nil because I is not as strong a base as II since only the latter contains a primary amino group. There was no interference from the antioxidant, sodium bisulfite (0.2%), and the preservatives, methylparaben (0.02%) and propylparaben (0.01%). The best pH range for the extraction of the phenylpropanolamine–dye complex with chloroform appears to be from 5.8 to 6.4 (Fig. 2). A pH value of 6.4 was preferred for these studies due to low blank values. The effect of buffer concentration on the extraction of the complex appears to be negligible (Fig. 1). To confirm this finding, three more amines (chlorpheniramine, ephedrine, and phenylephrine) were tested and the results were identical (Fig. 1). Compound I can be easily assayed (Table II) using the Koshy–Mitchner method (2) with borate buffer without any interference from II, the antioxidant, and the preservatives.

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Quantitative GLC Determination of Resorcinol Monoacetate in Dermatological Products

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Abstract □ A GLC procedure employing an internal standard of orcinol is described for the analysis of resorcinol monoacetate in dermatological preparations. The analysis of a cream or lotion is performed by the addition of an internal standard, acetylation, extraction with benzene, evaporation of benzene, addition of chloroform, and then chromatography on a 5% cyano ethyl silicone column.

Keyphrases □ Resorcinol monoacetate creams and lotions—GLC analysis □ Dermatological creams and lotions, resorcinol monoacetate—GLC analysis □ Cream, resorcinol monoacetate—GLC analysis □ Lotion, resorcinol monoacetate—GLC analysis □ GLC—analysis, resorcinol monoacetate in creams and lotions

Due to its mild action, resorcinol monoacetate has been incorporated in dermatological products primarily for the treatment of eczema, psoriasis, and seborrheic dermatitis. In addition to the base, the dermatological preparations frequently contain sulfur, hydrocortisone, and hexachlorophene.

Due to the complex matrix present in dermatological creams and lotions, the quantitative determination of resorcinol monoacetate requires extensive cleanup procedures.

Methods of analysis for resorcinol monoacetate reported in the literature have included UV absorption (1, 2) and photometry after reaction with picric acid (3) or *p*-dimethylaminobenzaldehyde (4). Paper chromatography and TLC techniques have also been used extensively (5, 6), and methods describing the use of GLC for phenolic compounds have been reported (7, 8). None of these methods has been used for the quantitative determination of resorcinol monoacetate in a pharmaceutical matrix.

Table I—Statistical Data from GC Analysis of Resorcinol Monoacetate (RMA) in Cream Base Placebo

RMA Added, mg.	RMA Found, mg.	Bias, mg.	*SD*, mg.	*df*	*CV*, %
13.50	13.45	−0.05	0.193	5	1.43
15.00	14.94	−0.06	0.187	6	1.25
16.50	16.53	+0.03	0.249	5	3.51

The method described here utilizes an internal standard technique and a simple cleanup procedure involving acetylation and extraction. It allows the separation and determination of resorcinol monoacetate by GLC without interference from the excipients commonly present in dermatological creams and lotions. This method can be adapted to the quality control of resorcinol monoacetate in creams and lotions.

EXPERIMENTAL[1]

Chromatographic Conditions—A 1.22-m. (4-ft.), 2-mm. i.d., stainless steel column packed with 5% cyano ethyl silicone on diatomite aggregate (high performance)[2], 80–100 mesh, was used for the assay. The column temperature was 170°, and the detector and injection port temperatures were 220°. The helium carrier gas flow rate was 15 ml./min. A flame-ionization detector was used with a hydrogen flow rate of 30 ml./min. and an air flow rate of 450 ml./min.

Reagents and Solutions—The following were used: resorcinol monoacetate NF; orcinol, 95–99% pure[3]; acetic anhydride, reagent grade; and pyridine, reagent grade.

[1] A Hewlett-Packard 7620A research chromatograph with 7127A strip chart recorder and a 7670A automatic sampler was used.

[2] Five percent XE-60 on Chromosorb G (HP), Supelco, Inc., Bellefonte, Pa.

[3] K & K Laboratories, Plainview, NY 11803

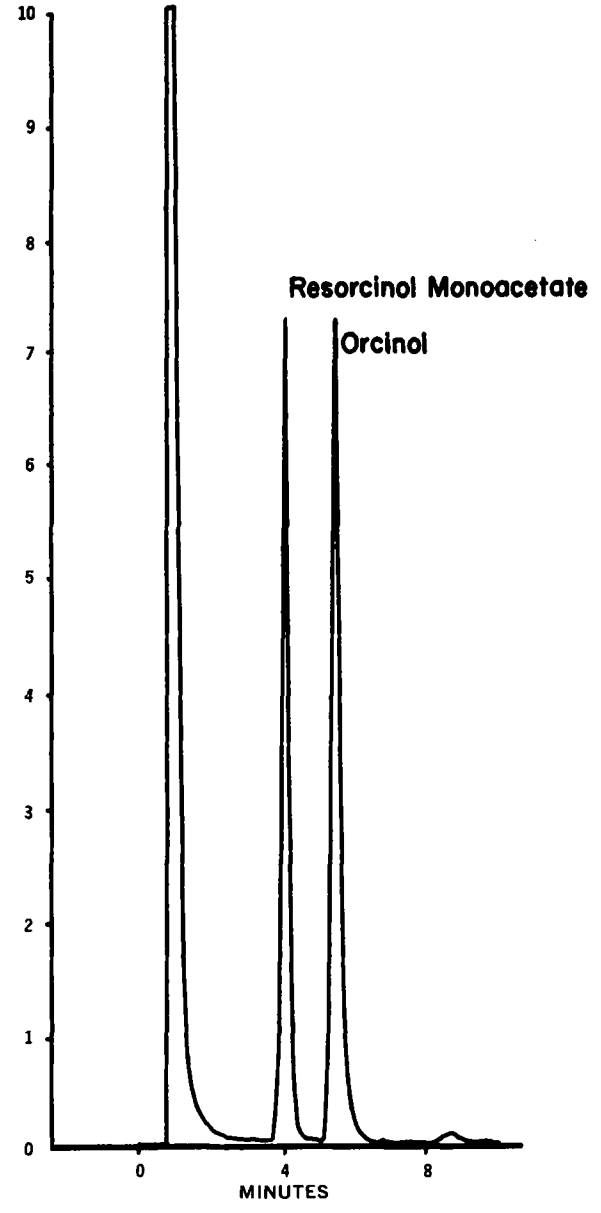

Figure 1—*A typical chromatogram of standard solution of resorcinol monoacetate and orcinol as internal standard, acetylated and extracted.*

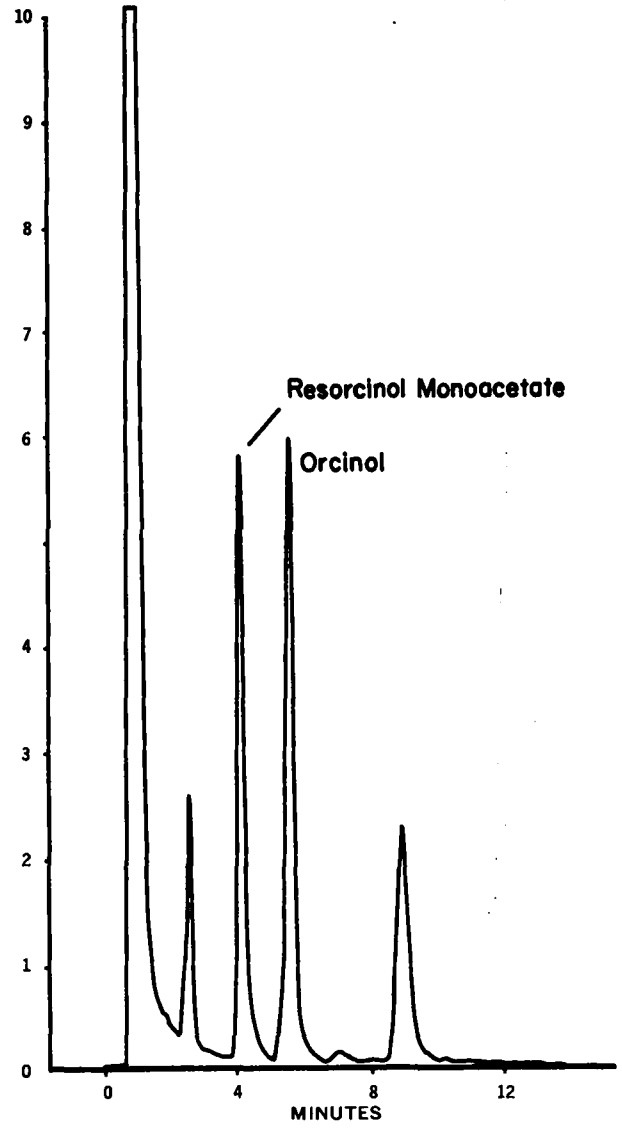

Figure 2—*Chromatogram of sample solution containing orcinol as internal standard, acetylated and extracted.*

For the standard resorcinol monoacetate solution, prepare a standard solution containing, accurately weighed, about 300 mg. of resorcinol monoacetate in 100 ml. of pyridine. For the internal standard orcinol solution, prepare an internal standard solution containing about 300 mg. of orcinol in 100 ml. of pyridine.

For the working standard solution preparation, pipet 5.0 ml. of standard solution and 5.0 ml. of internal standard solution into a 125-ml. glass-stoppered boiling flask. Pipet 10 ml. of pyridine and 4 ml. of acetic anhydride into the flask. Connect an air condensor to the flask and heat on a steam bath for 30 min.

Sample Preparation—Transfer an accurately weighed sample containing about 15 mg. of resorcinol monoacetate into a 125-ml. boiling flask. Pipet 5.0 ml. of orcinol internal standard solution, 15 ml. of pyridine, and 4 ml. of acetic anhydride into the flask. Heat on a steam bath for 30 min. using an air condenser.

Procedure—Cool the working standard and sample preparations. Add 50 ml. of benzene to each, mix well, and transfer to respective separators. Wash each mixture three times with 50 ml. of distilled water, discarding the lower (aqueous) layer each time. Gravity filter the upper (benzene) layer (through anhydrous sodium sulfate in a folded glass fiber filter) into a 125-ml. glass-stoppered boiling flask. Place the flasks in a rotary vacuum evaporator in a hot water bath and evaporate the solvent until only an oily residue remains. Add 5 ml. of chloroform to each flask and swirl to dissolve the sample. Inject 1 or 2 μl. of the sample and standard solutions into a gas chromatograph.

Calculation—Resorcinol diacetate elutes before orcinol diacetate under the conditions of the analysis. Determine the peak height ratio for each standard and sample solution:

$$\frac{A}{W} \times \frac{\text{(RDA/ODA) for sample}}{\text{(RDA/ODA) for standard}} \times 100 = \text{percent resorcinol monoacetate} \quad \text{(Eq. 1)}$$

where:

RDA = resorcinol diacetate peak height
ODA = orcinol diacetate peak height
A = milligrams of resorcinol monoacetate in working standard solution
W = sample weight in milligrams

RESULTS AND DISCUSSION

To determine the accuracy and precision of the proposed method, a statistical study was done. Samples were prepared containing three different levels of known amounts of resorcinol monoacetate. The

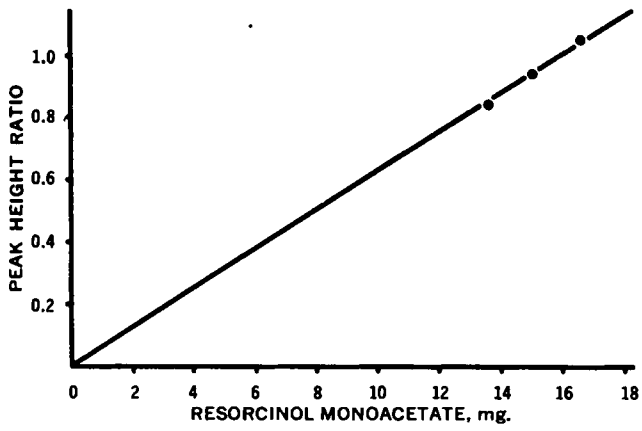

Figure 3—*Standard curve of resorcinol monoacetate concentration* versus *peak height ratio.*

statistical data are shown in Table I. The sample cream base formulated was composed of sorbitan monolaurate, glycerin, polyoxyethylene (20), glyceryl monostearate, hexachlorophene, hydrocortisone acetate, propylene glycol, cetyl alcohol, and colloidal sulfur. The statistical evaluation of the results indicates that the method had no bias at any of the three levels of resorcinol monoacetate. The average coefficient of variation was 1.40%. For 16 replicate samples, the average recovery was 99.76%.

A typical chromatograph of the standard mixture is shown in Fig. 1, and a chromatograph obtained from the extract of the dermatological preparation is shown in Fig. 2. The correlation coefficient for concentration of resorcinol monoacetate *versus* peak height ratio (resorcinol diacetate/orcinol diacetate) was found to be 1.025. A calibration curve for milligrams of resorcinol monoacetate *versus* peak height ratio is shown in Fig. 3.

The statistical results indicate that the method is accurate and reproducible for quality control of resorcinol monoacetate in dermatological preparations.

Table II—Determination of Resorcinol Monoacetate in Commercial Preparations

Sample	Number of Samples	Label Claim, %	Found, % ($\bar{x}$)
Cream I	20	3.0	3.03
Lotion I	12	3.0	3.09
Cream II	16	3.0	3.04
Lotion II	9	3.0	2.88

This method has been used in these quality control laboratories for over a year. The results obtained during this period are shown in Table II.

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GLC Analysis of Homatropine Methylbromide in Tablets and Elixirs

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Abstract □ A GLC assay was developed for the determination of homatropine methylbromide in both tablets and elixirs. The method allows for assaying the drug in the presence of other tropine derivatives and the usual constituents of tablets and elixirs. An aqueous suspension of tablets or a sample of elixir was adjusted to pH 2.2 with hydrochloric acid buffer USP and extracted with ether. This preliminary extraction of the buffered sample removes interfering substances and excludes any hydrolyzed material in the sample from analysis. The homatropine methylbromide was then hydrolyzed by adding 10% sodium hydroxide solution to pH 10–11 and boiling the solution for 20 min. After acidification with hydrochloric acid buffer, the resulting mandelic acid was extracted with ether. The trimethylsilyl derivative of the mandelic acid resulting from hydrolysis was then chromatographed, with the trimethylsilyl derivative of 2-naphthol as the chromatographic standard. A blank elixir preparation with added homatropine methylbromide (0.12 mg./ml.) assayed with an accuracy of 99.12% of the calculated value. This procedure was applied to various commercial preparations containing homatropine methylbromide, with reproducible results ranging from 97.59 to 100.86% of the labeled amount of homatropine methylbromide.

Keyphrases □ Homatropine methylbromide tablets and elixir—GLC analysis □ GLC—analysis, homatropine methylbromide tablets and elixir

Many esters of the amino alcohol tropine exhibit strong anticholinergic activity (1) and, as a result, are found in several pharmaceutical preparations. Analysis of both naturally occurring and semisynthetic derivatives, particularly those contained in pharmaceutical preparations, has been of interest to the pharmaceutical chemist for many years (2). Several of the official procedures (3) for the analysis of these compounds, how-