Phytochemistry, Vol. 25, No. 10, pp. 2343–2347, 1986.
Printed in Great Britain.

0031–9422/86 $3.00 + 0.00
Pergamon Journals Ltd.

THE CONSTITUTION OF ESSENTIAL OILS FROM *ARTEMISIA HERBA ALBA* POPULATIONS OF ISRAEL AND SINAI

I. FEUERSTEIN, D. MÜLLER*, K. HOBERT*, A. DANIN† and R. SEGAL‡

The Department of Natural Products, The Hebrew University, Jerusalem, Israel; *Lehrstuhl für Strukturchemie, Abteilung für Chemie, Ruhr-Universität, Bochum, West Germany; †Department of Botany, The Hebrew University, Jerusalem, Israel

(*Revised received* 7 *January* 1986)

Key Word Index—*Artemisia herba alba*; Compositae; essential oils; monoterpenes; chemotypes.

Abstract—The essential oils of *Artemisia herba alba* populations, four from Israel and one from Sinai, were analysed. Identification of components was achieved either by isolation of pure components or by GC and GC/MS. The composition of the oils differed in the various populations. All the oils contained 1,8-cineole in varying concentrations. Irregular monoterpenes were found in two populations, in one of them at high concentration. Two main types of oils were discerned, the cineole–thujane–bornane type and the pinane type. The differences in the composition of the essential oils in the *A. herba alba* populations investigated are in line with the variations of their sesquiterpene lactones.

INTRODUCTION

Artemisia herba alba Asso. is a common shrub in the Irano-Turanian phytogeographic region. In Israel it abounds over large areas in the Negev and the Judean deserts. The plant is widely used by the local population wherever it grows, mainly for the treatment of gastric disturbances such as diarrhoea, abdominal cramps and for healing external wounds [1, 2]. The vapours generated by heating the leaves and flowers in hot water relieve symptoms of colds and coughs.

A systematic survey of the sesquiterpene lactones of the plants growing in Israel [3–6] revealed the existence of five chemotypes which differ from those found in Sinai [7–10], Egypt and Spain [11]. Their essential oils exhibit pronounced antispasmodic and mild antibiotic activities [12–14]. Their wide application in folk medicine may at least partly be ascribed to these properties.

The essential oils of various *A. herba alba* populations have previously been analysed [15–18]. They differed in their reported aroma, physico-chemical properties and in the composition of their main constituents.

Of the Israeli plants, so far only the essential oil of the Sde Boker population has been partially analysed [19] and found to contain four irregular monoterpene alcohols in high concentrations. The aim of the present study was a comprehensive investigation of the composition of essential oils from four Israeli chemotypes and one from the Sinai desert.

RESULTS

The essential oils were prepared by steam distillation of air dried inflorescences, leaves and small stems of *A. herba alba* plants which were collected from four locations in Israel: Sde Boker, Mizpe Ramon (both in the central Negev), Maale Edumim (Judean Desert) and Elat (southern Negev). One sample was from Santa Katarina (Sinai Desert).

From the Elat oil, when stored at −20°, crystals precipitated while all the other oils preserved the liquid state under the same conditions. This precipitate was identified as xantoxyline (2-hydroxy-4,6-dimethoxy acetophenone) by comparison of its mp and spectroscopic properties with literature data [20, 21].

The major components of the oils could mostly be isolated and identified by spectroscopic methods and by comparison with pure authentic samples. The minor components were mostly identified by GC/MS methods and screening of the fragmentation patterns obtained by a computer search or by comparison with literature data [22–27]. Retention time data, when available, were used for confirmation.

The results so obtained are summarized in Table 1 which is arranged according to the structural types of components. All the oils tested contained 1,8-cineole in varying concentrations. It constitutes 50% of the oil from the Judean Desert and was found in considerable amounts in the oils of Sde Boker and Mizpe Ramon. Its concentration is however relatively small in the oils from Elat and Sinai. Monoterpenes possessing the thujane skeletons (mostly thujone and isothujone) and bornane skeleton are found especially in the Sde Boker, the Judean Desert and in the Mizpe Ramon plants. Their concentration is low in the oils from Sinai and especially from Elat. Of special interest is the great concentration of the irregular monoterpenes present mainly in Sde Boker and to a smaller extent in the second population from the central Negev, i.e. Mizpe Ramon. These compounds were absent in all other populations investigated. The pinane derivatives (especially those derived from chrysanthenol) are very abundant in the Elat and Sinai oils, whereas they appear in low concentration in the others. Xanthoxylin, which has not yet been found in *A. herba alba* oils, was present in high concentration in the Elat variety which also contained relatively large amounts of davanone.

Since the composition of the essential oils is subject to seasonal changes, some of the plants were collected at

‡Author to whom correspondence should be addressed.

Table 1. Composition (%) of the essential oils of *A. herba alba* collected from various localities (late spring)

Terpenoid	Site of collection: Sde Boker	Mizpe Ramon	Maale Edumim	Elat	Sinai	Mode of identification*	Reference
Monocyclic monoterpenes							
p-Cymene	1.5	2.0	2.1	0.3	1.2	a	
γ-Terpinene	trace	—	0.5	—	—	d	22, 24, 29
δ-Terpineol	trace	0.5	0.7	—	—	d	29
Terpinen-4-ol	1.5	5.0	3.5	0.5	0.5	b	22
α-Terpineol	0.4	0.9	0.5	—	0.5	b	22, 25, 26
p-Cymen-8-ol	—	—	—	trace	0.6	d	27, 29
Piperitol	0.7	0.4	—	—	0.2	d	28, 29
Terpenyl acetate	0.6	—	0.3	—	0.1	c	28
Thymol	—	0.2	—	trace	trace	a	
1,8-Cineole	13.0	38.0	50.0	4.8	7.4	a	
Total	17.7	47.0	57.6	5.6	10.5		
Monoterpenes with thujane skeleton							
α-Thujene	trace	0.1	0.4	—	—	d	28
Sabinene	0.4	0.3	0.4	—	—	c	28, 29
cis-Sabinene hydrate	—	1.9	1.6	—	—	b	28, 30
Thujone	4.2	1.4	27.0	—	—	c	28, 29
Isothujone	12.4	0.7	0.5	—	—	c	28, 29
Total	17.0	4.4	29.9	—	—		
Monoterpenes with bornane skeleton							
Camphene	0.5	3.4	0.8	0.4	—	a	
Camphenilone	—	1.0	—	—	—	d	29, 31
Camphor	9.0	25.0	3.0	0.1	0.7	a	
Borneol	11.0	3.0	2.4	—	—	a	
Bornyl acetate	0.3	0.4	0.2	—	0.3	c	23, 27, 29
Total	20.8	32.8	6.4	0.5	1.0		
Monoterpenes with pinane skeleton							
α-Pinene	—	0.4	trace	—	—	c	
β-Pinene	—	0.4	0.3	—	—	c	
Chrysanthenone	—	—	—	4.4	1.0	d	32
cis-Chrysanthenol	—	—	—	24.5	7.1	d	17
cis-Chrysanthenyl acetate	0.2	0.1	—	6.4	25.0	b	17, 32
trans-Pinocarveol	—	0.8	0.7	1.9	1.8	c	28, 29
Pinocarvone	0.3	0.4	—	0.6	trace	d	29
Myrtenal	—	0.4	0.3	trace	—	d	22, 28
Myrtenol	—	trace	0.3	—	0.3	d	22, 28
Myrtenyl acetate	1.5	0.4	—	trace	—	d	28
Total	2.0	2.9	1.6	37.8	35.2		
Irregular monoterpenes							
Artemisia triene	0.8	0.6	—	—	—	d	33
Artemisia alcohol	10.0	0.4	—	—	—	a	19, 33
Santolina alcohol	6.0	0.7	—	—	—	b	19, 34
Yomogi alcohol	8.8	0.3	—	—	—	b	19, 33, 35
Lyratol	5.7	3.4	—	—	—	b	36–38
Total	31.3	5.4	—	—	—		
Sesquiterpenes							
β-Cubebene	trace	2.2	0.3	2.8	—	d	28, 39
γ-Elemene	—	0.2	trace	1.2	—	c	
α-Copaene	—	—	—	0.6	—	c	

Table 1. (*Continued*)

Terpenoid	Site of collection: Sde Boker	Mizpe Ramon	Maale Edumim	Elat	Sinai	Mode of identification*	Reference
Davanone	—	—	—	2.0	0.6	c	
Unidentified sesquiterpenes	—	—	—	9.4	—		
	—	—	—	—	—	—	
Total	—	2.4	0.3	16	0.6		
Miscellaneous compounds							
cis-Jasmone	—	trace	—	1.1	4.0	b	28, 29, 40
Xanthoxylin	—	—	—	9.1	—	b	20, 21

*(a) Purified compound identified by comparison with authentic sample. (b) Purified compound identified by comparison of spectroscopic data with literature data. (c) Identified by comparison of GC/MS data with those of authentic sample. (d) Identified by comparison of GC/MS data with literature data.

Table 2. Seasonal variations of the major components in the essential oils from the Negev population*

Compound	Sde Boker			Mizpe Ramon		
	March	May	November	March	May	November
Camphene	0.2	0.5	1.0	2.9	3.4	3.5
p-Cymene	0.3	1.5	0.7	3.0	2.0	2.1
1,8-Cineole	6.6	13.0	4.0	23.5	38.0	35.0
Thujone	1.2	4.2	9.0	5.1	1.4	2.4
Isothujone	13.0	12.4	10.0	8.0	0.7	7.5
Camphor	9.0	9.0	10.5	21.0	25.4	21.2
Borneol	2.0	11.0	5.4	2.5	3.0	2.8
Terpinen-4-ol	0.9	1.5	2.1	4.1	5.0	2.4
cis-Chrysanthenyl acetate	0.3	0.2	—	0.3	0.1	0.1
β-Cubebene	0.6	trace	6.0	0.6	2.2	0.2
Artemisia alcohol	11.0	10.0	5.2	0.6	0.4	0.4
Santolina alcohol	12.8	6.0	5.0	n.d.†	0.7	0.3
Yomogi alcohol	9.6	8.8	5.0	0.5	0.3	0.3
Lyratol	5.0	5.7	8.2	7.5	3.4	4.8

*Expressed as percentage of oil.
†n.d., Not detectable.

different vegetation periods and the main constituents of their essential oils were determined. The results summarized in Tables 2 and 3 show that although quantitative differences exist, the general chemical profile of the oils remains unaltered.

DISCUSSION

Essential oils were obtained from all *A. herba alba* populations in relatively high yield. This explains the strong aromatic odour perceived in those arid zones inhabited by *A. herba alba*.

The Sde Boker, Mizpe Ramon and Judean Desert populations grow in great abundance and are easily accessible. The great quantities of plant material which could be collected and the large amounts of essential oils obtained made possible an almost complete elucidation of the composition of these three oils (more than 90%). The plants from the Elat region yielded in the GC a great number of peaks in the region characteristic for sesquiterpenes [26]. Only a few of these have been described in the literature. Since the plants grow sparsely in this region, these components could not be isolated in sufficient yield to be subjected to vigorous spectroscopic and chemical analysis and thus they remained unidentified.

Table 3. Seasonal variations in major components in the essential oil from Elat Region

Compound	May (%)*	August (%)
trans-Pinocarveol	1.9	0.9
cis-Chrysanthenol	24.5	6.5
cis-Chrysanthenyl acetate	6.4	31.0
β-Cubebene	2.8	7.1
Xanthoxylin	9.0	3.0

*Expressed as percentage of oil. The variations in the concentrations of the following components did not exceed 100%; terpinen-4-ol: *cis*-jasmone; *α*-copaene; *γ*-elemene; davanone.

Several investigations [41] on the essential oils of various *Artemisia* species showed that 1,8-cineole and derivatives of the thujane and bornane skeletons charac-

terize most species of these plants. This pattern fits our findings mainly for three populations (Sde Boker, Mizpe Ramon and Judean Desert). The Elat and Sinai populations are characterized by their high content of pinane derivatives which are only sparsely represented in the Negev and Judean Desert types (Table 1).

The distribution of the irregular monoterpenes is very limited in the plant kingdom and is restricted to the Anthemidea tribe of the Compositae [38]. They were found exclusively in two populations of *A. herba alba*, namely Sde Boker and Mizpe Ramon. They may thus serve as taxonomic markers for the *A. herba alba* plants from the Negev.

Since no significant qualitative differences were observed in the constitution of the essential oils collected at different seasons of the year, the composition of the essential oils may serve chemotaxonomic purposes for differentiating the *A. herba alba* populations growing in the Near East. We may distinguish between two major types: (a) the cineole–thujane–bornane type to which the Sde Boker, Mizpe Ramon and Judean Desert populations belong, and (b) the pinane type to which the Elat and Sinai populations are related. Type (a) can be further subdivided according to the presence and absence of irregular monoterpenes (Sde Boker and Mizpe Ramon versus Maale Edumim).

The differences in the composition of the essential oils in the populations investigated by us are in line with the variations in their sesquiterpene lactone constitution [3–9]. The greatest resemblance was found in the sesquiterpene lactones of the Sde Boker and Mizpe Ramon chemotypes. These could be related to the lactones isolated from the Judean Desert types. The plants from Elat were devoid of sesquiterpene lactones, while those from Sinai possessed a completely different hydroxylation pattern.

The chemical variations in the different populations growing in the Near East may be due to environmental conditions.

EXPERIMENTAL

Materials. Artemisia herba alba Asso. was collected at Maale Edumim (Judean Desert) March 1980 (0.68), May 1982 (0.73), June 1983 (1.7), November 1982 (0.93); Mizpe Ramon (Negev) March 1980 (0.4), May 1983 (0.9), November 1981 (1.2); Elat March 1981 (0.37), May 1983 (0.34), August 1980 (0.08); Sinai Desert (near Santa Katarina) August 1980 (0.18—figures given in parentheses refer to yield of essential oil as percentage of air dried weight). Voucher samples are deposited at the Herbarium of the Hebrew University. The essential oils were steam distilled and stored under N_2 at $-20°$. 1,8-Cineole, thujone, borneol, *p*-cymene and camphor were obtained from Fluka A. G., Switzerland, camphene, α-pinene, β-pinene, terpenyl acetate and *cis*-jasmone from Carl Roth, GmbH, Germany, linalool from Dragoco, Germany, and pinocarveol from Haarmann Riemer, Germany. Davanone was obtained from Dr. L. H. Zalkow, Georgia Institute of Technology, Atlanta, GA.

General experimental procedures. NMR: $CDCl_3$ with TMS as internal standard using Brucker WP 60, WH 80 or AM-400 spectrometers.

Mass spectra were taken with a Finnigan MAT CH-5 direct inlet mass spectrometer with data system SS 100. Ionization potential 70 eV; temp. of ion source 250°.

Analytical GC. (a) A Perkin–Elmer F-2 FE gas chromatograph, equipped with FID and a 50 m OV-101, 0.28 mm i.d. glass capillary column was used. Carrier gas was He at 2 ml/min. Injector and detector temps 200° and 250° respectively. Injector split oven temp. 60–200°, programmed to 5°/min. R_ts were referred to the homologous series of C_8–C_{17} *n*-alkanes as standards. Peak areas were determined with the aid of a Hewlett–Packard 3380-A integrator. (b) Pye Unicam GCV instrument with FID detector system was used. A 2.2 m glass column, i.d. 4 mm, packed with 5% OV 17 on chromosorp WAP (100–120 mesh) was used. Working conditions: injector and detector temps 200° and 250° respectively. Oven temp. 60° for initial 2 min, then programmed 5°/min to 200° final temp. Carrier gas, 35 ml N_2/min. Solns of 2 μl of 2% oil in CH_2Cl_2 were injected.

Prep. GC was performed on a Pye Unicam GCV instrument using a 2.5 m glass column, i.d. 8 mm, packed with 3% OV-17 on chromosorb WHP (60–80 mesh). Working conditions: injector and detector temps 190° and 240° respectively. Oven temp. was programmed from 70 to 160°, 5°/min; carrier gas 30 ml N_2/min. A splitter (1:50) was installed at the end of the column. Pure compounds were collected in ice cooled U-tubes on the basis of the analytical results.

GC/MS. Measurements were performed on the above GC instrument interfaced with a Varian-MAT CH-7 mass spectrometer. For data reduction a Varian MAT SS 200 data system was used. A 50 m OV-101 glass capillary column was used. The operating conditions were: injector, interface and ion source 220°, 300° and 250° respectively. Carrier gas, He 1 ml/min. Temp. programming 80–200° at 5°/min; accelerating voltage 3 kV; trap current 150 μA; scan 1 sec/decade. Pure compounds were obtained by CC on silica gel 60 eluted with petrol (30–40°)–Et_2O gradient, or by prep. GC.

Acknowledgements—I.F. and R.S. thank the DAAD and the Alexander-von-Humboldt Stifftung respectively for fellowships supporting this research. We are grateful to Dr. D. Henneberg and Dr. R. Rienaeker of the Max Planck Institut für Kohlenforschung, Muelheim for putting their MS computer services at our disposal and to Prof. G. Snatzke for his valuable discussions and continuous encouragement.

REFERENCES

1. Taeckholm, V. (1939) *Hort. Rev. Egypt. Hort. Soc.* **27**, 22.
2. Bailey, C. and Danin, A. (1981) *Econ. Botany* **35**, 145.
3. Segal, R., Sokoloff, S., Haran, B., Zaitschek, D. V. and Lichtenberg, D. (1977) *Phytochemistry* **16**, 1237.
4. Segal, R., Feuerstein, I., Duddeck, H., Kaiser, M. and Danin, A. (1983) *Phytochemistry* **22**, 129.
5. Segal, R., Eden, L., Danin, A., Kaiser, M. and Duddeck, H. (1984) *Phytochemistry* **23**, 2954.
6. Segal, R., Eden, L., Danin, A., Kaiser, M. and Duddeck, H. (1985) *Phytochemistry* **24**, 1381.
7. Zalkow, L. H. and Gordon, M. M. (1979) *J. Nat. Prod.* **42**, 681.
8. Zalkow, L. H., Gordon, M. M., Dickinson, C. and Gelbaum, L. T. (1980) *Planta Med.* **39**, 265.
9. Gordon, M. M., van Derveer, D. and Zalkow, L. M. (1981) *J. Nat. Prod.* **44**, 432.
10. Khafagy, S. M., Gharbo, S. A. and Sarg, T. M. (1971) *Planta Med.* **20**, 90.
11. Gomis, J. D., Marco, J. A., Pedro Llinares, J. R., Parareda, J. S., Sendra, J. M. and Seoane, E. (1979) *Phytochemistry* **18**, 1523.
12. Ross, S. A., Keltawi, N. E. and Megalla, S. E. (1980) *Fitoterapia* **51**, 201.
13. Yashphe, J., Segal, R., Breuer, A. and Erdreich-Naftali, G.

(1979) *J. Pharm. Sci.* **68**, 924.
14. Yashphe, J., Feuerstein, I. and Segal, R., *Int. J. Crude Drug Res.* (in press).
15. Gildmeister, E. and Hoffmann, H. (1961) *Die Ätherischen Öle* (Treibs, W. and Bourmol, K. eds) Vol. VII, 4th edn. Akademie Verlag, Berlin.
16. Bengilali, B. and Richard, M. (1980) *Rev. Ital. E.P.P.O.S.* **62**, 69.
17. Bengilali, B., Sarris, J. and Richard, H. (1982) *Sci. Aliments* **2**, 515.
18. Lemberg, S. (1982) *Perfumer and Flavorist* 7, 58.
19. Segal, R., Breuer, A. and Feuerstein, I. (1980) *Phytochemistry* **19**, 2761.
20. Karrer, W. (1958) *Konstitution und Vorkommen der Organischen Pflanzenstoffe.* Birkhauser, Basel.
21. Hussein Ayoub, S. M. and Elassam, O. E. (1981) *Fitoterapia* **6**, 247.
22. Swigar, A. A. and Silverstein, R. (1981) *Monoterpenes: Infrared, Mass, ^1H NMR and ^{13}C NMR Spectra and Kovats Indices.* Aldrich Chemical Company, Milwaukee, WI.
23. Masada, Y. (1976) *Analysis of Essential Oils by Gas-chromatography and Mass Spectrometry.* John Wiley, New York.
24. Stenhagen, E., Abrahamsson, S. and McLafferty, F. W. (1974) *Registry of Mass Spectral Data.* John Wiley, New York.
25. von Sydow, E., Anjou, K. and Gunilla, K. (1970) *Archives of Mass Spectral Data* (Stenhagen, E., Abrahamsson, S. and McLafferty, F. W., eds) Vol. 1, pp. 387–578. Interscience, New York.
26. Jennings, W. and Shibamoto, T. (1980) *Qualitative Analysis of Flavour and Fragrance Volatiles by Glass Capillary Gas Chromatography.* Academic Press, New York.
27. Mass Spectra Collection of the Max Planck Institute, Muelheim, West Germany.
28. Mass Spectra Computer Service of the Max Planck Institute, Muelheim, West Germany.
29. Haarmann and Reimer Computer Services, Holzminden, West Germany.
30. Fanta, W. I. and Erman, W. F. (1968) *J. Org. Chem.* **33**, 1656.
31. von Sydow, E. (1984) *Acta Chem. Scand.* **18**, 1009.
32. Uchio, Y. (1978) *Bull. Chem. Soc. Jap.* **51**, 2342.
33. Epstein, W. W., McGee, L. R., Poulter, C. D. and Marsh, L. L. (1976) *J. Chem. Engng. Data* **21**, 500.
34. Chretien-Bessiere, Y. (1968) *Bull. Soc. Chim. Fr.* 2018.
35. Hayashi, S., Yano, K. and Matsura, T. (1968) *Tetrahedron Letters* 6241.
36. Devgan, O. N., Bokadia, N. M., Bose, A. K., Tibetts, M. S., Trivedi, J. K. and Chakravarti, K. K. (1967) *Tetrahedron Letters* 5337.
37. Devgan, O. N., Bokadia, M. M., Bose, A. K., Trivedi, G. K. and Chakravarti, K. K. (1969) *Tetrahedron* **25**, 3217.
38. Epstein, W. W. and Poulter, C. D. (1973) *Phytochemistry* **12**, 737.
39. NIH-EPA MSSS Data System according to Biemen technique.
40. Bakuzis, P. and Bakuzis, M. L. F. (1977) *J. Org. Chem.* **42**, 2362.
41. Stangl, R. and Greger, H. (1980) *Plant Syst. Evol.* **136**, 125.