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Original Article

SIMULTANEOUS ESTIMATION OF PARACETAMOL, CETIRIZINE AND DEXTROMETHORPHAN USING SECOND DERIVATIVE SPECTROPHOTOMETRY

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ABSTRACT

Objective: In the present study, a spectrophotometric method that does not require prior separation for simultaneous estimation of three drugs: paracetamol, cetirizine and dextromethorphan in tablet formulation have been reported. To develop and validate a simple and rapid method for simultaneous estimation of paracetamol, cetirizine and dextromethorphan from pure and dosage form.

Methods: The method was based on derivative spectroscopy and the absorbances were measured at 267.72, 232.71 and 292.68 nm being the zero crossing points for paracetamol, cetirizine and dextromethorphan respectively.

Results: All the three drugs obeyed Beer's law in the concentration range 6.25 – 50 µg/ml, 0.125 – 1 µg/ml and 0.5 – 4 µg/ml for paracetamol, cetirizine and dextromethorphan respectively.

Conclusion: The optimized method was validated for various parameters according to International Conference on Harmonization Q2B guidelines. The utility of the developed method has been demonstrated by analysis of laboratory prepared synthetic mixtures.

Keywords: Derivative spectrophotometry, Validation, Paracetamol, cetirIzine, Dextromethorphan

INTRODUCTION

Paracetamol (PCM) is N-(4-hydroxyphenyl) acetamide. It is a popular analgesic and antipyretic used for the relief of fever, head ache and other minor aches and pains. Cetirizine hydrochloride (CTZ), chemically [2-[4-[(4-chlorophenyl) phenyl methyl] 1-piperazinyl] ethoxy] acetic acid, belongs to the group of second generations antagonists of H_1 receptors. Dextromethorphan (DTM) is antitussive drug used for the pain relief and in psychological conditions. Chemically it is morphinan, 3-methoxy 17-meth (9, 13, 14) hydrobromide. The combination therapy of Paracetamol, Cetirizine and Dextromethorphan was superior when compared to monotherapy of Paracetamol, Cetirizine and Dextromethorphan. The combination acts well in patients with cold, fever, body pain and in any minor inflammations.

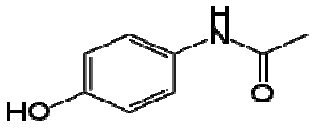
Cetirizine hydrochloride is official in BP and IP, both describes potentiometric method of assay. Literature reveals that many analytical methods are specified for the determination of PCM, CTZ and DTM as individual and combined dosage form with other combination of drugs and also in biological fluids viz., UV Visible Spectrophotometry [1, 2], HPLC [3-14] and HPTLC [15] method. Since no Spectrophotometric method is reported for simultaneous estimation of all three drugs in combined dosage form, an attempt has been made to estimate these drugs simultaneously without prior separation.

(1) Chemicals and Reagents

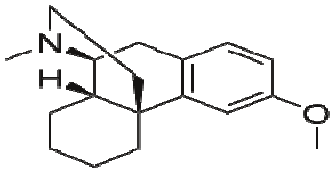
All spectrophotometric measurements were made using Perkin Elmer UV visible spectrophotometer equipped with Lamda 25 software. Pure drugs of PCM, CTZ and DTM were obtained as gift sample from Madras Pharmaceuticals, Chennai. All the chemicals and reagents used for the study were procured from Ranchem, India.

(2) Preparation of standard solutions

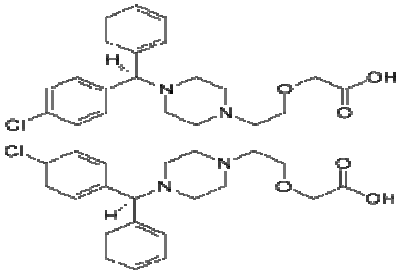
The standard stock solutions of PCM, CTZ and DTM were prepared by dissolving 125 mg, 2.5 mg and 10 mg of respective drugs in 100 ml of water in separate 100 ml volumetric flasks. Aliquot dilutions were made separately from standard stock solutions to get a concentration of 125µg/ml for Paracetamol, 2.5µg/ml for Cetirizine and 10µg/ml for Dextromethorphan respectively. These solutions were scanned in the range 200 – 400 nm to obtain second derivative overlain spectra for all the three drugs.



Paracetamol



Dextromethorphan



Cetrizine

Fig. 1: Structure of selected drugs

(3) Derivative Spectrophotometry

The second derivative (D_2) overlain spectra (fig 2) of each drug was found to show zero crossing point and assisted in their simultaneous estimation. The second derivative wavelengths considered for PCM, CTZ and DTM were 267.72 nm, 232.71nm and 292.68 nm respectively at which the other two drugs show zero absorbance. Calibration curves were plotted between D_2 values measured at selected wavelengths against the concentrations in the range of 6.25 – 50 µg/ml, 0.125 – 1.0 µg/ml and 0.5 – 4.0 µg/ml for PCM, CTZ and DTM respectively. Estimation of all three drugs was done by solving the following regression equations.

y = 0.003x + 0.001 ----- (1), for PCM

y = 0.081x + 0.001 ----- (2), for CTZ

y = 0.011x + 0.002 ----- (3), for DTM

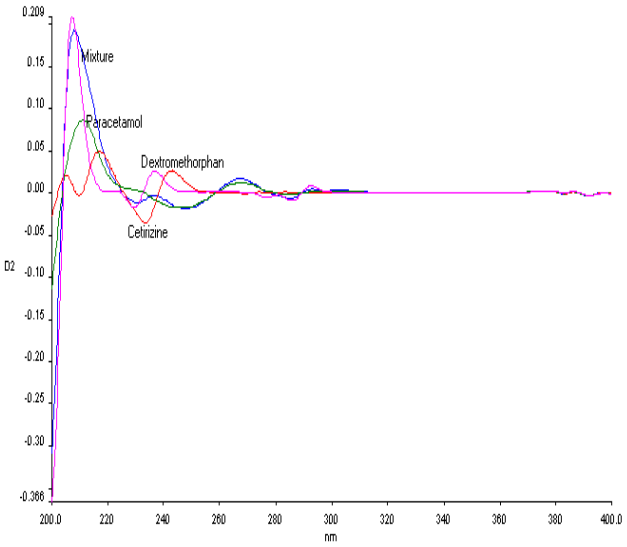


Fig. 2: Overlay spectrum of Paracetamol, Cetirizine and Dextromethorphan in D_2 mode

(4) Sample Preparation and Analysis

The synthetic mixture was prepared by mixing 250 mg of Paracetamol, 5 mg of Cetirizine, 20 mg of Dextromethorphan, 130 mg of lactose, 40 mg of talc, 50 mg of starch and 5 mg of magnesium stearate by geometric dilution, triturated well using a mortar and pestle. An amount equivalent to 250 mg of drug PTM was weighed from the mixture and transferred to a 100 ml standard flask and diluted with 30 ml of distilled water.

Table 1: Analysis data of synthetic mixture

Parameters	PCM	CTZ	DTM
Drug Content[a]	100.6	98.6	98.6
± SD	0.3	0.529	0.577
% RSD	0.298	0.536	0.584
SE	0.173	0.305	0.333

Amount of drug in synthetic mixture (mg/500 mg) – 250 - PCM, 5 - CTZ and 20 – DTM, a – Value for Drug Content (%) is the mean of 5 estimations; SD – Standard Deviation; RSD – Relative Standard Deviation; SE – Standard Error of mean.

This solution was sonicated for 15 mins, final volume was made up to the mark with distilled water. The extracts were filtered through whatmann no. 41 filter paper. The sample solutions of 10 ml of each were prepared in water by transferring appropriate amount of each filtrate to obtain an equimolar solution containing 6.25 µg/ml, 0.125 µg/ml and 0.5 µg/ml of PCM, CTZ and DTM respectively. The solutions were scanned in second derivative mode and the results were recorded (Table 1).

(5) Validation of the developed method

The method was validated according to International Conference on Harmonization (ICH) Q2B guidelines for validation of analytical procedures in order to determine linearity, sensitivity, accuracy and precision for each analyte. Both precision and accuracy were determined with standard samples prepared in triplicates at different concentration levels covering the entire linearity range.

RESULTS AND DISCUSSION

Linearity

The linearity range was optimized with 6.25 – 50 µg/ml, 0.125 – 1.0 µg/ml and 0.5 – 4.0 µg/ml for PCM, CTZ and DTM respectively. Linear regression analysis of the responses (y) on the theoretical concentrations (x) gave the following equations: at 267.72 nm, y = 0.003x + 0.001 (for PCM, r^2 = 0.999); at 232.71 nm, y = 0.081x + 0.001 (for CTZ, r^2 = 0.998); at 292.68 nm, y = 0.011x + 0.002 (for DTM, r^2 = 0.998) for the proposed method.

Accuracy

The validity and reliability of the proposed method was assessed by recovery studies by standard addition method. The results are shown in Table 2. The SD value for the mean of recovery (%) was found to be less than 2.0, which indicate excellent recovery ranging from 98.0 to 100.9 %. These results reveal that any small change in the drug concentration can be accurately determined by the proposed method.

Table 2: Results of Recovery studies

Drug	Amount taken (µg/ml)	Amount Added (µg/ml)	% Recovery* ± SD
PCM	12.5	6.25	100.9 ± 0.051
		12.5	99.5 ± 0.062
		18.75	99.6 ± 0.043
CTZ	0.25	0.125	101.3 ± 0.06
		0.25	98.6 ± 0.043
		0.375	98.7 ± 0.061
DTM	1.0	0.5	99.2 ± 0.012
		1.0	99.5 ± 0.034
		1.5	99.6 ± 0.023

* - Mean of five determinations; SD – Standard Deviation

Precision

Precision was determined by studying the repeatability and intermediate precision. Repeatability results indicate the precision under the same operating conditions over the short interval time and inter-assay precision. The intermediate precision study is expressed within the laboratory variation on different days. The % RSD for both inter and intra day precision was not more than 2 % which indicates excellent repeatability and good intermediate precision. The results are presented in Table 3.

LOD and LOQ

The values of LOD and LOQ were found to be 0.714 and 2.165 µg/ml for PCM, 0.023 and 0.071 µg/ml for CTZ and 0.136 and 0.412 µg/ml for DTM respectively.

Assay of synthetic mixture

The assay values of PCM, CTZ and DTM were found to be 100.5, 98.1 and 98.6 respectively. The standard deviation value for all drugs was found to be less than 1.0. The assay values indicate that interference of excipients is insignificant in the estimation of PCM, CTZ and DTM by the proposed method. The results of analysis are shown in Table 1.

Table 3: Optical characteristics and validation data of PCM, CTZ and DTM

Parameters	PCM	CTZ	DTM
Wavelength (nm)	267.72	232.71	292.68
Linearity range (µg/ml)	6.25 – 50	0.125 – 1.0	0.5 – 4.0
Precision			
Intra day precision (% RSD)*	0.296	0.0855	0.0324
Inter day precision (% RSD)*	0.323	0.0677	0.0329
LOD (µg/ml)	0.714	0.023	0.136
LOQ (µg/ml)	2.165	0.071	0.412
Regression values			
Slope	0.003	0.081	0.011
Intercept	0.001	0.001	0.002
Correlation Coefficient (r^2)	0.999	0.998	0.998

* - Mean of five determinations; LOD – Limit of Detection; LOQ – Limit of Quantification

CONCLUSION

The proposed second derivative method for simultaneous estimation of PCM, CTZ and DTM is simple, rapid and precise. It employs the use of UV Visible spectrophotometer, which is easy to perform. Hence the proposed method can be used for routine quality control analysis of these drugs in pure and dosage forms.

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