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Spectrophotometric estimation of paracetamol and promethazine in tablet dosage forms

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ABSTRACT

Two cost effective spectrophotometric methods are developed and validated for quantitative determination of paracetamol (PCT) and promethazine hydrochloride (PMZ) in tablet dosage form. Method I is based on the simultaneous equation and Method II on the absorbance ratio. The absorption maxima were found to be at 244 nm and 254 nm in distilled water for both the drugs. Beer's law is obeyed in the concentration range of 5-25 µg/ml for paracetamol and promethazine hydrochloride with correlation coefficient within range of 0.996 - 0.998. The simultaneous equation method is based on the additivity of absorbencies and the absorbance ratio method involves determination of the ratio of absorbance at 254 nm, the absorption maxima of promethazine and isoabsorptive wavelength 248 nm. The accuracy was assessed by recovery studies.

Keywords: Simultaneous equation method, absorption ratio method, paracetamol, promethazine.

INTRODUCTION

Paracetamol (PCT) is one of the most popular over-the-counter analgesic and antipyretic drugs. It is available in different dosage forms like tablets, capsules, drops, elixirs, suspensions and suppositories. Dosage forms of paracetamol and its combinations with other drugs have been listed in various pharmacopoeias [1, 2]. Numerous methods have been reported for the analysis of paracetamol and its combinations in pharmaceuticals or in biological fluids. Paracetamol has been determined in combination with other drugs using titrimetry [3,4] voltametry [5], fluorimetry [6], spectrophotometry [7-9], quantitative thin layer chromatography [10], high performance liquid chromatography [11-16] and gas chromatography [17] in pharmaceutical preparations.

Promethazine hydrochloride (PMZ) is H₁ receptor antagonist, used as an antiemetic in motion sickness and antipsychotic [18]. Numerous methods have been reported for the analysis of PMZ and its combination with other drug like HPLC [19-22], UV-spectrophotometry [23-25], nephelometry [26] and capillary isotachopheresis [27].

The combination of paracetamol with promethazine hydrochloride is commercially available in tablet dosage form as antipyretic and antiemetic. The structure of PCT and PMZ are shown in Figure 1 and 2 respectively. Literature survey reveals that HPLC [28] method is available for the simultaneous determination of these two drugs in combination but no UV-spectrophotometric method is available. So we communicate here rapid and cost-effective

quality-control tool for their routine quantitative analysis in pure and combined dosage forms by UV-spectrophotometry.

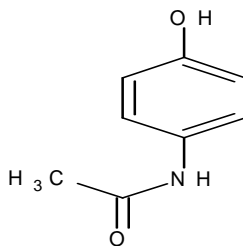


Figure 1. Chemical structure of paracetamol

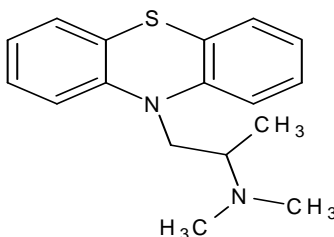


Figure 2. Chemical structure of promethazine

MATERIALS AND METHODS

Instrumentation

A UV-Visible double beam spectrophotometer of Jasco Model: V-630, with a fixed bandwidth 2 nm and a pair of 1cm matched quartz cell were used for all spectrophotometric measurements.

Selection of common solvent

After assessing the solubility of both drugs in different solvents distilled water was selected as a common solvent for developing spectral characteristics.

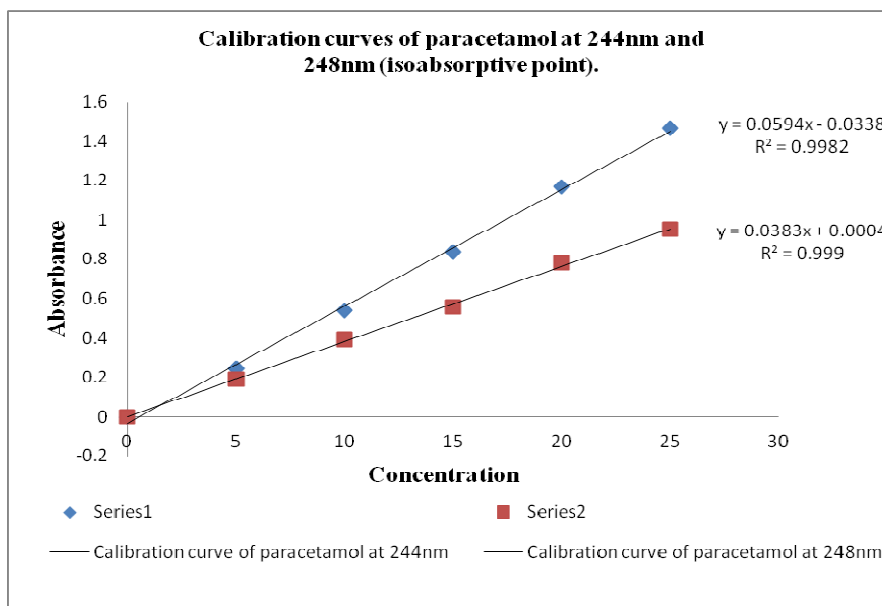


Fig. 3: Standard calibration curve of PCT

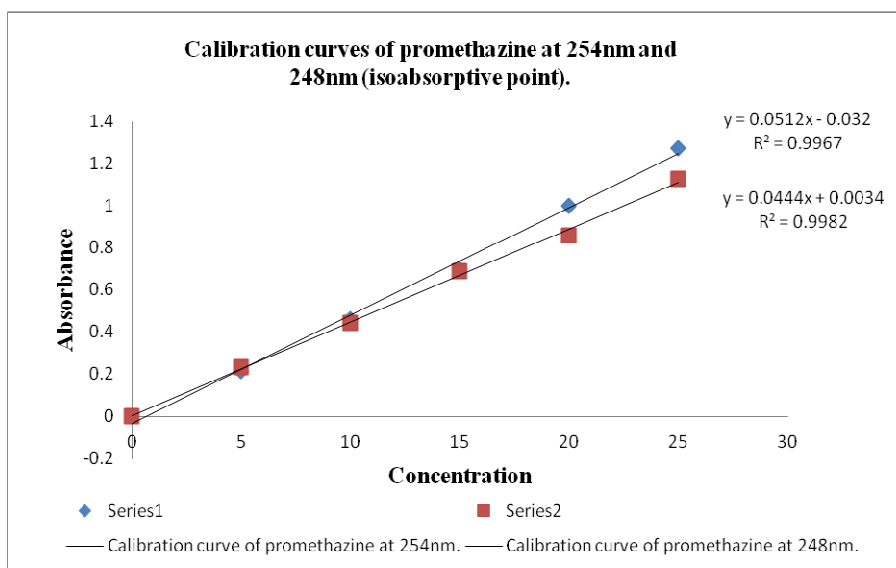


Fig. 4: Standard calibration curve of PMZ

Preparation of standard solution

The standard stock solutions of PCT and PMZ were prepared by dissolving 10 mg of each drug in 40 ml of distilled water and final volume was adjusted with distilled water to get a solution with strength of 100 µg/ml of each drug.

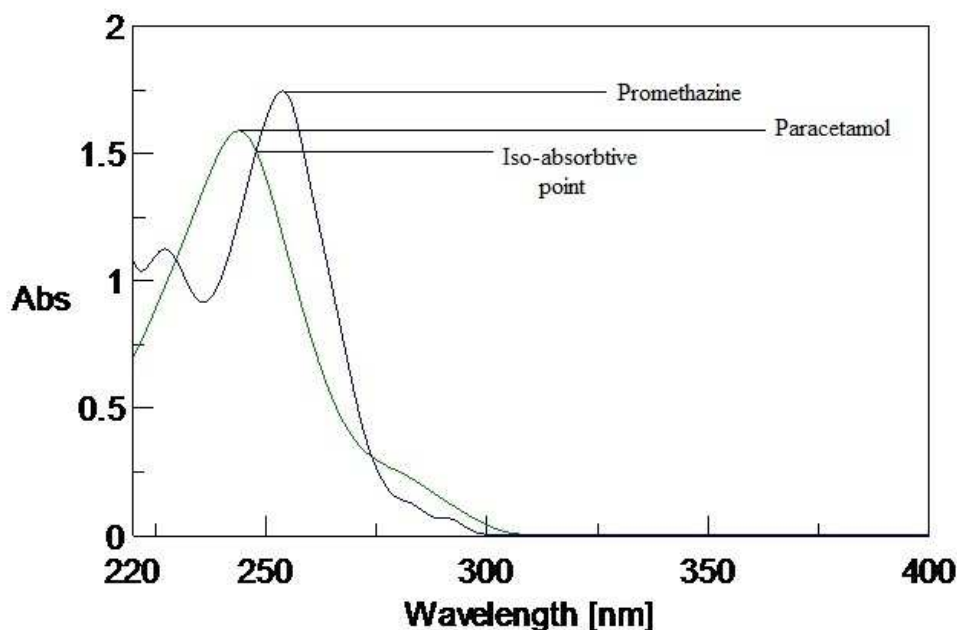


Figure 5: Overlain spectra of PCT and PMZ

For the selection of analytical wavelength, standard solution of PCT (20 µg/ml) and PMZ (20 µg/ml) were prepared separately by appropriate dilution of standard stock solution with distilled water and scanned in the entire UV range to determine λ_{max} of both the drugs. The λ_{max} of PCT and PMZ were found to be 244 nm and 254 nm, respectively where as 248 nm is isobestic wavelength. A series of standard solutions were prepared with strength in the range of 5-25 µg/ml for both PCT and PMZ. The absorbance of resulting solutions was measured at 244 nm, 248 and 254 nm,

and calibration curves were plotted. Both the drugs obeyed linearity in the concentration range under study. The standard calibration curve of PCT and PMZ are shown in Figure 3 and 4.

Method I: Simultaneous equation method

This method of analysis was based on the absorption of PCT and PMZ at the wavelength maximum of each other. Two wavelengths selected for the development of simultaneous equations were 244 nm and 254 nm which are λ_{\max} of PCT and PMZ respectively. The absorbances of PCT and PMZ were measured at the selected wavelengths. The absorptivity values $E(1\%, 1\text{cm})$ were determined for both the drugs at the selected wavelengths. These values are mean of five estimations. Overlain spectra of PCT and PMZ are shown in Figure 5.

The concentration of both drugs in mixture can be calculated by using following equations-

$$C_x = \frac{A_1 a_{y2} - A_2 a_{y1}}{a_{x1} a_{y2} - a_{x2} a_{y1}} \quad \text{Eq (1)}$$

$$C_y = \frac{A_1 a_{x2} - A_2 a_{x1}}{a_{y1} a_{x2} - a_{y2} a_{x1}} \quad \text{Eq (2)}$$

Where, A_1 and A_2 are absorbances of mixture at 244 and 254 nm respectively

a_{x1} and a_{x2} are absorptivities of PCT at 244 and 254 nm respectively

a_{y1} and a_{y2} are the absorptivities of PMZ at 244 and 254 nm respectively

C_x and C_y are the concentrations of PCT and PMZ respectively.

Analysis of marketed formulation

Twenty tablets were accurately weighed; average weight was determined and finely powdered. An accurately weighed quantity of tablet powder equivalent to 20 mg of PCT was transferred to 100 ml volumetric flask and dissolved by sonication with sufficient quantity of distilled water and volume was made to the mark with distilled water. The solution was then filtered through Whatmann filter paper no. 41. A 1 ml portion of the filtrate was taken in 10 ml volumetric flask and to it adds 1.96 ml of standard solution of PMZ and final volume was adjusted with distilled water. The above mixture was analyzed at 244, 248 and 254 nm wavelengths and values of the absorbance were substituted in respective equations (Eqn. 1 and 2) to obtain the content of PCT and PMZ respectively. The results of analysis are mentioned in Table 1.

Table 1: Result of Tablet Analysis

Drug	Label Claim (mg/tablet)	Amount of drug estimated (mg/tablet)		% Label claim estimated \pm S.D.*	
		Method I	Method II	Method I	Method II
PCT	500	497.55	505	99.51 \pm 0.34	101.1 \pm 0.49
PMZ	10	9.997	9.96	99.97 \pm 0.17	99.6 \pm 0.39

* Mean of six determinations.

Method II: Absorption ratio method

In quantitative assay of two components by absorption ratio method (Q-analysis), absorbencies were measured at the isobestic wavelength (248) and λ_{\max} of one of the two components. From the overlain spectra of PCT and PMZ shown in figure 5, absorbencies were measured at 248 nm (isobestic wavelength) and 254 nm (λ_{\max} of PMZ). From the following sets of equations, the concentration of each component in sample solution can be calculated.

$$C_x = \frac{(Q_0 - Q_2) \times A_1}{(Q_1 - Q_2) \times a_1} \quad \text{Eq(3)}$$

$$C_y = \frac{(Q_0 - Q_1) \times A_1}{(Q_2 - Q_1) \times a_2} \quad \text{Eq(4)}$$

Where, C_x and C_y are the concentration of PCT and PMZ respectively.

A_1 = absorbance of sample at 248 nm

Q_0 = (absorbance of sample at 254 nm)/ (absorbance of sample at 248 nm)

Q_1 = (absorptivity of PCT at 254 nm)/ (absorptivity of PCT at 248 nm)

Q_2 = (absorptivity of PMZ at 254 nm)/ (absorptivity of PMZ at 248 nm)

a_1 and a_2 are the absorptivity values of PCT and PMZ at 248 nm respectively.

RESULTS AND DISCUSSION

Two cost effective spectrophotometric methods are developed for quantitative determination of paracetamol and promethazine hydrochloride in tablet dosage form. Method I is based on the simultaneous equation and Method II on the absorbance ratio. The developed methods for simultaneous estimation of PCT and PMZ were validated as per ICH guidelines.

Accuracy

To check the accuracy of the developed methods and to study the interference of formulation additives, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). The results of recovery studies expressed as percent recovery were satisfactory and are presented in Table 2.

Table 2: Results of recovery studies

Method	Level of Recovery (%)	% Recovery \pm S.D. #	
		PCT	PMZ
I	80	99.75 \pm 0.0456	100.01 \pm 0.1045
	100	99.51 \pm 0.0345	99.97 \pm 0.3567
	120	99.50 \pm 0.2321	99.76 \pm 0.5578
II	80	100.40 \pm 0.2341	100.53 \pm 0.3784
	100	100.91 \pm 0.1679	99.63 \pm 0.234
	120	99.50 \pm 0.2451	99.33 \pm 0.2452

#mean of three determinations, SD: Standard Deviation

Intermediate precision (inter-day and intra-day precision)

The reproducibility of the proposed methods was determined by analyzing tablets at different time intervals on same day (Intra-day assay precision) and on three different days (Inter-day assay precision). The results are presented in Table 3.

Limit of detection (LOD) and Limit of quantitation (LOQ)

The LOD and LOQ were separately determined based on the standard deviation of y-intercept of the calibration curve. The limit of detection (LOD) and limit of quantification (LOQ) were determined by visual methods as suggested in ICH guidelines and shown in Table 3.

Table 3: Optical characteristics and validation parameters

Statistical parameters	PCT		PMZ	
λ max (nm)	244	248	254	248
Concentration range (μ g/ml)	5-25	5-25	5-25	5-25
Regression Equation ($y = mx + c$)				
Slope (m)	0.0594	0.0383	0.0512	0.0441
Intercept (c)	0.0338	0.0004	0.032	0.0034
Correlation Coefficient (r^2)	0.9982	0.999	0.9967	0.9982
LOD (μ g/ml)	0.0346	0.0117	0.1251	0.0233
LOQ (μ g/ml)	0.1153	0.039	0.417	0.0776
Precision (COV*): Interday (n = 3)	0.1507	0.0572	0.2231	0.0662
Intraday (n = 3)	0.1705	0.5816	0.2563	0.6922

* COV is Coefficient of variance

CONCLUSION

The proposed UV spectrophotometric methods are simple, cost effective and validated hence can be used for routine analysis of paracetamol and promethazine hydrochloride in pharmaceutical dosage forms.

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