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Determination of Paracetamol, Pseudoephedrine Hydrochloride and Chloropheneramine Maleate in Dosage Forms by Quantitative Thin Layer Chromatography

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A quantitative thin layer chromatographic (TLC) method has been developed for the determination of paracetamol, pseudoephedrine hydrochloride and chlorpheneramine maleate in drug preparations. The method involves the separation of the three constituents by TLC technique, extraction of the components with ethanol and measurement of their absorption in the UV-range.

INTRODUCTION

The combination of paracetamol (**PAC**), pseudoephedrine hydrochloride (**PEH**), chlorpheneramine maleate (**CPM**) are widely marketed preparations for antihistaminic and bronchodilator properties.[1, 2] Many methods have been investigated for the determination of **PAC, PEH** and **CPM** and in some cases in presence of one another or two drug constituents.[3–9] However there are no reports of their analysis performed in the form of their present formulations containing a combination of three drug constitutents. The present work describes their determination in the form of three drug constituents by TLC method.

EXPERIMENTAL

Potassium iodo bismuthate 10 g of (+) tartaric acid was dissolved in 40 mL of water. To this solution was added 0.85 g of bismuthate oxynitrate and stirred continuously for 1 h. Thereafter 20 mL of 40% w/v solution of potassium iodide was added and shaken well. Finally the mixture was allowed to stand for 24 h and filtered.

Standard Curve

Thin layer chromatographic plates (20 × 20 cm) coated with silica gel G (0.5 mm thick) were prepared. The plates were activated at 100°C for 30 min before use. Pure **PAC** solutions in concentration of 200 mg/mL, 40 mg/mL, 50 mg/mL and 100 mg/mL in ethanol were prepared by first making a stock solution from 2.5 g in 25 mL of ethanol. Each of the solution in the amount 0.02 mL was spotted on the TLC plates in duplicate. The chromatographs were developed in solvent system consisting of ethyl acetate : metahnol : ammonia (85 : 10 : 5) in closed chromatographic chamber at room temperature by ascending technique. The

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chromatographic spots ($R_f = 0.91$) were detected by spraying with a solution of 5% w/v phosphomolybdic acid and subsequently heating the plates at 80°C to obtain purple coloured spots. The chromatographic spots were scraped and collected in clean centrifuge tubes. 5 mL of the extraction solvent (99% methanol and 1% 1 N HCl) was added and vigorously shaken to acheve proper dissolution. 1 mL of this solution was diluted to 10 mL with extraction solvent. The absorbances of these solutions were measured at 242 nm on a Carry 17D UV-visible scanning spectrophotometer.

The duplicate uncoloured spots which were not sprayed with detecting agent were scrapped and used for both the samples. Blanks were prepared by scrapping of silicagel-G from an equivalent area of TLC plates to that of the sample spot from a point at the same migration distance from the start as the sample and parallel to it by processing exactly in the same manner as the sample.

Following a similar procedure the pure samples of **PEH** were prepared in the concentration of 3 mg/mL, 4 mg/mL, 5 mg/mL, 6 mg/mL and 10 mg/mL in ethanol and for **CPM** in the concentration of 0.05 mg/mL, 0.1 mg/mL, 0.15 mg/mL, 0.2 mg/mL and 0.3 mg/mL in ethanol. The loading of TLC plates was done in duplicate by using 0.02 mL of solution per spot. The development of the chromatograms was done in the same solvent system as previously mentioned under similar conditions of temperature. The spots ($R_f = 0.55$ and 0.44) were then detected by solution of potassium iodo bismuthate for **CPM** and 0.2% w/v ninhydrin solution for **PEH** respectively. Red and rose coloured spots were produced for **CPM** and **PEH** respectively. The uncoloured duplicate spots were scraped and dissolved in 10 mL of water, centrifuged and the supernatant clear solution was taken for the **PEH**. The absorbance as measured at 257 nm. Further

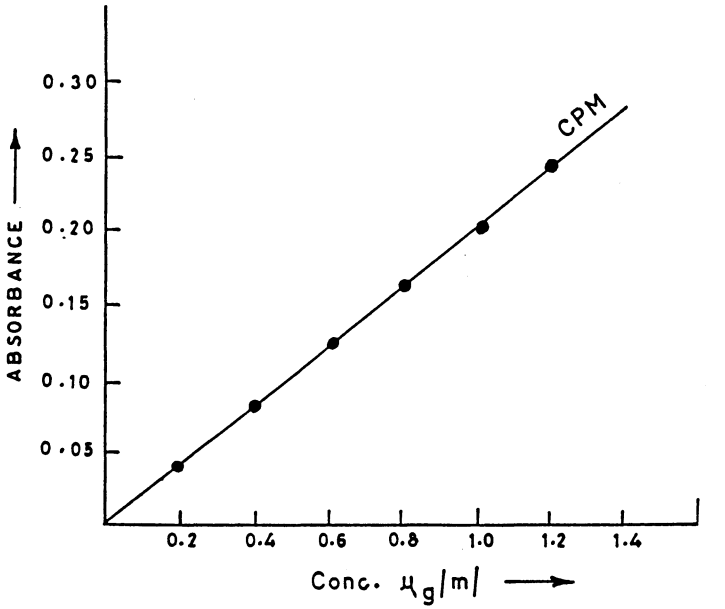

Fig. 1 Calibration curve for CPM.

the scraped substance for **CPM** was extracted with 5 mL of 0.05 M sulfuric acid and the absorbance of the clear solution was measured at 265 nm. From the absorbance values thus obtained, the standard curves for **PAC, PEH** and **CPM** were prepared and are shown in Fig. 1 and Fig. 2.

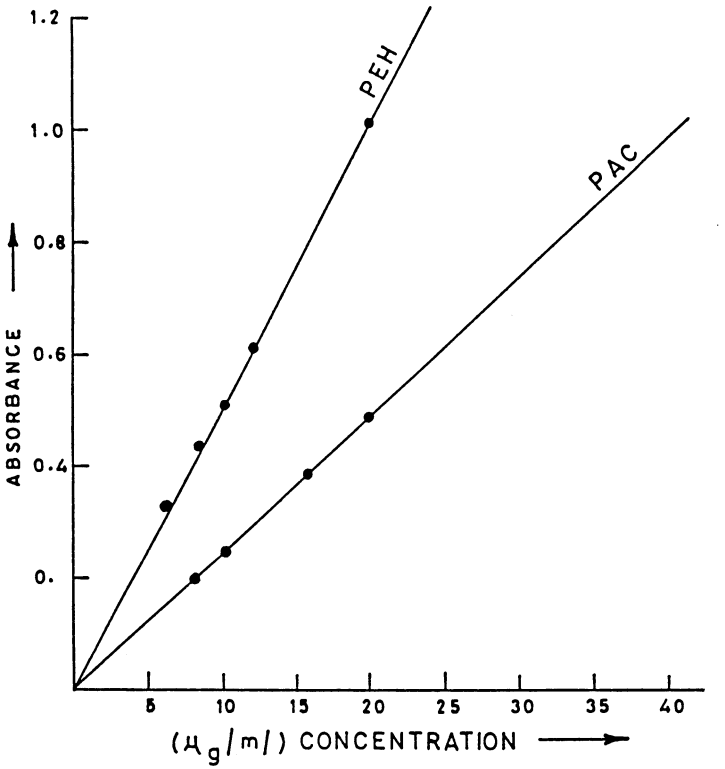

Fig. 2 Calibration curves for PAC and PEH.

Tablet Preparation

Twenty tablets were finely powdered and the powder equivalent to the average weight of one tablet was dissolved in 10 mL of ethanol. The solution was centrifuged and the supernatant solution was used for spotting on the TLC plates.

TABLE-1
RESULTS OF ESTIMATION OF PAC, CPM AND PEH IN COMBINED TABLET FORMULATION

Formulation	Labelled amount (mg/tab)	Amount found* (mg/tab)	% Recovery
PAC	500	499.00	99.8 ± 0.008
CPM	4	4.12	103 ± 0.13
PEH	60	58.85	98.15 ± 0.036

*Each value is an average of five determinations.

The development, detection and extraction of the separated constituents were done in the same manner as of pure drug samples. The absorbances of the solutions were measured at 242, 257 and 265 nm for **PAC, PEH** and **CPM** respectively. The results of the estimation are shown in Table 1.

RESULTS AND DISCUSSION

Various difficulties were encountered while devising a simultaneous assay procedure for the drug formulations described in this work. The selection of the solvent system and spraying agents was also not easy as it involves a large number of trials.

The results of this study show that the amounts **PAC, PEH** and **CPM** contained in the aforesaid formulation confirm to the individual content as specified in USP[2]. Currently various individual methods reported for the assay of **PAC** involves titrimetric, electrometric, colorimetric, fluorimetric and chromatographic methods like GLC and HPLC. The individual methods of analysis for **PEH** are nonaqueous titration, UV spectrophotometric, colorimetric and chromatographic methods like HPLC, TLC, GC. For **CPM**, the various assay methods described have been acid-base titrations, colorimetric, fluorimetric and chromatographic methods like TLC, GLC, HPLC.

Since an official method is not available for the analysis of these drug preparations containing the three drug constituents simultaneously, the proposed method of quantitative TLC analysis which we have developed now was found to be comparatively cheap, accurate and reproducible. This was evidenced by the standard deviations obtained by us on these formulations. We beleive the proposed method should become valuable in the routine analysis of present combined formulations containing three drug constitutents namely **PAC, PEH** and **CPM**.

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REFERENCES

1. Martindale, The Extra Pharmacopoeia, Royal Pharmaceutical Society of Great Britian, 30th edn., pp. 1254, 933, 27–28 (1993).
2. The United States Pharmacopoeia, 22nd revision, U.S. Pharmacopoeil Convention, Rockville, MD, pp. 1186–1188, 12, 290–291 (1990).
3. A. Steven, D. Benezra and J.W. McRae, Analytical Profiles of Drug Substances, Vol. 8, pp. 489–507 (1979).
4. G.E. Charles and T. Mecorkle, Analytical Profiles of Drug Substances, Vol. 7, pp. 43–80 (1978).
5. H.A. El-Obeid and A.A. Al-Badr, Analytical Profiles of Drug Substances, Vol. 14, pp. 553–590 (1985).
6. K. Marumato and L. Tashiro, *J. Chromatogr. Biomed. Appli*, **381**, 323 (1986).
7. M.H. Barary and A.M. Wahabi, *Drug Dev. Ind. Pharm.*, **17**, 457 (1991).
8. F.D. Fabrizio, *J. Pharm. Sci.*, **63**, 91 (1974).
9. T.W. Lawrence, G.P. Gnanaprakasam and B.H. Thomas, *J. Pharm. Sci.*, **65**, 1064 (1976).

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