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Research Article

SPECTROPHOTOMETRIC ESTIMATION OF ACECLOFENAC AND PARACETAMOL FROM TABLET DOSAGE FORM

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ABSTRACT
An attempt has been made to develop a simple, economic, sensitive and reproducible spectrophotometric method for quantitative estimation of Aceclofenac and Paracetamol from bulk drug and in pharmaceutical formulations.The method employing Q absorbance ratio method is very simple method and can be employed for routine analysis of Aceclofenac (ACE) and Paracetamol (PARA). The proposed method for simultaneous estimation of Aceclofenac and Paracetamol utilizes the spectrum mode of analysis of Jasco V-530 spectrophotometer. The method utilizes 274 nm and 268 nm as an analytical wavelength for estimation of Aceclofenac and Paracetamol. Once the absorptivity values are determined very little time is required for analysis, as it would only require determination of absorbance's of the sample solution at two selected wavelengths and few simple calculations. The accuracy of the method was determined by investigating the recovery of the two drugs using spiked concentrations of the standard drug. The results indicated excellent recoveries ranging from 100.49 to 101.33 % for the two drugs. Precision for tablet analysis was determined by analysis of tablets containing Aceclofenac and Paracetamol. Result of tablet analysis indicated that there was no interference of the common excipients used in the tablet formulation. Validation of this method is done as per ICHQ2B guidelines. The proposed method is highly sensitive and successfully applied for the analysis of Aceclofenac and Paracetamol in tablet formulation.

KEYWORDS: Aceclofenac, Paracetamol, Glass distilled water, Methanol.

INTRODUCTION
Aceclofenac [(2, 6-Dichlorophenylamino) phenyl] acectoxyacetic acid is a phenyl acetic acid derivative that shows analgesic properties and good tolerability profile in a variety of painful conditions.[1-5] It is used in the treatment of rheumatic disorders and soft tissue injuries. Aceclofenac inhibits the cyclooxygenase enzyme and thus exerts its anti-inflammatory activity by inhibition of prostaglandin synthesis. This effect seems to be correlated to the appearance of acute protocolitis associated with nonsteroidal anti-inflammatory drug therapy.[6, 7] The European pharmacopoeia supplement 2000 and the British pharmacopoeia reported HPLC methods for the determination of aceclofenac in presence of diclofenac.[1,2] Other methods include titrimetric,[1] electrochemical,[2,8]spectrophotometric,[8] spectrofluorometric[8] and chromatographic[11] methods.
Paracetamol (acetaminophen, *N*-acetyl-*p*-amino-phenol) is a safe and effective analgesic and antipyretic agent although its anti-inflammatory effect is weak. In case of an overdose, it may cause severe hepatic necrosis. Paracetamol is rapidly absorbed from the gastrointestinal tract but it is incompletely available due to first pass effect. Extensive metabolism occurs, predominantly in the liver, the major metabolites being the sulphate and the glucuronide conjugates.
In the present communication, this spectrophotometric method has been used for quantitative estimation of Aceclofenac and Paracetamol from tablets. Results of analysis have been validated as per ICHQ2B guidelines. Results of tablet analysis have been compared with other spectrophotometric method.

MATERIALS AND METHODS

Apparatus

A PC based Jasco V-530 recording spectrophotometer with spectral bandwidth of 2 nm and wavelength accuracy ± 0.5 nm (with automatic wavelength correction) was employed for all measurements using a matched pair of 10 mm quartz cell. Shimadzu AY 120 analytical balance was used for weighing.

Selection of Common Solvent

Methanol: Glass distilled water was selected as a common solvent for developing spectral characteristics of drugs. The selection was made after assessing the solubility and stability of both the drugs in different solvent.

Pharmaceutical Preparation

A commercial pharmaceutical preparation (Asthalin tablets, Cipla Laboratories, India, Batch No: DG 6370) was used for analysis. Each tablet contains 100 mg of aceclofenac.

Preparation of Standard Solutions

Standard stock solution containing Aceclofenac (ACE) and Paracetamol (PARA) was prepared by dissolving 10 mg of Aceclofenac and Paracetamol separately in 20 ml of methanol and then final volume of both the solutions was made up to 100 ml with Glass distilled water to get stock solution containing 100 µg/ml of Aceclofenac and 100 µg/ml of Paracetamol in two different 100 ml volumetric flask.

Procedure for Determining the Sampling Wavelength for Simultaneous Analysis:

By appropriate dilution of two standard drug solutions with methanol: Double distilled water, solutions containing 10 µg/ml of Aceclofenac and 10 µg/ml of Paracetamol were scanned separately in the range of 200-400 nm to determine the wavelength of maximum absorption for both the drugs. Aceclofenac showed absorbance maxima at 274 nm. This is absorptive point was obtained at 268 nm. Individual and overlain spectra for both the drugs are shown in **Fig. 1 to 3.**

Selection of Method and Wavelength

Absorbance ratio method was used to determine Aceclofenac and Paracetamol. In the Absorbance ratio method developed for simultaneous estimation of Aceclofenac and Paracetamol, the wavelengths were selected from the overlain spectra shown in **Fig. 3.** The wavelengths selected were 274 nm (λ_{max} of ACECLOFENAC) and 268 nm (**is absorptive point**).

Procedure for Determination of Absorptivity

By appropriate dilution of two standard drug solutions with methanol: Double distilled water, six different solutions containing 10 µg/ml of Aceclofenac and 10 µg/ml of Paracetamol were prepared separately and scanned in the range of 200-400 nm. The absorbances were recorded at the selected wavelengths and the absorptivity values were determined for Aceclofenac and Paracetamol. The absorptivity values at 274 nm and 268 nm are given in **Table 1.**

Derivation of Equations

From the absorptivity values determined at 274 nm and 268 nm the simultaneous equation is derived for determination of Aceclofenac and Paracetamol in pure drug mixed standards and in its pharmaceutical formulation.

$$C_1 = \frac{Q_0 - Q_2}{Q_1 - Q_2} \times \frac{A}{a} \quad \text{.....(1)}$$

$$C_2 = \frac{Q_0 - Q_1}{Q_2 - Q_1} \times \frac{A}{a} \quad \text{.....(2)}$$

Where,

C_1 = concentration of Paracetamol in gms/dm^3

C_2 = concentration of Aceclofenac in gms/dm^3

a = absorptivity of Paracetamol and Aceclofenac at 268 nm

$$Q_0 = \frac{\text{Absorbance of sample at 274 nm}}{\text{Absorbance of sample at 268 nm}}$$

$$Q_1 = \frac{\text{Absorptivity of PARA at 274 nm}}{\text{Absorptivity of PARA at 268 nm}}$$

$$Q_2 = \frac{\text{Absorptivity of ACE at 274 nm}}{\text{Absorptivity of ACE at 268 nm}}$$

After calculating the values of Q_1 and Q_2, we get
$Q_1 = 0.6057$
$Q_2 = 1.0838$
Substituting these values in equation (1) and (2), we get

$$C_1 = \frac{Q_0 - 1.0838}{0.4781} \times \frac{A}{345.40} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

$$C_2 = \frac{Q_0 - 0.6057}{0.4781} \times \frac{A}{360.05} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Sample preparation

Marketed tablet formulations containing 100 mg of Aceclofenac and 500 mg of Paracetamol were analyzed by this method. From the triturate of 20 tablets, an amount equivalent to 10 mg of Aceclofenac was weighed and transferred to 100 ml volumetric flask. The contents of the flask were dissolved in the 20 ml of the methanol, and then final volume of the solution was made up to 100 ml with double distilled water to get a stock solution containing 100 µg/ml of Aceclofenac and 500µg/ml of Paracetamol. Solutions were ultrasonicated for 10 min. The solution was filtered through Whatman filter paper no. 41 after appropriate dilutions, the absorbances were measured and the concentration of each analyte was determined with the equations generated. The statistical data obtained after replicate determinations (n = 5) is shown in **Table 2**

Validation

The proposed method has been statistically validated for accuracy, precision, repeatability and reproducibility. The results of validation data has been represented in Table 4 to Table 7

RESULTS AND DISCUSSION

The proposed method for Q Absorbance Ratio of Aceclofenac and Paracetamol utilizes the spectrum mode of analysis of Jasco V-530 spectrophotometer. The method utilizes 274 nm and 268 nm as an analytical wavelength for estimation of Aceclofenac and Paracetamol. The method employing simultaneous equation is very simple method and can be employed for routine analysis of Aceclofenac and Paracetamol. Once the absorptivity values are determined very little time is required for analysis, as it would only require determination of absorbance's of the sample solution at two selected wavelengths and few simple calculations.

The accuracy of the method was determined by investigating the recovery of the two drugs using spiked concentrations of the standard drug. The results indicated excellent recoveries ranging from 100.49 to 101.33 % for the two drugs. Precision for tablet analysis was determined by analysis of tablets containing Aceclofenac and Paracetamol. Result of tablet analysis indicated that there was no interference of the common excipients used in the tablet formulation.

CONCLUSION

Excellent statistical parameters and recovery data indicate that the method can be employed for efficient, rapid, accurate and precise analysis of the two drugs from multicomponent formulation. The result of

analysis clearly indicates absence of interference from the excipients in the formulation.

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Table 1: Absorptivity Values

Conc. (10µg / ml)	Absorptivities for ACE		Absorptivities for PARA	
	274 nm	268 nm	274nm	268 nm
1	390.68	359.8	211.3	346.23
2	389.79	360.29	208.17	343.43
3	390.68	359.8	208.41	346.53
4	389.79	359.7	211.3	346.23
5	390.68	360.39	208.17	343.43
6	389.79	359.9	208.41	346.23
Mean	390.24	360.05	209.21	346.53

*Average of five determinations

Table 2: Result of Analysis of Tablet Formulation

Formulation	Drug	Label Claim (mg)	% Label Claim estimated * (Mean ± S.D.)	Coefficient of variance
Tablet-1	ACE	100	99.38 ± 1.46	1.47
	PARA	500	98.33 ± 0.73	0.73

SD stands for Standard Deviation; *Average of five determinations

Table 3: Result of Recovery Studies

Formulation	Drug	Label Claim (mg)	% Recovery estimated* (Mean ± S.D.)	Coefficient of variance
Tablet	ACE	100	101.6 ± 1.17	1.18
	PARA	500	99.43 ± 0.296	0.297

*Average of five determinations; SD stands for Standard Deviation.

Table 4: Result of Analysis

Parameters	ACE	PARA
λ_{max}	274	248
Beer's law limit (µg ml^{-1})	1-5 µg/ml	5-25 µg/ml
Accuracy	101.6 %	99.43 %

*Average of five determinations

Table 5: Result of Precision Parameter Studies

Analyte	Tablet Analysis		Recovery Study	
	% Label claim Estimated * (Mean ± SD)	R.S.D	% Recovery Estimated* (Mean ± SD)	R.S.D
Intra-day -Interday				
Day I				
Morning				
ACE	99.91 ± 1.89	1.89	100.76 ± 1.33	1.35
PARA	98.29 ± 0.44	0.44	99.46 ± 0.28	0.28
Evening				
ACE	102.91 ± 1.63	1.64	98.52 ± 1.70	1.71
PARA	98.96 ± 0.96	0.97	99.25 ± 0.73	0.74
Day II				
Morning				
ACE	99.42 ± 1.66	1.67	101.6 ± 1.17	1.18
PARA	99.09 ± 1.18	1.19	99.43 ± 0.296	0.297

*Average of five determinations; SD stands for Standard Deviation.
R.S.D. stands for Relative Standard Deviation.

Table 6: Results of Reproducibility

Analyte	Tablet Analysis		Recovery Study	
	% Label claim Estimated * (Mean ± SD)	R.S.D	% Recovery Estimated* (Mean ± SD)	R.S.D
Reproducibility				
ACE	101.83 ± 1.81	1.82	97.52 ± 1.63	1.65
PARA	99.98 ± 1.32	1.34	99.95 ± 0.73	0.74

*Average of Five determinations; SD stands for Standard Deviation.
R.S.D., Relative Standard Deviation

Table 7: Limit of detection and limit of quantitation

Drugs	LOD (µg ml^{-1})*	LOQ (µg ml^{-1})*
ACE	0.296	0.756
PARA	0.986	2.52

*Average of Five determinations

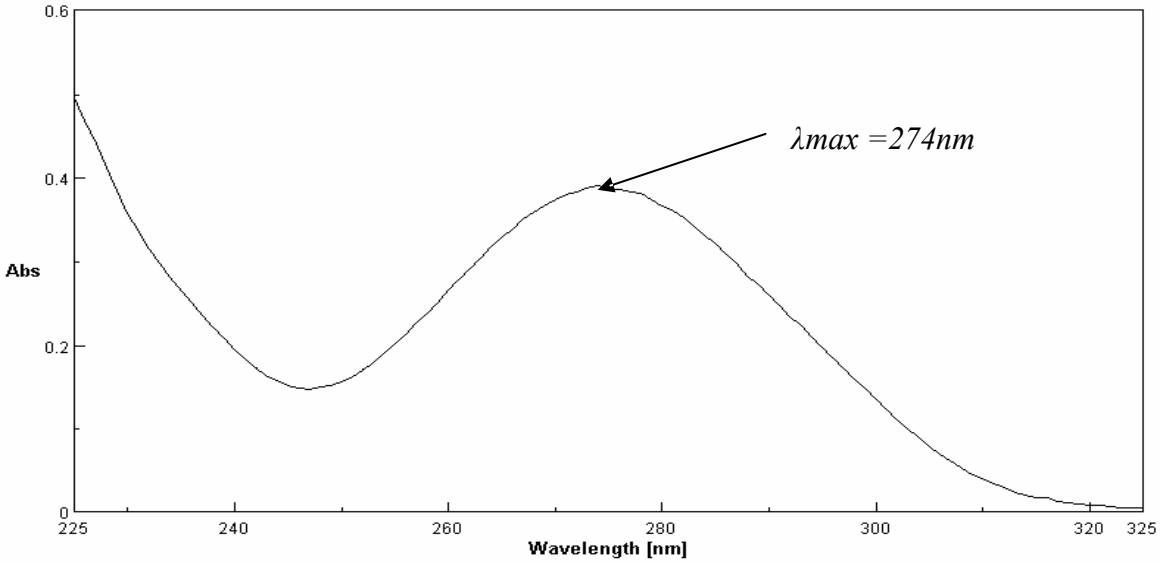

Fig. 1: UV spectra of ACE

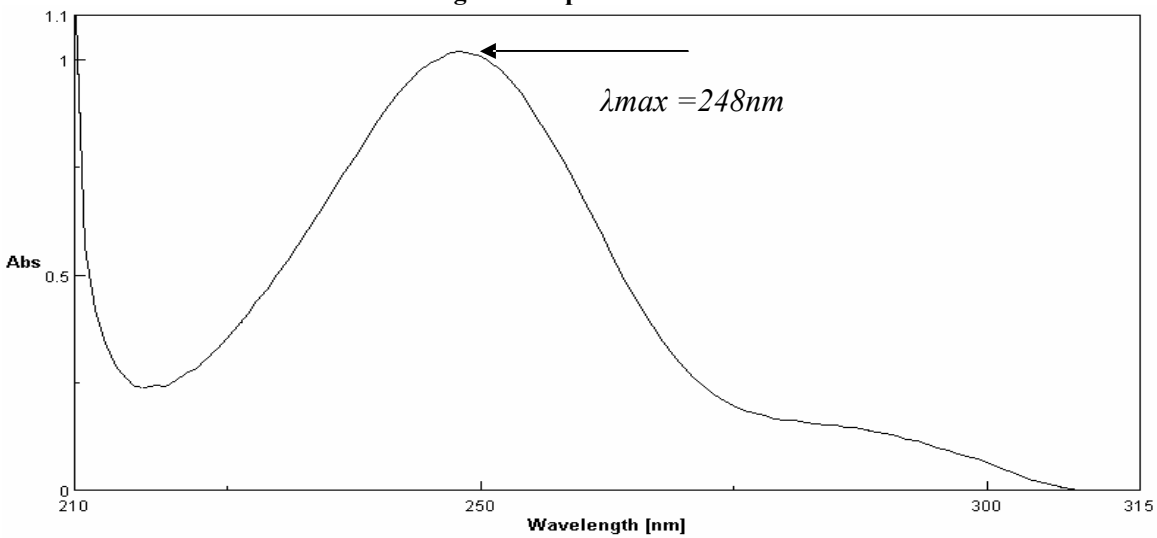

Fig. 2: UV spectra of PARA

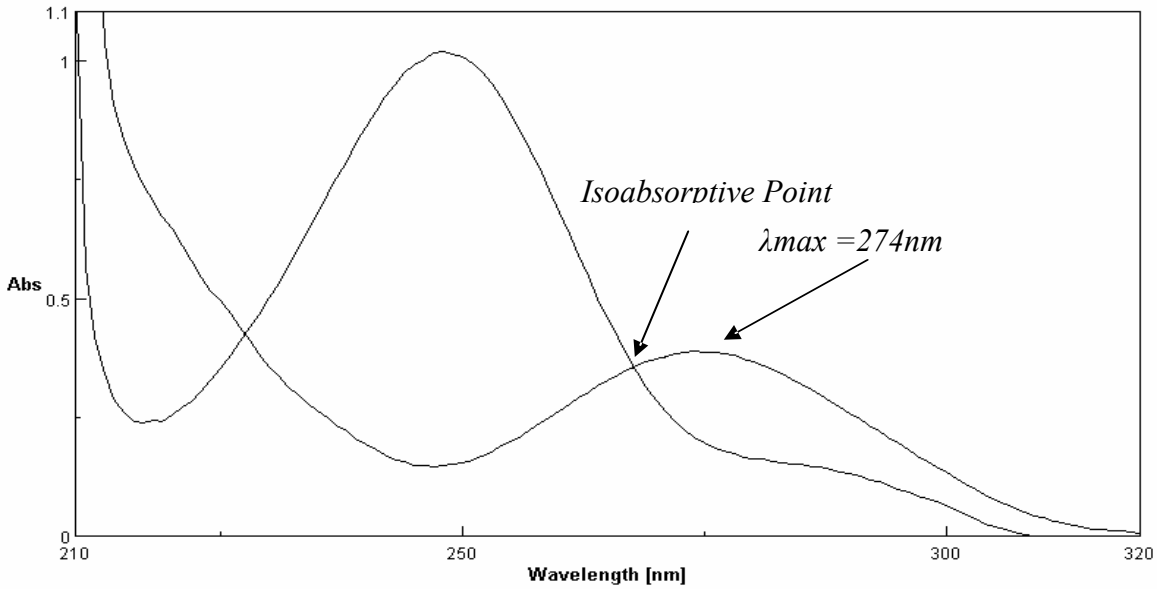

Fig. 3: Overlain spectra of ACE and PARA

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