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Derivative spectrophotometric method for determination of diacerhein and aceclofenac in pharmaceutical formulations

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ABSTRACT

A simple, accurate and precise spectrophotometric method was developed for simultaneous estimation of Diacerhein and Aceclofenac in tablets by using first order derivative zero-crossing method. Aceclofenac showed a zero crossing point at 275.8 nm while Diacerhein showed a zero crossing point at 293.4 nm. The dA/dλ was measured at 293.4 nm for Aceclofenac and 275.8 nm for Diacerhein and calibration curves were plotted as dA/dλ versus concentration, respectively. The method was found to be linear in the range of 10-50 μg/mL for both the drugs. The limit of detection was found to be 0.48 and 0.53 μg/mL for Aceclofenac and Diacerhein respectively. The limit of quantitation was 1.46 and 1.6 μg/mL for Aceclofenac and Diacerhein respectively. The method was successfully applied for simultaneous determination of Aceclofenac and Diacerhein in formulation.

KEYWORDS

Aceclofenac;
Diacerhein;
Derivative spectroscopy;
Zero crossing method.

INTRODUCTION

Diacerhein is chemically known as 4,5-Bis(acetyloxy)-9,10-dioxo-2-anthracenecarboxylic acid[1]. Aceclofenac is chemically known as 2-[2-[2-(2,6-Dichlorophenyl) aminophenyl]cetyl] oxyacetic acid[2]. Diacerhein is used treatment of osteoarthritis. Aceclofenac is used as anti-inflammatory drug. Literature survey reveals that assay of Aceclofenac as bulk and its dosage form is official in British Pharmacopoeia 2007[3] and Indian Pharmacopoeia 2007[4]. Several analytical methods reported for estimation of Aceclofenac include Spectrophotometry[5,6], High Performance Liquid Chromatography (HPLC)[7-10], Thin Layer Chromatography (TLC)[11,12], Liquid Chromatography - Mass Spectrometry (LC-MS)[13] and Fluorimetry[14]. Analytical methods reported for the estimation of Diacerhein are Spectrophotometry[15], HPLC[16] and flow injection Chemiluminescence[17]. To the best of our knowledge, there is no published derivative spectrophotometric method for this combination. The present paper describes a simple, accurate and precise method for simultaneous estimation of Diacerhein and Aceclofenac in combined tablet dosage form. The proposed method is optimized and validated as per the International Conference on Harmonization (ICH) guidelines[18].

EXPERIMENTAL

Chemicals

Working standard of Diacerhein was procured from

M/s. Lupin Research Park, Pune, India and Aceclofenac was procured from M/s. NuLife Pharmaceuticals, Pune, India as gift samples. Marketed formulation Dycerin A (Diacerhein-50 mg/tablet and Aceclofenac-100 mg/tablet) was purchased from local market.

Instrumentation

First order derivative spectrum was recorded in the wavelength range 200 – 400 nm using UV-Visible double beam spectrophotometer of make Jasco, model V-550 with 1 cm matched quartz cells. The instrumental parameters optimized for the first order derivative spectrum were:

Bandwidth : 1 nm
Scanning speed : 400 nm/min
Data pitch : 0.2 nm

Preparation of stock solution

Standard stock solutions of Diacerhein and Aceclofenac were prepared by separately dissolving 10 mg each in 1 mL of dimethylacetamide and further making the volume to 10 mL with methanol. Appropriate volumes were diluted with methanol in volumetric flasks to get concentrations in range of 10-50 µg/mL for each drug.

Preparation of sample solution

20 tablets were weighed and crushed to obtain fine powder. An accurately weighed tablet powder equivalent to 10 mg of Diacerhein and 20 mg of Aceclofenac was transferred to 10 mL volumetric flask. 2 mL Diamethylacetamide was added in the flask and sonicated for 15 min. The volume was then made up to 10 mL using methanol as solvent. The resulting solution was filtered first through Whatmann filter paper No. 41 and if the particles were found to be present then the solution was again filtered through membrane filter paper. Filtrate was appropriately diluted to get concentration of 10 µg/mL of Diacerhein and 20 µg/mL of Aceclofenac.

Procedure

Firstly the solutions of Aceclofenac and Diacerhein were scanned from 200 – 400 nm. The first derivative spectrum was found to provide a better resolution of the overlaying absorption bands. The absorbance values of the first derivative spectrum at 293.4 nm for Aceclofenac (zero crossing point of Diacerhein) and 275.8 nm for Diacerhein (zero crossing point of Aceclofenac) were then selected (Figure 1 and 2). Absorbances of sample solutions were recorded at 293.4 nm and 275.8 nm. The calibration curves were constructed by plotting dA/dλ versus concentration and regression equations were further computed. The con-

TABLE 1 : Validation parameters for first derivative method

Parameters	Diacerhein	Aceclofenac
Beers law range	10 - 50 µg/mL	10 - 50 µg/mL
Wavelength (nm)	275.8 nm	293.4
Correlation coefficient	0.9994	0.9939
Linearity equation = y = mx + c		
Slope	0.0031	0.0011
Intercept	0.0078	0.0033
LOD (µg/mL)	0.53	0.48
LOQ (µg/mL)	0.16	1.46
Precision (% RSD)		
Intraday precision	0.34	0.51
Interday precision	1.24	1.15

TABLE 2 : Recovery studies

% Level	Sample (µg/ml)	Std. added (µg/ml)	Amount recovered (mg)	% Recovery ± SD*
Diacerhein				
80	20	16	35.94	99.83 ± 0.41
100	20	20	39.94	99.84 ± 0.36
120	20	22	43.78	99.50 ± 0.43
Aceclofenac				
80	20	16	36.13	100.37 ± 0.25
100	20	20	39.94	99.84 ± 0.27
120	20	22	44.00	100.00 ± 0.30

***SD – Standard deviation**

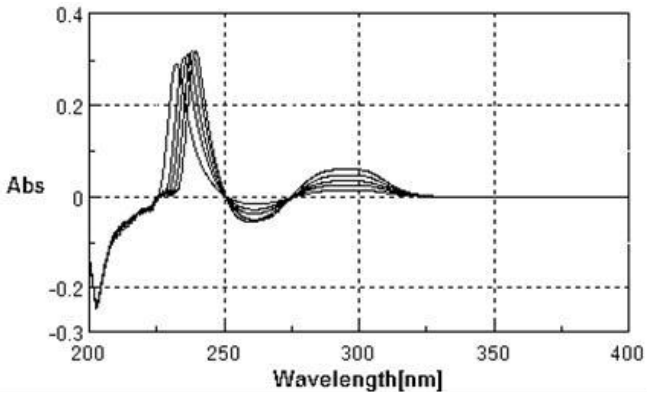

Figure 1 : Overlain first derivative spectrum of aceclofenac (Concentration 10-50 µg/mL)

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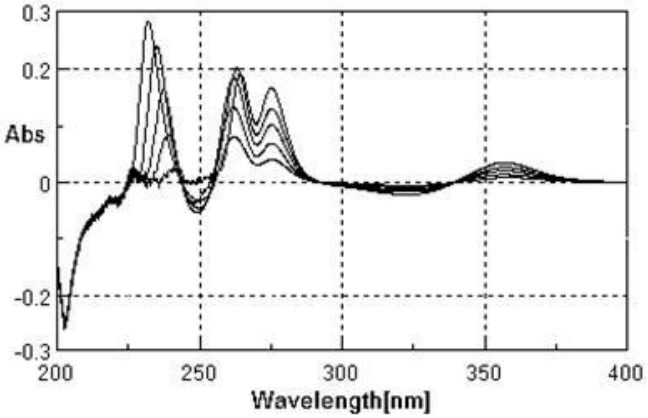

Figure 2 : Overlain first derivative spectrum of diacerhein (Concentration 10-50 µg/mL)

centrations of two drugs in the sample were then determined by using the calibration equations 1 and 2.

$$C_{Dia} = (dA/d\lambda - 0.0078)/ 0.0031 \quad (1)$$

$$C_{Aceclo} = (dA/d\lambda - 0.0033)/ 0.0011 \quad (2)$$

Method validation

Linearity and range

The linearity for both Diacerhein and Aceclofenac were determined at five concentration levels ranging from 10 µg/mL – 50 µg/mL.

Precision

Precision was checked by performing interday and intraday variation studies. In interday variation, the absorbance for standard solution was measured on three consecutive days. In intraday variation, the absorbance was measured three times in a day. The percent Relative Standard Deviation (% RSD) values were determined for interday and intraday variation.

Accuracy

To check accuracy of the method, recovery studies were carried out by standard addition method, to pre-analyzed sample solution at three different levels 80, 100 and 120 %. Mean percentage recovery was determined.

Limit of detection and limit of quantitation

The limit of detection (LOD) is smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula:

$$LOD = \frac{3.3\,\sigma}{S}$$

Where, σ = Standard deviation of the response, S = slope of the calibration curve

The LOQ is the smallest concentration of the analyte, which gives a response that can be accurately quantified. LOQ was calculated using the following formula:

$$LOD = \frac{10\,\sigma}{S}$$

Where, σ = Standard deviation of the response, S = slope of the calibration curve

Robustness

Robustness of the method was determined by making slight deliberate changes in data pitch, such as from 0.2 to 1 nm. It was observed that there were no marked changes in the calibration data, which demonstrated that the spectrophotometric method developed is robust.

RESULTS AND DISCUSSION

The linearity in the proposed method for determination of Diacerhein and Aceclofenac was found in the concentration range of 10-50 µg/mL. Marketed brand of tablet was analyzed and the percentage label claim estimated was 100.79 % ± 0.52 for Diacerhein and 99.55 % ± 0.19 for Aceclofenac. This derivative spectroscopic method was validated as per ICH guideline. The accuracy of method was determined at 80, 100 and 120 % level. The % recovery ranges from 99.53 % to 100.55 % for Aceclofenac and 99.10 % to 100.28 % for Diacerhein. Precision was calculated as interday and intraday variations (% RSD is less than 1.5) for both drugs.

CONCLUSION

The validated spectrophotometric method was found to be simple, accurate and rapid for the routine determination of Diacerhein and Aceclofenac in tablet formulation. The proposed method can therefore be successfully used for simultaneous estimation of Diacerhein and Aceclofenac in combined dosage form.

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