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Spectrophotometric Determination and Validation of Paracetamol and Mefenamic Acid in Pure and Tablet Dosage Form.

***Pawar P.Y., Jadhav K.B., Thube U.S. and Dhaygude S.M.**

P.D.V.V.P.F's College of Pharmacy, Post - MIDC, Vilad Ghat, Ahmednagar 414111, (MS), India.

Abstract

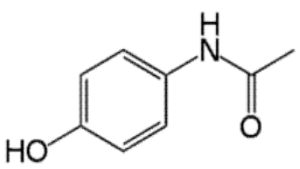
Two simple, precise, accurate and economical UV Spectrophotometric methods have been developed and validated for the routine estimation of Paracetamol (PARA) and Mefenamic acid (MEF) in bulk drug and pharmaceutical preparations. The drug shows maximum absorption at 250nm. and 271nm.Obeyed Beer-Lambert's law in the concentration range of 5-25µg/ml.. The same spectrum was derivatised into first order derivative the amplitude of trough at 231 nm and 255 nm for D_1 were measured. In D_1 method the drug showed linearity in the concentration range of 5-25µg/ml. Recovery studies were carried out by addition of known amount of standard drug (80,100 and 120% of labeled claim of a tablet) to the preanalysed tablet solution. The % recovery was found to be 98.55 & 99.73, which indicates accuracy and reliability of the validated method as well as noninterference from excipients to the developed method. The intraday and inter day assay was within 2%. The methods were then validated statistically as per the ICH guidelines which yielded good results concerning range, precision, accuracy, specificity and repeatability.

Key Words

Paracetamol, Mefenamic acid**,** λmax, Absorbance ratio method and Derivative spectroscopy.

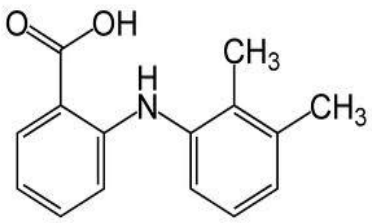
Introduction

Paracetamol (PARA) and Mefenamicacid (MEF) combination is used to treat the mild to Analgesic anti-inflammatory. Several methods have been reported for estimation of drug from Pharmaceutical dosage form. Extensive literature survey reveals that no Spectrophotometric method is available for simultaneous determination of Paracetamol and Mefenamic acid in combined tablet dosage form. Aim of present work was to develop simple, precise, accurate and economical Spectrophotometric methods for simultaneous determination of binary drug formulation. The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines.



Structure of Paracetamol

***Corresponding Author:**
kanchan.jadhav27@gmail.com



Structure of Mefenamic acid

Materials and Methods

UV-visible double beam spectrophotometer, JASCO-V630 with spectral bandwidth of 1 nm, wavelength accuracy of ± 0.3 nm and a pair of 10 mm matched quartz cells were used. The commercially available tablet, (Label claim: Paracetamol450 mg and Mefenamic acid 500 mg) was procured from local market.

Selection of solvent

After assessing the solubility of drugs in different solvents Methanol has been selected as solvent for developing spectral characteristics.

Preparation of standard stock and Calibration curve

The standard stock solutions of drugs was prepared by dissolving 10 mg of drug in 10mL methanol in 10mL volumetric flask, final volume was adjusted with methanol and sonicated for about 10 min to get 100 µg/mL. Working standard solutions of 10 µg/mL were scanned in the entire UV range of 400-200 nm to obtain the absorbance spectra. The absorbance of resulting solutions were measured at respective λmax at 250nm 283 nm plotted a calibration curve against concentration to get the linearity and regression equation. The same spectrum was derivatised into first order derivative, the amplitude of trough at 231 nm, and at 255 nm was measured.

Experimental

Method A: Absorbance ratio method

Two wavelengths selected for the method are 250 nm and 271 nm that are absorption maxima. The stock solutions of both the drugs were further diluted separately with distilled water to get a series of standard solutions of 5-25µg/mL concentrations of Paracetamol and 5-25µg/mL concentrations of Mefenamicacid. The absorbance was measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs at both wavelengths were determined as mean of six independent determinations. Concentrations in the sample were obtained by using following equations,

Cx = (Qm-Qy). A1 / (Qx-Qy).Ax1

Cy = (Qm-Qx). A1 / (Qy-Qx).Ay1

Where; Qm = A2/ A1

Qx = ax2/ ax1

Qy = ay2/ ay1

Where, A1 and A2 are absorbance's of mixture at 250 nm and 283 nm respectively ax1 and ax2 are absorptivities of paracetamol at λ1 and λ2 respectively and ay1 and ay2 are absorptivities of Mefenamic acid.

Method B: Derivative spectroscopy (D^1)

The Zero order spectra of both the drugs were derivatised. The same spectrum was derivatised into first order derivative the amplitude of trough at 231 nm and 255 nm for D_1

were measured. In D_1 method the drug showed linearity in the concentration range of 5-25µg/ml.

Analysis of tablet

Twenty tablets were weighed accurately and reduced to fine powder, drug equivalent to 10mg .of powder was weighed and dissolved in 10 ml of methanol in a 100ml volumetric flask, final volume was made with methanol and sonicated for about 10min. The above solution was filtered by using Whatmann filter paper No.41. Analysis procedure was repeated five times with tablet formulation. Aliquot was scanned in the UV range (200-400nm). The same spectrum was derivatised into first order, amplitude of the trough at 231 nm, and at 255 nm for D_1. The amount of drug present in the tablet was calculated from the standard graphs.

Method Validation

Linearity

Appropriate concentration of stock solution was assayed as per developed methods. Beer-Lambert's concentration range was found to be 5- 25µg/ml.

Accuracy

The accuracy of the methods was determined by performing recovery studies on tablet formulation and for prepared solutions containing known amount of drug by standard addition method in which preanalysed samples were taken and standard drug was added at three different levels 80%.100% and 120% as per ICH guidelines.

Precision

To check the degree of repeatability of methods, suitable statistical evaluation was carried out. Repeatability was performed for five times with tablets formulation. The standard deviation, coefficient of variance and standard error was calculated.

Intermediate Precision (Interday and Intraday precision)

The experiments were repeated three times in a day to determine intraday precision and on three different days to determine interday precision.

Limit of Detection (LOD) and Limit of Quantization (LOQ)

The LOD and LOQ of Paracetamol & Mefenamic acid by proposed methods were determined using calibration standards.LOD and LOQ were calculated as $3.3\sigma/S$ and $10\sigma/S$ respectively, where S is the slope of the calibration curve and σ is the standard deviation of response.

Results and Discussion

The proposed methods are simple, rapid and precise and do not suffer from any interference due to excipients of tablet. The proposed Spectrophotometric methods were found to be linear in the range of 5-25µg/ml at 250 nm and 271 nm. absorbance ratio method with correlation coefficients (R^2) 0.986 and 0.9941 while in D_1 5-25 µg/ml at 231nm.and 255 nm with correlation coefficients (R^2) for D_1were found to be 0.986 and 0.990 respectively. The methods were validated in terms of accuracy, precision, repeatability and the results are recorded in Table. The accuracy of the method was determined by performing recovery

studies by standard addition of method in which preanalysed samples were taken and standard drug was added at three different levels. Values of recovery greater than 98.0% indicate that proposed method is accurate for the analysis of the drug. The precision of the proposed method was estimated in terms of interday precision and intraday precision wherein the method was repeated on three different days and repeated for three different time periods in the same day respectively. The selectivity of the method was checked by monitoring a standard solution of Drugs in presence of excipients at the same concentration level as used in tablet using the method described in the procedure for calibration curve in pharmaceutical tablets. The excipients did not show any effect on the estimation of Paracetamol and Mefenamic acid. Rigorous analysis of the results indicates that the presence of excipients in tablet formulation did not interference with the final determination of the active component. This reveals that the potential utility of this method for the routine analysis of Paracetamol and Mefenamic acid in pharmaceutical preparations.

Conclusion

Two new, simple precise, accurate and selective Spectrophotometric methods were developed for the analysis of Paracetamol and Mefenamic acid in bulk and in pharmaceutical formulation. The Absorbance ratio method is useful for tablet formulations where there is no interference of excipients in the absorbance of Paracetamol and Mefenamic acid, method D_1 can be utilized for formulations containing any interfering excipients. The developed methods were also validated and from the statistical data, it was found that methods were accurate, precise, reproducible and can be successfully applied to the pharmaceutical formulations without interference of excipients.

Acknowledgement

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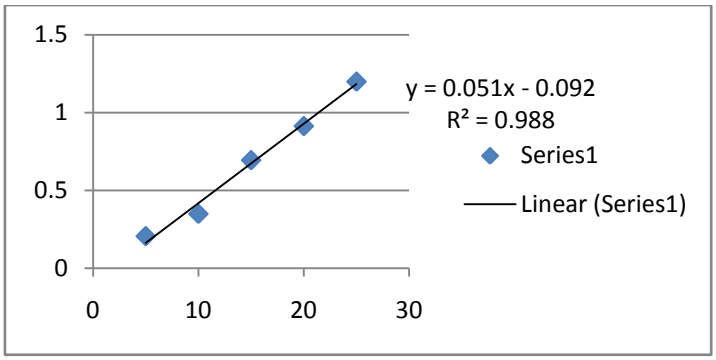

Fig. 1: linearity curve for PARA.

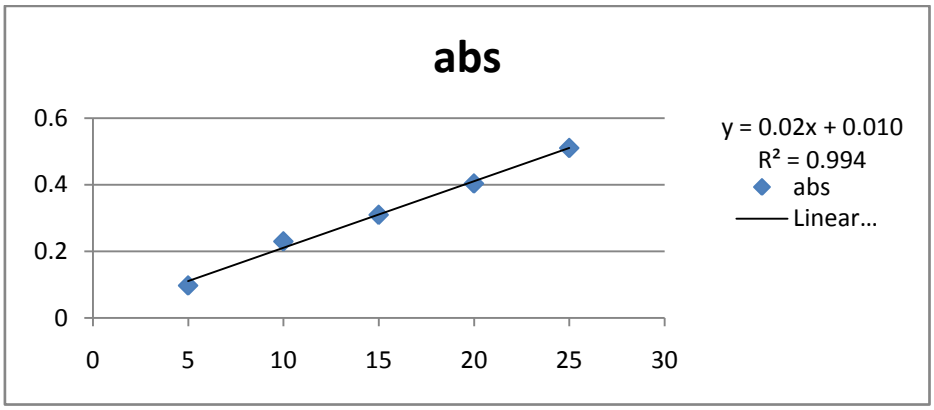

Fig. 2: linearity curve for MEF.

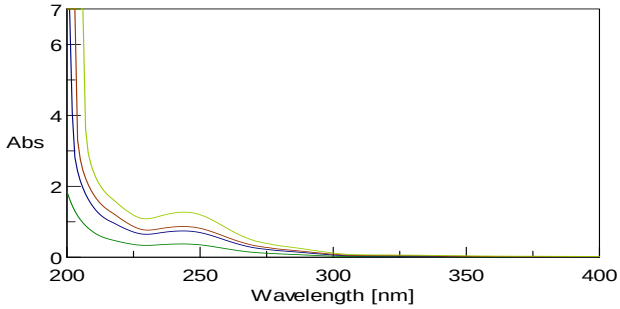

Fig. 3: UV-spectra for PARA.

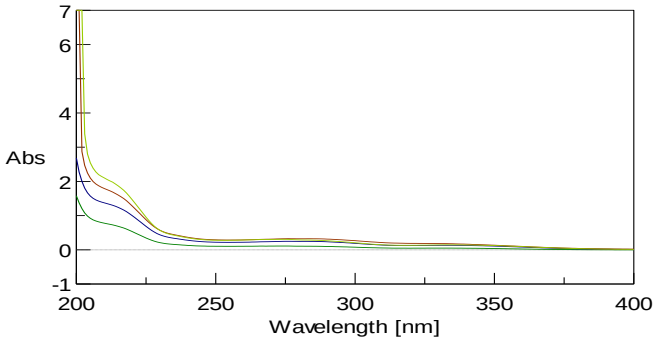

Fig. 4: UV-spectra for MEF.

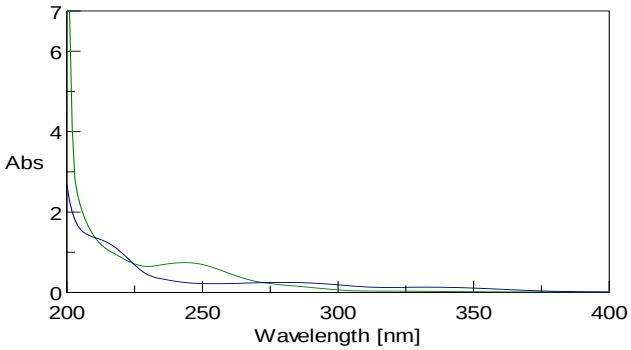

Fig.5: Overlain spectra of PARA and MEF.

Table 1: Analysis of Tablet formulation.

Drug	Label claim (mg/ tab.)	Amount found (mg)	%Drug found ±SD
PARA	450	447	99.33±0.21
MEF	500	495	99.00± 0.23

Table 2: Recovery study of PARA and MEF.

Drug	Level of addition (%)	Formulation Conc.(µg/mL)	Amount of Drug Added (µg/mL)	Amount recovered (µg/mL)	% Recovery
PARA	80%	10	8	17.89	99.13±0.50
	100%	10	10	19.95	99.75±0.27
	120%	10	12	21.95	99.77±0.23
MEF.	80%	10	8	17.93	99.61±0.28
	100%	10	10	19.98	99.99±0.29
	120%	10	12	21.92	99.63±0.33

Table 3: Optical characteristics data and validation parameters.

Parameters	**PARA**	**MEF**
Absorption maxima (λ max)	250	283
Beer's law limit (µg/ml)	5-25	5-25
Regression Equation	y = 0.051x - 0.0924	y = 0.02x + 0.0102
Correlation coefficient (R2)	0.9886	0.9941
Accuracy (%Recovery ± SD)	99.55±0.33	99.74±0.30
Precision		
Intraday*(Analyst 1)	99.35±0.35	99.51±0.42
Interday*(Analyst 2)	98.59±0.56	98.57±0.51
LOD (µg/ml)	0.62	0.55
LOQ (µg/ml)	1.25	1.08

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