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Sesquiterpene Lactones and Other Constituents from The Aerial Parts of *Tanacetum Abrotonifolium* Druce, Collected in East Turkey

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Abstract: In these notable study successful by chemical composition of the aerial parts of *Tanacetum abrotonifolium* Druce, collected in eastern region of Anatolia in Turkey and was study for the first time. Eight known sesquiterpene lactones, namely tanachin (**1**), tavulin (**2**), tamirin (**3**), spiciformin (**4**), isospiciformin (**5**), 1β-hydroxy-6α-angeloxy-oxygermacra-4(5),10(14),11(13)-trien-8,12-olide (**6**), dentatin A (**7**), 1-β-hydroxy-6α-angeloyloxyeudesm-4(15), 11(13)-dien-8,12-olide (**8**) as well as α-amyrin (**9**) and β-sitosterol (**10**) were isolated by using ethyl acetate and MeOH extracts from the aerial parts of *Tanacetum abratonifolium* Druce. The structures were isolated and identified by comparing their physical and spectroscopic data with those given in the literature.

Keywords: *Tanacetum abrotonifolium*, Asteraceae, Compositae, sesquiterpene lactones, eudesmanolides

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INTRODUCTION

The genus *Tanacetum* is distributed in Europe and in Western part of Asia throughout the northern temperate regions. *Tanacetum* genus has about 200 (1, 2) species and is represented by 44 species altogether 59 taxa in Turkey, 17 of them being endemic (3). Since some *Tanacetum* species which belong to the family of Asteraceae have been used as folk remedies for centuries in all over the world, it seemed to be important to investigate the genus being one of the riches genera in the flora of Turkey (4). Although many species of the genus *Tanacetum*, such as *T. annuum*, *T. balsamita*, *T. indicum*, *T. nubigenum*, *T. santolinoides*, *T. microphyllum*, *T. artemisioides*, *T. vulgare* and *T. parthenium* are used therapeutically around the world the last two are the most studied and the best characterized (5-8).

Tanacetum abrotanifolium Druce. (Asteraceae) is a tall (60–100 cm), perennial herb that finds a natural habitat on rocky slopes or in Quercus woods at 1630–2300 m altitude. This species intrinsically grows in eastern and northeastern Asia Minor (1).

Previous investigations on the essential oils of *T. abrotanifolium* were documented comprehensively in the literature (9, 10). Aerial part of T. abrotanifolium was also documented in the literature for biological activity tests (11). Flavonoids and essential oils are also pointed out as active substance in *T. abrotonifolium* (9, 10).

However, to the best of our knowledge, there is no report on constituents of the aerial parts of *T. abrotanifolium*. In the course of our studies on *Tanacetum* species growing in Turkey, we investigated the chemical composition of *Tanacetum abrotonifolium* which afforded eight sesquiterpene lactones as well as α-amyrin and β-sitosterol.

MATERIAL AND METHODS

General

CC was carried out on Kieselgel 60 (0.063-0.200 mm, Merck), TLC was performed on precoated silica gel 60 F_{254}, 0.2 mm plates (Merck), spots were detected under UV light and spraying acidified ceric sulfate followed by heating. FTIR spectra were recorded on a Mattson 1000 on NaCl cells at Yıldız Technical University; ^{1}H NMR spectra were recorded at 400 MHz on a Bruker-Spectrospin Avance DPx400 Ultrashield NMR instrument at Middle East Technical University (Ankara).

List of abbreviations: Thin Layer Chromatography (TLC); Ultraviolet (UV); Fourier-transform infrared spectroscopy (FTIR); Nuclear magnetic resonance spectroscopy (NMR); Column Chromatography (CC).

Plant Material

T. abrotanifolium was collected from Muradiye – Van at 2494 m altitude in its flowering period. Voucher specimen has been deposited in the Herbarium of the Faculty of Pharmacy, Istanbul University, Turkey (Voucher no. ISTE 83755). Plant materials were identified by Dr.Kerim Alpinar.

Extraction and Isolation

The extraction of 2800 gr dried and powdered aerial parts of *T. abrotanifolium* collected from Muradiye – Van at 2494 m altitude in its flowering period. Voucher specimen has been deposited in the Herbarium of the Faculty of Pharmacy, Istanbul University, Turkey (Voucher no. ISTE 83755). Plant materials were identified by Dr.Kerim Alpinar. 2800 g of viscous mass which subjected to column chromatography on silica gel with n-hexane, ethyl acetate, and MeOH. The ethyl acetate and MeOH extracts (93.80 g) were combined and treated with MeOH in order to remove the long-chain saturated hydrocarbons.

The residue was applied on a silica gel column to afford 8 fractions and eluted successively with the following solvent systems in increasing polarity: Fraction 1) n-hexane (1500 mL), Fraction 2) dichloromethane-hexane (750:750 mL), Fraction 3) dichloromethane (1500 mL), Fraction 4) dichloromethane-ethyl acetate (750:750 mL), Fraction 5) ethyl acetate (1500 mL), Fraction 6) ethyl acetate-methanol (750:750 mL), 77) methanol (1500 mL) and 8) methanol-dist. H_2O (750-750 mL).

The fractions from CC were controlled by TLC and similar fractions were combined and further separated on silica gel columns and by prep. TLC. Thus Fraction 2 by elution with dichloromethane-hexane (%50:% 50) yielded 1β-hydroxy-6α-angeloxy-oxylgermacra-4(5),10(14),11(13)-trien-8,12-olide (**6**) (3 mg), dentatin A (**7**) (27.10 mg), 1-β-hydroxy-6α-angeloyloxyeudesm-4(15), 11(13)-dien-8,12-olide (**8**) (4.50 mg). Fraction 3 gave α-amyrin (**9**) (50.80 mg) by column chromatography on silica gel using % 100 dichloromethane; Fraction 4 by elution with by CC on silica gel using dichloromethane-ethyl acetate (%50:%50) yielded β-sitosterol (**10**) (383.20 mg) ; Fraction 5 gave tanachin (**1**) (359.52 mg) and tavulin (**2**) (301.32 mg) by column chromatography on silica gel using % 100 ethyl acetate, Finally from the fraction 6 that was submitted to CC with ethyl acetate-methanol (%50:%50 mL) tamirin (**3**) (14 mg), spiciformin (**4**) (355.61 mg), isospiciformin (**5**) (449.88 mg) was obtained. (Fig. 1).

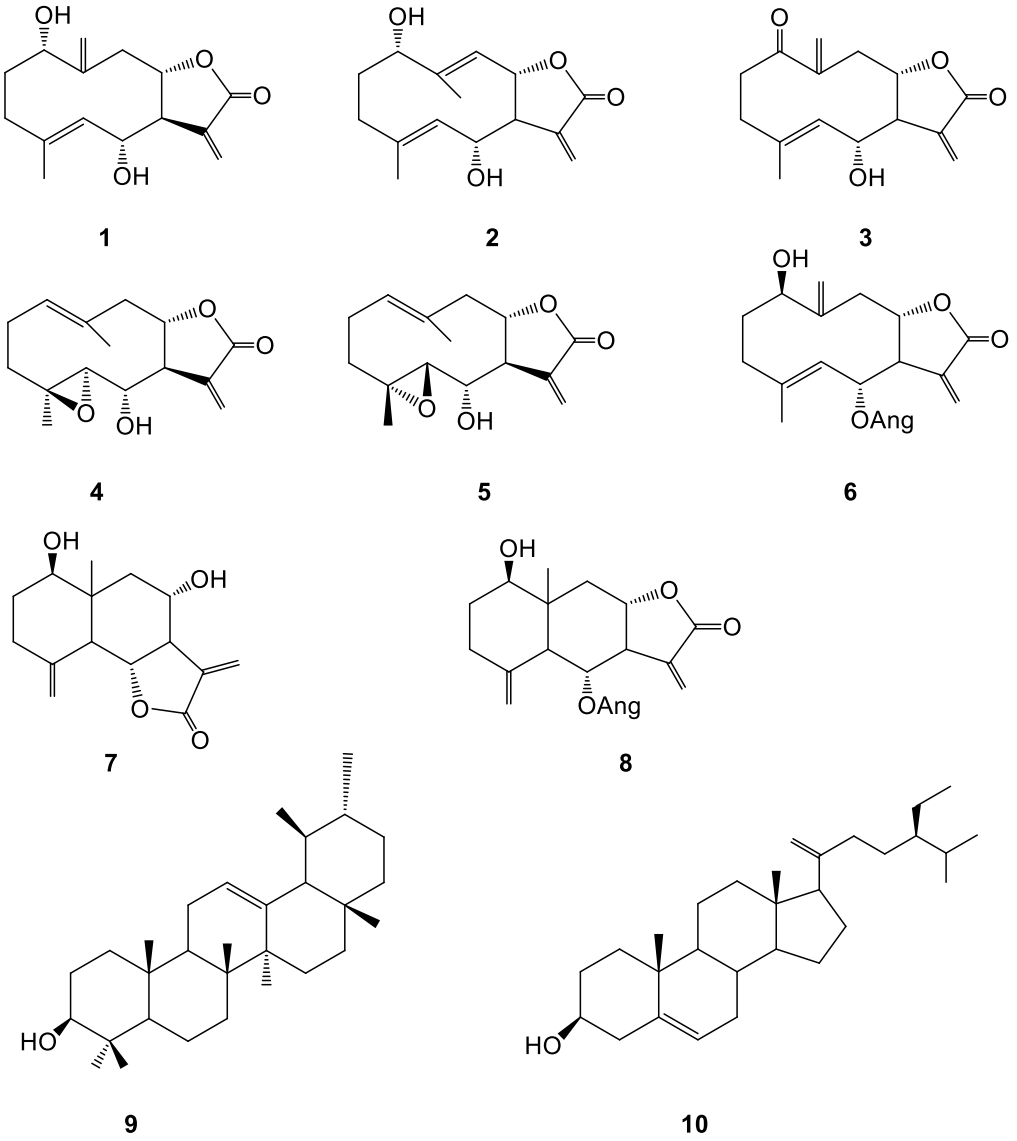

Figure 1: Compounds isolated from *T. Abrotonifolium.*

RESULTS AND DISCUSSION

In this study, the chemical compositions of the aerial parts of *T. abrotonifolium* collected from Eastern Turkey is reported for the first time.

The genus *Tanacetum* belongs to family Asteraceae or Compositae. Interest is increasing in species of *Tanacetum* due to constituents and the presence of sesquiterpene lactones, which exhibited biological activities like cytotoxicity, antimicrobial activity, and growth regulation.(7). *Tanacetum* species have been used for centuries as folk remedies due to their diverse biological activities. Sesquiterpenoids which are the main components of the genus, supposed to be active principles of the plants. The lactone ring of sesquiterpene lactones, having exocyclic methylene group, has been suggessed to be responsible for biological activities of sesquiterpenoids (7) Biological activities of the sesquiterpene lactones from *Tanacetum* genus were reported extensively. Tavulin, isospiciformin, tanachin, and dentatin A were isolated from *T.*

argyrophyllum var. argyrophyllum, exhibited bactericidal effects against *Staphylococcus aureus*, and *Escherichia coli* (12). Tavulin, spiciformin, dentatin A isolated from *T. densum ssp. sivasicum,* were found to be active activity against human epidermoid (KB) cells, with the IC_{50} values of 3.2, 2.9 and 2.4 μgm^{-1}, respectively (13). The sesquiterpene lactones tavulin, tanachin and tamirin isolated from *Tanacetum praeteritum* ssp. *praeteritum* showed cytotoxic activity against the human pulmonary carcinoma cell line GLC_4 and the colorectal cancer cell line COLO 320 as well as antibacterial activities against the bacteria *Bacillus subtilis, Staphylococcus aureus, Proteus mirabilis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus*, beta-hemolytic *Streptococcus*, and the yeast *Candida albicans* (14).

In Table 1 shows that, biological activities and active principles in *Tanacetum* species which also analyzed in chemical structure of *T. abrotonifolium*.

Table 1. Biological active principles in *T. abrotonifolium*

Sources	Name	Activity	References
T. argyrophyllum var.argyrophyllum T. densum ssp Sivasicum	Tanachin	Antimicrobial activity	(12, 13)
T. argyrophyllum var.argyrophyllum T. densum ssp Sivasicum	Tavulin	Antimicrobial activity Cytotoxic activity	(12, 13)
	Spiciformin	Cytotoxic activity	(13)
T. argyrophyllum	Isospiciformin	Antimicrobial activity	(12)
var.argyrophyllum		Antimicrobial activity	(12)
T. densum ssp Sivasicum	Dentatin A	Cytotoxic activity	(13)
T. praeteritum ssp. Praeteritum	Tamirin	Antimicrobial activity Cytotoxic activity	(14)

Polatoglu *et al.* investigated on the phytochemistry and the essential oils composition of *T. abrotonifolium* and they reported that insecticidal and biological activity of this species. (9)
Gecibesler *et al*. reported of the essential oils components of *T. abrotonifolium* by using HS-SPME-GC-MS method. (10) Gecisler also investigated biological activity studies of aerial parts this species. According to this report aireal parts of *T. abrotonifolium* were shown that anti-cancer, anti-microbial anti-oxidant activity (11).
However, the chemical constituents of aireal parts of *T. abrotanifolium* species have not been investigated. It is important to know the chemical structures of the air parts of *T. abrotonifolium* for scientific studies and future drug investigations.

Therefore, the aim of the study presented here was to examine the chemical compositions of the aerial parts of *T. abrotonifolium*.

The aerial parts of *T. abrotonifolium* yielded the known compounds tanachin (**1**) (15), tavulin (**2**) (16), tamirin (**3**) (16, 17), spiciformin (**4**) (18, 13), isospiciformin (**5**) (13, 12), 1β-hydroxy-6α-angeloxy-oxygermacra-4(5),10(14),11(13)-trien-8,12-olide (**6**) (19), dentatin A (**7**) (20), 1-β-hydroxy-6α-angeloyloxyeudesm-4(15), 11(13)-dien-8,12-olide (**8**) (19). β-sitosterol (**10**) (21)which is the common steroids in the genus and α-amyrin (**9**) (22) which is only few common triterpenes were also isolated from *T. abrotonifolium.*

The ^{1}H-NMR spectrum of some compounds which belongs to *T. abrotonifolium* and ^{13}C-NMR spectrum of compounds were given in Table 2 and Table 3 respectively.

Table 2. The ^{1}H-NMR spectrum of some compounds which belongs to *T. abrotonifolium* (400 MHz; a. $CDCl_3$ b. $CDCl_3$+ CD_3OD)

H	1[a] (15)	2[a] (16)	3[a] (16, 17)	7[b] (20)
1	4.02 brd	4.38 brd.d		3.54 d.d
2		2.05-1.85 m	3.27 m	1.85 d.d.d
2′		2.05-1.85 m	3.27 m	1.55d.d.d
3	2.30-1.90 m	2.29 brd.d	2.30-2.60 m	
3′		1.78 m	2.30-1.60 m	
5	5.25 brd	4.99brd	5.07 brd	2.19 brd
5′				
6	4.41 d.d	4.50 d.d.d	4.15 d.d	4.04 d.d
7	2.88 d.d.d.d	2.80 d.d.d.d	2.73 d.d.d.d.d	2.62 d.d.d.d
8	3.94 d.d.d	4.54 d.d	3.95 d.d.d	4.10 d.d.d
8′				
9	3.05 d.d.d.d	5.32 brd	3.40 d.d.d.d.d	2.38 d.d
9′	2.41 d.d		2.15 d.d	1.33 d.d
13	6.30 d.d	6.30 d.d	6.37 d.d	6.18 d.d
13′	6.18 d.d	6.21 d.d	6.17 d.d	5.99 d.d
14		1.83 d	5.83 d	0.82 s
14′	5.16 d		5.78 d	
15	1.70 d	1.78 brs	1.65 d	5.0 brs
15′				4.87 brs

Table 3. The ^{13}C-NMR and the ^{1}H-NMR data of the compounds isolated from *T. abrotonifolium* (50-50.75 MHz; a. $CDCl_3$ b. $CDCl_3$+ CD_3OD)

C	1[a] (15)	2[a] (16)	3[a](16, 17)	7[b] (20)
1	76.6	66.9	203.1	67.7

2	36.3	27.2	36.4	31.4
3	36.5	35.3	35.6	46.3
4	138.2	135.3	136.5	141.8
5	127.9	129.9	131.5	52.0
6	71.4	71.1	70.2	78.0
7	58.1	52.3	50.5	55.2
8	83.5	74.2	76.8	67.7
9	41.9	126.8	40.2	33.6
10	152.9	142.5	146.6	42.2
11	137.3	137.6	136.3	136.6
12	170.1	169.9	169.6	170.6
13	124.5	123.7	124.2	119.8
14	113.0	16.8	126.0	12.8
15	17.8	15.7	17.3	110.8

CONCLUSIONS

Tanacetum species have been used for centuries as folk remidy since their various biological activity. *T. abrotanifolium* is used by the people for cure purposes, even sold by herbalists, in Turkey. Phytochemical investigation on the essential oil composition of *T. abrotonifolium* and biological activity studies of this species is reported but the chemical constituents of aerial parts of *T. abrotanifolium* species have not been reported so far. Therefore, the main goal of this study of the chemical constituents of aerial parts of *T. abrotonifolium*. It is important to know the chemical structures of the aerial parts of *T. abrotonifolium* for scientific studies and future drug investigations. Further study should be carried out to the active compounds for pharmaceutical and industrial purposes.

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REFERENCES

1. Davis P. Flora of Turkey and the East Aegean Islands. Vol. 5. Edinburgh: Edinburgh University Press. 1975; 256-292.

2. Duke J. CRC Handbook of Medicinal Herbs. England: CRC Press. 1987; 474-475.

3. Abad M, Bermejo P, Villar A. An approach to the genus *Tanacetum* L.(Compositae): phytochemical and pharmacological review. Phytotherapy Research. 1995; 9(2):79–92.

4. Davis P, Mill R, Tan K, editors. Flora of Turkey and the East Aegean Islands (supplement). Edinburgh: Edinburgh University Press; 1998. 5.5. Lahlou S, Tahraoui A, Israili Z, Lyoussi B. Diuretic activity of the aqueous extracts of *Carum carvi* and *Tanacetum vulgare* in normal rats. J. Ethnopharmacol. 2007; 110: 458-463.

6. Akpulat H.A, Tepe B, Sokmen A, Daferera D, Polissiou M. Composition of the essential oils of *Tanacetum argyrophyllum* (C. Koch) var. *argyrophyllum* and *Tanacetum parthenium* (L.) Schultz Bip. (Asteraceae) from Turkey. Biochem. Syst. Ecol. 2005; 33: 511-516.

7. Gören N, Arda N, Çalışkan Z. Chemical Characterization and Biological Activities of the genus *Tanacetum* (Compositae). Studies in Natural Products Chemistry 2002; 27: (Bioactive Natural Products (Part H)): 547-658. Publisher: (Elseiver Science B.V.,) CODEN:SNPCE2

8. Brown A.M.G, Love K.C, Davey M.R, Power J.B. Plant Science. 1996; 116: 223.

9. Polatoglu K, Karakoc O.C, Yucel Y, Betul Demirci B, Goren N, Baser K.H.C. Composition, insecticidal activity and other biological activities of *Tanacetum abrotanifolium* Druce. essential oil. Industrial Crops and Products. 2015; 71: 7–14.

10. Geçibesler I.H, Demirtas I, Koçak A. Based on the Quantity, Temperature and Time, The Examination of Variability in Odorous Components of *Tanacetum abrotanifolium* from Turkey: An Exclusive Gradient Work. Journal of Essential Oil Bearing Plants. 2015; 18 (4): 840–843.

11. Geçibesler I.H. *In vıtro* bıologıcal activity studies on *Tanacetum abrotanifolium* (L.) Druce (Asteraceae). Anadolu Univ. J. of Sci. and Technology A-Appl. Sci. and Eng. 2017; 18(2).
12. Gören N, Jakupovic J, Topal Ş. Sesquiterpene lactones with antibacterial activity from *Tanacetum argyrophyllum* var. *argyrophyllum*. Phytochemistry. 1990 Jan; 29(5):1467–1469.

13. Gören N, Bozok-Johansson C, Jakupovic J, Lee-Juian L, Hui-Ling S, Cordell GA, et al. Sesquiterpene lactones with antibacterial activity from *Tanacetum* densum subsp.*sivasicum*. Phytochemistry. 1992 Jan; 31(1):101–104.

14. Gören N, Woerdenbag H, Bozok-Johansson C. Cytotoxic and Antibacterial Activities of Sesquiterpene Lactones Isolated from *Tanacetum praeteritum* subsp. *praeteritum*. Planta Medica. 1996 Oct; 62(05):419–422.

15. Yunusov A, Kasymov S.Z, Sidyakin G. Lactones of *Tanacetum pseudoachillea*. Chemistry of natural compounds. 1973; 9(2):267–167.

16. Nano G, Appendino G, Bicchi C, Frattini C. Wild Piedmontese Plant. Part III. On a chemotype of *Tanacetum vulgare* L. containing sesquiterpene lactones with germacrene skeleton. 1980.

17. Mnatsakanyan V, Revazova L. Phytochemıcal analysis of plant tanacetum myriophyllum willd. 1. sesquiterpenic lactones-tamirin. Armyanskii Khimicheskii Zhurnal. 1973; 26(11):914–919.

18. Gören N, Arda N, Çaliskan Z. Chemical characterization and biological activities of the genus Tanacetum (Compositae). In: Studies in Natural Products Chemistry [Internet]. Elsevier; 2002

19. Gören N, Tahtasakal E. Sesquiterpenoids from *Tanacetum argenteum* subsp. *canum* var. *canum*. Phytochemistry. 1997; 45(1):107–109.

20. Yunusov A, Abduazimov B.K, Sidyakin G. Dentatin A from *Tanacetum vulgare*. Khim Prir. Soedin. 1980; 4:573.

21. Gören N, Tahtasakal E, Pezzuto J.M, Cordell G.A, Shwarzt B, Prokscht P. Sesquiterpene lactones from *Tanacetum argenteum*. Phytochemistry. 1994 May; 36(2):389–392.

22. Gören N, Tahtasakal E. Constituents of *Tanacetum densum* subsp. *eginense*. Phytochemistry. 1994 Aug;36(5):1281–1282.