Spectrophotometric Determination of Acetaminophen, Phenylephrine Hydrochloride, Codeine Phosphate, and Pyrilamine Maleate in Tablets or Powder

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An ultraviolet spectrophotometric method has been developed for the determination of acetaminophen, phenylephrine hydrochloride, codeine phosphate, and pyrilamine maleate after a partial separation of them by means of column chromatography using alginic acid; codeine phosphate and phenylephrine hydrochloride are both eluted with 0.01 *N* HCl and determined simultaneously while acetaminophen and pyrilamine maleate are determined separately.

NO STANDARD ANALYTICAL PROCEDURE exists for acetaminophen, codeine phosphate, phenylephrine hydrochloride, and pyrilamine maleate in this common pharmaceutical combination[1]; however, various assays were reported for each of the components alone or in other combination (1–4). To achieve the separation of the components, the author employed a chromatography technique using alginic acid 40–100 mesh prepared after the process of Foster and Murfin (5). This cation-exchange medium has been used largely to determine many organic bases, to separate codeine phosphate from aspirin and phenacetin in APC tablets B.P. (6), strychnine from nux vomica (7), and to determine thiamine nicotinamide, and pyridoxine in vitamin B complex tablets (8). In this investigation it was found that acetaminophen was not held by the alginic acid used, as was foreseen in a previous theoretical study of the problem, but passed through the prepared column; codeine phosphate and phenylephrine hydrochloride are both eluted with 0.01 *N* HCl and simultaneously determined at two different wavelengths. Finally, pyrilamine maleate is eluted with 0.1 *N* HCl and determined at 316 mμ.

EXPERIMENTAL

Apparatus—Spectrophotometer, Beckman DB, and 1-cm. square fused silica cells were used. Glass column 35 × 2 cm. with stem (5 cm.) was fitted with a buret key.

Reagents—Cation-exchange resin alginic acid, 40–100 mesh, available from British Drug House (B.D.H.): hydrochloric acid 2 *N* in water; 0.1 *N* hydrochloric acid in water; 0.01 *N* hydrochloric acid in water; 0.01 *N* hydrochloric acid in 80% ethanol in water. Except where otherwise specified all reagents were of B.D.H. analar quality.

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[1] Marketed as Mepacod.

Standard Solutions—The following solutions were prepared with suitable reference standard: (*a*) acetaminophen, 0.75 mg./250 ml. in 0.1 *N* hydrochloric acid in 80% ethanol in water; (*b*) codeine phosphate, 8.1 mg./250 ml. in 0.01 *N* hydrochloric acid in water; (*c*) phenylephrine hydrochloride, 5 mg./250 ml. in 0.01 *N* hydrochloric acid in water, (*d*) codeine phosphate and phenylephrine hydrochloride in a mixture in 0.01 *N* hydrochloric acid in water; (*e*) pyrilamine maleate, 20 mg./250 ml. in 0.1 *N* hydrochloric acid in water.

Column Preparation—Alginic acid, about 4 Gm. is slurried in water and allowed to soak 4 hr. The slurry is poured into a glass column that has been fitted with glass wool plug and allowed to settle. The column is washed with 2 *N* hydrochloric acid until the absorbance of the eluate (pathlength 1 cm.) is less than 0.005 at 250 mμ and 273 mμ, and then washed with distilled water until the eluate is neutral to litmus solution.

Sample Treatment—Powder 20 tablets and weigh an amount of powder equivalent to one tablet. Place this in a 50-ml. volumetric flask, add water to volume, and mix. Allow to stand for 30 min., shaking occasionally, then centrifuge about 40 ml. of solution. Pipet 20 ml. of the clear solution onto the prepared alginic acid column; place a 1-L. volumetric flask under the column and start collecting the eluate at the rate of 1 ml./min. Then add 200 ml. of water and allow to pass through at the same rate. Adjust the rate to 2 ml./min. and pass more water through the column to the 1-L. mark. Remove and shake. This eluate contains the acetaminophen. Bring the layer of the liquid in the column to just above the glass wool pledget. Elute the column with 0.01 *N* HCl at the rate of 2 ml./min. Discard the first 15 ml. of eluate and collect the rest in a 100-ml. volumetric flask to volume. This solution contains codeine phosphate and phenylephrine hydrochloride. Again allow the level of the liquid in the column to drop to just above the glass wool pledget. Elute the column with 0.1 *N* HCl at the rate of 2 ml./min., collecting the eluate in a 250-ml. volumetric flask. This solution contains pyrilamine maleate.

Determination—Following the base-line technique compare the absorbances of the standard solutions passed through the column with those of the samples. Quantitatively adjust the claimed concentrations of the sample eluates as closely as possible to the corre-

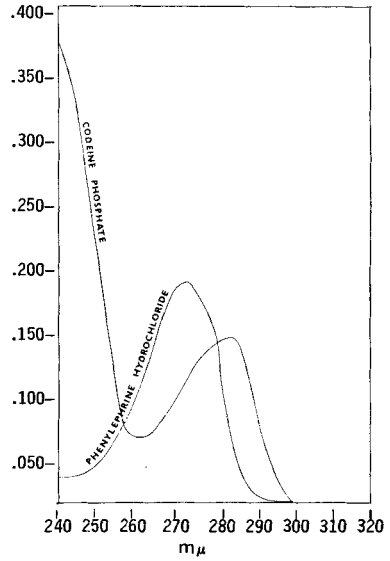

Fig. 1—Spectra of 0.0324 mg./ml. of codeine phosphate and of 0.02 mg./ml. of phenylephrine hydrochloride in 0.01 N HCl.

sponding standard solutions. Calculate the amount of acetaminophen in the sample from the value of the absorptivity of the corresponding standard at 249 mμ. Similarly calculate pyrilamine maleate at 316 mμ and codeine phosphate and phenylephrine hydrochloride at both wavelengths of 250 and 273 mμ.

RESULTS AND DISCUSSION

The first step in the chromatographic procedure was the determination of the "breakthrough" point of each component separately and in a mixture. As previously mentioned, acetaminophen and pyrilamine maleate are separated by the column and their spectrophotometric determination does not present any difficulty. Further study was necessary to choose two different wavelengths where the interferences of codeine phosphate and phenylephrine hydrochloride, contained in the same solution, were as low as possible. In a series of 40 determinations the most favorable system was to be found at the wavelengths of 273 mμ and 250 mμ. However at 250 mμ, the corresponding point lies on the steep part of the curve (see Fig. 1). The error using this wavelength gave a value much lower than the one computed at 248 (the peak), 240, and 245 mμ. The results of 10 determinations of mixtures of codeine phosphate and phenylephrine hydrochloride at 250 and 273 mμ are shown in Table I.

Five mixtures prepared in this laboratory containing acetaminophen, codeine phosphate, phenylephrine hydrochloride, and pyrilamine maleate gave mean values as shown in Table II.

TABLE I—DETERMINATIONS OF MIXTURES OF CODEINE PHOSPHATE AND PHENYLEPHRINE HYDROCHLORIDE

Material	Mean of 10 Determinations, % of Theoretical	S.D. of 10 Determinations, % of Theoretical
Codeine phosphate	98.8	±2.1
Phenylephrine hydrochloride	98.4	±1.0

TABLE II—MEAN VALUES OF FIVE MIXTURES

Material	Taken	Found, % of Amt. Taken
Acetaminophen	150 mg.	99.85
Codeine phosphate	8.1 mg.	98.70
Phenylephrine hydrochloride	5.0 mg.	98.50
Pyrilamine maleate	10.0 mg.	98.97

The total error was about −4 mg. and the mean relative deviation ±2.6%. As can clearly be seen, the proposed method yields results acceptable for routine analysis. In the spectrophotometric determination of pyrilamine maleate, slight differences between the absorbance observed in the standard solution as is and the one passed through the column were taken into account. Finally some water-soluble excipients and dyes, generally used in the manufacture of tablets and powder, pass through the alginic acid column together with acetaminophen; they do not affect the results at 249 mμ as they are in such high dilution.

REFERENCES

(1) Hiskey, C. F., and Levin, N., *J. Pharm. Sci.*, **50**, 393(1961).
(2) Berggrent, A., and Björling, C. O., *J. Pharm. Pharmacol.*, **5**, 393(1961).
(3) Higuchi, T., and Brochmann-Hanssen, E., "Pharmaceutical Analysis," Interscience Publisher, New York, N. Y., 1961, pp. 546–554.
(4) "British Pharmacopoeia," The Pharmaceutical Press, London, England, 1963, p. 477.
(5) Foster, J. S., and Murfin, J. W., *Analyst*, **86**, 462(1961).
(6) Garrat, D. C., "The Quantitative Analysis of Drugs," 3rd ed., Chapman & Hall, London, England, 1964, pp. 13–14.
(7) *Ibid.*, pp. 461–462.
(8) "British Pharmaceutical Codex," The Pharmaceutical Press, London, England, 1963, pp. 1237–1238.

Keyphrases

Drug mixtures—analysis
Acetaminophen, phenylephrine HCl, codeine PO_4, pyrilamine maleate—analysis
Cation exchange resin—separation
UV spectrophotometry—analysis