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ESTIMATION OF LORNOXICAM AND DIACEREIN IN DOSAGE FORM BY SIMULTANEOUS EQUATION AND Q-ANALYSIS METHOD USING UV SPECTROSCOPIC TECHNIQUE

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ABSTRACT

Two simple sensitive accurate uv spectroscopic methods were developed for the simultaneous estimation of diacerein and lornoxicam in pharmaceutical dosage form. In this communication simultaneous equation method and absorbance ratio method (Q value) were reported for the assay of both the drugs in the pharmaceutical dosage form. In simultaneous equation method the absorbance of the sample was measured at 341 nm and 398 nm respectively which was further applied for determining the concentration of the both the drugs. In absorbance ratio method (Q value) the absorbances were measured at wavelengths 341 nm and 398 nm and other at the isosbestic point i.e. 372 nm. The proposed methods were validated statistically for specificity, linearity, accuracy and precision. Recoveries of methods were carried out by standard addition method. The low values of standard deviation and percentage RSD indicated high precision of methods. These methods were successfully used for routine analysis of diacerein and lornoxicam in combination dosage form with good recoveries.

KEYWORDS

Diacerein ,Lornoxicam,Simultaneous equation method, Absorbance ratio method

INTRODUCTION

The present research article proposes a novel analytical methods for simultaneously determining lornoxicam and diacerein in pharmaceutical dosage form. Lornoxicam is a non-steroidal anti-inflammatory drug of the oxicam class with analgesic, antiinflammatory and antipyretic properties. Diacerein is the first interleukin 1 (Il-1) inhibitor in osteoarthritis used for the treatment of degenerative joint diseases. Lornoxicam is (3*E*)-6-chloro-3-[hydroxy(pyridin-2-ylamino)methylene]-2-methyl-2,3-dihydro-4*H*-thieno[2,3-*e*][1,2]thiazin-4-one 1,1-dioxide. Diacerein is 4,5-diacetyloxy-9,10-dioxo-anthracene-2-carboxylic acid. The spectral data of lornoxicam and diacerein showed absorbance maxima at 398 nm and 341 nm respectively with the isosbestic point at 372 nm. Literature survey reveal no official method for assay of lornoxicam whereas diacerein is reported in IP[1]. In the proposed work optimization and validation of uv spectroscopic methods[2] for simultaneous determination of lornoxicam and diacerein were presented. The developed method can be used for the routine analysis in quality control laboratories for simultaneous determination of lornoxicam and diacerein in combination dosage form.

EXPERIMENTAL

Materials

A SHIMADZU UV-160A double beam uv-visible recording spectrophotometer with pair of 5 mm matched quartz cells was used to measure absorbance of the solution. A sartorious analytical balance with a least count of 0.01 mg was used. Lornoxicam and diacerein were obtained from reputed firms with certificate of analysis. Dimethyl acetamide of A.R grade were used in the study.

Preparation of standard solution

Stock solution of lornoxicam (160 µg/ml) and diacerein (1000 µg/ml) was prepared in dimethyacetamide. From this stock solution standard solution of lornoxicam (16 µg/ml) and diacerein (100 µg/ml) for method I and II were prepared using appropriate dilutions.

Preparation of sample solution

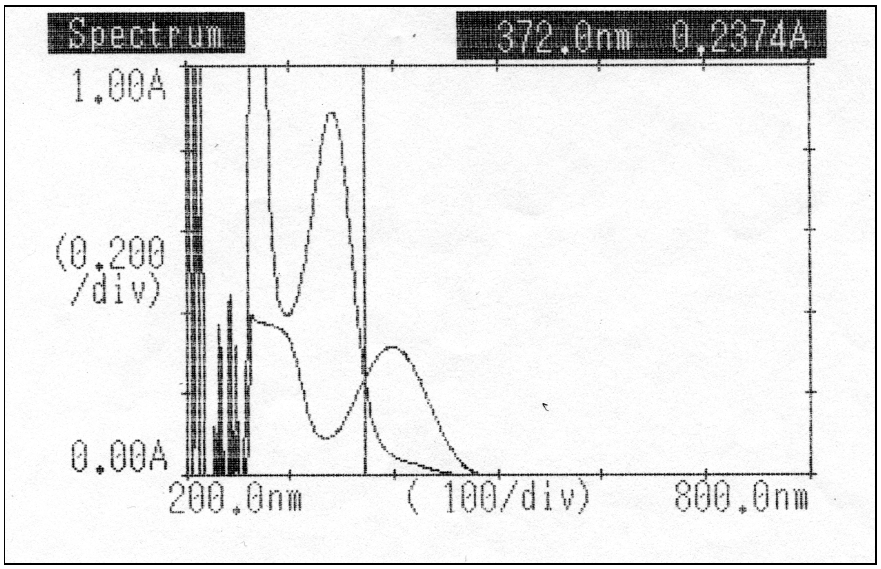
About 20 tablets were crushed to powder and powder equivalent to 16 mg of lornoxicam and 100 mg of diacerein was accurately weighed and transferred to 100 ml of volumetric flask. About 70 ml of dimethyl acetamide was added to it and sonicated for 30 minutes. Further the volume was made upto the mark with dimethyl acetamide to give a concentration of 160 µg/ml of lornoxicam and 1000 µg/ml of diacerein. Further 5 ml of the above solution was diluted to 50 ml with dimethyl acetamide to give a concentration of 16 µg/ml of lornoxicam and 100 µg/ml of diacerein.

Methods of estimation

Method I (Simultaneous equation method)

In simultaneous equation method (vierodt's method) two wavelengths were selected i.e. 341 nm and 398 nm which were absorbance maximas of diacerein and lornoxicam respectively (Figure 1). Standard stock solution of lornoxicam (160 µg/ml) and diacerein (1000 µg/ml) were prepared in dimethyacetamide. The stock solutions of both the drugs were further diluted separately with dimethyl acetamide to get a series of standard solutions containing 8 – 24 µg/ml of lornoxicam and 50 – 150 µg/ml of diacerein respectively. The absorbances for both the drugs were measured at selected wavelengths over the linear range and the mean absorbance was determined. The content of both ingredient in the sample were obtained by using following equations:

Figure.1
Overlain spectra of diacerein and lornoxicam



$$Cx = \frac{A_2 ay_1 - A_1 ay_2}{ax_2 ay_1 \quad ax_1 ay_2}$$

$$Cy = \frac{A_1 ax_2 - A_2 ax_1}{ax_2 ay_1 \quad ax_1 ay_2}$$

where,
A_1 = Absorbance of the diluted sample at 341 nm
A_2 = Absorbance of the diluted sample at 398 nm
ax_1 = Absorptivity of diacerein at 341 nm
ay_2 = Absorptivity of lornoxicam at 398 nm
Cx = Concentration of diacerein in the diluted sample
Cy = Concentration of lornoxicam in the diluted sample

Method II (Absorbance ratio - Q analysis method)
In this method the ratio of absorbances at any two wavelengths is a constant value independent of concentration or wavelength. In the assay of the drug product under study which contains two active ingredient i.e. diacerein and lornoxicam the absorbances were measured at two wavelengths, one being the λ_{max} of diacerein (341 nm) and other being the wavelength of equal absorptivity of the two components i.e. an isosbestic point (372 nm). The content of both ingredient in the sample were obtained by using following equations :

$$Cx = \frac{Q_m - Q_x}{Q_y - Q_x} \times \frac{A_1}{ax_1}$$

$$Cy = \frac{Q_m - Q_y}{Q_x - Q_y} \times \frac{A_1}{ay_1}$$

Instrumental Parameters

A SHIMADZU UV-160A double beam uv-visible recording spectrophotometer with pair of 5 mm matched quartz cells with wavelengths of 341 nm and 398 nm which were absorption maxima of diacerein and lornoxicam respectively were selected. The isosbestic point selected was 372 nm. The diluent used for preparing standard and sample solution was dimethyl acetamide.

Method Development

The initial development was started with selection of proper diluent. Different solvents like water, methanol, acetonitrile, ethanol were used as diluent but none of them showed stability of diacerein. Finally dimethyl acetamide showed excellent stability for both diacerein and lornoxicam. The wavelength maxima of both the drugs were determined as 341 nm and 398 nm. Different quantitation methods like derivative spectroscopy, multi-component spectroscopy etc were evaluated for simultaneously determining diacerein and lornoxicam in finished dosage form. Finally simultaneous equation method and absorbance ratio method were more sensitive for accurate measurement of diacerein and lornoxicam in finished dosage form i.e. tablet.

RESULT AND DISCUSION

The results of analysis shows that the proposed analytical methods are capable of estimating diacerein and lornoxicam in finished dosage form like tablet. The developed uv spectroscopic methods were validated for parameters like system suitability, specificity, linearity, accuracy, precision etc.

Method Validation

The suitability of the proposed analytical procedure for determining the assay of both the drugs i.e. diacerein and lornoxicam was demonstrated by statistically evaluating different validation characteristics like linearity, accuracy, precision etc.

Specificity

Specificity of the method was established by evaluating the interference of the placebo at wavelength maxima of diacerein and lornoxicam. The placebo showed no uv absorption at 341 nm and 398 nm. Also at the isosbestic point 372 nm the placebo showed no interference. Thus the specificity was established for both simultaneous equation and absorption ratio method. The overlain spectra of both the drugs is given in figure 1.

Linearity

Under the experimental conditions described above, calibration curves were plotted for both diacerein and lornoxicam. Regression analysis was done on the absorbance (y) v/s concentration (x). The linear range for diacerein was found to be 50 – 150 µg/ml whereas for lornoxicam it was found to be 8 – 24 µg/ml. The results of the same are tabulated in Table 1.

Table 1

Statistical evaluation of the test data subjected to regression analysis

Parameters	*Diacerein*	*Lornoxicam*
Correlation Coefficient (r)	0.9999	0.9999
% Intercept (y)	1.8	2.3
Slope (m)	0.0088	0.0204

Accuracy

The accuracy of the analytical method was established by spiking diacerein and lornoxicam in the placebo at 50%, 100% and 150% of the label claim. The recoveries were found be between 98.0 to 102.0 by simultaneous equation method and Q-analysis method. The results of the same are tabulated in Table-2

Table 2
Recovery study of synthetic mixture of diacerein and lornoxicam

	Diacerein					Lornoxicam				
Level (%)	Amount of drug added (mg)	Amount of drug recovered (mg)	% Recovery	% Error	% RSD	Amount of drug added (mg)	Amount of drug recovered (mg)	% Recovery	% Error	% RSD
Method I (Simultaneous equation method)										
50	50.31	50.65	100.7	0.00		7.82	7.81	99.9	0.01	
	51.15	50.85	99.4			7.91	7.83	99.0		
	49.83	49.70	99.7			7.89	7.86	99.6		
100	99.75	99.34	99.6	0.01	0.55	16.23	16.11	99.3	0.01	0.69
	100.52	99.45	98.9			16.11	16.16	100.3		
	100.28	99.27	99.0			16.27	16.02	98.4		
150	150.23	148.73	99.0	0.01		24.49	24.29	99.2	0.00	
	149.35	148.89	99.7			24.37	24.26	99.5		
	150.18	148.87	99.1			24.12	24.28	100.7		
Method II (Absorbance ratio - Q analysis method)										
50	40.8	41.2	100.9	0.01		6.80	6.71	98.7	0.00	
	40.7	40.9	100.4			6.71	6.65	99.2		
	41.0	41.4	100.9			6.69	6.74	100.7		
100	102.3	103.7	101.4	0.01	1.3	16.78	16.89	100.7	0.01	0.83
	102.8	104.2	101.4			16.93	16.97	100.3		
	102.5	104.5	101.9			16.86	17.01	100.9		
150	148.1	145.4	98.2	0.02		23.50	23.67	100.7	0.00	
	147.3	145.6	98.9			23.90	23.71	99.2		
	147.9	145.6	98.5			23.62	23.72	100.4		

Method Precision

The distribution of the data points between a series of measurements was obtained by multiple sampling of a homogenous sample and determining the coefficient of variation for diacerein and lornoxicam by simultaneous equation method and Q-analysis method. The results of the same are tabulated in Table-3

Table 3
tatistical evaluation of the test data subjected to method precision

Sample Number	% Assay			
	Simultaneous equation		Q-Analysis	
	Diacerein	Lornoxicam	Diacerein	Lornoxicam
1	99.13984	15.43	97.6	15.4
2	99.36692	15.46	97.2	15.2
3	99.42373	15.46	97.5	15.2
4	99.23438	15.46	97.1	15.6
5	99.36692	15.46	97.5	15.2
6	99.42755	15.45	97.6	15.4
Mean	99.33	15.45	97.4	15.3
SD	0.11512	0.009368	0.2262	0.1474
% RSD	0.12	0.06	0.23	0.96

CONCLUSION

The proposed uv spectrophotometric methods of estimation i.e. simultaneous equation and Q analysis method showed good agreement of the estimated concentrations of both the active ingredients with declared label claims. Both the method of estimation showed good recoveries close to 100 % and % coefficient of variation was less than 1.0 % for both diacerein and lornoxicam. Hence the proposed uv spectrophotometric method is strongly recommended for the quality control of the finished dosage form.

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