

## Q-Absorbance Ratio Spectrophotometric Method for the Simultaneous Estimation of Paracetamol and Propyphenazone in their Combined Pharmaceutical Dosage Form

**Mehul G. Kakdiya\***, Viral M. Kakdiya, Darshan Madiya  
 Department of Quality Assurance,  
 Smt. R. D. Gardi B. Pharmacy College, Rajkot, Gujarat, India  
 \*kakdiyamehul@gmail.com



### ABSTRACT

The present manuscript describes simple, sensitive, rapid, accurate, precise and economical Q-absorbance ratio method for the simultaneous determination of Paracetamol and Propyphenazone in their combined pharmaceutical dosage form. Absorbance ratio method uses the ratio of absorbance at two selected wavelengths, one which is an isoabsorptive point and other being the  $\lambda$ -max of one of the two components. Paracetamol and Propyphenazone show an isoabsorptive point at 264 nm in methanol. The second wavelength used is 249 nm, which is the  $\lambda$ -max of Paracetamol in methanol. The linearity was obtained in the concentration range of 1-12  $\mu\text{g/ml}$  for Paracetamol and 5-24  $\mu\text{g/ml}$  for Propyphenazone. The concentrations of the drugs were determined by using ratio of absorbance at isoabsorptive point and at the  $\lambda$ -max of Paracetamol. The method was successfully applied to pharmaceutical dosage form because of no interference. The results of analysis have been validated by recovery studies.

**Keywords:** Paracetamol, Propyphenazone, Methanol, Q-Absorbance Ratio method

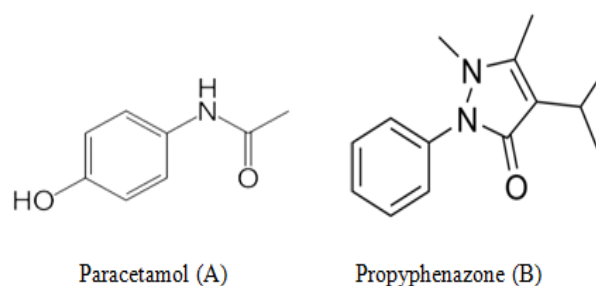
### INTRODUCTION

Paracetamol (PCM) is chemically 4-hydroxyacetanilide (Figure 1-A)<sup>[1]</sup>. paracetamol is common analgesic that is used for the relief of fever, headaches, and other minor aches and pains.<sup>[2]</sup>

Propyphenazone (PP) , is a pyrazolone derivative having mainly anti-inflammatory, analgesic, and anti-pyretic activity, introduced in 1951 for the treatment of rheumatoid disorders<sup>[3]</sup>

Both drug showing the mechanism through inhibiting the cyclo oxygenase enzyme involved in prostaglandin synthesis.<sup>[1,2]</sup>

The chemical structures of Paracetamol and Propyphenazone are shown in Figure 1 (A), (B).<sup>[1,3]</sup>



**Figure-1:** Chemical structure of (A) Paracetamol and (B) Propyphenazone

Paracetamol is official in all major compendia like IP, BP and USP and is estimated by UV-Visible Spectrophotometric method as per IP, USP and BP. <sup>[4,5,6]</sup> Propyphenazone is official in IP, BP Pharmacopoeia but not in USP.<sup>[4,5]</sup> It is assayed by potentiometrically as per IP, BP.

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Literature review also reveals HPLC, UV spectrophotometric and HPTLC method for the estimation of PCM with other drugs are available today.<sup>[7,8,9]</sup> Literature survey does not reveal any simple spectrophotometric method of Paracetamol and Propyphenazone in Pharmaceutical dosage form. So the objective of this work was to develop simple and economical method and validate that method.

## MATERIALS AND METHODS

### Instrumentation

Double beam UV-visible spectrophotometer (helios Alpha, Model - V 7.09) having two matched quartz cells with 1 cm light path. An Electronic analytical balance (Contech, CA34 Model) was used in the study.

### Material and reagent

Paracetamol (PCM) was obtained from Meghmani pharma pvt. ltd. and Propyphenazone (PP) bulk powder was kindly gifted by Vani pharma Pvt. Ltd, Hyderabad. Methanol reagent was supplied by college.

### Preparation of Standard Stock solution of PCM and PP:

Accurately weighed quantity 100 mg of PCM and PP were transferred into separate 100 ml volumetric flask, dissolved and diluted up to mark with Methanol (100 ml). This will give a stock solution having strength of 1000 µg/ml of each.

### Preparation of Working Standard Solution of PCM and PP:

100 µg/ml of PCM and PP solution were prepared by diluting 10 ml of stock solution to 100 ml with Methanol in separate 100 ml volumetric flask.

Suitable aliquots of this solution were diluted up to the mark with Methanol to get the concentration range of 1, 3, 5, 7, 9 µg/ml for PCM and 7, 11, 15, 19, 23 µg/ml for PP.

### Selection of analytical wavelength:

From working standard solution of PCM (100 µg/ml) and PP (100 µg/ml), prepare 10 µg/ml for PCM and PP both. The scanning for solution of PCM and PP were carried out in the range of 200-400 nm against using Methanol as a blank. The maximum absorption ( $\lambda_{max}$ ) of PCM was found at 249 nm and iso-absorptive point at 264 nm. Absorption and absorptivity for a series of standard solutions were recorded at selected wavelengths.

### Preparation of calibration curve:

Standard solutions of PCM in the concentration range of 1 to 12 µg/ml obtained by transferring (0.1, 0.3, 0.5, 0.7, 0.9 ml) of PCM stock solution (100 µg/ml) to the series of 10 ml volumetric flasks and standard solutions of PP in the concentration range of 5 to 24 µg/ml were obtained by transferring (0.7, 1.1, 1.5, 1.9, 2.3 ml) of PP stock solution (100 µg/ml) to the series of 10 ml volumetric flasks. Then volume was adjusted up-to mark with Methanol. All dilutions were scanned in wavelength range of 200 nm to 400 nm. The absorbance was plotted against the respective concentrations to obtain the calibration curves.

## VALIDATION PARAMETERS

Validation of developed method was carried out as per ICH guideline.<sup>[10]</sup> Parameters such as Linearity and range, Accuracy, Precision, LOD and LOQ were taken up as tests for analytical method validation.

### Linearity and Range:

Linearity is expressed in terms of correlation coefficient of linear regression analysis. The linearity responses was determined in the range of 1-12 µg/ml for PCM and 5-24 µg/ml for PP. Plot the calibration curve of absorbance verses concentration at specified wavelength and determine correlation coefficient and regression equations for PCM and PP.

### Precision

Precision of the method was determined in the terms of Repeatability, Intraday and Interday precision. Repeatability (% RSD) was assessed by analyzing test drug solution within the calibration range, six times on the same day. Intraday variation (% RSD) was determined by analysis of this solution three times on the same day. Interday precision (%RSD) was determined by analysis of this solution on three different days.

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

They were calculated as  $3.3 \sigma/S$  and  $10 \sigma/S$  respectively. Where  $\sigma$  is the standard deviation of the response (y-intercept) and  $S$ , is the mean of the slope of calibration plot.

### Recovery Studies:

Recovery studies were done so as to check the accuracy of the method. Known amounts of standard solutions of PCM and PP were added to pre-quantified sample solutions of PCM and PP and absorbance were determined at 264nm and 249nm. Concentration of the drug in the mixture was calculated using the equations. The analysis was done in a set of 3 replicates.

### Application of Proposed Method to dosage form:

The powder of 20 Tablets were weighed. An accurately weighed quantity of the powder equivalent to about 100 mg of Paracetamol and 100 mg of Propyphenazone was taken in 100 ml volumetric flask and dissolved with methanol and further diluted upto the mark with same solvent. The solutions were then filtered through the Whatmann filter paper No. 41. Necessary dilutions are made with methanol to give final concentration of  $10 \mu\text{g/ml}$  of PCM and  $10 \mu\text{g/ml}$  of PP respectively. The solutions are then scanned between 200-400nm and absorbances are measured at respective wavelengths.

### Formation of Simultaneous Equation:<sup>[11]</sup>

A set of two equations were framed using the mean absorptivity.

$$C_x = \frac{Q_m - Q_y}{Q_x - Q_y} * \frac{A_1}{ax_1}$$

$$C_y = \frac{Q_m - Q_x}{Q_y - Q_x} * \frac{A_1}{ay_1}$$

$$Q_m = \frac{\text{Absorbance of sample solution at 249 nm (A2)}}{\text{Absorbance of sample solution at 264 nm (A1)}}$$

$$Q_x = \frac{\text{Absorptivity of PCM at 249 nm}}{\text{Absorptivity of PCM at 264 nm}}$$

$$Q_y = \frac{\text{Absorptivity of PP at 249 nm}}{\text{Absorptivity of PP at 264 nm}}$$

Where,  $Q_x$  and  $Q_y$  are value of PCM and PP respectively,  $ax_1$  and  $ay_1$  are absorptivity value at iso-absorptive point for PCM and PP.

## RESULTS AND DISCUSSION

### Absorption Maxima:

Iso-absorptive wavelength of PCM (10 ppm) and PP (10 ppm) were recorded as 264 nm ( $\lambda_1$ ) and overlain spectra were recorded in Fig: 2. 249 nm wavelength was used as  $\lambda_2$ . Regression characteristics for PCM and PP are shown in Table 4.

### Method Validation:

The linearity range for PCM and PP were 1-12  $\mu\text{g/mL}$  and 5-24  $\mu\text{g/mL}$  respectively. Recovery studies was carried out by addition of standard drug solution to pre-analyzed dosage form solution at three different concentration levels taking into consideration percentage purity of added bulk drug sample. The results of the recovery studies are found to besatisfactory for PCM and PP and shown in Table 1 and 2 respectively. The result of assay procedure obtained was showed in Table 3. Summary of Other validation parameters including Repeatability, Intraday, Interday, LOD and LOQ were found to be satisfactory and are shown in Table 5.

## CONCLUSION

The proposed dosage form chosen with justification like in earlier days paracetamol formulation comes in very large dose amount of PCM so by adding another NSAID to existing one is also new approach and we can minimize dose of individual drug.

The results obtained by such procedures, it is proved that the proposed method is accurate, precise, simple and economical and can be applied successfully for routine analysis for the estimation of PCM and PP in their combined

pharmaceutical dosage form as well as in bulk dosage form. The developed method was validated as per ICH guidelines.

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## Figures and tables

Figure-2: Overlain Spectrum of Paracetamol and Propyphenazone in methanol

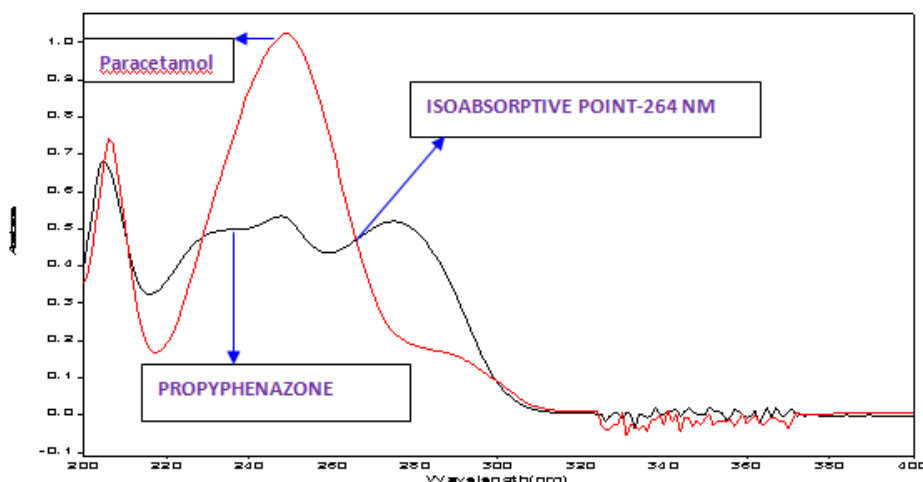


Table-1 Result of Recovery Studies for PCM in Dosage form:

Amount of PCM in mixture (µg/ml)	Amount of Std PCM added (µg/ml)	Total amount of PCM (µg/ml)	Total amount of PCM found (µg/ml) Mean* ± SD	%Recovery
3	0	3	2.96 ± 0.0331	98.66
3	2.4	5.4	5.41 ± 0.079	100.201
3	3	6	6.03 ± 0.099	100.526
3	3.6	6.6	6.54 ± 0.019	99.122

[\*=mean value of 3 determination]

Table-2 Result of Recovery Studies for PP in Dosage form:

Amount of PP in Mixture ( $\mu\text{g/ml}$ )	Amount of Std PP added ( $\mu\text{g/ml}$ )	Total amount of PP ( $\mu\text{g/ml}$ )	Total amount OfPP found ( $\mu\text{g/ml}$ ) Mean* $\pm$ SD	%Recovery
11	0	11	10.94 $\pm$ 0.1081	99.4545
11	8.8	19.8	20.29 $\pm$ 0.1201	102.491
11	11	22	22.29 $\pm$ 0.4101	101.318
11	13.2	24.2	24.56 $\pm$ 0.1069	101.487

[\*=mean value of 3 determination]

Table-3: Analysis of PCM and PP in Dosage form:

Tablet dosage form	Label claim(mg)		%Recovery $\pm$ SD (% of label claim*)	
	PCM	PP	PCM	PP
100mg	100mg	100mg	99.8048 $\pm$ 0.7443	102.073 $\pm$ 1.8490

[\*=mean value of 5 determination]

Table-4: Regression Characteristics:

Characteristics	PCM		PP	
	264( $\lambda_1$ )	249( $\lambda_2$ )	264( $\lambda_1$ )	249( $\lambda_2$ )
Wavelength (nm)	264( $\lambda_1$ )	249( $\lambda_2$ )	264( $\lambda_1$ )	249( $\lambda_2$ )
Linearity ( $\mu\text{g/ml}$ )	1-12	1-12	5-24	5-24
Regression Equation	$y = 0.048x + 0.022$	$y = 0.092x + 0.029$	$y = 0.181x - 0.169$	$y = 0.050x - 0.105$
Slope	0.048	0.092	0.181	0.050
$r^2$	0.999	0.997	0.998	0.998
Intercept	0.022	0.029	0.169	0.105
S.D. of Intercept	0.001528	0.001155	0.002646	0.003

TABLE-5: VALIDATION PARAMETERS:

Parameters	PCM		PP	
	264( $\lambda_1$ )	249( $\lambda_2$ )	264( $\lambda_1$ )	249( $\lambda_2$ )
Wavelength(nm)	264( $\lambda_1$ )	249( $\lambda_2$ )	264( $\lambda_1$ )	249( $\lambda_2$ )
Repeatability(%RSD)(n=6)	0.8173	0.6783	0.6026	0.4775
Precision (%RSD)				
Intra-day (n=3)	0.5978-1.2364	0.9541-1.6558	0.8724-1.0388	0.8160-0.9214
Inter-day (n=3)	0.9—1.81	0.36-1.03	0.32-1.54	0.366-1.06
LOD ( $\mu\text{g/ml}$ )	0.107285	0.04188	0.19845	0.20204
LOQ ( $\mu\text{g/ml}$ )	0.3251	0.12692	0.60136	0.612244
% Recovery (n=3)	98.66%-100.52%		99.45%-102.49%	
Assay(mean $\pm$ S.D.)(n=5)	99.80% $\pm$ 0.744		102.07% $\pm$ 1.84	

LOD: Limit of Detection, LOQ: Limit of Quantitation, R.S.D.: Relative standard deviation, S.D.: Standard deviation

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