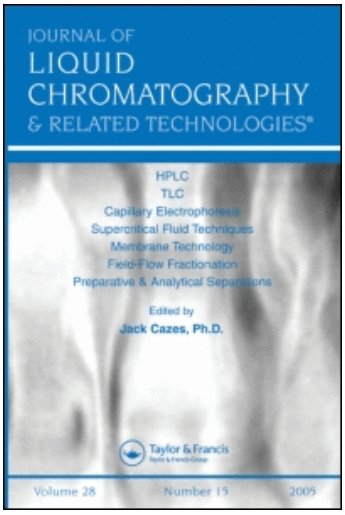

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Separtion of Menthol Isomers by Normal Phase High Performance Liquid Chromatography (1)

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SEPARATION OF MENTHOL ISOMERS BY NORMAL PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (1)

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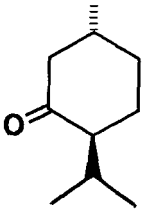
ABSTRACT

An HPLC method has been developed for the separation of the four isomers of menthol using isocratic and normal phase ethyl acetate/isooctane systems. This method has been used to detect and measure these isomers in peppermint oils. The method has several advantages over existing techniques. It is more rapid than GC which in addition requires unstable columns for similar analysis. Because solvent and column are normal phase and isocratic, the method and sample preparation are very simple.

INTRODUCTION

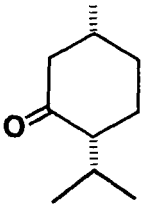
A variety of methods (2,3) have been devised for the GC determination of the isomers of menthone and menthol (1-6). Only one paper, however, has appeared using HPLC and that concerned itself with 1 and 2 (4). There have also been HPLC papers published dealing with p-menthane and monoterpene derivatives other than menthols in essential oils (5,6).

Recently we have developed an HPLC method which is useful for menthol isomers. These compounds can be rapidly identified



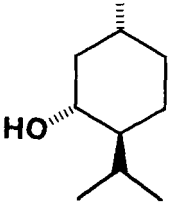
1

MENTHONE



2

ISOMENTHONE



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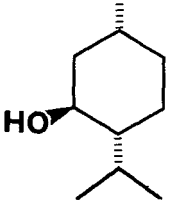
MENTHOL



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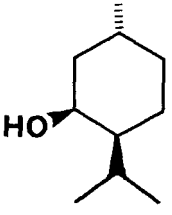
ISOMENTHOL



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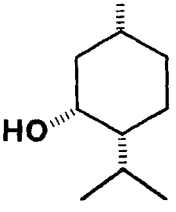
NEOMENTHOL



6

NEOISOMENTHOL

without the need for unstable GC phases (eg. Hyprose), expensive reverse phase HPLC systems, or tedious sample preparation.

EXPERIMENTAL

The instrumentation involved a Waters Associates Liquid Chromatograph, Model ALC-201, equipped with a U6K loop injector, a Radial Compression Separation System (10 cm x 0.8 cm Radial Pak B μ-Porasil cartridge, RCM-100 module) (7), and a Model 401 Differential Refractometer.

Menthones and menthols used for standards were obtained from SCM Organic Chemicals. In all cases HPLC identities were substantiated by GC[3] comparison to these authentic materials.

Liquid chromatography grade solvents obtained from Waters Associates were filtered through 0.45μ Millipore filters prior to use.

All samples were prepared for HPLC by dissolution in 3% ethyl acetate/isooctane and filtration through 0.45μ Millipore filters. Injection volumes were adjusted to apply about 0.1 mg of total sample to the HPLC column on each run.

DISCUSSION

As can be seen in Figure 1, each component is completely resolved using 3% ethyl acetate/isooctane.

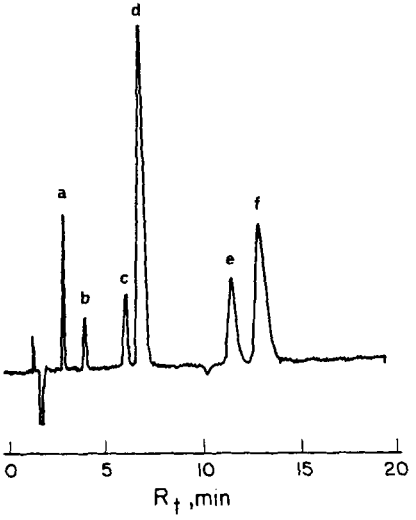


FIGURE 1 HPLC of Menthone and Menthol Isomers
Solvent = 3% ethyl acetate/isooctane, Flow Rate = 3mL/min
(a) Menthone (b) Isomenthone
(c) Neoisomenthol (d) Neomenthol
(e) Menthol (f) Isomenthol

In order to test the applicability of this method in determining the presence of 1-6 in a complex mixture, a sample of corn mint oil (George Uhe Company, Inc.) was run under the same conditions as Figure 1. The resulting chromatogram is shown in Figure 2. The presence of 1, 2, 3 and 4 can readily be determined.

Further work on similar isomeric separations is currently underway in our laboratories.

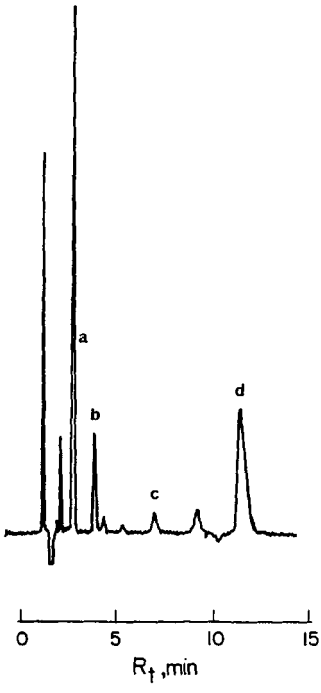


FIGURE 2 HPLC of Corn Mint Oil
Solvent = 3% ethyl acetate/isoctane, Flow Rate-3mL/min
(a) Menthone (b) Isomenthone
(c) Neomenthol (d) Menthol

ACKNOWLEDGMENTS

Our thanks to Ms. Mayada Logue for adapting the literature GC methods for our use and to Mr. Al Correia of Waters Associates for his cooperation.

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7. The standard 3.9mm x 30cm μPorasil steel column works equally as well. Equilibration time is longer and pressures at similar flow rates are much higher. Use of the RCM Module allows for decreased analysis time by further increasing the flow rate if desired without serious resolution loss.