Sesquiterpenoids from *Cynara scolymus* [J]. *Heterocycles*, 65: 287—291

Schütz K, Kammerer D, Carle R *et al.*, 2004. Identification and quantification of caffeoylquinic acids and flavonoids from artichoke (*Cynara scolymus* L.) heads, juice, and pomace by HPLC-DAD-ESI MS [J]. *Journal of Agricultural and Food Chemistry*, 52: 4090—4096

Shimoda H, Ninomiya K, Nishida N *et al.*, 2003. Anti-Hyperlipidemic sesquiterpenes and new sesquiterpene glycosides from the leaves of artichoke (*Cynara scolymus* L.): structure requirement and mode of action [J]. *Bioorganic & Medicinal Chemistry Letters*, 13: 223—228

Wang MF, Simon JE, Aviles IF *et al.*, 2003. Analysis of antioxidative phenolic compounds in artichoke (*Cynara scolymus* L.) [J]. *Journal of Agricultural and Food Chemistry*, 51: 601—608

Zhu XF, Zhang HX, Lo R, 2004. Phenolic compounds from the leaf extract of artichoke (*Cynara scolymus* L.) and their antimicrobial activities [J]. *Journal of Agricultural and Food Chemistry*, 52: 7272—7278