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High-performance liquid chromatographic assay for the determination of paracetamol, pseudoephedrine hydrochloride and triprolidine hydrochloride

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Abstract: The different UV absorption characteristics of paracetamol, pseudoephedrine hydrochloride and triprolidine hydrochloride have been used to facilitate their determination in pharmaceutical preparations by HPLC. The method developed involves isocratic, reversed-phase chromatography. A 'wavelength switching' programme is preferred to the use of a compromise wavelength for all three compounds. This gives reasonable UV responses despite widely different UV characteristics and concentrations of drugs. The limits of quantitation are found to be within 200–700 μg ml^{-1} for paracetamol, 24–84 μg ml^{-1} for pseudoephedrine HCl and 1.0–4.0 μg ml^{-1} for triprolidine HCl. The method performs well in terms of precision and accuracy as indicated by linear regression analysis.

Keywords: *Reversed-phase liquid chromatography; UV detection; wavelength switching; paracetamol; pseudoephedrine hydrochloride; triprolidine hydrochloride.*

Introduction

Paracetamol, pseudoephedrine hydrochloride and triprolidine hydrochloride have been analysed by reversed-phase LC using a Spherisorb S5W silica column with methanolic ammonium perchlorate (10 mM, pH 6.7) as eluent and electrochemical detection [1]. Although UV absorption and fluorescence detection have been widely used in the analysis of basic drugs, oxidative electrochemical detection [2] has been restricted to compounds containing relatively easily oxidized groups such as phenolic hydroxyl or phenothiazine sulphur.

There are a number of pharmaceutical preparations containing various combinations of paracetamol, pseudoephedrine HCl and triprolidine HCl, which are used for the symptomatic relief of colds and allergic rhinitis. Normal doses of drugs in a unit dose preparation contain 500 mg paracetamol, 60 mg pseudoephedrine HCl and 2.5 mg triprolidine HCl.

Widely different UV characteristics of all these three components can be judged from the specific absorption value at different wavelengths. The absorbance (1%, 1 cm) of a solution of paracetamol, at 249 nm is about 880, whilst for triprolidine HCl, the absorbance at 290 nm is about 1.2.

In the range 230–350 nm, a 0.05% (w/v) solution of pseudoephedrine hydrochloride exhibits three maxima, at 251, 257 and 263 nm, respectively. The absorbance at 251 nm is about 0.75, at 257 nm, about 0.98 and at 263 nm about 0.78 [4]. Quantitative analysis of all three drugs normally requires two separate isocratic high-performance liquid chromatographic (HPLC) systems because of the widely different doses and different UV characteristics.

A reversed-phase LC method using Partisil 10 columns and an eluent based on alcohol and aqueous ammonium acetate [3], with the emphasis on the use of UV detection with the 'wavelength' switching programme, has been developed to determine simultaneously all three active components. Details of the method and its validation are now reported.

Materials

Ammonium acetate GR, ACS, ISO, and alcohol were obtained from Merck. All stock solutions were prepared by dissolving USP reference standards of paracetamol, pseudoephedrine HCl and triprolidine HCl.

HPLC method

The chromatograph used in this study consisted of a LC-6A pump (Shimadzu, Japan), a SIL-6A injector, a SPD-6AV detector and a C-

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R3A integrator. Partisil 10 250 × 4 mm columns were used, protected by ODS pre-columns.

A degassed and filtered mixture of alcohol and 0.015 M aqueous ammonium acetate (70:30, v/v) was used as eluent. The flow rate was maintained at 1.5 ml min^{-1}. Detection was performed at 300 nm followed by a wavelength switching programme entered in 'time programme' mode of a system controller SCL-6A module (Shimadzu) which provides a 'built-in' facility to change parameters such as wavelength, flow rate, etc. automatically during an analysis. Selection from the menu of the time programme mode, enabled entry of the parameters to be changed after certain periods of time. The method presented, required a change of wavelength from 300 to 257 nm after 5.6 min and stopping the run time after 16 min. All separations were carried out at ambient temperature.

Preparation of standard solutions

A 150 mg quantity of pseudoephedrine HCl, (USP reference standard), accurately weighed, was transferred to a 100 ml volumetric flask. It was dissolved in and made up to volume with an equivolume mixture of alcohol and water, mixed well. This was designated solution 'A'.

A 125 mg quantity of triprolidine HCl, (USP reference standard), accurately weighed, was transferred to a 200 ml volumetric flask. It was dissolved in and diluted to volume with an equivolume mixture of alcohol and water, mixed well. This was designated solution 'B'.

A 125 mg quantity of paracetamol, (USP reference standard), accurately weighed, was transferred to a 250 ml volumetric flask. The contents were dissolved in about 100 ml of an equivolume mixture of alcohol and water.

A 10 ml aliquot of solution A and 1 ml of solution B were transferred into the flask (250 ml) containing paracetamol. The contents of the flask were diluted to volume with an equivolume mixture of alcohol and water and well mixed. This was the reference standard solution. The solution was filtered through a 0.45 μm membrane filter before injection into the liquid chromatograph.

Preparation of test solution

A test solution containing paracetamol (500 μg ml^{-1}) pseudoephedrine HCl (60 μg ml^{-1}) and triprolidine HCl (2.5 μg ml^{-1}) was prepared using an equivolume mixture of alcohol and water as diluent. The solution was filtered through a 0.45 μm membrane-filter before injection.

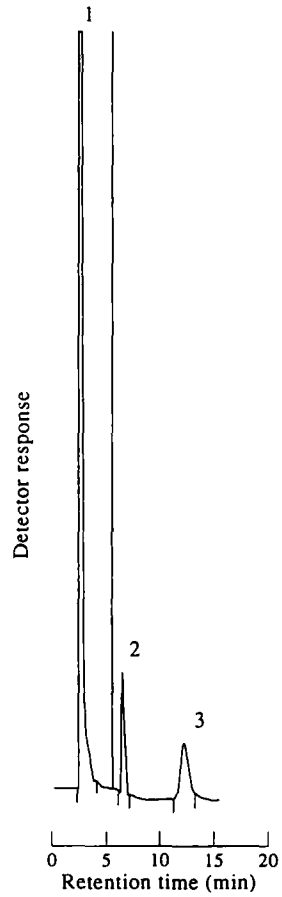

Figure 1
Chromatogram of authentic mixture containing 500 μg ml^{-1} of paracetamol (1), 60 μg ml^{-1} of pseudoephedrine HCl (2) and 2.5 μg ml^{-1} of triprolidine HCl (3).

Table 1
Regression analysis of the calibration data

Drug	Slope	Intercept	Correlation coefficient	(n = 5)
Paracetamol	2.23294	39.7738	0.9989	0.9989
Pseudoephedrine HCl	26.5503	2.06787	0.9989	0.9989
Triprolidine HCl	11.8345	−11.1079	0.9997	0.9997

Experimental conditions as given in the text.

Table 2
Simultaneous analysis of paracetamol, pseudoephedrine HCl and triprolidine HCl by the proposed HPLC method

Paracetamol			Pseudoephedrine HCl			Triprolidine HCl		
Amount added ($\mu g\ ml^{-1}$)	Amount found ($\mu g\ ml^{-1}$)	Recovery* (%)	Amount added ($\mu g\ ml^{-1}$)	Amount found ($\mu g\ ml^{-1}$)	Recovery* (%)	Amount added ($\mu g\ ml^{-1}$)	Amount found ($\mu g\ ml^{-1}$)	Recovery* (%)
312.58	318.5	101.85	35.27	34.55	97.97	1.432	1.368	95.56
412.58	418.02	101.32	47.37	48.14	101.64	2.432	2.352	96.70
512.58	509.27	99.35	59.47	60.51	101.75	2.932	2.789	98.12
612.58	611.55	99.83	71.57	72.05	100.67	3.432	3.450	100.57
712.58	708.46	99.42	83.67	84.12	100.53	3.932	4.050	103.10
Mean		100.35			100.51			98.81
SD		1.15			1.52			3.04
RSD		1.14			1.51			3.07

* Average of five experiments.

Approximate retention times

The approximate retention times of the reference compounds were found to be 2.5, 6.7 and 12.5 min for paracetamol, pseudoephedrine HCl and triprolidine HCl, respectively.

Results and Discussion

Individual test/standards containing 40, 80, 100, 120 and 140% of the theoretical assay concentration of each of the active ingredients were examined by the HPLC method and the responses measured. In each case, test and standard, a linear relationship of peak height and concentration was observed. A typical chromatogram is shown in Fig. 1.

Regression analysis of the data (n = 5) for each component gave the values for slope, intercept and correlation coefficient for each calibration curve (summarized in Table 1).

The validity of the listed regression data was tested by the assay of an authentic mixture containing known quantities of paracetamol, pseudoephedrine HCl and triprolidine HCl. The result showed good accuracy (as revealed by the percentage recovery; see Table 2). The recovery data were generated by the assay of solutions containing 60, 80, 100, 120 and 140% of the theoretical assay concentration. The proposed method has been found to be highly sensitive, time saving and appropriate for use in Quality Control and R&D laboratories for similar type and composition of products.

References

[1] I. Jane, A. McKinnon and R.J. Flanagan, *J. Chromatogr.* **323**, 191–225 (1985).

[2] B. Fleet and C.J. Little, *J. Chromatogr. Sci.* **12**, 747–752 (1974).

[3] *United States Pharmacopeia*, XXII, p. 1187, 1425 (1990).

[4] *British Pharmacopoeia*, pp. 414, 478, 588. Her Majesty's Stationery Office, London (1988).

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