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Research Article

DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF FAMOTIDINE AND DICLOFENAC POATASSIUM IN COMBINED TABLET DOSAGE FORM BY FIRST ORDER DERIVATIVE METHOD

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ABSTRACT

In the present study analytical research worka simple, accuratefirst order derivative method was developed and validated for simultaneous estimation of Famotidine and Diclofenac Potassium in combined tablet dosage form. Here methanol was used as a solvent and wavelength of detection was selected as 253.6 nm and 287.6 nm for Famotidine and Diclofenac Potassium respectively.The method obeyed Beer's law in the concentration range of 2-12 µg/ml with a (r^2) value of 0.9988 for Famotidine and 5-30 µg/ml with a (r^2) value of 0.9999 for Diclofenac Potassium in the combined tablet formulation. The percentage of Famotidine and Diclofenac Potassium in marketed formulation was found to be 98.23 ± 0.2753 % and 99.85 ± 0.0702%, respectivelyby first order derivative method.The developed method was validated as per International Conference on Harmonisation (ICH) guidelines. The limit of detectionwas found to be 0.1 µg/ml and 0.07µg/mlandlimit of quantitationwas found to be 0.21µg/ml and 0.6 µg /ml for Famotidine and Diclofenac Potassium respectively. The results indicated that the developed method can be precisely used for the routine determination of Famotidine and Diclofenac Potassium in pharmaceutical combined dosage forms.

Keywords: Famotidine, Diclofenac Potassium, validation, first order derivative spectroscopy.

INTRODUCTION

Combination of Famotidine and Diclofenac Potassium is used to relieve pain and to treat ulcer induced by long term treatment with NSAID's. Famotidine is given to patients before they undergo surgery to prevent postoperative nausea and to reduce the risk of aspiration pneumonitis.[1]Diclofenac potassium is used to reduce pain, inflammation, swelling, and/or stiffness caused by several conditions, osteoarthritis or rheumatoid arthritis, painful menstrual periods, and general pain.

[2]Famotidine(FAMO) chemically,(3-([2-(diamino methyleneamino)thiazol-4-yl]methylthio)- *N'*-sulfamoyl-propanimidamideis an H_2 histamine-receptor antagonist, also known as an H_2-blocker. Histamine is a chemical present in some cells of the body that causes production of acid in the stomach.[3] H_2-blockers inhibit histamine action, and therefore reduce gastric secretion or the amount of acid produced.[4]Diclofenac Potassium(DICLO) chemically,2[(2,6-dichlorophenyl)amino] enzene acetic acid potassium saltis a non-steroidal anti-

inflammatory drug(NSAID). The primary mechanism responsible for its anti-inflammatory, antipyretic and analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclo-oxygenase (COX).[5] It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis.[6]

Literature review revealed that only a few analytical methods are reported for estimation of Famotidine and Diclofenac Potassium in combined tablet dosage form.[7]Hence, in this present study attempts were made to develop a fast, simple, economical, selective and sensitive analytical method for the estimation of FAMO and DICLO in their combined dosage form using first order derivative spectroscopic method.[8]

MATERIALS AND METHODS

Chemicals and reagents used

The Famotidine and Diclofenac Potassium standard pure powders were procured from Alembic Analytical Lab.,[Baroda Gujarat India] as gift samples. Tablet formulation, Diclosef (Sun Pharma, Baroda), was obtained commercially with the labelled amount of 20 mg FAMO and DICLO 50mg. Methanol used as a solvent was purchased from E.Merck (Mumbai, India). All chemicals used were of analytical grade.

Instruments used

UV-Visible Spectrophotometer 1800, Shimadzu, software Version 2.23 using 10 mm quartz cell with a slit width of 1 mm and scanning speed is medium, Electronic weighing balance(Shimadzu analytical balance).

Preparation of standard stock solution

Standard stock solutions of FAMO and DICLO were prepared by dissolving 100 mg of each drug in two separate 100 ml volumetric flasks using methanol to give a concentration of 1000 µg/ml. Further dilutions were made to obtain a concentration of 6µg/ml for FAMO and 15 µg/ml of DICLO.Thesolutionswere scanned in the spectrum mode from 200 nm - 400 nm. Overlay spectra of FAMO and DICLO was studied.

Standard stock solution of mixture of FAMO and DICLO

100 mg of standard FAMO and 100 mg of standard DICLO was weighed, transferred to 100 ml volumetric flask and dissolved in 25 ml methanol by gentle shaking and volume was made up to the mark with same solvent to obtain final concentration of 1000 µg/ml FAMO and 1000 µg/ml of DICLO. Further dilutions were made to obtain final concentration of 100 µg/ml of FAMO and 100 µg/ml of DICLO.

Selection of wavelength

While using the first order derivative method, spectra showed overlapping. The zero crossing point (ZCP) value of FAMO at which the DICLO showed derivative response was recorded. The wavelength 253.6 nm was selected for the quantification of FAMO(while the derivative response for DICLO was zero) and 287.6 nm was selected for the quantification of DICLO(where the derivative response for FAMO was zero). Characteristic wavelength (ZCP) for FAMO and DICLO were confirmedby varying the concentration of both drugs.

Analysis of tablet formulations

Twenty tablets were weighed and ground to fine powder. An accurately weighed powder sample equivalent to 20 mg of FAMO and 50 mg DICLO were transferred to a 50 ml volumetric flask volume as made up to the mark with methanol. The solution was filtered through Whatmann filter paper No. 41 and the solution was diluted to obtain solution having concentrations equivalent to 4 µg/ml of FAMO and 10 µg/ml of DICLO. The solutions were then analysedin the multicomponent mode of the instrument in the same manner as the mixed standard solution of pure drugs were analysed.

Validation of spectrophotometric method[9-12]

The methods were validated according to ICH Q2 (R1) guidelines for validation of analytical procedures.

(a) Accuracy

Recovery studies were carried out by standard addition method by adding known amount of FAMO and DICLO to the pre-analyzed sample at three different concentration level that is 80%, 100%, 120% of assay concentration and percentage recoveries were calculated. [11]

(b) Precision

Repeatability was assessed by analyzing six different standard solutions of FAMO (2, 4, 6, 8, 10, and 12 µg/ml) and DICLO (5, 10, 15, 20, 25, and 30 µg/ml) and recording their first order derivative spectra. The inter day and intraday precision was evaluated by analyzing three different samples per day for three different days and on three different intervals on the same day respectively.

(c) Linearity and Range

Six concentrations of the standardsolutionsof FAMO (2, 4, 6, 8, 10, and 12 µg/ml) and DICLO (5, 10, 15, 20, 25, and 30 µg/ml) were analyzed. Calibration curves were constructed byplotting absorbance versus concentrations.Linearity was found using theregression equations. The range of analytical method was decided from the interval between upper and lower level of calibration curves.

(d) Ruggedness

The study was carried out to evaluate the effect of various parameters like different laboratories, different analysts, inter day and intraday variations.

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

Detection limit and quantitation limit were determined based on the standard deviation of y-intercepts of six calibration curves and average slope of six calibration curves.

$$LOD = 3.3 \times \frac{\text{Standard Deviation of intercept}}{\text{Slope}}$$

$$LOQ = 10 \times \frac{\text{Standard Deviation of intercept}}{\text{Slope}}$$

RESULTS AND DISCUSSION

In the present study, the first order derivative spectroscopy was employed for eliminating the spectral interference from one of the two drugs while estimating the other. Based on the overlain spectra of the two drugs, 287.6 nm and 253.6 nm were selected as the wavelength for the quantification of DICLO and FAMO respectively (Figure 1 and 2). From the calibration curve, the responses were found to be linear in the concentration range of 2 – 12 µg/ml for FAMO and 5 -25µg/ml for DICLO (Figure 3 and 4). The assay value was found to be 98.23 ± 0.2753 %for FAMO and 99.85 ± 0.0702 % for DICLO (Table 1). For accuracy, the recoveries were well within the acceptable limits which showed that the developed method was accurate. The repeatability values demonstrated a high precision of the method (Table 2). LOD for FAMO was found to be 0.1µg/ml and that for DICLO was 0.07µg/ml and LOQ 0.21µg/ml for FAMO and 0.6µg/ml DICLO, the results for which are tabulated in Table 3.

Table 1: Assay resultsfor marketed formulation

Formulation	Labelled amount (mg)		FAMO (%)* (Mean± SD)	DICLO (%)* (Mean± SD)
	FAMO	DICLO		
Tablet	20	50	98.23 ± 0.2753	99.85 ± 0.0702

*Mean of 3 estimations

Table 2: System suitability parameters for FAMO and DICLO

Parameters	FAMO	DICLO
Recovery %	98.33 – 99.72	98.26 – 101.16
Repeatability (RSD, n=5)	0.9318	0.6255
Precision(CV) intra-day(n=3) inter-day(n=3)	1.41 --- 5.09 1.04 --- 3.69	-1.33 --- -1.65 -2.41--- -3.69

Table 3: Linear regression analysis for calibration curves of FAMO and DICLO

Parameters	FAMO	DICLO
Linearity Range (µg/ml)	2-12	5-25
Slope	0.0005	-0.0010
Intercept	0.0001	0.0008
Correlation coefficient (r^2)	0.9988	0.9999
LOD (µg/ml)	0.1	0.07
LOQ (µg/ml)	0.21	0.6

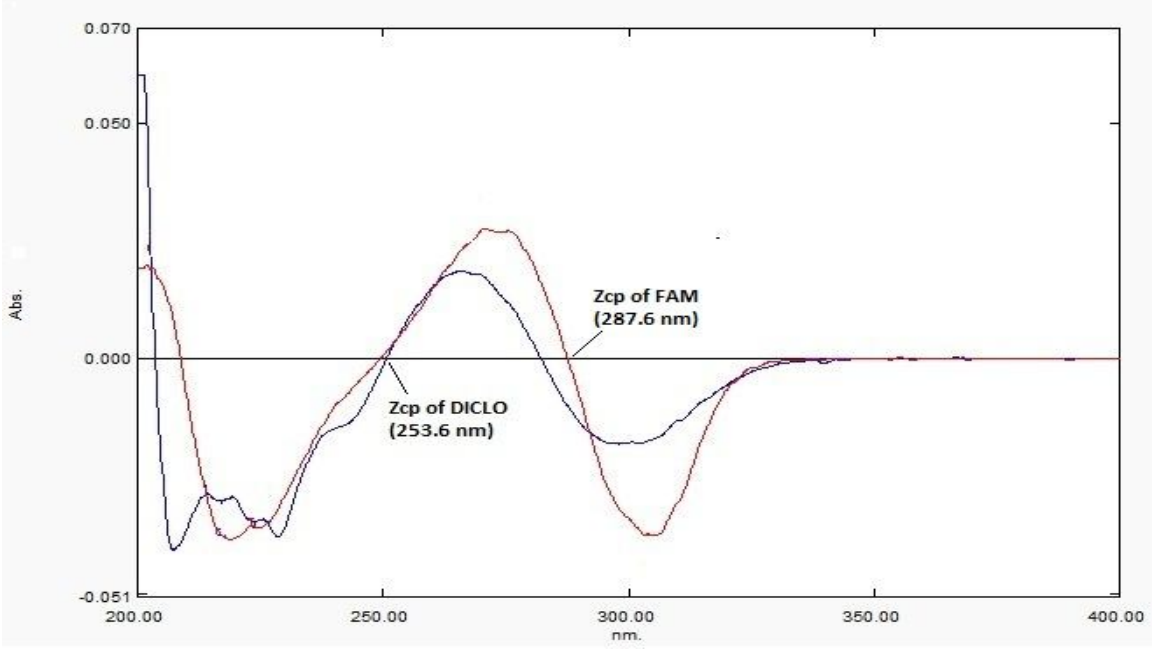

Fig. 1: Overlain spectra of mixed standard solution of FAMO (4 µg/ml) and DICLO (10µg/ml)

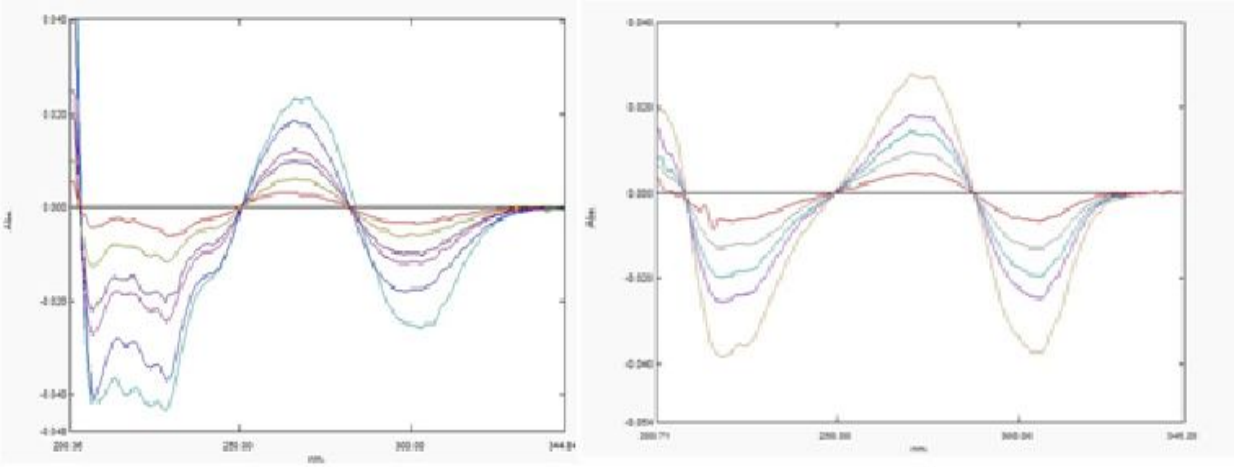

Fig. 2: Overlain spectra of serial dilutions of (a) FAMO (2-12 µg/ml) at 253.6 nm for calibration curve and (b) DICLO(5-30 µg/ml) at287.6 nm for calibration curve

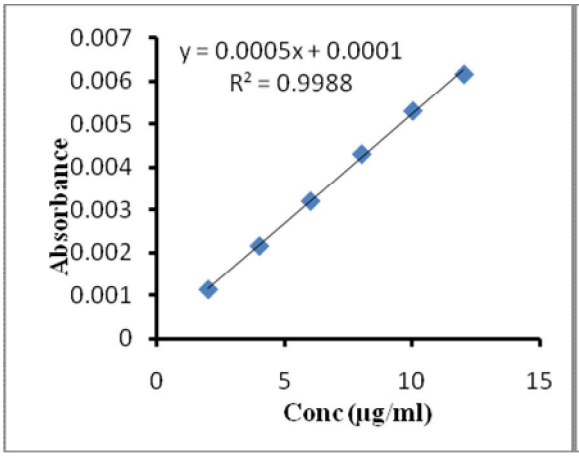

Fig. 3: Calibration Curve of FAMO at 253.6 nm

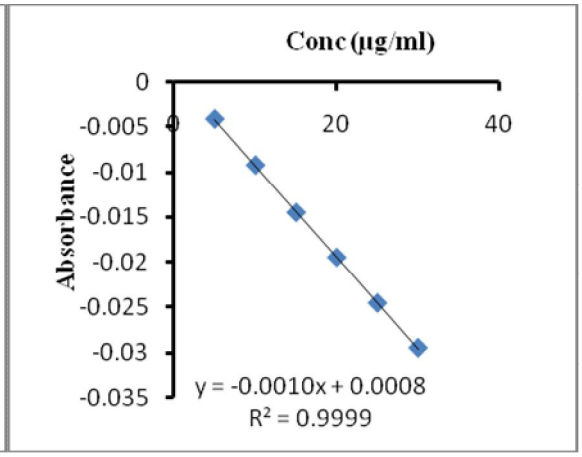

Fig. 4: Calibration Curve of DICLO at 287.6 nm

CONCLUSION

From the obtained data, the developed and validated UV spectrophotometric (First Order Derivative Spectroscopic method) was found to be simple, rapid, accurate, sensitive, precise and robust for determination of Famotidine and Diclofenac Potassium in combined tablet dosage formulation.The excipients usually present in the pharmaceutical formulation did not interfere with determination of Famotidine and Diclofenac potassium. Thus the developed methods can be successfully used for routine quality control of Famotidine and DiclofenacPotassium in their combined tablet dosage form.

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