

Ulubelenolide: A New triterpene lactone from *Tanacetum chilliophyllum* (Fisch. & Mey.) var. *monocephalum* Grierson

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Abstract: A further investigation on *Tanacetum chilliophyllum* var. *monocephalum* ethyl acetate extract afforded a new triterpene lactone Ulubelenolide (olean-12-ene-3 β ,10 β -olide) (**1**). The structure of (**1**) was determined with spectral analysis including FTIR, ¹H, ¹³C NMR, APT, DEPT, COSY, HMQC, HMBC, and APCI-MS.

Keywords: Ulubelenolide; triterpene lactone; olean-12-ene-3 β ,10 β -olide; *Tanacetum chilliophyllum* var. *monocephalum*; Astereaceae. © 2015 ACG Publications. All rights reserved.

1. Plant Source

In our previous investigation of *T. chilliophyllum* var. *monocephalum* we have reported a new sesquiterpene lactone 1-*epi*-chilliophyllin together with known neolupenyl acetate (lup-12-ene-3 β -acetate), 4',5,7-trihydroxy-3',8-dimethoxyflavone, 4',5,7-trihydroxy-8-methoxyflavone from ethyl acetate extract [1]. The ethyl acetate and methanol extracts of the plant also showed significant contact toxicity against *Sitophilus granarius* and DPPH scavenging activity [1].

Plant materials were collected during the flowering period from Güzeldere-Van at an altitude of 2594 m in 2006. A voucher specimen was deposited at the Herbarium of the Faculty of Science, İstanbul University (Voucher no. ISTE 83478), Turkey. Plant material was identified by Dr. Kerim Alpınar.

2. Previous Studies

Previously the essential oil composition, chemotype variation, flavones, flavonols and sesquiterpene lactones of *T. chilliophyllum* var. *chilliophyllum* were reported [2-7]. New sesquiterpene lactones chilliophyllin and heimerlein together with known ones were also reported from *T. chilliophyllum* var. *heimerlei* [8,9]. Until now essential oils that contains (+)-linalool and camphor main components were reported for *T. chilliophyllum* var. *monocephalum* [10,11]. New sesquiterpene lactone 1-*epi*-chilliophyllin together with known neolupenyl acetate (lup-12-ene-3 β -acetate), 4',5,7-trihydroxy-3',8-dimethoxyflavone, 4',5,7-trihydroxy-8-methoxyflavone content were also reported from the ethyl acetate extract of *T. chilliophyllum* var. *monocephalum* [1].

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3. Present Study

Air dried and powdered aerial parts (1.2 kg) of the plant were extracted with hexane, ethyl acetate and methanol, respectively. Each extract from different solvent was concentrated under reduced pressure to give solvent free residue: 2.6 g crude hexane extract, 17.1 g crude ethyl acetate extract and 60 g crude methanol extract were obtained. Ethyl acetate extract was fractionated with a SiO₂ column using hexane, ethyl acetate, methanol as eluents in increasing polarity. The fraction obtained from hexane/ethyl acetate (1:1) elution was refractionated with a silicagel column using hexane, dichloromethane, chloroform, diethyl ether, ethyl acetate eluents in increasing polarity. The fraction obtained from dichloromethane/chloroform (1:1) was separated further on silicagel TLC using hexane/chloroform/dichloromethane (6:2:2) eluents and compound **(1)** (8.2 mg) was obtained. The structure of the pure compounds were identified using spectral methods including FTIR, ¹H, ¹³C NMR, APT, COSY, HMQC, HMBC, DEPT and APCI-MS. The NMR spectra were acquired in CDCl₃ with 400 MHz Varian Mercury-VX 400 BB. The Infra red spectra were acquired by Perkin Elmer FT-IR with ATR attachment. The Mass spectra were obtained with Thermo LCQ Deca Ion Trap Mass Spectrometer. APCI was used as an ion source in mass spectrometry. Structure of new compound **(1)** was given in Figure 1.

Ulubelenolide (olean-12-ene-3 β ,10 β -olide) (**1**): White amorphous powder; IR-ATR λ_{\max} 2921, 2851, 1732, 1463, 1380, 1176, 755 cm⁻¹; ¹H NMR (400MHz, CDCl₃, δ) and ¹³C NMR (100.6 MHz, CDCl₃, δ) were given in Table 1; APCIMS *m/z*: 423.60 [M-CH₃]⁺(17), 410.13 [M-CO]⁺(100), 391.80 [M-2-COOH]⁺(9), 287.07(2), 279.13(7), 205.53 [423.60-C₁₆H₂₆]⁺ (Retro Diels-Alder fragmentation)(3), 149.27(4), 95.20(4).

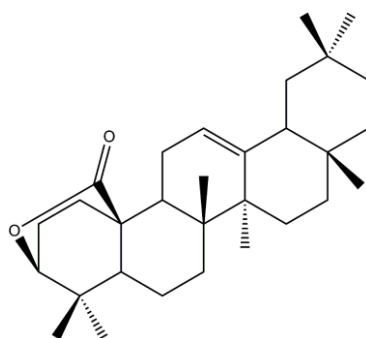


Figure 1. Structure of Ulubelenolide (**1**) isolated from *T. chiliophyllum* var *monocephalum* ethyl acetate extract.

Compound **(1)** gave a red-brownish spot on TLC when treated with Ce(SO₄)₂. The APCI-MS spectrum showed [M-CH₃]⁺ peak at *m/z*: 423.60 (Calculated for C₂₉H₄₃O₂, 423.66), The FT-IR spectrum gave the bands at 1732 cm⁻¹ indicating a lactone group in the molecule. Seven methyl groups were observed in the ¹H NMR spectrum suggesting the compound could be a triterpene (Table 1).

The ¹H NMR spectrum of **(1)** gave peaks at δ 5.11 (H-12, dd, J=4; 4 Hz) and 4.43 (H-3, dd, J=6; 6 Hz) indicating the unsaturation and the proton attached to an oxygen function, respectively. Biogenetically oleanane type triterpenes have oxygen function at the C-3 as β position, and a double bond at the position between C-12 and C-13 [12]. The APT spectrum of the compound showed only two unsaturated carbon atoms at δ 121.8 (-) and δ 145.4 (+) indicating endocyclic nature of the double bond. In the APT spectrum a signal at δ 173.9 (+) indicated that existence of a carbonyl group which might be a lactone carbonyl according to the IR spectrum. In the HMQC spectrum the signal at δ 4.43 (H-3) coupled with the methine carbon at δ 80.8 (-). The HMBC experiments supported the location of lactone ring between C-3 and C-25. In the HMBC spectrum, correlations were observed between 173.9 (C=O, C-25) and the peaks δ 4.43 (H-3), and δ 2.22 (H-1) which were further coupled with δ 1.60 (H-2, m), observed in COSY and spin decoupling experiments. In the formation of a lactone ring biosynthetically in the structure, probably C-25 methyl group first oxidized an acid moiety, then a five membered lactone ring is formed between C-25 acid and C-3 β hydroxyl groups through an aldol

condensation with a loss of H₂O [12]. The HMBC experiments also showed correlations between C-3 and H-23 and H-24 supporting the position of the lactone ring. The position of the remaining methyl signals were elucidated by HMBC correlations and with the spectral data of the similar oleanane type pentacyclic triterpenes in the literature [13,14]. The specific Retro-Diels Alder fragmentation observed in MS at *m/z* 205.53 [423.60-C₁₆H₂₆]⁺ was further improved that the compound was an oleanane type triterpene. The compound (**1**) was named as ulubelenolide in the honor of Prof. Dr. Ayhan Ulubelen for her outstanding contributions to the Natural Products Chemistry.

Table 1. ¹H NMR (400MHz, CDCl₃, δ); ¹³C NMR (100.6 MHz, CDCl₃, δ), HMQC and HMBC of (**1**)

H	¹ H NMR	HMQC	HMBC	C	¹³ C NMR APT ^a	DEPT
1	2.22 ddd (J=3;7;7 Hz)	C-1	C-25	1	35.1 (+) ^a	CH
2	1.60 m*	C-2		2	25.4 (+) ^a	CH ₂
3	4.43 dd (J=6;6Hz)	C-3	C-25	3	80.8 (-) ^a	CH
				4	37.4 (+) ^b	C
5	0.84 m ^{*,b,c}			5	55.5 (-) ^b	CH
6	1.40, 1.50 ^{*,b,c}			6	18.5 (+) ^b	CH ₂
7	1.32, 1.52 ^{*,b,c}			7	32.7 (+) ^b	CH ₂
				8	40.0 (+) ^b	C
9	1.54 m ^{*,c}			9	47.8 (-) ^b	CH
				10	37.1 (+) ^b	C
11	1.85 m*	C-11		11	23.7 (+) ^a	CH ₂
12	5.11 t (J=4 Hz)	C-12		12	121.8 (-) ^a	CH
				13	145.4 (+) ^a	C
				14	41.9 (+) ^b	C
15	0.78, 1.96 ^{*,b,c}			15	27.2 (+) ^b	CH ₂
16	1.74, 0.98 ^{*,b,c}			16	26.4 (+) ^b	CH ₂
				17	32.2 (+) ^b	C
18	1.94 m ^{*,b,c}			18	47.5 (-) ^b	CH
19	1.60, 1.00 ^{*,b,c}			19	47.0 (+) ^b	CH ₂
				20	31.3 (+) ^b	C
21	1.08, 1.37 ^{*,b,c}			21	34.9 (+) ^b	CH ₂
22	1.24, 1.44 ^{*,b,c}			22	35.0(+) ^b	CH ₂
23	0.80 s	C-23	C-3	23	28.2 (-) ^a	CH ₃
24	0.80 s	C-24	C-3	24	23.9 (-) ^a	CH ₃
25	-	-		25	174.0 (+) ^a	C
26	0.81 s	C-26		26	14.3 (-) ^a	CH ₃
27	1.06 s	C-27	C-13	27	26.1 (-) ^a	CH ₃
28	0.78 s	C-28		28	28.6 (-) ^a	CH ₃
29	0.90 s	C-29		29	17.0 (-) ^a	CH ₃
30	0.89 s	C-30		30	15.7 (-) ^a	CH ₃

* Overlapped Signals.

^a Chemical shift of carbon atoms were assigned with HMQC experiment.

^b The ¹H NMR and ¹³C NMR peaks were assigned using the spectral data of the similar oleanane type pentacyclic triterpenes in the literature [13,14].

^c Chemical shift of hydrogens were determined with COSY.

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