J. Soc. Cosmet. Chem., 43, 49–54 (January/February 1992)

Percutaneous absorption of lavender oil from a massage oil

W. JÄGER, G. BUCHBAUER, L. JIROVETZ, and
M. FRITZER, *Institute of Pharmaceutical Chemistry (W.J., G.B., L.J.) and Institute of Medical Chemistry (M.F.), University of Vienna, Währinger Straße 10, A-1090 Vienna, Austria.*

Received July 12, 1991. Presented in part at the Forum Cosmeticum Viennensis, Vienna, Austria, November 16, 1991.

Synopsis

In the present study, the percutaneous absorption of the essential oil of lavender from a massage oil was investigated. It was shown that lavender oil penetrates the skin of a male subject. Within five minutes of finishing, the massage traces of linalool (1) and linalyl acetate (2) as the main constituents of lavender oil could be detected in the blood. After 20 minutes, 100 ng/ml for 2 and 121 ng/ml for 1 showed up as the maximum concentration. Within 90 minutes, most of the lavender oil was eliminated. The sedative and relaxing effect of lavender oil after a massage may be based on two different ways of incorporation: the inhalation of fragrant molecules and the penetration through the skin.

INTRODUCTION

The essential oil of lavender, a pale-yellow liquid with a characteristic slightly camphoraceous odor, is obtained from *Lavendula angustifolia* Mill. (syn. *L. officinalis* Chaix, *L. vera* D.C.) (1). The medical effects of lavender oil have been discussed for a long time (2–7). Due to its sedative and spasmolytic effects, this essential oil is used as a mild sedativum in the case of psychosomatic disorders, insomnia, and nervousness (8). Owing to these effects, it is increasingly used by aromatherapists and cosmetic chemists, and in folk medicine. In combination with other essential oils, it is applied as a massage treatment (9) and used for baths and inhalation in the case of nervous tension, migraine, rheumatism, and several skin disorders such eczema and dermatitis. It is also used as a very important oil in the fragrance industries (10). In spite of its widespread use, little research about the absorption via lung or skin has been described. In previous animal experiments we showed that lavender oil can lead to sedation after inhalation (11). The blood samples after one hour inhalation were investigated by gas chromatographic-spectroscopic analyses in order to identify 1 and 2 as main components of the essential oil (12–13). To confirm the results of the GC-FID measurements, analyses were carried out by GC-MS total ion current (TIC), with retention time and mass spectra comparison and single-ion monitoring (SIM) over ion profiles of the main fragments at m/z 71 amu,

93 amu, and 121 amu by electron impact (EI). Therefore, our aim was to study a possible absorption of the essential oil of lavender from a massage oil during a massage and to analyze the volatile components quantitatively in defined intervals.

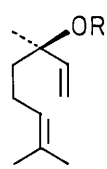
MATERIALS AND METHODS

MATERIALS

Lavender oil (24.79% 1, 29.59% 2), linalool, linalyl acetate, tiglinic acid benzyl ester (ST), and peanut oil are products of Dragoco Comp. (Austria). Heparine (5000 I.U./ml) was obtained from Immuno Austria and methanol p.a. from Merck (BRD). Massage oil: lavender oil/peanut oil (2:98, W/W).

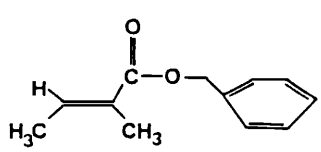
EXPERIMENTAL CONDITIONS

One and one-half grams of massage oil were spread on a defined skin area of the stomach (27×14 cm $= 376$ cm^2) from a male subject (body weight 60 kg, age 34). For ten minutes the oil was gently massaged into the skin and the remaining oil was completely removed. Blood samples (3.0 ml) were drawn from the left cubital vein 0, 5, 10, 15, 20, 30, 45, 60, 75, and 90 minutes after finishing the massage. Heparine was added to the samples, the plasma centrifuged (2500 rpm, ten minutes), and the samples stored



1: R = H

2: R = $COCH_3$



ST

at −20°C until chromatographic and spectroscopic investigations. For statistics, each experiment was repeated three times on the same human subject.

EXTRACTIONS

The plasma was extracted by using a Bond-Elut-C18 column (100 mg, Analytichem Int. Comp., USA). After preconditioning with 3.0 ml methanol and 2.0 ml water bidest., the fragrances were eluted nearly quantitatively with 0.5 ml methanol (recovery rate: 88.2–93.1%; standard deviation: ±6.2%; concentration range 1–150 ng/ml).

GC-FID

An HRGC-Mega-Series (Carlo Erba Comp.) and a 25-m HP-5 fused silica column (i.d. 0.32 mm; film thickness: 0.17 μm) were used. Carrier gas: hydrogen; split-ratio: 1:20; injector temperature: 250°C; detector temperature (FID): 320°C; temperature program: 60 to 300°C, rate of 6°C/min; injected volume: 1 μl.

GC-MS

An HP-5890A gas chromatograph and an HP-5970B-Mass Selective Detector mass spectrometer (Hewlett-Packard Comp.) with data system HP-59970C-Chem-Station were used. Interface-heating: 300°C; mass range: 40 to 450 amu; 70 eV for electron impact; carrier gas: helium.

QUANTIFICATION

GC-FID measurements with tiglinic acid benzyl ester (ST) as an internal standard (1 μg/ml methanol) were employed.

CALCULATIONS

Statistics were performed by an Atari 1040 personal computer (program "WISTAT"). Pharmacokinetic parameters were determined using an IBM AT 286 PC (program NONLIN).

RESULTS AND DISCUSSION

In the first step of this work the main constituents of lavender oil (linalool 1 and linalyl acetate 2) were quantified time dependently by GC-FID in the blood of the subject after the massage. As can be seen from Figure 1, 1 and 2 were well separated from the matrix peaks (t_R 1 = 5.03 minutes; t_R 2 = 10.21 minutes), and there is no overlap with the internal standard (t_R ST = 15.37). The plasma concentration versus time data were fitted to an open two-compartment standard pharmacokinetic model (for serum concentration time curves for 1 and 2, see Figure 2; the corresponding pharmacokinetic

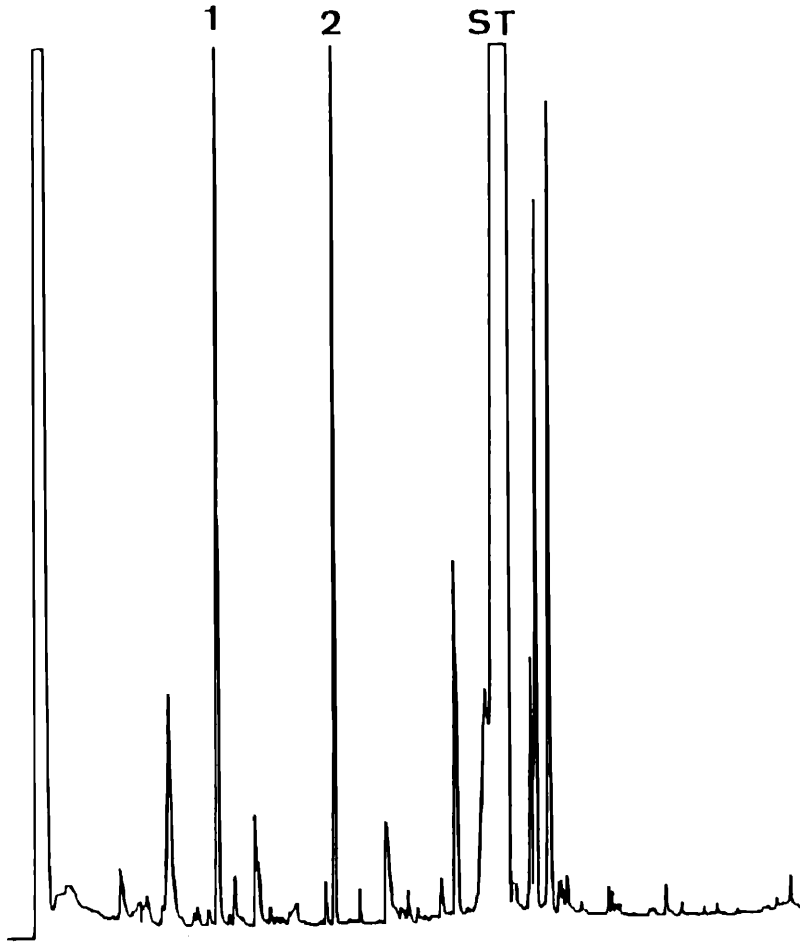


Figure 1. GC-FID of extracted blood sample ten minutes after finishing the massage: 1 linalool (t_R = 5.03 min); 2 linalyl acetate (t_R = 10.21 min); ST tiglinic acid benzyl ester (t_R = 15.37 min).

parameters are summarized in Table I). 1 and 2 were absorbed quickly from the skin and could be detected in the blood five minutes after finishing the massage. 1 and 2 showed a nearly identical behavior of resorption and elimination. No significant difference could be found in the invasion rate constant (0.11 min^{-1}), elimination rate constant (0.46 min^{-1} and 0.48 min^{-1}, respectively), half life of invasion (6.16 min and 6.29 min, respectively) and biological half life (13.76 min and 14.30 min, respectively). The peak plasma concentration for 1 and 2 occurred at 19 minutes, with a mean plasma concentration of 100 ng/ml for 1 and 121 ng/ml for 2. Subsequently, the plasma concentration versus time curve slowly decreased, reaching a minimum after 90 minutes. In spite of native lavender oil (24.79% 1 and 29.59% 2), the plasma concentration of 1 was significantly higher than that of 2, represented by a larger area under the curve compared to 2. This difference was detected in most of the samples and is probably owing to an increased enzymatic catabolism of 2 to 1 by unspecific esterases in blood. The

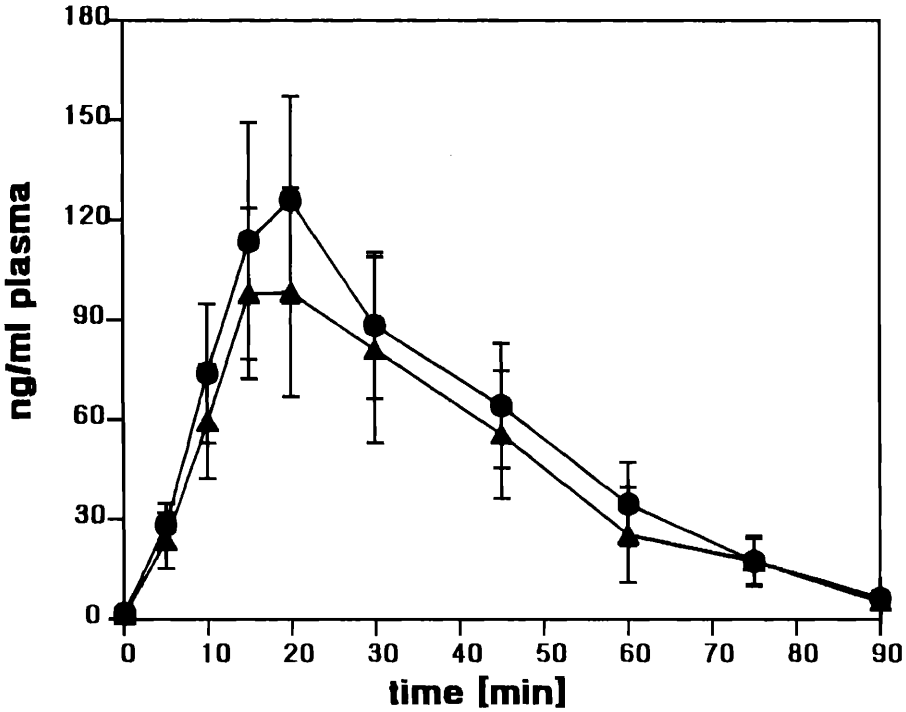


Figure 2. Blood levels of 1 (●) und 2 (▲).

previously mentioned effects of lavender oil may be based partly on sufficient absorption through the skin.

ACKNOWLEDGMENTS

We would like to thank the Fonds zur Förderung der wissenschaftlichen Forschung (projects P6090C and P8299-CHE) and Dragoco Company, Vienna-Liesing, for the

Table I
Pharmakokinetic Parameters of 1 and 2

Parameter	1	2
Dose [mg]	7.23	8.64
kg [kg]	60.00	60.00
k(in) [1/min]	0.11	0.11
k(el) [1/min]	0.46	0.48
$t_{1/2}$ in [min]	6.16	6.29
$t_{1/2}$ biol [min]	13.76	14.30
t(p) [min]	18.76	19.55
c(tp) [ng/ml]	121.08	100.17
$AUC_{(0-90)}$ [(ng/ml)min]	4927.25	4174.50

kg, body weight; k(in), invasion rate constant; k(el), elimination rate constant; $t_{1/2}$ in, half life of invasion; $t_{1/2}$ biol, biological half life; t(p), time to reach the peak; c(tp), concentration at the time to reach the peak; $AUC_{(0-90)}$, area under the curve (0 bis 90 min).

fragrance samples and their interest. Also the skilful massage by Linda Böhm, Cosmetic institute, A-M70 Vienna, Rosenackev, tm. 23, is gratefully acknowledged.

REFERENCES

(1) Fenaroli, *Fenaroli's Handbook of Flavor Ingredients* (CRC Press, Ohio, 1975), pp. 386–387.
(2) S. Atanassova-Shopova, K. S. Roussinova, and I. Boycheva, On certain central neurotropic effects of lavender essential oils. II. Studies on the effects of linalool and of terpineol, *Izv. Inst. Fiziol. Bulg. Akad. Nauk,* **15**, 149–156 (1973); (A. Pg, 58356 (1974).
(3) M. J. Gamez, J. Jimenez, C. Navarro, and A. Zarzuelo, Study of the essential oil of Lavendula dentata L., *Pharmazie,* **45**, 69–70 (1990).
(4a) D. L. J. Opdyke, Linalool, *Food Cosmet. Toxicol.,* **13** (suppl.), 827–832 (1975).
(4b) D. L. J. Opdyke, Lavender oil, *Food Cosmet. Toxicol.,* **14** (suppl.), 451 (1976).
(5) D. V. Parker, K. H. M. Q. Rahman, and R. Walker, The absorption, distribution and excretion of linalool in the rat, *Biochem. Soc. Trans.,* **2**, 612–615 (1974).
(6) D. V. Parker, K. H. M. Q. Rahman, and R. Walker, Effect of linalool on hepatic drug-metabolizing enzymes in the rat, *Biochem. Soc. Trans.,* **2**, 615–618 (1974).
(7) H. Schilcher, Ätherische Öle—Wirkungen und Nebenwirkungen, *Dtsche Apoth. Ztg.,* **124**, 1433–1442 (1984).
(8) M. Wichtl, *Teedrogen* (Wiss. Verlagsgesellschaft, Stuttgart, 1989), p. 303.
(9) S. Price, *Praktische Aromatherapie* (Urania Verlags AG, Neuhausen, 1988), pp. 137–138.
(10) K. Bauer and D. Garbe, *Common Fragrance and Flavor Materials* (VCH Verlagsgesellschaft mbH, Weinheim, 1985), pp. 129–130.
(11) G. Buchbauer, L. Jirovetz, W. Jäger, H. Dietrich, C. Plank, and E. Karamat, Aromatherapy: Evidence for sedative effects of the essential oil of lavender after inhalation. *Z. Naturforsch.,* **46C**, 1067–1072 (1991).
(12) L. Jirovetz, G. Buchbauer, W. Jäger, V. Raverdino, and A. Nikiforov, Determination of lavender oil fragrance compounds in blood samples, *Fres. J. Anal. Chem.,* **338**, 922–923 (1991).
(13) L. Jirovetz, G. Buchbauer, W. Jäger, and W. Balba, A simple and efficient trapping-system for the investigation of exhalation-samples, *Fres. J. Anal. Chem.,* **340**, 785–786 (1991).