International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.5, No.4, pp 1802-1807, April-June 2013

Simultaneous Estimation Of Paracetamol And Pamabrom Inbulk Drugs And In Pharmaceutical Formulation By Spectrophotometry

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Abstract: Two simple, rapid, precise and accurate spectrophotometric methods have been developed for simultaneous analysis of Paracetamol (PCM) and Pamabrom in bulk drugs and pharmaceutical formulation. MethodA, Second derivative zero crossing spectrophotometry which involve conversion of zero order spectra into second order derivative spectra and measure zero cross points, at 227 nm PCM has zero cross point so Pamabrom can be measured and at 268 nm Pamabrom has zero crossing point so PCM can be measured. The concentrations can be calculated from the derived equations. Method B, Single divisor ratio derivative spectrophotometry, in which zero order spectra of one drug was divided by minimum concentration of other drug which give higher R^2 value and ratio spectra of drug was converted into first order spectra for better visualisation.Amplitude at 270.9 nm and 231.9 nm were selected in the ratio derivative spectra to determine Pamabrom and PCM, respectively Developed methods werevalidated according to ICH guidelinesQ2 (R_1)[11]. The calibration graph follows Beer's law in the range of 1 to 35µg/ml forPamabrom and 5.0 to 30 µg/ml for PCM with R^2 value greater than 0.999. Accuracy of all methods wasdetermined by recovery studies and showed % recovery between 98 to 102%. Intraday and interday precision waschecked for all methods and mean %RSD was found to be less than 2 for all the methods. The methods weresuccessfully applied for estimation of Pamabrom and PCM in pharmaceutical formulation.

Key Words: Paracetamol, Pamabrom,Second Derivative Spectrophotometry, Single Divisor Ratio Spectrophotometry.

INTRODUCTION:

Paracetamol (PCM), [8] [1] [2] [3] chemically it is N-(4-hydroxyphenyl) acetamide (Fig. 1); it is classified as a mild analgesics. PCM is official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United States Pharmacopoeia (USP).

Pamabrom[7][3] chemically it is 8-Bromotheophylline compound with 2-amino-2-methyl-1-propanol (1:1) (Fig. 2), is a diuretic, available in combination with acetaminophen (Paracetamol) for various conditions such as back pain and menstrual relief. Pamabrom is official in US Pharmacopoeia.

Survey of literature revealed that number of methods has been reported in literature for the individual analysis of PCM and Pamabrom by UV spectrophotometric and RP-HPLC method.UV spectrophotometric method available in literature for simultaneous determination of PCM with other drugs like Diclophenac sodium [4], Meloxicam [5], Tizanidine [6]. However, to our knowledge, there is no reported u.v-spectrophotometric method available for simultaneous estimation of PCM and Pamabrom.

The aim of the present work was to develop easy, economic, accurate, specific and precise spectrophotometric methods for simultaneous estimation of PCM and Pamabrom in bulk drugs and pharmaceutical formulation and validation of newly developed analytical methods.

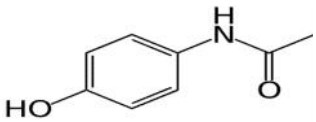

Fig.1 Paracetamol

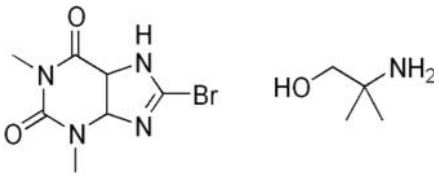

Fig. 2 Pamabrom

EXPERIMENTAL:

Apparatus And Software: Shimadzu UV-1700 double beam spectrophotometer connected to a computer loaded with Shimadzu UVProbe 2.10 software was used for all the spectrophotometric measurements. The absorbance spectra of the reference and test solutions were carried out in 1cm quartz cells over the range of 200-400 nm. The samples were weighed on electronicanalytical balance (A×120, shimadzu).

Preparation Of Stock Solution: Accurately weighed PCM and Pamabrom (in quantities of 25.0 mg) were transferred to two separate 25 ml volumetric flasks, dissolved with the use of water and volume was made up to the mark with water to obtain stock solution of PCM(1000 µg/ml) and Pamabrom (1000 µg/ml)

Preparation Of Working Standard Solution: From the above solution, standard stocks solutions of PCM (100 µg/ml) and Pamabrom (100 µg/ml) were prepared by transferring 5 ml aliquots to 50 ml volumetric flasks and making up the volume with water.

Preparation Of Calibration Curve Of Standard PCM And Pamabrom: From working std. solution of PCM (100 µg/ml) 1.3, 1.56, 1.82, 2.08 and 2.34 ml were transferred to 10 ml volumetric flasks and volume were made up to the mark with water. This gives 13 to 23.4 µg/ml of PCM. From working std. solution of Pamabrom (100 µg/ml) 0.1, 0.12,0.14,0.16 and 0.18 ml were transferred to 10 ml volumetric flasks and volume were made up to the mark with water. This gives 1.0 to 1.8 µg/ml of Pamabrom.

Method A-

Second Derivative Zero Crossing Spectrophotometry [10]:

The solutions of standard PCM and Pamabrom were prepared in the range of 13 to 23.4 µg/ml and 1 to 1.8 µg/ml respectively. The absorption spectra of the solutions of PCM and Pamabrom were recorded in the range of 200 nm to 400 nm and were stored in the memory of the instrument and transformed to second derivative with $\Delta\lambda$ = 8 nm and scaling factor 100. At 227nm, PCM, having zero crossing point and Pamabrom can be determined. At 268 nm, Pamabrom, having zero crossing point and PCM can be determined. The amplitudes at 227 nm were plotted against respective concentrations of Pamabrom and the amplitudes at 268nm were plotted against the respective concentrations of PCM for the preparation of calibration graph.

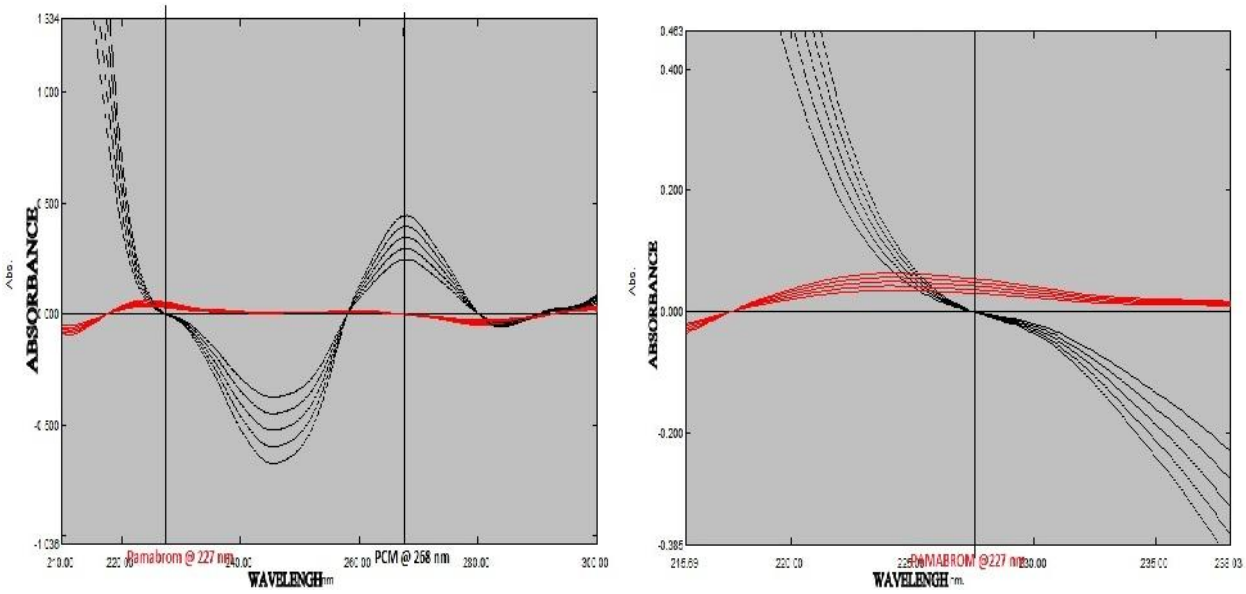

Fig -3.1 and 3.2, Zero order overlain spectra of PCM (13, 15.6, 18.2, 20.8 and 23.4 µg/ml, black) and Pamabrom (1, 1.2, 1.4, 1.6 and 1.8 µg/ml, red)

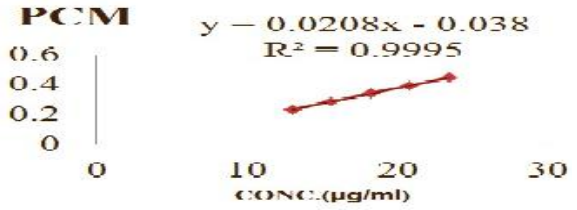

Fig. – 4.1 Calibration graph of PCM.

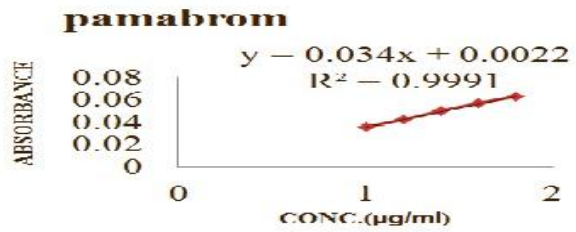

Fig. – 4.2 Calibration graph of Pamabrom.

Method B-

Single Divisor Ratio Derivative Method[10]:

The spectra of PCM and Pamabrom were divided by one standard spectrum of PCM and Pamabrom respectively. For selecting the standard solution as divisor, appropriate concentrations of PCM and Pamabrom were tested and based on better coefficient of correlation, 1.2 µg/ml of Pamabrom and 13 µg/ml of PCM were selected as divisor. The spectra of PCM (5 to 30 µg/ml) were divided by standard spectrum of 1.2 µg/ml Pamabrom to obtain ratio spectra. These ratio spectra were derivatised with $\Delta\lambda$ = 8 nm and scaling factor 100. Analytical wavelength of 231.9 nm was selected because of higher correlation co efficient for estimation of PCM. Similarly, the spectra of Pamabrom (1 to 35 µg/ml) were divided by standard spectrum of 13 µg/ml PCM and derivatised with $\Delta\lambda$ = 8 nm and scaling factor 100. For estimation of Pamabrom, analytical wavelength of 270.9 nm was selected.

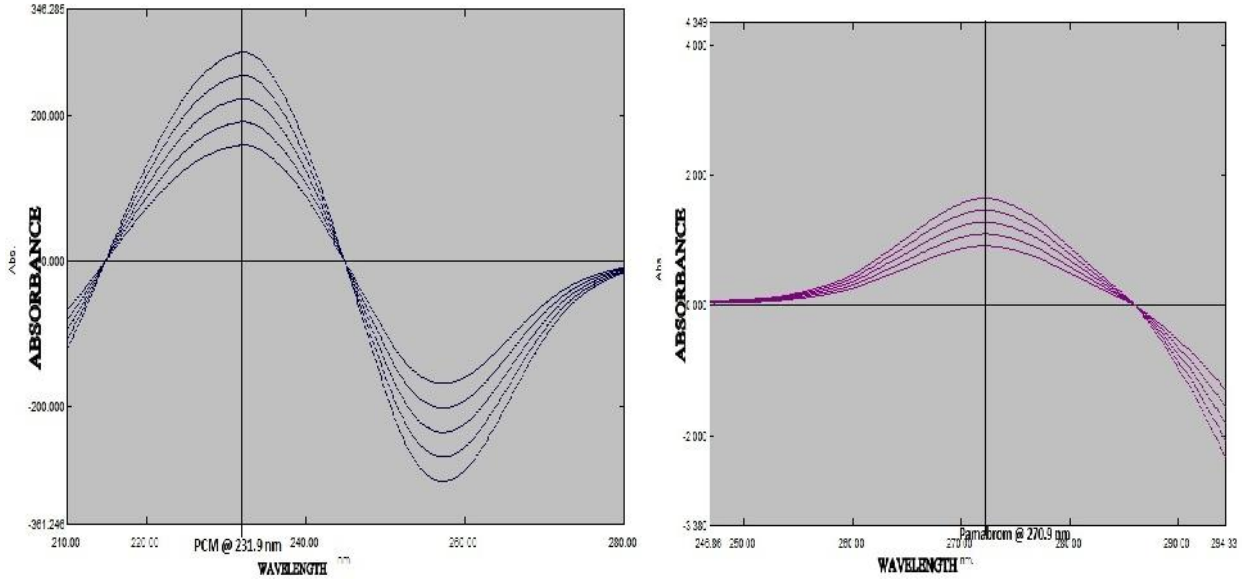

Fig -5.1 Ratio der. overlain spectra of PCM (13, 15.6, 18.2, 20.8, 23.4 µg/ml, blue) and Pamabrom (1, 1.2, 1.4, 1.6, 1.8 µg/ml, violet).

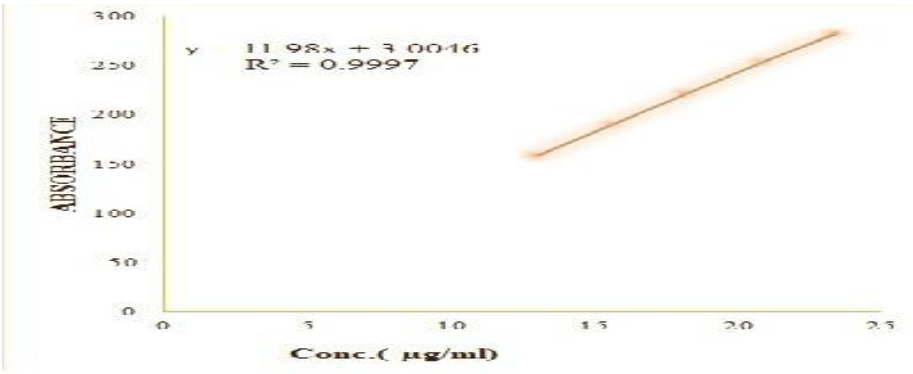

Fig. – 6.1 Calibration graph of PCM at 231.9 nm

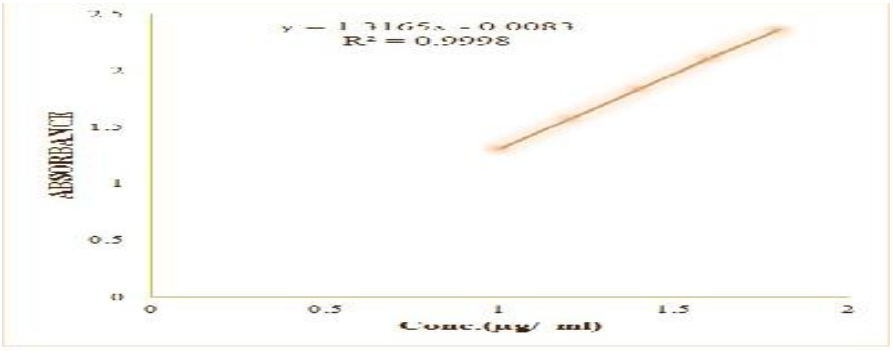

Fig. – 6.2 Calibration graph of Pamabrom at 270.9 nm.

Assay of pharmaceutical formulation by Method A and B:

20 tablets were powdered and an amount equivalent to 32.5 mg PCM and 2.5 mg Pamabrom was weighed and dissolved in 100 ml water. Solutions were filtered using whatmann filter paper grade 1. Appropriate dilutions were prepared in water, taking suitable aliquots of the clear filtrates and subjected to analysis using all the four methods described above. The result of analysis is reported (Table 1).

Table 1: Results of Simultaneous Estimation of Marketed Formulation for Method A and B:

Formulation:- Fem Relief Tablets		
Labeled Claim :- PCM : Pamabrom (325 mg : 25mg)		
Method	**PCM*±SD**	**Pamabrom*±SD**
A	99.71 ± 1.34	101.18 ± 0.92
B	100.12 ± 0.77	99.36 ± 1.32

*****Mean value of five determinations

RESULTS AND DISCUSSION:

Developed spectrophotometric methods for the simultaneous estimation of PCM and Pamabrom were validated according to ICH guidelines Q2 (R_1) [11] and data complying with the standards were obtained[11]. The results of validation parameters for all the three developed methods are reported (Table 2 and 3).

Table 2: Summary of Validation Parameters by Developed Methods:

Parameters	**Method - A**		**Method - B**	
	PCM	**Pamabrom**	**PCM**	**Pamabrom**
Analytical wavelength (nm)	268	227	231.9	270
Beer's range (µg/ml)	5-30	1-35	5-30	1-35
Slope	0.0208	0.034	11.98	1.3165
Intercept	0.038	0.0022	3.0046	-0.0083
Correlation coefficient	0.9995	0.9991	0.9997	0.9998
Intraday precision (%RSD)	0.5996	0.7671	0.699	0.7599
Interday precision (%RSD)	0.7468	1.5306	0.8304	1.2873
LOD (µg/ml)	0.9538	0.1929	1.2834	0.1336
LOQ (µg/ml)	2.86	0.5728	3.8502	0.40086

Table 3: Results Of Recovery Study Of Pcm And Pam By Developed Methods

Method	**% Spiking**	**C_{ACTUAL}** µg/ml		**C_{ADDED}** µg/ml		**C_{FOUND}*** µg/ml		**%Recovery ± S.D.**	
		PCM	**PAM**	**PCM**	**PAM**	**PCM**	**PAM**	**PCM**	**Pamabrom**
A	**50**	13	1	6.5	0.5	19.34	1.49	99.17±0.0765	99.33±0.1061
	100	13	1	13	1	26.39	2.01	101.5±0.0406	100.49±0.1768
	150	13	1	19.5	1.5	32.6	2.48	100.30±0.1267	99.2±0.0778
B	**50**	13	1	6.5	0.5	19.38	1.48	99.38±0.0768	98.66±0.0644
	100	13	1	13	1	26.52	1.99	102±0.1353	99.5±0.1058
	150	13	1	19.5	1.5	32.2	2.53	99.07±0.0557	101.2±0.1127

* Mean of three determinations

CONCLUSION:

TwoSpectrophotometric methods (Second derivative zero crossing spectrophotometry and single divisor Ratio spectrophotometry) were developed for simultaneous estimation of PCM and Pamabrom inbulk drugs and pharmaceutical formulation. Methods were found to be precise and accurate as can be reflected from validation data. Developed methods were successfully applied for estimation of PCM and Pamabrom in pharmaceutical formulation.

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