ASIAN JOURNAL OF PHARMACY & LIFE SCIENCE

Simultaneously Estimation of Paracetamol, Aceclofenac and Rabeprazole in Tablet Dosage Form Using UV Spectroscopy

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ABSTRACT

Paracetamol {N- (4-hydroxyphenyl) acetamide} and Aceclofenac {2-[(2, 6-dichlorophenyl) amino] phenyl acetoxy acetic acid} are NSAIDs which acts by inhibiting the synthesis of prostaglandins. Rabeprazole {2-[(4-(3-methoxypropoxy)-3-methyl-pyridine–2-yl) Methylsulfinyl- 1H benzoimidazole} is an anti ulcer drug which is a proton pump inhibitor. No spectroscopic method has been reported for the Simultaneous estimation of Paracetamol, Aceclofenac and Rabeprazole in Combined Tablet Dosage Formulation. Hence simple, sensitive, reliable and rapid spectroscopic methods have been developed for the determination of paracetamol, aceclofenac and rabeprazole in combined tablet dosage form. Determinations were performed on Shimadzu UV-Visible double beam recording spectrophotometer (Model UV-1700). The linearity of paracetamol, aceclofenac and rabeprazole was found to be 3-30µg/ml, 2-20 µg/ml, and 2-20µg/ml respectively. The stability of the solution was found to be 72 hrs. The method was validated for accuracy, precision, repeatability as per ICH Guidelines. This method can be used commercially for routine estimation of various compounds in pharmaceutical dosage forms.

Key-words – Paracetamol, aceclofenac, rabeprazole, multi-component, derivative spectroscopy, validation.

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Received: 27/05/11 Accepted: 12/07/11

INTRODUCTION

Combination of paracetamol (PCM), aceclofenac (ACF) and rabeprazole (RAB), in the tablet dosage form is widely used as an analgesic. The official monograph describes the procedure for individual assay of PCM [1], [2] and ACF [3], where as RAB is not official in any pharmacopoeia. The IP (1996) and BP (2003) both suggest titrimetric and UV spectrophotometric assay method for PCM in bulk and tablet formulations. Literature survey revealed that HPLC [4] , densitometric [5] , spectrofluorimetric [6] and colorimetric [7] methods have been reported for the estimation of ACF in pharmaceutical dosage forms. Method for simultaneous analysis of PCM and ACF by UV spectroscopy [8] and RP-HPLC [9] has been reported. But no method was reported on the combination of PCM, ACF and RAB.

In the present study, methods for simultaneous quantification methodology of PCM, ACF and RAB in tablet by UV spectroscopy were developed and the developed methods were validated as per ICH guideline. [10], [11]

MATERIALS AND METHODS

Instrumental:

Analysis were carried out on SHIMADZU UV 1601 UV-VIS spectrophotometer, a double beam high speed scanning spectrophotometer with a photomultiplier tube detector and having spectral bandwidth of 1nm (190.0nm to 900.0nm.)

Chemicals and reagents:

PCM, ACF and RAB were received as gratis sample by Ipca Laboratories Ltd., India, Commercial tablets containing PCM (500mg), ACF (100mg), and RAB (10mg) Ace-Proxyvon (Wockhardt Pharmaceuticals Ltd, India) were used for study. All the chemicals used were of analytical grade (E. Merck, India.)

Low concentration of RAB in the dosage necessitate the requirement of its spiking (10 times) to produce appropriate absorbance, same stock solution were used to spike the concentration of RAB in mixed standard analysis and analysis of commercial preparation and all the apparatus were calibrated before use.

METHOD - I

Multi-component method -

Standard solutions:

Three stock solutions were prepared by dissolving 50, 10, and 1mg (spiked to 10 mg) of PCM RAB and RAB in 100 ml of methanol respectively and again 1 mg of the above solution was taken and diluted up to 100 ml, in this solution the concentration of RAB was spiked to 10 times. Six mixed standards were prepared from the stock solution with different concentration ranging from 5-30, 2-12 and 2-12 µg/ml of PCM ACF and RAB respectively. All the mixed standard solutions were scanned over the range of 390-190 nm in multi-component mode using three sampling points 249, 276 and 284 nm. These solutions were used to calculate the linear dynamic range and for the relative quantification of tablet.

Sample preparation:

Twenty tablets of Ace-Proxyvon (label claim as containing 500 mg of PCM, 100 mg of ACF and 10 mg of RAB) were weighed, crushed and powder equivalent to 50 mg of PCM, 10 mg of ACF and 1 mg RAB (tablet contains 500 mg PCM, 100 mg ACF and 10 mg RAB) was extracted four time with 20 ml methanol each time and volume was made up to 100 ml. residue was filtered using Whatman grade filter paper.. The filtrate was further diluted and concentration of Rabeprazole was spiked 10 times to get final concentration of all three drugs in the linearity range. Absorbance of tablet preparation was noted at the selected wavelengths.

METHOD II -

Derivative spectroscopy -

Standard solutions:

Stock solution of PCM (100 µg/ml) was prepared by dissolving 100mg of PCM in 75 ml of methanol and the volume was made up to the mark with methanol (1000 µg/ml) . 10 ml of the above solution was diluted up to 100ml with methanol to produce final stock solution of 100 µg/ml of PCM. Standard stock solution of ACF and RAB was prepared similarly as that of PCM. Then the resulting solutions were scanned over the range of 390-190 nm to give their absorbance spectra then their spectra were converted to their first derivative spectra.

Zero crossing wavelength technique was used to select the working wavelength for each of three drugs from the overlay derivative spectra of the PCM, ACF and RAB (fig 1). From the technique the working wavelength was found 271, 257, and 297 for PCM, ACF and RAB respectively.

Sample preparation:

Twenty tablets of Ace-Proxyvon (label claim as containing 500 mg of PCM, 100 mg of ACF and 10 mg of RAB) were weighed, crushed and powder equivalent to 50 mg of PCM, 10 mg of ACF and 1 mg RAB (tablet contains 500 mg PCM, 100 mg ACF and 10 mg RAB) was extracted four time with 20 ml methanol each time and volume was made up to 100 ml. residue was filtered using Whatman grade filter paper.. The filtrate was further diluted and concentration of Rabeprazole was spiked 10 times to get final concentration of all three drugs in the linearity range. Resulting solutions were scanned over a range of 390-190 nm and the resulting absorbance spectra were converted to first derivative spectra and absorbance of all three drug were measured at their respective zero crossing wavelength points, Table 2.

RESULTS AND DISCUSSION

The reproducibility, repeatability and accuracy of the proposed method were found to be satisfactory (Table 3) which is evidenced by low values of standard deviation, percent relative standard deviation and standard error. The percent range of error (within 95% confidence limits) showed precision of the method. The accuracy and reproducibility of the proposed method was confirmed by recovery experiments, performed by adding known amount of the drugs to the pre analyzed formulations and reanalyzing the mixture by proposed method. The percent recovery obtained indicates non-interference from the excipients used in the formulations. Thus the method developed in the present investigation found to be simple, sensitive, accurate and precise and can be successfully applied for the simultaneous estimation of PCM, ACF and RAB in tablets.

TABLE 1: QUANTIFICATION PARAMETERS OF PCM, ACF AND RAB.

S. No.	Drug	Mean %± S.D.	% CV	S.E.
1.	PCM	99.00±1.19	1.19	0.532
2.	ACF	99.52±0.454	0.45	0.203
3	RAB	100.38±1.19	1.19	0.532

TABLE 2: QUANTIFICATION PARAMETERS OF PCM, ACF AND RAB.

S. No.	Drug	Mean %± S.D.	% CV	S.E.
1.	PCM	99.11±0.407	0.43	0.23
2.	ACF	99.54±0.501	0.50	0.29
3	RAB	99.37±0.371	0.37	0.31

TABLE 3: VALIDATION OF DEVELOPED METHODS

S.N.	Validation Parameter	Method (Mean %± S.D.)					
		Multi-component			Derivative spectroscopy		
		PCM	ACF	RAB	PCM	ACF	RAB
1	Linearity Range	2-30 µg/ml	5-70 µg/ml	4-60 µg/ml	2-30 µg/ml	5-70 µg/ml	4-60 µg/ml
2	Accuracy	99..13 ± 1.19	99.52 ± 0.454	100.38 ± 1.19	99.02± 1.18	99.44± 1.071	99.36± 0.71
3	Precision, Intraday	99.52±0.370			99.49±0.485		
	Interday	99.52±0.370			99.72±0.445		
4	Recovery 80%	99.11± 0.358	99.54± 0.501	99.37± 0.371	99.11± 0.407	99.54± 0.501	99.37± 0.371
	100%	99.26± 0.489	99.56± 0.501	99.37± 0.501	99.26± 0.462	99.56± 0.501	99.37± 0.501
	120%	98.80± 0.553	99.09± 0.490	98.42± 0.587	98.80± 0.568	99.09± 0.490	98.42± 0.587
5	LOD (µg/ml)	0.32	0.76	0.52	1.015	2.48	6.6
6	LOQ (µg/ml)	0.95	2.31	1.60	3.15	3.15	20.0

7	Robustness	98.52± 0.438	99.38± 0.794	99.67 ± 0.454	98.62± 0.38	99.36± 0.24	99.81± 0.18

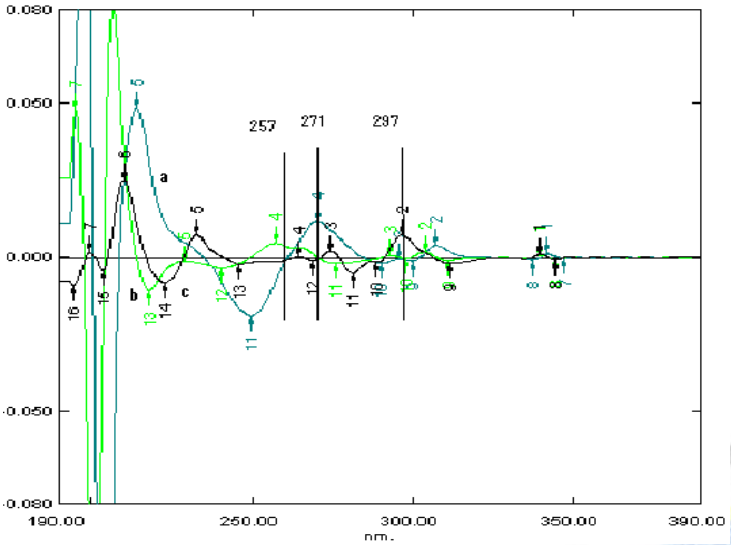

FIG 1: FIRST ORDER DERIVATIVE OVERLAY SPECTRA OF PCM (a), ACF (b) & RAB(c).

ACKNOWLEDGEMENTS

The authors are thankful to Ipca laboratories, Mumbai for providing gift samples of aceclofenac and paracetamol and Cadila Pharmaceuticals Ltd., Ahmedabad for providing a gift sample of rabepracole. The authors are grateful to College of pharmacy, IPS academy, Indore for providing facilities to carry out this work.

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