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Simultaneous Determination of Paracetamol and Diclofenac Sodium from Combined Dosage Forms by Absorbance Difference Method

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A new spectrophotometric method for the simultaneous and separate estimation of paracetamol and diclofenac sodium in binary tablet formulations has been described. The method is based on the estimation of one drug in presence of another drug by absorbance difference method. The paracetamol and diclofenac sodium solutions were scanned over the range of 210 to 304 nm. In this method, two wavelengths 230 and 254 nm were chosen for paracetamol; at these wavelengths the absorbance was almost zero and in case of diclofenac sodium it should be considerable absorbance difference. Similarly the two wavelengths 260 and 292 nm were chosen for diclofenac sodium; at these two wavelengths absorbance difference was almost zero and it should be considerable absorbance difference in case of paracetamol. In the mixture of paracetamol and diclofenac sodium solution the absorbance values of four wavelengths 260, 292, 230 and 254 nm were measured. The amount of paracetamol is directly proportional to the absorbance difference between 230 and 254 nm. Similarly the amount of diclofenac sodium is directly proportional to the absorbance difference between 260 and 292 nm

Key Words: Paracetamol, Diclofenac sodium, Spectrophotometric determination.

INTRODUCTION

The combination formulations of paracetamol and diclofenac sodium have been in the market for their use as anti-inflammatory and antipyretic. The literature describes various specrophotometric methods for the analysis of paracetamol[1–6] and diclofenac sodium[7–9] as individual drug products. Few methods such as rapid liquid chromatographic method[10], HPTLC method[11], HPLC method[12, 13] and spectrophotometric method[14], for simultaneous analysis of paracetamol and diclofenac sodium, have been cited. No method for the simultaneous analysis of paracetamol and diclofenac sodium in binary tablet formulations has been reported by absorbance difference method. The objective of the present investigation is to develop a simple, rapid, precise, reproducible and economical method for the simultaneous analysis of the binary drug formulations by using absorbance difference method without any interference from each other.

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EXPERIMENTAL

A spectronic 1001 spectrophotometer with 10 mm quartz cells was used for absorbance values of the drug solution. All the chemicals used were of analytical grade. A.R. grade methanol was used as solvent.

Preparation of standard paracetamol solution: 50 mg of pure paracetamol was dissolved in 50 mL methanol. Therefore, 1.0 mL of the stock solution was further diluted to 50 mL with methanol to get working concentration of 50 μg/mL.

Preparation of standard diclofenac sodium solution: 50 mg of pure diclofenac sodium was dissolved in 50 mL methanol to obtain the working concentration of 1 mg/mL. 1.0 mL of the above stock solution was further diluted to 50 mL with methanol to get working concentration of 30 μg/mL

Preparation of mixed solution: Two solutions, the first containing 50 μg/mL of paracetamol and the second containing 30 μg/mL of diclofenac sodium were used as mixed solutions. Four mixed standard solutions were made by taking 4, 3, 2 and 1 mL of paracetamol solution into a series of test tubes and the diclofenac sodium stock solution was also added to a series of test tubes to keep the total volume at 5 mL.

Preparation of calibration curve: Various aliquots (5, 6, 7 and 8 mL) of paracetamol solution were transferred into a series of 10 mL standard flasks and the volume in each flask was adjusted to 10 mL with distilled water. The absorbances of these solutions were scanned over the range of 210 to 304 nm. Overlain spectrum of paracetamol is shown in Fig. 1. Again various aliquots of diclofenac sodium solution were transferred into a series of 10 mL volumetric flask and the volume in each flask was adjusted to 10 mL with distilled water. These solutions were scanned over the range of 210 to 304 nm. Overlain spectrum of diclofenac sodium is shown in Fig. 2. Two wavelengths 230 and 254 nm are chosen for paracetamol, at these two wavelengths the absorbance values are almost zero and diclofenac sodium at the same wavelengths 230 and 254 nm has maximum absorbance difference. A calibration curve was drawn between the absorbance difference values of diclofenac sodium and the amount of diclofenac sodium in μg/mL. The amount of diclofenac sodium present in the sample was computed from the calibration curve. Similarly two wavelengths 260 and 292 nm were chosen for diclofenac sodium; at these two wavelengths the absorbance difference was almost zero and paracetamol has maximum absorbance difference values at the same wavelengths 260 and 292 nm. A calibration curve was drawn between absorbance difference values of paracetamol and amount of paracetamol in μg/mL. The amount of paracetamol present in the sample was computed from calibration curve.

Various aliquots of mixture of paracetamol and diclofenac sodium solutions in different proportions were transferred into a series of test tubes and the volume in each test tube was kept at 5 mL with distilled water. The absorbance values were measured at two wavelengths 260 and 292 nm for estimation of paracetamol and two wavelengths 230 and 254 nm for estimation of diclofenac sodium. A calibration curve was drawn between the absorbance difference values of paracetamol and the amount of paracetamol present in μg/mL. A calibration graph was drawn between

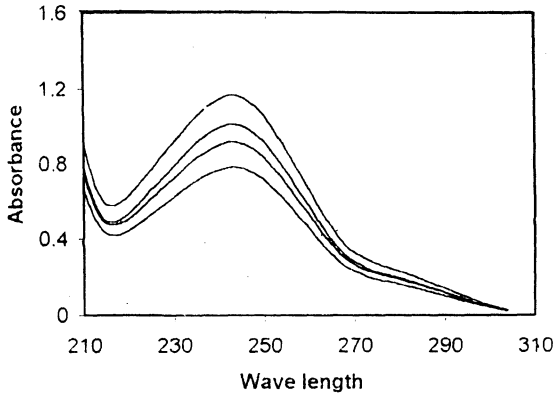

Fig. 1. Overlain spectrum of paracetamol

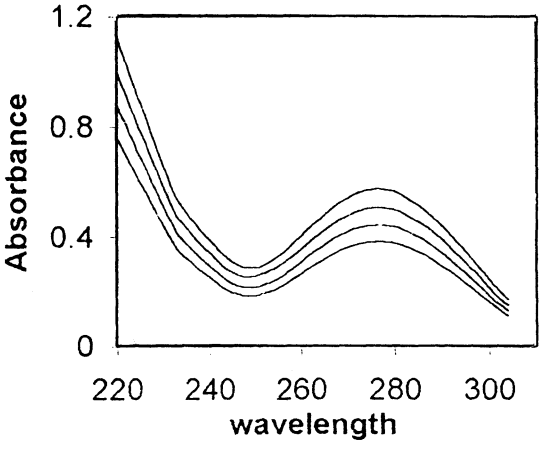

Fig. 2. Overlain spectrum of diclofenac sodium

the absorbance difference values of diclofenac sodium and the amount of diclofenac sodium present in μg/mL. A linear curve in each case was obtained. The linearity of the curves obtained indicates it obeys Beer's law and the suitability of this method for the simultaneous determination of the two drugs in admixture.

Estimation of paracetamol in formulation

Twenty tablets were weighed and powdered. An average weight of the tablet containing the two drugs paracetamol and diclofenac in the ratio of 1 : 10 and 50 mg powder of these tablets was dissolved in 30 mL methanol by vigorously shaking and the volume was made up to the mark. The solution was then filtered through Whatman filter paper No. 41 and the solution was diluted to get a final concentration of 20 μg/mL of paracetamol and 2 μg/mL of diclofenac sodium. The sample solutions were measured at 260 and 292 nm for paracetamol and 230 and 254 nm for

diclofenac sodium in a spectronics 1001 spectrophotometer. The results are represented in Table-2.

TABLE-1
CONCENTRATION OF TWO COMPONENTS IN FOUR MIXED STANDARDS

Standard No.	Volume of paracetamol (mL)	Concentration of paracetamol (μg/mL)	Volume of diclofenac sodium (mL)	Concentration of diclofenac sodium (μg/mL)
1	4	80	1	20
2	3	60	2	40
3	2	40	3	60
4	1	20	4	80

TABLE-2
ESTIMATION OF PARACETAMOL AND DICLOFENAC SODIUM IN PHARMACEUTICAL PREPARATIONS

S. No.	Label Claim (mg/tab)		Found* (mg/tab)		% Recovery*	
	Paracetamol	Diclofenac sodium	Paracetamol	Diclofenac sodium	Paracetamol	Diclofenac sodium
T_1	500	50	498.6	49.6	99.8	99.6
T_2	500	50	498.3	49.2	99.6	99.8
T_3	500	50	499.3	50.48	100.0	98.6
T_4	500	50	500.1	48.96	100.2	100.4

*Average of five determinations based on the label claim.

TABLE 3
STATISTICAL ANALYSIS OF ESTIMATION OF PARACETAMOL AND DICLOFENAC SODIUM

S. No.	Label claim (mg/tab)		Standard deviation		Coefficient of deviation	
	Paracetamol	Diclofenac sodium	Paracetamol	Diclofenac sodium	Paracetamol	Diclofenac sodium
T_1	500	50	1.1400	0.9838	0.2286	1.9830
T_2	500	50	1.9230	0.7348	0.3859	1.4930
T_3	500	50	0.7328	0.4813	0.1467	0.9534
T_4	500	50	1.0545	0.5176	0.2108	1.0570

*Average of five determinations based on the label claim.

Validation of method

The method was validated in terms of linearity, accuracy, precision, specificity and reproducibility of the sample applications. The linearity of the method was investigated by serially diluting the stock solutions of paracetamol (20 μg/mL), diclofenac sodium (2 μg/mL) and measured the absorbance values at 260 and 292 nm for paracetamol and 230 and 254 nm for diclofenac sodium in the Spectronics 1001 spectrophotometer. Calibration curves were constructed by plotting the absorbance difference values against the amount of drug in μg/mL.

Statistical analysis

The statistical analysis was performed on the statistically significant variables using the statistical software. The coefficient of variation and standard deviation were determined.

Recovery experiment

To ensure the accuracy and reproducibility of the results obtained, recovery experiments were performed by adding a known amount of standard drug to previously analysed pharmaceutical preparations. The results are recorded in Table-2.

RESULTS AND DISCUSSION

The present study was carried out to develop a simple, rapid, sensitive, precise, reproducible and accurate spectrophotometric method for the estimation of simultaneous determinations of paracetamol and diclofenac sodium in pharmaceutical dosage forms. The content of paracetamol and diclofenac sodium in four different tablet dosage forms is shown in Table-2. The absorbance of various aliquots of mixture of paracetamol and diclofenac sodium solutions were measured at two wavelengths 260 and 292 nm for paracetamol and 230 and 254 nm for diclofenac sodium. A calibration curve was drawn between the absorbance difference values of paracetamol and the amount of paracetamol present in μg/mL. Similarly, for the estimation of diclofenac sodium, a calibration graph is plotted the absorbance difference values of diclofenac sodium against the amount of diclofenac sodium in μg/mL. The amount of diclofenac sodium in the sample was read from calibration curve.

The results obtained by the proposed method are in good agreement with the label claims. The additives and excipients usually present in the tablet do not interfere. The tablets were found to contain 98.6 to 100.3%. As a check on accuracy of the method, a recovery experiment was performed and per cent recovery values were also tabulated (Table-2). The statistical analysis was studied by the proposed method The values of standard deviation and coefficient of variation values were satisfactorily low, indicating accuracy and the reproducibility of the method.

In conclusion, the results indicate that the proposed absorbance difference method is simple, rapid, precise, highly accurate and less time consuming. Hence it can be used for the routine analysis of simultaneous determination of paracetamol and diclofenac sodium in pharmaceutical formulations.

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