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SIMULTANEOUS ESTIMATION OF PARACETAMOL AND ACECLOFENAC IN TABLET DOSAGE FORM USING UV SPECTROSCOPY

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ABSTRACT

The present study deals with UV spectrophotometric method development & validation for estimation of Paracetamol & Aceclofenac in bulk drug & tablet dosage form by viedort's method & first order UV derivative spectrophotometry. The vierodt's method involves measurement of absorbance at λmax of Paracetamol & Aceclofenac at 248 nm & 276 nm respectively. The linearity of paracetamol and aceclofenac was found to be 3-30µg/ml and 2-20 µg/ml respectively. The % recovery of Paracetamol & Aceclofenac was found out to be 99.72 % & 99.69 %s respectively. First order UV derivative spectrophotometry (D_1 method), the zero crossing method was chosen as paracetamol could be easily analyzed without any interference from Aceclofenac and vice-versa. Paracetamol was determined by measurement of its D_1 amplitude at the zero crossing point of Aceclofenac at (276 nm), While Aceclofenac was determined by measurement of its D_1 amplitude at zero crossing point of Paracetamol at (248 nm) 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.

Key words: - Paracetamol, Aceclofenac, Derivative spectroscopy, Validation.

INTRODUCTION

Aceclofenac [(2, 6-Dichlorophenylamino) phenyl] acetoxy acetic acid is a phenyl acetic acid derivative that shows analgesic properties and good tolerability profile in a variety of painful conditions.[1-3] 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] Since no spectrophotometric method is reported for simultaneous estimation of in combination using methanol & phosphate buffer. Paracetamol and Aceclofenac in Combined Tablet Dosage Formulation. Hence simple, sensitive, reliable and rapid spectroscopic methods have been developed for the determination of Paracetamol and Aceclofenac in combined tablet dosage form. Determinations were performed on Shimadzu UV-Visible double beam recording spectrophotometer (Model UV-1700). 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.

MATERIALS AND METHODS

Apparatus

UV/Visible spectrophotometer (Shimadzu Model 1700) was employed with spectral bandwidth of 1nm and wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 1 cm matched quartz cells). Mettler M80 analytical balance was used for weighing. Analytical grade reagents and solvents were used for the study; Combined Aceclofenac and Paracetamol tablets were procured from the local market.

Preparation of standard and sample

Selection of Common Solvent

Methanol: 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 (Lekace-P tablets, JB Chemicals, India, was used for analysis. Each tablet contains 100 mg of aceclofenac and 325 mg of Paracetamol.

Preparation of Standard Solutions

Standard stock solution containing Aceclofenac (ACE) and Paracetamol (PARA) was prepared by dissolving 100 mg of Aceclofenac and Paracetamol separately in mixture of 10 ml of methanol to get standard stock solution of 1000 µg/ml respectively by sonicating for 15 min and 1 ml was pipette out and further volume was made up to 10 ml with phosphate buffer to obtain concentration of 100 µg/ml. Further dilutions were made in phosphate buffer from stock solution to get concentrations of 1-10 µg/ml of ACE & 2-20 µg/ml of paracetamol.

Procedure for Determining the Sampling Wavelength for Simultaneous Analysis

By appropriate dilution of two standard drug solutions of 100 µg/ml working standard solutions of drug were prepared by appropriate dilutions were prepared in phosphate buffer, were scanned in entire UV range to determine λmax 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 and Paracetamol showed absorbance maxima at 274 nm and 248 nm respectively. Individual and overlain spectra for both the drugs are shown in Fig. No.1 to 3.

Selection of Method and Wavelength

Viedort's method was used to determine Aceclofenac and Paracetamol. the method developed for simultaneous estimation of Aceclofenac and Paracetamol, the wavelengths were selected from the overlain spectra shown in Fig. No.3. For Aceclofenac the wavelength selected was 274 nm and 248 nm for Paracetamol respectively.

Procedure for Determination of Absorptivity

By appropriate dilution of two standard drug solutions with methanol: Glass 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 for Aceclofenac and Paracetamol are given in Table. No. 1. Absorptivity values determined for Aceclofenac at 274 nm and 248 nm were 390.24 and 150.62, while respective values for Paracetamol were 209.21 and 1013.34

Derivation of Equations

From the absorptivity values determined for Aceclofenac and Paracetamol the simultaneous

equation is derived for determination of Aceclofenac and Paracetamol in pure drug mixed standards and in its pharmaceutical formulation.

$A1 = 390.24\ C1 + 209.21\ C$ …… .at 274nm (1)

$A2 = 150.62\ C1 + 1013.34\ C2$ …… ..at 248 nm (2)

Hence,

$$C_2 = \frac{A1 - 150.62\ C1}{1013.34} \quad \text{……(3)}$$

$$C_1 = \frac{A1 - 0.2065\ A_2}{359.14} \quad \text{…… (4)}$$

Sample Preparation

Marketed tablet formulations containing 100 mg of Aceclofenac and 325 mg of Paracetamol were analyzed by this method. From the triturate of 20 tablets, an amount equivalent to 100 mg of Aceclofenac was weighed and transferred flask and make up volume with methanol to get stock solution of 1000 µg/ml, Further dilutions was made with phosphate buffer to get a stock solution containing 100 µg/ml of Aceclofenac and 325 µg/ml of Paracetamol. Solutions were ultrasonicated for 10 min. The solution was filtered through Whatmann filter paper no. 41 after appropriate dilutions, the absorbance was 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 No. 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 No.4 to Table no.7.

RESULTS AND DISCUSSION

The proposed method for simultaneous estimation of Aceclofenac and Paracetamol utilizes the spectrum mode of analysis of Schimadzu 1700 spectrophotometer. The method utilizes 274 nm and 248 nm as 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.

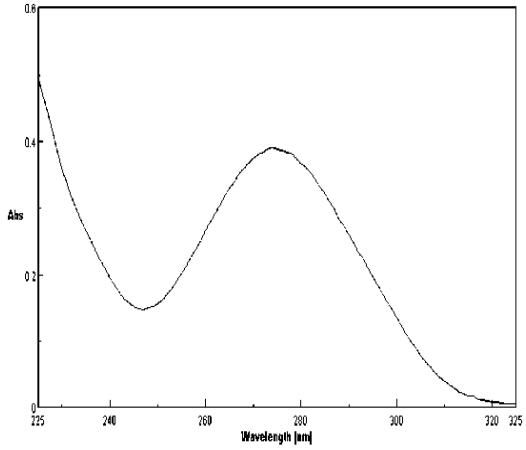

Fig. 1: UV spectra of Aceclofenac

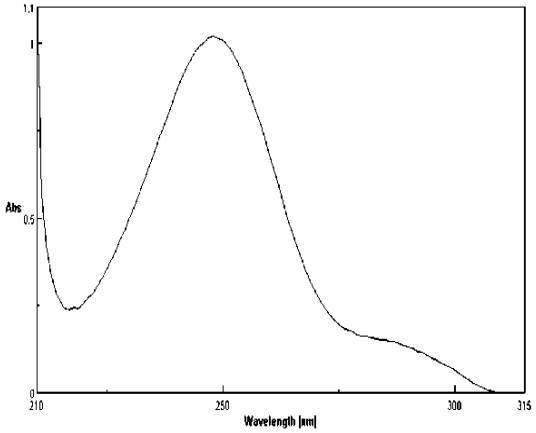

Fig. 2: UV spectra of Paracetamol

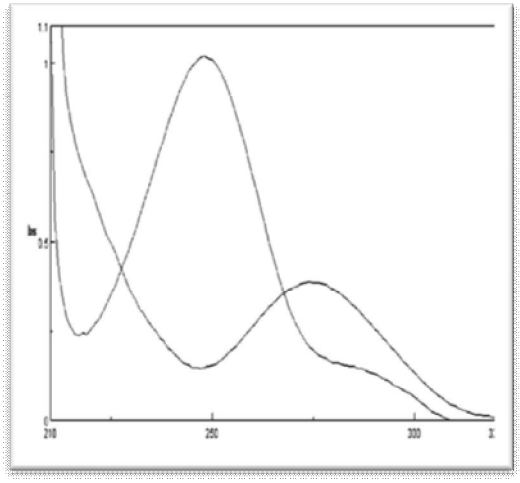

Fig. 3: Overlain spectra of ACE and PARA.

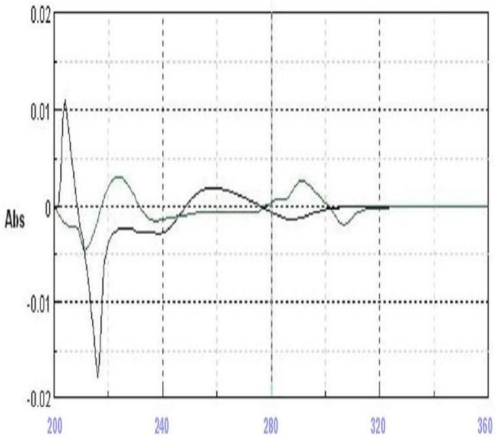

Fig. 4: ZERO order spectra of ACE and PARA

Conc. (10 g/ ml)	Absorptivity for Aceclofenac		Absorptivity for Paracetamol	
	274 nm	248 nm	274nm	248 nm
1	390.68	150.37	211.3	1012.03
2	389.79	150.86	208.17	1009.62
3	390.68	150.37	208.41	1018.38
4	389.79	150.86	211.3	1013.03
5	390.68	150.37	208.17	1009.62
6	389.79	150.86	208.41	1018.38
Mean	390.24	150.62	209.21	1013.34

Recovery Studies

To study the accuracy of the proposed method, recovery studies were carried out at three different levels 80%, 100% and 120% by addition of known amount of Aceclofenac and Paracetamol to a known concentration of the commercial tablet.

Level of % recovery	% mean recovery *		Standard deviation		% RSD	
	ACE	PARA	ACE	PARA	ACE	PARA
80	98.42	99.66	1.08	0.94	0.208	0.234
100	99.24	99.74	1.04	1.08	0.246	0.292
120	100.64	101.34	1.16	1.46	0.324	0.378

Table 1: Validation As Per ICH

Parameters	Method I		Method II	
	ACE (274nm)	PARA (248nm)	ACE (274nm)	PARA (248nm)
Linearity range(µg/ml)	1-10 µg/ml	3.25-32.5 µg/ml	1-10 µg/ml	3.25-32.5 µg/ml
Correlation coefficient (r^2)	0.999	0.998	0.998	0.997
Interday	0.26	0.07	0.43	0.09
Intraday	0.54	0.12	0.74	0.10
Slope	0.0342	0.1124	0.0326	0.348
Intercept	0.0017	0.0003	0.0027	0.0019

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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