Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

Behavior of (-)-α-Bisabolol and (-)-α-Bisabololoxides A and B in Camomile Flower Extraction with Supercritical Carbon Dioxide

Branislav Pekić[a]; Zoran Zeković[a]; Lidija Petrović[a]; Aleksandar Tolić[a]
[a] DEPARTMENT OF PHARMACEUTICAL ENGINEERING FACULTY OF TECHNOLOGY, UNIVERSITY OF NOVI SAD, NOVI SAD, YUGOSLAVIA

To cite this Article Pekić, Branislav , Zeković, Zoran , Petrović, Lidija and Tolić, Aleksandar(1995) 'Behavior of (-)-α-Bisabolol and (-)-α-Bisabololoxides A and B in Camomile Flower Extraction with Supercritical Carbon Dioxide', Separation Science and Technology, 30: 18, 3567 — 3576
To link to this Article: DOI: 10.1080/01496399508015137
URL: http://dx.doi.org/10.1080/01496399508015137

SEPARATION SCIENCE AND TECHNOLOGY, **30**(18), pp. 3567–3576, 1995

Behavior of (−)-α-Bisabolol and (−)-α-Bisabololoxides A and B in Camomile Flower Extraction with Supercritical Carbon Dioxide

BRANISLAV PEKIĆ,* ZORAN ZEKOVIĆ, LIDIJA PETROVIĆ, and ALEKSANDAR TOLIĆ
DEPARTMENT OF PHARMACEUTICAL ENGINEERING
FACULTY OF TECHNOLOGY
UNIVERSITY OF NOVI SAD
BOULEVARD CARA LAZARA 1, 21000 NOVI SAD, YUGOSLAVIA

ABSTRACT

A systematic study of the extraction behavior of selected components of camomile flowers in extraction with supercritical carbon dioxide was carried out. (−)-α-Bisabolol and its A and B oxides, which have a wide importance in pharmacology and standardization of camomile flower products, were selected. The dependence of the yield of selected components on the pressure and/or temperature of supercritical extraction was investigated. The results obtained were correlated.

INTRODUCTION

Camomile essential oil has a complex composition since it contains many different components. From the pharmacological point of view, chamazulene, (−)-α-bisabolol, (−)-α-bisabololoxides A and B, and en-in-dicycloethers (Fig. 1) are especially important. The antiphlogistic (anti-inflammation) activity of camomile essential oil was ascribed to chamazulene for a long time. However, a very distinct antiphlogistic effect of monocyclic sesquiterpene alcohol (−)-α-bisabolol has been proved. The antiphlogistic effect of its oxides, (−)-α-bisabololoxides A and B, is twice

* To whom correspondence should be addressed.

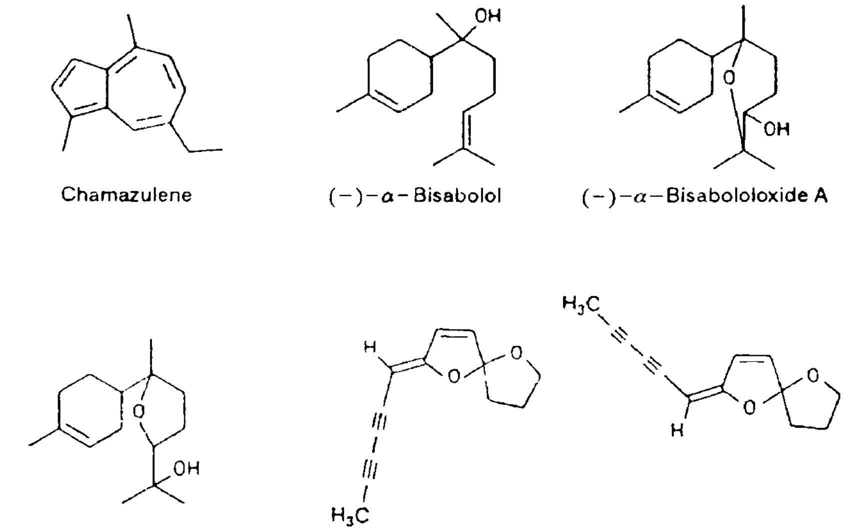

FIG. 1 Structural formulas of important camomile oil components.

as weak. En-in-dicycloethers also contribute to the antiphlogistic activity of camomile essential oil (1–3).

The camomile essential oil obtained by steam distillation is colored intensive blue, the consequence of the presence of chamazulene, which originates from proazulenes (matricine and matricarin) at increased temperatures in the presence of organic acids contained in the camomile flowers (4). The extracts obtained by camomile extraction with supercritical carbon dioxide, as well as essential oils obtained from CO_2 extracts by steam distillation, are yellow, since chamazulene is not contained in them. However, their antiphlogistic effect depends, in the first place, on the presence of (−)-α-bisabolol and its oxides.

Some camomile essential oils contain up to 50% (−)-α-bisabolol. Because of the therapeutic importance of this sesquiterpene alcohol, chemotypes of camomile with minimal contents of proazulenes and high contents of (−)-α-bisabolol were obtained by selection. Determination of the content of (−)-α-bisabolol and its A and B oxides, as well as of en-in-dicycloethers, is important for the standardization of camomile products (3).

Previous investigations of camomile flower extraction with supercritical carbon dioxide, including ours (5–7), have referred to the integral observance of extraction and did not include the extraction behavior of each individual camomile flower component.

On the basis of all these facts, the behaviors of selected components, (−)-α-bisabolol and (−)-α-bisabololoxides A and B, in camomile flower extraction with supercritical carbon dioxide were investigated for this paper. The dependence of the yield of selected components on selected values of pressure and temperature were investigated, and the results obtained were correlated. Our intention to investigate the extraction behavior of *cis*- and *trans*-en-in-dicycloethers was not possible to realize, primarily due to the unsatisfactory reliability of the determinations.

EXPERIMENTAL

All investigations were carried out on camomile flowers (*Chamomillae flos*) obtained from the Institute for Hop, Broomcorn and Medicinal Plants, Bački Petrovac, Yugoslavia (1992). There was 0.4352 g essential oil per 100 g of the material. Essential oil contents were determined by the procedure described in Ref. 8.

Commercial carbon dioxide was used as the extracting agent.

The extraction was carried out on a laboratory-scale High Pressure Extraction Plant—HPEP (NOVA-Swiss, Switzerland) (Fig. 2).

The samples for extraction (50 g) were previously milled (ratio of the fraction between the sieves with 0.5 and 0.315 mm was 96.2%, whereas the remainer was 3.8%). The samples were extracted for 2 hours at a carbon dioxide flow rate of 53.5 dm^3/h (expressed at normal conditions), and at different combinations of pressure and temperature. Deviation of the flow rate during the investigations, as well as of the pressure and temperature, did not exceed ±3 and ±2%.

To determine the total extraction yield, the extract obtained in the separator was quantitatively dissolved in petroleum ether (bp 40–60°C) and the solvent was removed by the procedure for the determination of camomile essential oil given in Ref. 8. The same procedure, i.e., steam distillation, was employed to determine the essential oil content in the extracts.

For determination of important camomile components (bisabolol and bisabololoxides A and B) and other active components (chamazulene and *cis*- and *trans*-en-in-dicycloethers) in the camomile essential oils, a gas chromatograph (Hewlett-Packard 5890 A) with a split/splitless injector and a mass detector (Hewlett-Packard 5971 A) were used. For treatment of the results obtained, MS Chem Station and HP 9000 serial 300 were used. For identification of components, the Wiley database and our own database were used (9, 10).

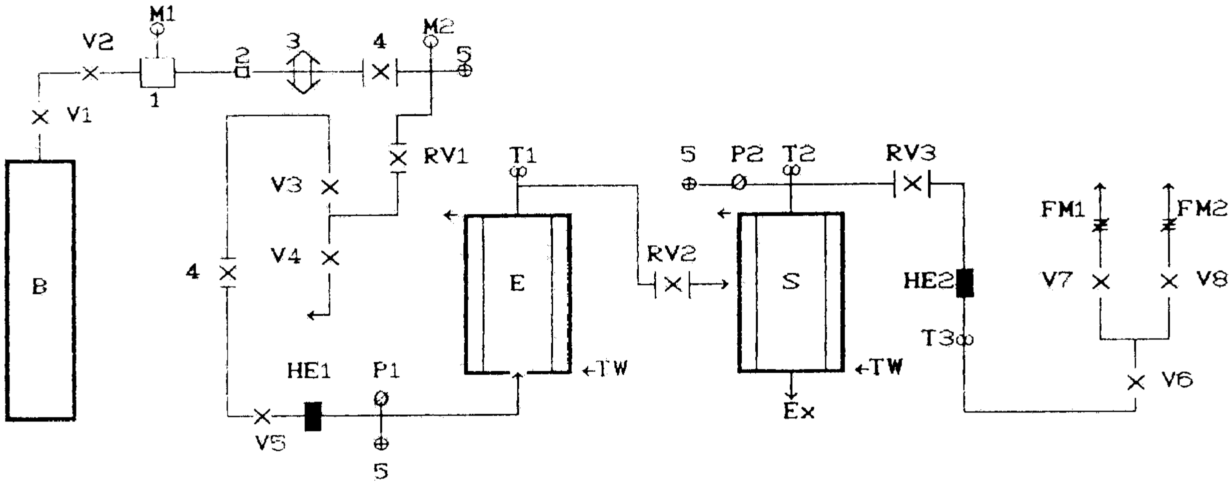

FIG. 2 Flow sheet of the high pressure extraction plant (HPEP): (1) measuring connector; (2) filter; (3) diaphragm compressor; (4) control valve; (5) safety valve; RV, regulation valve; V, valve; HE, heat exchanger; B, carbon dioxide bottle; P, pressure gauge; T, thermometer; TW, thermostatted water; M, manometer; E, extractor ($V = 200$ cm^3); S, separator ($V = 200$ cm^3); FM, flow meter; Ex, extract.

RESULTS AND DISCUSSION

The selection of pressure and temperature ranges in the extraction of camomile flowers with supercritical carbon dioxide is based on the fact that an outstanding change in the density and dielectric constant of carbon dioxide occurs between 70 and 160 bar and, in order to prevent thermal decomposition of some camomile flower components, the temperature should not exceed 353 K (11). For these reasons the extraction process was studied in the range of 80–160 bar and 313–353 K.

After the formulation of a two-factor plan, the experiments on camomile, which were the subject of a previous investigation (7), were carried out, and the composition of essential oils separated from the extracts obtained was determined. These results are presented in Table 1.

On the basis of the data presented in Table 1, the essential oils separated from CO_2 extracts do not contain chamazulene, which is in accordance with the fact that it is not a native substance contained in camomile flowers. However, the essential oil obtained by steam distillation contains chamazulene. The contents of (−)-α-bisabolol and (−)-α-bisabololoxides A and B in essential oils separated from the CO_2 extracts obtained at 80 bar are higher than those obtained at higher pressures (120 and 160 bar)

TABLE 1
Experimental Conditions and Results of Camomile Extraction

No.	p (bar)	T (K)	Content of component in essential oil obtained from CO_2 extract in percent and its yield in mg/100 g camomile[a]		
			Bisabolol	Bisabololoxides A and B	Chamazulene
1	120	333	11.96 (62.16)	5.70 (29.62)	0 (0)
2	160	333	12.32 (124.31)	5.90 (59.53)	0 (0)
3	80	333	18.69 (24.20)	9.47 (12.26)	0 (0)
4	120	353	11.12 (60.86)	5.63 (30.81)	0 (0)
5	160	353	10.99 (73.85)	5.30 (35.62)	0 (0)
6	80	353	18.36 (11.34)	8.95 (5.53)	0 (0)
7	120	313	11.35 (95.41)	5.50 (46.23)	0 (0)
8	160	313	14.24 (140.83)	6.62 (65.47)	0 (0)
9	80	313	17.81 (20.41)	10.49 (12.02)	0 (0)
Content of Component in Camomile Essential Oil Obtained by Steam Distillation					
			18.78 (81.73)	10.13 (44.09)	6.55 (28.51)

[a] Value in parentheses.

and similar to the contents in essential oil obtained by steam distillation of camomile flowers.

By observing the absolute yield values of the components of camomile essential oil obtained by extraction with supercritical carbon dioxide (Table 1, values in parentheses), it could be concluded that the extraction yield is considerably higher than the yield obtained by steam distillation. For example, the yield of (−)-α-bisabolol, i.e., (−)-α-bisabololoxides A and B, achieved by CO_2 extraction at 313 K and 160 bar is 1.72, i.e., 1.48 times higher than the yield achieved by steam distillation. These results confirmed our previous conclusion (6, 7) that the yield of essential oil, i.e., essential oil components, obtained by extraction of camomile flowers with supercritical carbon dioxide is considerably higher than the yield obtained by steam distillation.

The experimental data were obtained in accordance with the two-factor plan (Table 1). On the basis of these data, a regression equation was derived describing the dependence of the extraction yield of a selected component (y) on the pressure (p) and temperature (T).

1. For (−)-α-bisabolol:

$$y = -1692 + 8.416p + 8.081T - 0.01812pT - 0.005p^2 - 0.01025T^2$$
$$\sigma = \pm 6.64 \quad (1)$$

2. For (−)-α-bisabololoxides A and B:

$$y = -684.9 + 3.604p + 3.270T - 0.00725pT - 0.00269p^2 - 0.00425T^2$$
$$\sigma = \pm 3.59 \quad (2)$$

where y is expressed in milligrams of the selected component per 100 g camomile flowers (mg/100 g), p is in bar, T is in K, and the standard deviation (σ) is in mg/100 g.

By introducing the values from Table 1 for a constant pressure and temperature into Eqs. (1) and (2) for selected components, the systems of equations for the investigated components were obtained. The equations for the extraction at constant pressure (Eqs. A, B, and C, i.e., a, b, and c) and at constant temperature (Eqs. D, E, and F, i.e., d, e, and f) are presented in Table 2.

The corresponding graphical presentations, together with the experimental points, are given in Figures 3, 4, 5 and 6.

Judging from the fit of curves obtained (Figs. 3–6) and the standard deviation values obtained (Table 2), the validity of integral Eqs. (1) and (2) of selected components describing quantitatively the extraction process for the case of boundary states (p, i.e., T constant) is confirmed.

TABLE 2
Expressions Obtained from Eqs. (1) and (2) by Introducing the Condition of Constant Pressure or Constant Temperature

Constant parameter	Analytical expression	Equation identification	Standard deviation ($\pm\ \sigma$)
	(−)-α-*Bisabolol, Eq. (1)*		
p = 80 bar	$y = -1051 + 6.63T - 0.0102T^2$	A	2.14
p = 120 bar	$y = -754.1 + 5.91T - 0.0102T^2$	B	9.53
p = 160 bar	$y = -473.4 + 5.18T - 0.0102T^2$	C	6.09
T = 313 K	$y = -166.6 + 2.74p - 0.005p^2$	D	3.44
T = 333 K	$y = -137.4 + 2.38p - 0.005p^2$	E	9.77
T = 353 K	$y = -116.5 + 2.02p - 0.005p^2$	F	5.99
	(−)-α-*Bisabololoxides A and B, Eq. (2)*		
p = 80 bar	$y = -413.8 + 2.69T - 0.00425T^2$	a	0.99
p = 120 bar	$y = -291.2 + 2.40T - 0.00425T^2$	b	5.05
p = 160 bar	$y = -177.1 + 2.11T - 0.00425T^2$	c	6.06
T = 313 K	$y = -77.7 + 1.33p - 0.00269p^2$	d	1.58
T = 333 K	$y = -67.2 + 1.19p - 0.00269p^2$	e	5.22
T = 353 K	$y = -80.1 + 1.04p - 0.00269p^2$	f	2.92

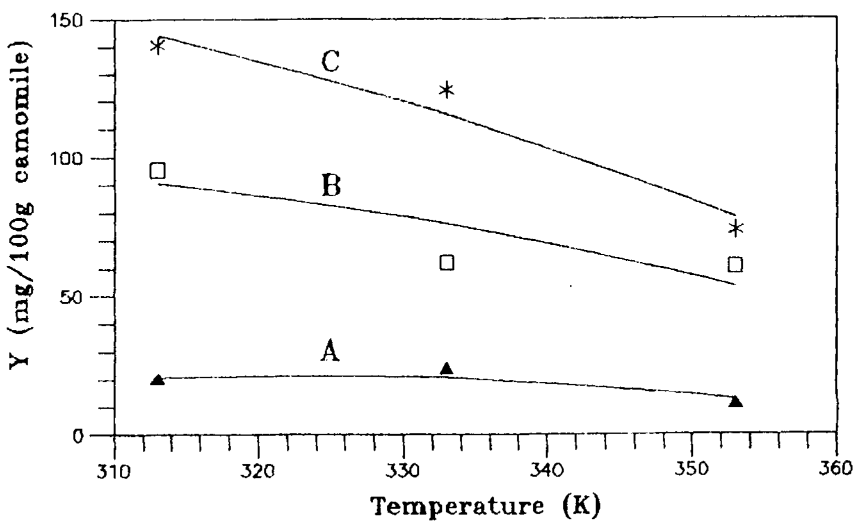

FIG. 3 Graphical presentation of Equations A, B, and C and the corresponding experimental values.

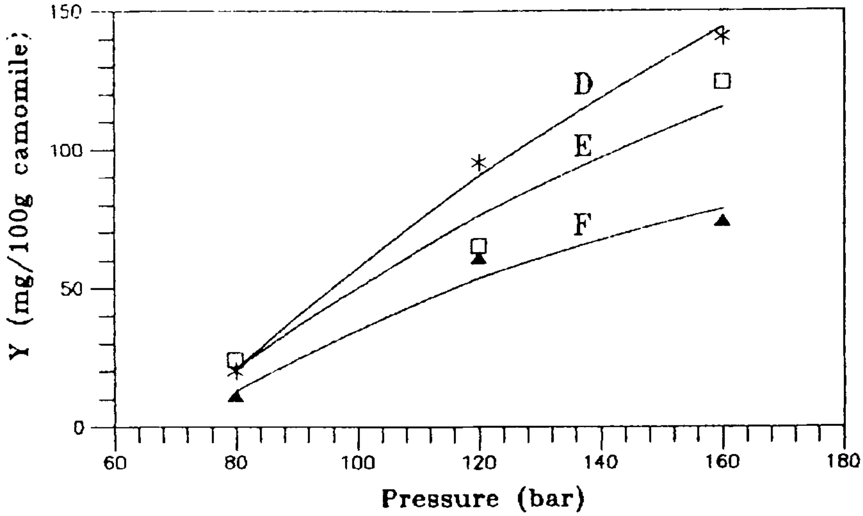

FIG. 4 Graphical presentation of Equations D, E, and F and the corresponding experimental values.

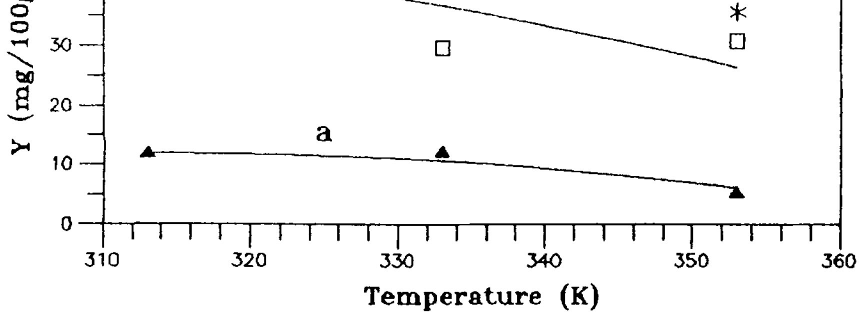

FIG. 5 Graphical presentation of Equations a, b, and c and the corresponding experimental values.

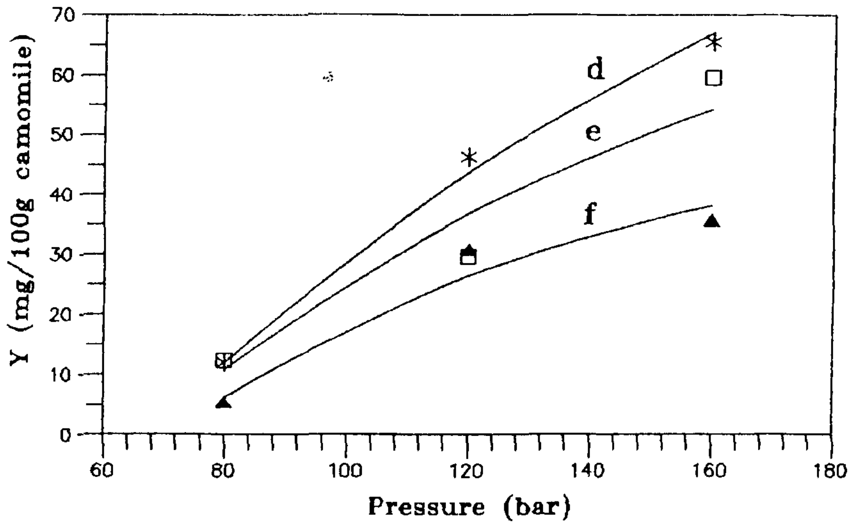

FIG. 6 Graphical presentation of Equations d, e, and f and the corresponding experimental values.

The integral equations of selected components derived in this way (Eqs. 1 and 2) represent a potential means of defining the dependence of selected component yield on the pressure and temperature in camomile extraction with supercritical carbon dioxide—within the whole range of investigated values of the pressure and temperature.

REFERENCES

1. V. Jakovlev, O. Isaac, K. Thiemer, and R. Kunde, "Pharmacological Investigations with Compounds of Chamomile. II. New Investigations on the Antiphlogistic Effects of (−)-α-Bisabolol and Bisabolol Oxides," *Planta Med.*, *35*, 125 (1979).
2. V. Jakovlev, O. Isaac, and E. Flaskamp, "Pharmacological Investigations with Compounds of Chamomile. VI. Investigations of the Antiphlogistic Effects of Chamazulene and Matricine," *Ibid.*, *49*, 67 (1983).
3. O. Isaac, "Pharmacological Investigations with Compounds of Chamomile. I. On the Pharmacology of (−)-α-Bisabolol and Bisabolol Oxides (Review)," *Ibid.*, *35*, 118 (1979).
4. B. Pekić, in *Chemistry and Technology of Pharmaceutical Products—Alkaloids and Essential Oils*, Faculty of Technology, University of Novi Sad, Yugoslavia, Novi Sad, 1983, p. 217 (in Serbian).
5. E. Stahl and E. Schütz, "Extraktion der Kamillenblüten mit Überkritischen Gasen," *Arch. Pharm. (Weinheim)*, *311*, 922 (1978).
6. B. Pekić, Z. Zeković, and A. Tolić, "Investigation of the Extraction Kinetics of Camomile Flowers by Supercritical Carbon Dioxide," *J. Serb. Chem. Soc.*, *59*(4), 249 (1994).

7. B. Pekić, Z. Zeković, and A. Tolić, "Study of the Extraction of Camomile Flowers with Supercritical Carbon Dioxide," *Ibid.*, To Be Published.
8. *Pharmacopoea Jugoslavica, Editio Quarta* (Ph. Jug. IV), Federal Institute of Public-Health, Belgrade, 1984, pp. 126–128 (in Serbian).
9. N. Marjanović, B. Pekić, L. Petrović, Ž. Lepojević, and Z. Zeković, "Determination of Different Components of Chamomile Essential Oil (*Aetheroleum chamomillae*) using GC + MS," *Proc. Fac. Technol. (Novi Sad)*, *23*, 189 (1992) (in Serbian).
10. Z. Zeković, B. Pekić, Ž. Lepojević, and L. Petrović, "Chromatography in Our Investigations of Camomile (*Matricaria chamomilla* L.)," *Chromatographia 39*(9/10), 587 (1994).
11. B. Pekić, "Extraction of Medicinal Plants Using Underpressure Gases," in *10th Congress of Pharmacists of Yugoslavia, Proceedings I*, Novi Sad, 1988, pp. 151–166 (in Serbian).

Received by editor March 29, 1995