

PHYTOCHEMICAL ANALYSIS OF SOME SIDERITIS SPECIES OF TURKEY

T. Kilic¹, Ya. K. Yildiz¹, A. C. Goren²,
G. Tumen³, and G. Topcu^{1,4}

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Linearol, foliol, epicandicandiol, siderol and ent-7 α ,18-dihydroxy-15 β ,16 β -epoxykaurane have been investigated for antibacterial activity test. Highest activity of epicandicandiol has been determined against E-coli.

Key words: Sideritis athoa, Sideritis trojana, Sideritis dichotoma, Sideritis Spilyea, Sideritis Argyrea, diterpenes, antibacterial activity.

Herbal parts of *Sideritis athoa*, *Sideritis trojana*, *Sideritis dichotoma*, *Sideritis Spilyea*, and *Sideritis Argyrea* which grow in the Balikesir region were investigated for their chemistry and biological activity. Dried aerial parts of the plants collected during flowering were successively extracted with hexane, acetone, and methanol. Diterpenes were isolated and characterized from the extracts using chromatographic-spectral techniques. As a result 41 diterpenoids were isolated from the five *Sideritis* species studied, corresponding to 27 single structures belonging to kaurene (**1–24**), beyerene (**25**), pimarene (**26**), and labdane (**27**) skeletons including the following five new kaurene diterpenes: *ent*-3 β ,7 α -dihydroxykaur-16-ene (**4**), *ent*-7 α ,17,18-trihydroxykaur-9,(11)-en-12-one (Athanolone) (**9**) from *Sideritis athoa*, *ent*-7 α -acetoxy-15 β ,16 β -epoxykaurane (**16**), 2 α -hydroxy-8(14),15-pimaradiene (**26**) from *Sideritis trojana*, and *ent*-6 β ,8 α -dihydroxylabda-13(16),14-diene (**27**) from *Sideritis Argyrea* (Table 1). Furthermore, linearol (**1**), foliol (**2**), 7-epicandicandiol (**6**), siderol (**10**), and *ent*-7 α ,18-dihydroxy-15 β ,16 β -epoxykaurane (**20**) compounds were used for antibacterial activity test [1–19].

Linearol (**1**), foliol (**2**), 7-epicandicandiol (**6**), siderol (**10**), and *ent*-7 α ,18-dihydroxy-15 β ,16 β -epoxykaurane (**20**) compounds were used for antibacterial activity test. First, as a qualitative criterion, inhibition zones were characterized by the disc diffusion method for diterpenic compounds, and for inhibition zones greater than 7 mm, “tube dilution tests” were performed quantitatively. *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Proteus mirabilis*, *Escherichia coli*, *Enterococcus faecalis*, and *candida albicans* were investigated, and MIC (minimum inhibitory concentration) values were found (Table 2). As a result, the highest activity from 7-epicandicandiol was observed against *E. coli*. In addition, the same compound was active against *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, and *E. faecalis*. *Ent*-7 α ,18-dihydroxy-15 β ,16 β -epoxykaurane (**20**) was moderately active against *B. subtilis*.

1) Balikesir University, Necatibey Education Faculty, Department of Chemistry, 10100 Balikesir; 2) TUBITAK, Marmara Research Center, MKTAE, PK.21, 41470 Gebze-Kocaeli; 3) Balikesir University, Science and Art Faculty, Department of Biology 10100 Balikesir; 4) Istanbul University, Faculty of Pharmacy, 34452 Beyazit-Istanbul. Published in Khimiya Prirodnykh Soedinenii, No. 5, pp. 373–374, September-October, 2003. Original article submitted July 8, 2003.

TABLE 1. Isolated Diterpenes

No.	Isolated Compound	<i>S. athoa</i>	<i>S. trojana</i>	<i>S. dichotoma</i>	<i>S. sipylea</i>	<i>S. Argyrea</i>
Kauren Diterpenes						
1. Linearol		+	-	-	+	+
2. Foliol		+	-	-	-	+
3. Sidol		+	-	-	-	+
4. Ent-3 β ,7 α -dihydroxykaur-16-ene		+	-	-	-	-
5. Ent-3 α ,18-dihydroxykaur-16-ene		+	-	-	-	-
6. 7-Epicandicadiol		+	+	-	+	+
7. 7-Epicandicadiol 18 monoacetate		-	-	-	-	+
8. Ent-3 β -hydroxykaur-16-ene		+	-	-		
9. Ent-7 α ,17,18-trihydroxykaur-9,(11)-en-12-one (Athonolone)		+	-	-	-	-
10. Siderol		-	+	+	+	+
11. Sideridiol		-	+	+	+	+
12. Candol B		-	-	-	-	+
13. Isocandol B		-	+	-	-	-
14. Candol A acetate		-	+	-	-	-
15. Ent-7 α -acetoxykaur-15-ene		-	+	-	-	-
16. Ent-7 α -acetoxy-15 β ,16 β -epoxykaurane		-	+	-	-	-
17. Ent-7 α -acetoxy-18-hydroxykaur-16-ene		-	-	-	-	+
18. Ent-7 β ,15 α ,18-trihydroxykaur-16-ene		-	-	+	-	-
19. Ent-7 β -acetoxy-15 α ,18-trihydroxykaur-16-ene		-	-	+	-	-
20. Ent-7 α ,18-dihydroxy-15 β ,16 β -epoxykaurane		-	-	+	-	-
21. Ent-7 α -acetoxy-18-hydroxy-15 β ,16 β -epoxykaurane		-	-	+	-	-
22. Isolinearol		-	-	-	+	-
23. Iisosidol		-	-	-	+	-
24. Epoxyisolinearol		-	-	-	+	-
Beyerene Diterpene						
25. Ent-7 α ,18-dihydroxybeyer-15-ene		+	-	+	-	-
Pimarane Diterpene						
26. 2 α -Hydroxy-8(14),15-pimaradiene		-	+	-	-	-
Labdane Diterpene						
27. Ent-6 β ,8 α ,dihydroxylabda-13(16),14-diene		-	-	-	-	+

TABLE 2. Antibacterial (MIC) Activity Test Results for Linearol (1), Foliol (2), Epicandicandiol (6), Siderol (10), and Ent-7 α ,18-dihydroxy-15 β ,16 β -epoxykaurane (20)*,**

	1	10	6	20	2
<i>B. subtilis</i>				> 625	> 625
ATCC 6633					
<i>S. aureus</i>			> 300		> 625
ATCC 6538					
<i>Ps. Aeruginosa</i>	> 625		> 300		
ATCC 9027					
<i>P. mirabilis</i>	> 625				> 625
ATCC 14153					
<i>E. coli</i>	> 625		> 300		
ATCC					
<i>K. pneumoniae</i>		> 600	> 300		
ATCC 4352					
<i>E. faecalis</i>	> 625		> 300		
ATCC 29212					
<i>C. albicans</i>					
ATCC 10231					

*Minimum inhibition concentrations for compounds have been given as a mg/mL.

**it is performed by prof. Dr. C. B. Johansson (Marmara University, Department of Microbiology).

EXPERIMENTAL

Plant Material: *Sideritis athoa*, *Sideritis trojana*, *Sideritis dichotoma*, *Sideritis Spilyea*, and *Sideritis Argyrea* were collected from the Kazdagı region in June 1995. The plants were identified by Prof. Dr. K. H. C. Baser (Eskisehir); a voucher specimen was deposited in the Herbarium of the Faculty of the Pharmacy, Anadolu University.

General: The spectra were recorded with the following instruments: IR: Perkin-Elmer 980 in CHCl₃; NMR: Bruker AC-200 L, 200 MHz and 50.32 MHz for ¹H and ¹³C-NMR, respectively, in CDCl₃; HRMS: VG ZabSPEC (maximum mass resolution 10.000). For isolation and purification of the compounds TLC: Kieselgel 60F₂₅₄ (E.Merc) precoated plates, CC: Silicagel 60 and Sephadex LH-20 (Fluka) were used.

REFERENCES

1. G. Topcu, A. C. Goren, Y. K. Yildiz, and G. Tumen, *Nat. Prod. Lett.*, **14**, 123 (1999).
2. G. Topcu, A. C. Goren, T. Kilic, Y. K. Yildiz, and G. Tumen, *Fitoterapia*, **67**, 1 (2001).
3. T. de Quesada, B. Rodriguez, S. Valverde, and S. Huneck, *Tetrahedron Lett.*, 2187 (1972).
4. E. Cabbera, A. Garcia-Granados, A. S. De Buruaga, and J. M. S. De Buruaga, *Phytochemistry*, **22**, No. 12, 2779 (1983).
5. B. M. Fraga, M. G. Hernandez, J. M. H. Santana, and J. M. Artega, *Phytochemistry*, **30**, No. 3, 913 (1991).
6. F. Piozzi, P. Venturella, A. Bellino, M. P. Paternostro, B. Rodriguez, and S. Valverde, *Chem. Ind.*, 962 (1971).
7. A. Garcia-Granados, M. Martinez, M. E. Onorato, and O. Socorro, *Phytochemistry*, **23**, 607 (1980).
8. P. Venturella, et al, *Experientia*, **33**, 1270 (1977).
9. M. A. Lopez Gomez, C. Marguez, R. M. Rabanal, and S. Valverde, *An Quim.*, **75**, 911 (1979).
10. C. A. Henrick and P. R. Jefferies, *Aust. J. Chem.*, **17**, 915 (1964).
11. F. Tetsuro, T. Sachiko, and F. Eiichi, *J. Chem. Soc., Perkin Trans, 1*, 910 (1979).

12. A. G. Gonzalez, B. M. Fraga, G. Hernandez, and J. G. Luis, *Phytochemistry*, **12**, 2721 (1973).
13. D. E. U. Ekong and A. U. Ogan, *J. Chem. Soc., Perkin Trans I*, 311 (1967).
14. P. Venturella, A. Bellino, and M. L. Marino, *Phytochemistry*, **22**, 2537 (1983).
15. Angela C. Pinto, Susan K. Do Prado, and Richard Pinchin; *Phytochemistry*, **20**, 520 (1981).
16. P. Venturella, A. Bellino, and M. L. Marino, *Phytochemistry*, **17**, 811 (1978).
17. P. Venturella, A. Bellino, and F. Piozzi, *Phytochemistry*, **14**, 1451 (1975).
18. E. Sezik, N. Ezer, J. Hueso-Rodriguez, and B. Rodriguez, *Phytochemistry*, **24**, 2739 (1985).
19. A. G. Gonzalez, J. G. Luis, and A. G. Ravelo, *Plants Iberoamericanas Fuentes de Moleculas Bioactivas*, **2**, Labiatae, Romero, Tenerife, Spain, (1990).