GLC Analysis of Menthol, Phenol, Benzocaine, and Pyrilamine Maleate in Aerosol Spray Lotion

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Abstract □ A GLC method is presented for the quantitative determination of menthol, phenol, benzocaine, and pyrilamine maleate. The propellent was exhausted from a pressurized can, and an aliquot of the alcoholic base was weighed. After the addition of the internal standard diluted with chloroform, 1 μl of the mixture was injected in the chromatograph with a flame-ionization detector and a glass column packed with 2.5% OV-225. Average recoveries were 100.3 ± 1.4, 100.0 ± 1.4, 101.3 ± 1.5, and 101.5 ± 1.5% for menthol, phenol, benzocaine, and pyrilamine maleate, respectively.

Keyphrases □ Aerosols—GLC analysis of menthol, phenol, benzocaine, and pyrilamine maleate □ GLC—analysis of menthol, phenol, benzocaine, and pyrilamine maleate in aerosol form □ Sprays—GLC analysis of menthol, phenol, benzocaine, and pyrilamine maleate

Menthol (I), phenol (II), benzocaine (III), and pyrilamine maleate (IV) are found in various preparations, such as creams, lotions, and dusting powders, used for the treatment of allergic conditions and analgesic applications. While analyses have been reported for the quantitation of I–III singly and in combination with other drugs in topical products, no analytical procedure was found for IV in lotion or cream form.

Douglas (1) used GLC to determine I, II, and methyl salicylate in several commercial preparations. Quantitative determinations of III by colorimetric (2), high-performance liquid chromatographic (HPLC) (3), and GLC (4) methods also were reported. Ghanekar and Gupta (5) used HPLC to determine the maleates of IV, chlorpheniramine, brompheniramine, and pheniramine. The method presented here permits the simultaneous determination and identification of the components analyzed with a single injection.

EXPERIMENTAL

Materials—A gas chromatograph[1] with a flame-ionization detector was fitted with a 1.8-m × 3-mm i.d. column packed with 2.5% OV-225 on Chromosorb W, 80–100 mesh. The reagents[2] chloroform, menthol, phenol, and dichloroxylenol[3] were used.

Solution Preparation—The stock standard solution was prepared by dissolving, per milliliter of chloroform, 7.9 mg of menthol, 7.9 mg of phenol, 7.8 mg of benzocaine[4], and 10.9 mg of pyrilamine maleate[4]. In 50 ml of chloroform was dissolved 1000 mg of dichloroxylenol, the internal standard solution.

Standard Preparation—Stock standard preparation (3 ml) was pipetted into a 50-ml volumetric flask, and 2 ml of the internal standard solution was added and diluted to the mark with chloroform. Then 1 μl was injected into the chromatograph.

Table I—Standard Preparation

Trial	Recovery, % I	II	III	IV
1	100.2	100.6	100.6	101.0
2	101.6	101.9	103.2	103.0
3	100.5	100.5	99.6	99.1
4	99.5	100.0	103.4	101.2
5	101.6	101.3	99.3	100.2
6	100.9	100.9	102.5	100.2
7	99.5	99.0	102.8	102.9
8	97.9	98.8	100.7	103.0
9	100.0	97.8	101.0	103.5
10	100.6	100.0	100.3	100.7
Mean	100.3	100.0	101.3	101.5
SD	±1.1	±1.4	±1.5	±1.5

Sample Preparation—A pressurized can was cooled in the freezer of an ordinary refrigerator for 1 hr. The can was removed and pierced in the shoulder plate (valve site). The propellent ejection was regulated by holding the piercing device into the perforated hole. When the propellent[5] pressure had ceased, the top of the can was cut, and the alcoholic base[6] was poured into a 250-ml conical flask. The flask was shaken mechanically for 20 min. All operations were carried out under a semiclosed hood. An aliquot of liquid (~2.5 ml) was weighed into a 50-ml volumetric flask, and 2 ml of the internal standard solution was added and diluted to volume with chloroform. Then 1 μl was injected into the chromatograph.

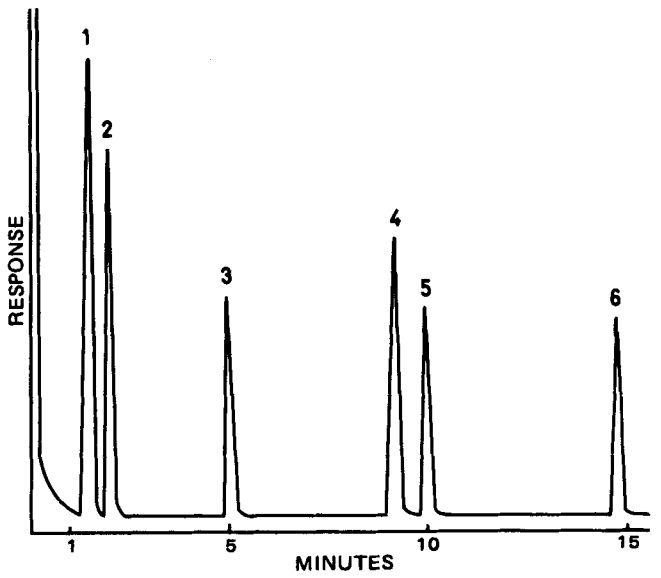

Figure 1—*Representative gas chromatogram, Key: 1, menthol; 2, phenol; 3, internal standard; 4, acetylated lanolin alcohol; 5, benzocaine; and 6, pyrilamine maleate.*

[1] Hewlett-Packard 5840-A.
[2] Unless otherwise specified, all reagents were from British Drug Houses.
[3] Pfaltz & Bauer.
[4] USP reference standard.
[5] Dichlorofluoromethane (Arcton 12), Imperial Chemical Industry Ltd.
[6] The preparation, excluding the propellent, contained, per gram, 13.3 mg of I, 13.3 mg of II, 12.5 mg of III, 18.3 mg of IV, ethanol, Myglyol, Crodolan LA, and Cetiol HE.

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Table II—Response Factors of I–IV with Respect to the Internal Standard [a]

Solution, %	Component	Response Factor	*RSD*, %
80	I	2.06	0.78
	II	1.79	0.71
	III	1.40	1.11
	IV	0.99	0.64
100	I	2.05	1.02
	II	1.81	0.82
	III	1.41	1.00
	IV	0.99	1.74
120	I	2.10	0.90
	II	1.84	1.14
	III	1.43	1.68
	IV	1.04	1.43

[a] Three solutions were prepared, and 18 measurements were made.

Table III—Precision Study of a Commercial Preparation

Parameter	Compound I	II	III	IV
Theoretical content, mg/g	13.3	13.3	12.5	18.3
$\bar{X}$ (n = 8)	13.0	13.1	12.3	18.3
RSD, %	0.75	0.76	1.2	1.2

RESULTS AND DISCUSSION

The recovery study was conducted by preparing a standard solution containing the internal standard and all of the ingredients in amounts as found in the commercial product. The solution was determined 10 times. The results (Table I) show that active ingredients can be separated (Fig. 1) and analyzed by direct injection into the chromatograph. Eventual interferences from other ingredients were investigated by preparing a solution that excluded the active components. The chromatogram of this solution showed a peak of one component[7] with a retention time at ~9.15 min, which did not interfere. Peaks of less volatile compounds[8] appeared between 25 and 28 min. Therefore, it was convenient to allow the instrument to run periodically for 30 min during the analysis.

The ratios of the area per weight of substance to the area per weight of internal standard were calculated for the active components over a range of 80–120% of the label claim. Results for three solutions (80, 100, and 120%) are reported in Table II. Several liquid phases were tried to accommodate compounds of different polarity in the same chromatogram. The response factors throughout the concentration range studied attest to the usefulness of OV-225 as the liquid phase.

Since the procedure was planned only to determine the active ingredients contained in the alcoholic base, it appeared preferable to remove first the propellent from the rest of the sample at a temperature (~0°) where the alcoholic vapor tension was considerably reduced. The residual propellent was eliminated by shaking the decanted sample for 20 min. Precision also was examined by analyzing a production lot commercial preparation. Results are reproduced in Table III.

The method presented is reasonably fast, and precision is consistent with accuracy.

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[7] Acetylated lanolin alcohol (Crodalan).

[8] Polyol fatty acid esters (Cetiol HE) and triglyceride mixture of saturated fatty acids (Myglyol 812).

Optical Characterization of a Low Solubility Organic Compound

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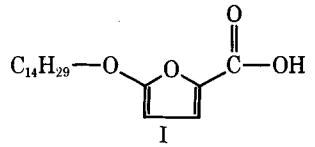
Received April 7, 1980, from *Merrell Research Center, Merrell-National Laboratories, Division of Richardson-Merrell Inc., Cincinnati, OH 45215.* Accepted for publication March 5, 1981.

Abstract □ The X, Y, and Z principal vibration directions along with the principal refractive indexes, optic angle, optical sign, birefringence, optical orientation, and crystal system for the low solubility compound 5-(tetradecyloxy)-2-furancarboxylic acid were determined with a polarizing microscope and spindle stage. The X and Z principal vibration directions are not coincident with the a and c crystallographic axes; however, the Y direction is considered to be coincident with the b axis. Therefore, the crystal is assigned to the monoclinic crystal system. The bladed/lath-shaped crystals rest on one of the two large orthopinacoid (100) faces and present the microscopist with a single plane of optical symmetry. A β refractive index of 1.555 is observed with the crystal axis of elongation parallel to the polarizer, and a γ' of ~1.600–1.660 is observed in the contiguous extinction position. Determination of the optic angle, principal vibration directions, and principal refractive indexes was facilitated by mounting the crystals on a spindle stage for rotation about the b crystallographic axis (optic normal).

Keyphrases □ 5-(Tetradecyloxy)-2-furancarboxylic acid—optical characterization using a polarizing microscope and spindle stage □ Optical characterization—low solubility compound, 5-(tetradecyloxy)-2-furancarboxylic acid □ Crystallography—optical characterization of a low solubility organic compound, 5-(tetradecyloxy)-2-furancarboxylic acid

Control of dosage formulation in the clinic by conventional aqueous dissolution methods was not possible with 5-(tetradecyloxy)-2-furancarboxylic acid[1] (I) because of its poor solubility in alcohol and/or water. A high concentration of surfactant and water was eventually utilized for the solvent, but other controls were necessary to ensure that changes in the crystalline structure between lots did not occur. Long-chain fatty acid compounds such as this one are well known for their polymorphic character (1).



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[1] RMI 14,514, Merrell Research Center.

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