RESULTS AND DISCUSSION

The presented method reaffirms that ion-exchange chromatography is an excellent general procedure for quantitatively separating alkaloid bases and organic acids. Initially, the choice of the most suitable solvent for readily dissolving all of the active ingredients as well as providing a solution with pH 3–4 (the optimum pH range for alginic acid absorption) was important. An equivalent mixture of 0.5% (v/v) acetic acid in water and ethanol was the most appropriate. Although this study did not present particular difficulties because a previous method served as its basis, attention was focused on the possibility of finding two different wavelengths where the interferences of phenylephrine hydrochloride and diphenhydramine hydrochloride, contained in the same eluate, were as low as possible. Several standard solutions, containing these two active ingredients in the same weight ratio as in the commercial formulation, were subjected to a spectrophotometric test at 285 nm (peak for diphenhydramine hydrochloride), 273 nm (peak for phenylephrine hydrochloride), 252, 243, and 236 nm. It was found that the most favorable results were obtained by using wavelengths at 273 and 236 nm, which correspond to the maximum and the minimum absorbances for phenylephrine hydrochloride, respectively (Fig. 1). The results of 10 determinations of mixtures containing phenylephrine hydrochloride are shown in Table I.

In the determination of acetaminophen, the effects of ascorbic acid, starch[4], and the alcoholic-acetic acid solvent which passed through the alginic acid column together with acetaminophen were investigated. Standard mixtures of these three ingredients in an alcoholic-acetic solution were subjected to the described procedure. It was found that they did not affect the results at 257 nm because they were in such high dilution. The accuracy of the proposed method was based upon results of 10 synthetic mixtures containing all ingredients and prepared in a manner similar to commercial formulations (Table II).

In the quantitative evaluation of ascorbic acid, the use of 2,6-dichloroindophenol yielded reasonable results. This titrant did not interfere with the other components present in this formulation. The possibility of utilizing other methods for the determination was not investigated.

This method provides a simple and rapid means by which the concentration of each component of this preparation is quantitatively determined.

[4] Starch was used as the excipient.

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Quantitative Determination of Resorcinol and Phenol in Resorcinol–Phenol–Boric Acid Solution

V. DAS GUPTA[x] and LINDLEY A. CATES

Abstract □ The quantitative determination of resorcinol and phenol in resorcinol–phenol–boric acid solution is reported. They are assayed by combining a bromination technique with NMR spectroscopy. There is no interference from other ingredients of the solution (acetone, alcohol, boric acid, and water).

Keyphrases □ Resorcinol and phenol in resorcinol–phenol–boric acid solution—analysis, bromination technique and NMR spectroscopy □ Phenol and resorcinol in resorcinol–phenol–boric acid solution—analysis, bromination technique and NMR spectroscopy □ NMR spectroscopy—analysis, phenol and resorcinol in resorcinol–phenol–boric acid solution

A colorless resorcinol–phenol–boric acid solution is used externally as an antifungal preparation. No method for analyzing resorcinol and phenol quantitatively in each other's presence has been reported. Most available methods (1, 2) such as the bromination technique and UV spectroscopy are useful for the combined determination of both ingredients. Two GLC procedures (3, 4) for the quantitative determination of phenolic compounds have also been reported. A method was suggested for the quantitative determination of resorcinol in Castellani's paint by condensing the former with 4-dimethylaminobenzaldehyde and measuring the intense violet color in acetone (5). Recently, the quantitative determination of resorcinol monoacetate in creams and lotions by GLC was reported (6).

This paper reports the quantitative determinations of resorcinol and phenol in resorcinol–phenol–boric acid solution. The method is based on the bromination technique for combined results. The individual quantities of resorcinol and phenol are then computed from the bromination value and the molar ratio obtained from the NMR spectroscopic analysis.

EXPERIMENTAL

Chemicals and Reagents—All chemicals and reagents were USP, NF, or ACS grade.

Preparation of Resorcinol–Phenol–Boric Acid—The solution

Table I—Assay of Resorcinol–Phenol–Boric Acid Solution

Experiment	Total Volume of 0.1 *N* Bromine Solution Used	Molar Ratio of Resorcinol–Phenol Found[a]	Average Volume of Solution Used against	
			Resorcinol[b]	Phenol[b]
1	20.62	1.920:1		
2	20.53	1.919:1		
3	20.65	1.912:1		
Average	20.60 (99.09%)[c]	1.917:1 (Calc. 1.899:1)	13.54	7.06
Average deviation (%)	0.23	0.17	(98.41%)	(98.47%)

[a] Average of at least four integrations as obtained by NMR spectroscopy. [b] The equivalent weights of both (resorcinol and phenol) equal one-sixth of their molecular weights. [c] The solution contains 10% resorcinol and 4.5% phenol.

was prepared according to directions in NF X (7) for Castellani's paint, except that no dye was added since many practitioners prefer this solution without the dye.

Determination of Total Volume of 0.1 *N* Bromine Solution Required for Analysis of Combined Phenol and Resorcinol—A 5.0-ml portion of resorcinol–phenol–boric acid was diluted to 100.0 ml with water. Then a 5.0-ml portion of the diluted solution was transferred to a glass-stoppered bottle. The remainder of the procedure was the same as previously reported (1), starting with: "Add 30 ml. of 0.1 *N* bromine . . .." Results are presented in Table I.

Determination of Molar Ratio of Phenol–Resorcinol Present in Resorcinol–Phenol–Boric Acid—Samples (0.8 ml) of solution were pipeted into an analytical NMR tube and examined[1] from δ 6 to 8, with peak field position being referred to tetramethylsilane

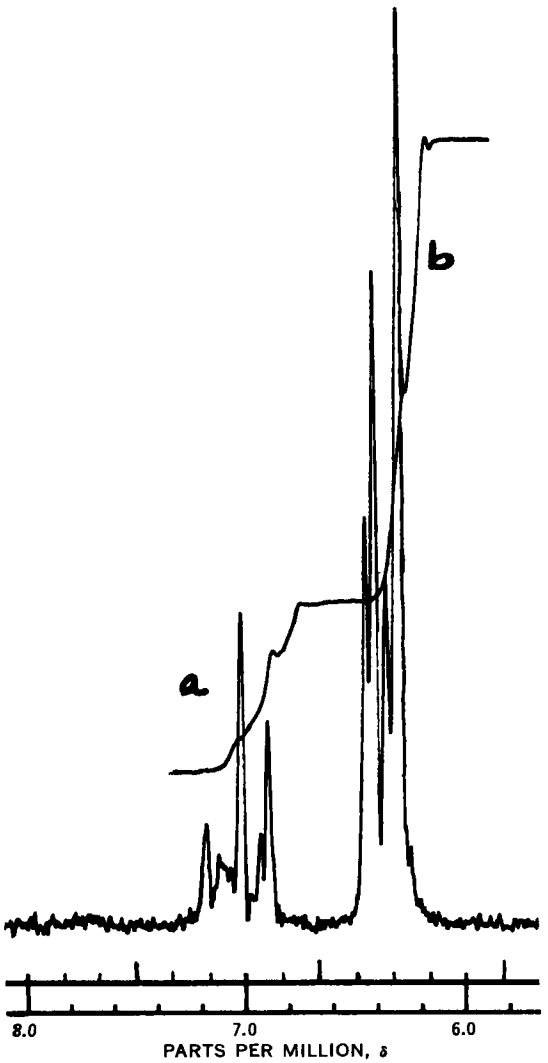
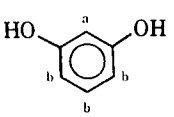


Figure 1—*NMR spectrum of resorcinol in deuterium oxide.*



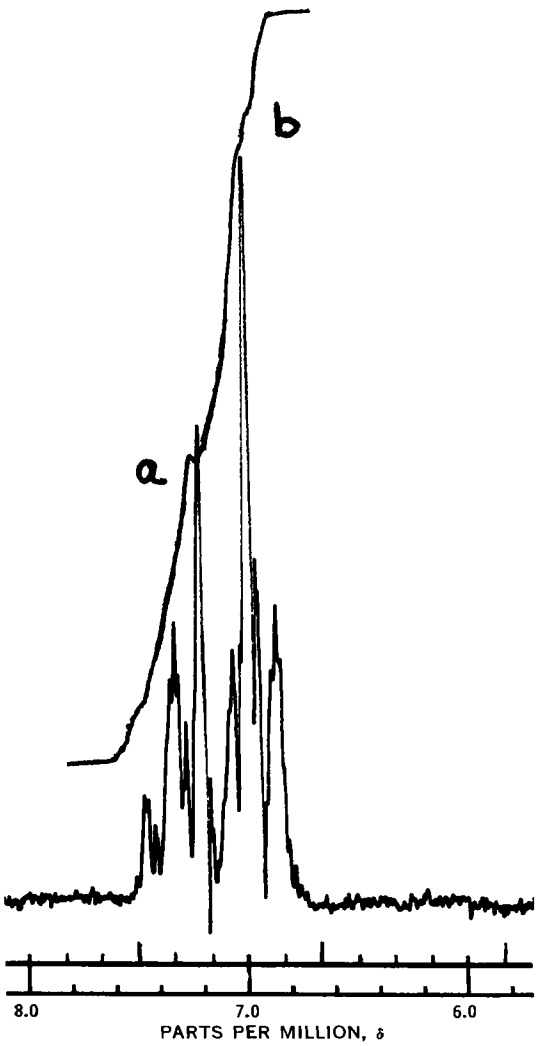
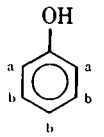


Figure 2—*NMR spectrum of phenol in deuterium oxide.*



[1] Varian T-60 NMR spectrometer.

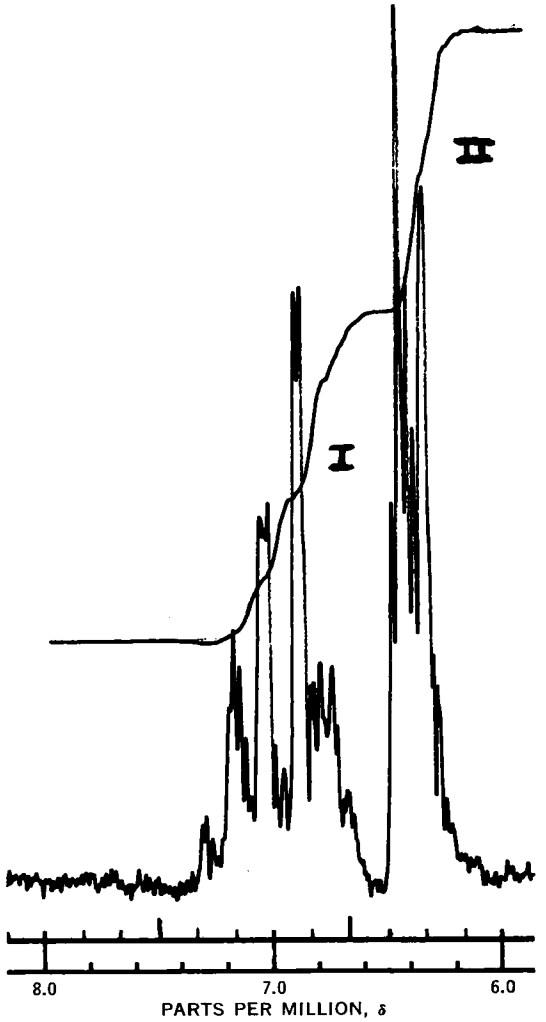


Figure 3—*NMR spectrum of resorcinol–phenol–boric acid solution. Key: I, integral for the C-2 proton of resorcinol and the five protons of phenol; and II, integral for the C-4, C-5, and C-6 protons of resorcinol.*

at 0 ppm. The peaks of interest were integrated at least four times, and the average was used to calculate the molar ratios of resorcinol to phenol as follows:

$$\text{resorcinol} = \frac{A_r}{3} \qquad \text{(Eq. 1)}$$

$$\text{phenol} = \frac{[A_{pr} - (A_r/3)]}{5} \qquad \text{(Eq. 2)}$$

where A_r = integral value of the signal representing three of the four aromatic protons in resorcinol, and A_{pr} = integral value of the signal representing the aromatic protons in phenol and one resorcinol aromatic proton. Results are presented in Table I.

DISCUSSION AND CONCLUSION

The results (Table I) indicate that resorcinol and phenol can be assayed when combined together. The combined result on phenol and resorcinol and the result on phenol are slightly low, probably due to slight impurities in the phenol.

Table II—Pure Mixtures of Resorcinol and Phenol Using NMR Spectra Taken in Deuterium Oxide[a]

Sample	Molar Ratio of Resorcinol to Phenol	
	Known	Found
1	1:1	12.33:12.42
2	1:1	11.33:11.27
3	2:1	12.2:6.1
4	1:2	6.3:12.5

[a] It is not necessary to use deuterium oxide because water gives similar results.

The ability to determine relative amounts of resorcinol and phenol in a mixture is based on the chemical shifts produced by certain protons contained in these similar substances. As seen in Fig. 1, resorcinol gives two NMR signals which are assigned to the more highly deshielded C-2 proton and the three remaining protons whose multiplet occurs more upfield. However, all five protons in phenol give a signal[2] at a downfield position (Fig. 2). Thus, in a mixture of resorcinol and phenol, there appears to be sufficient difference between the absorptions produced by the five aromatic protons of phenol plus the C-2 proton of resorcinol (about δ 6.6–7.6) and the C-4, C-5, and C-6 protons of resorcinol (about δ 6.0–6.6) to permit determination of their relative peak areas and, therefore, calculation of their molar ratios. To test this concept, several known resorcinol–phenol mixtures of varying concentration in deuterium oxide were examined. The results (Table II) indicate that the procedure was applicable. It was later found that the other ingredients in the product (acetone, ethanol, boric acid, and water) do not interfere with the ratio determination and, although there are slight differences in spectra due to solvent effect, the pertinent data can be obtained as well from the solution *per se* (Fig. 3) as from samples prepared (*i.e.*, using deuterium oxide as a solvent) for this product.

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[2] Although phenol actually gives two signals, integrating for two (C-2 and C-6) and three (C-3, C-4, and C-5) protons, this is not important to this analysis.