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SPECTROPHOTOMETRIC DETERMINATION OF DIACERIN IN BULK AND PHARMACEUTICAL FORMULATION

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ABSTRACT

It is a disease modifying anti-rheumatoid drug used in the treatment of Osteoarthritis and chronic inflammatory arthritis. Various methods of analysis are available but are time consuming and expensive. A simple, rapid and accurate colorimetric method has been developed for the estimation of diacerein in bulk and pharmaceutical dosage forms, method are based on pink colored complex formation between diacerein with sodium hydroxide which shows maximum absorbance at 514nm .The linearity was found to be 10-50µg/ml. The developed method was found to be precise and accurate form the statistical validation of the analysis data.

KEYWORDS

Diacerein, rhein, spectrophotometric, Diacetylrhein

INTRODUCTION

Diacerein is chemically 4, 5-diacetyloxy-9,10-dioxo-anthracene-2-carboxylic acid.

Diacerein **(DAR**), also known as diacetylrhein**,** is a drug used in the treatment of osteoarthritis[1,2]**.** It obtained from Aloe Vera**.** Diacerein and its active metabolite of rhein are anthraquinone compounds that ameliorate the course of osteoarthritis [3,4]. DAR is a slow acting symptomatic treatment of osteoarthritis, which has demonstrated efficacy on functional manifestations of osteoarthritis and on the structural component[5]. In a recent report, two mechanisms of action have been validated: in vitro inhibition of interleukin-1 (IL-1) synthesis, the main cytokine involved in cartilage destruction and activity on the synthesis of proteoglycans and hyaluronic acid, the principal component of cartilage[7]. Accordingly, a simple, rapid sensitive visible spectrophotometric method can be used for routine quality control analysis formulations containing the drug.

MATERIAL AND METHODS

Instruments:

A. A Shimadzu-1700 double beam UV/Vis spectrophotometer with

(a) Spectral bandwidth of 1 nm.

(b) Wavelength accuracy ±0.3 nm with a pair of 10 mm matched quartz cells.

B. Ultrasonicator.

Reagents:

All chemicals used in assay were of analytical grade and the reagent solutions were prepared using double distilled water. Diacerein pure drug was obtained as a gift sample from Glenmark pharma Mumbai.

Capsules of diacerein were purchased from local market for analysis. Sodium hydroxide is used for colour reaction.

EXPERIMENTAL

Determination of λ_{max}:

Weighed amount of diacerein was dissolved in Acetone to obtain 100mg/ml solution .This solution was scanned between 400-800 nm and absorption maximum was determined the effect of dilution on absorption maximum was studied by diluting the above solution to 20 µg/ml. The λmax of DAR was found to be 514 nm .

Preparation of standard solutions:

Standard DAR stock solution (1mg/ml) was prepared by dissolving 100mg in 100 ml volumetric flask.

Preparation of working standard solutions:

10 ml of the stock solution was diluted to 100 ml with the Acetone to obtained working standard solution (100µg/ml). From this solution prepared different concentration (10 to 50 µg/ml).Sodium hydroxide (2%) was prepared in distilled water. In case of formulation one brand of commercially available capsules were analysed by proposed method.

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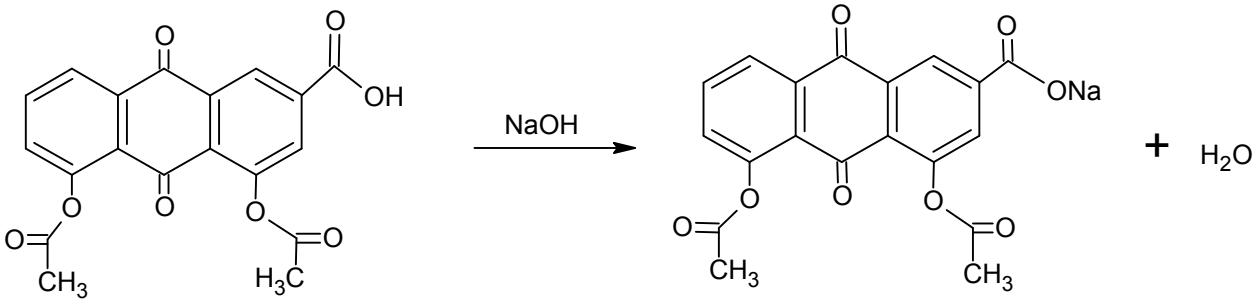
Assay:

Weighed accurately 20 capsule of DAR each contain 50mg DAR. Capsule powder equivalent to 50mg of DAR was taken and dissolve 50mg in 50 ml volumetric flask and made the volume to mark with Acetone. From this solution ranging from 1 –5ml (100µg/ml) were transferred into a series of volumetric flasks. To each of the above 1 ml of (2% NaOH) was added and made up to 10 ml with distilled water .The pink colour complex was formed and measure at 514 nm against reagent blank .The calibration curve is plotted between the concentration of DAR and respective measured absorbance



VALIDATION OF SPECTRO PHOTOMETRIC METHOD[6]:

The validation of spectrophotometric method was carried out by determining the selectivity, linearity, precision, accuracy, quantification and detection limit.

i. Linearity:

The aliquots working standard solution was diluted serially with sufficient Acetone to obtain final concentration range 10-50 µg/ml. The calibration curve for Diacerein was obtained by measuring the absorbance at λ_{max} of 514 nm. Statistical parameters like the slope, intercept, coefficient of correlation, standard deviation, relative standard deviation and error were determined.

ii. Precision:

The precision of spectrophotometric method reported, as %RSD was estimated by measuring repeatability time dependent intermediate precision and reproducibility by measuring absorbance of five-individual preparation of DAR standard solution.

iii. Recovery:

Recovery studies were performed to judge the accuracy of method. 1 ml of standard formulation was taken in three 10 ml volumetric flask and add to it 1 ml, 2ml and 3ml of working standard solution respectively and made the volume to mark. The respective absorbance at 514nm was recorded against the blank. The amount of added concentration was determined from the absorbance values obtained and percentage recovery was determined for each formulation.

iv. Robustness:

The evaluation of robustness was performed for system suitability to ensure the validity of analytical procedure. This was done by varying the instrument, analyst and time of study .The analysis was performed on UV-Vis Spectrophotometric model Shimadzu-1700 double beam UV/Vis spectrophotometer and Elico SL-159.Interday and intraday analysis was performed by changing the analyst.

RESULTS AND DISCUSSION

The Vis scan of solution between 400-800nm showed the absorbance maxima at 514nm, shown in fig. 1. The beer's law was verified from the calibration curve by plotting a graph of concentration vs. absorbance. The plot is showing in fig.2. Regression analysis showed very good correlation. The calibration plot revealed zero intercept which is clear by the regression equation Y= m X + C (Y is absorbance, m is the slope and x is the concentration of Diacerein in mcg/ml) as obtained are depicted in Table No. 1. The results of analysis for assay and recovery studies for three different formulations were studied and are show in Table No. II. No significance variation was observed on interday and intraday analysis. Also no significant variations were observed on changing the instrument make and model.

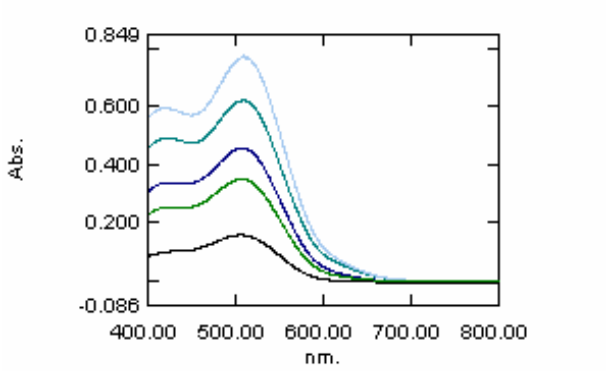


Fig .No.-1

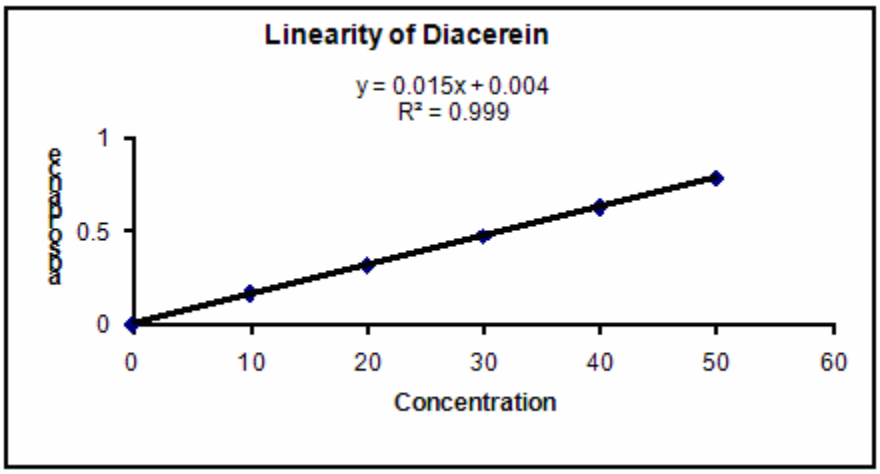


Fig.No -2
Calibration curve of diacerein

Table 1
Summary of validation parameters for diacerein by spectroscopic method

Parameters	Value
λ_{max}	514
Beer's law limit(mcg/ml)	10-50
Molar Absorptivity	$1.65*10^4$
Regression Equation (Y=ax+b)	
Intercept (a)	0.0157
Slope (b)	0.0046
Correlation coefficient (r^2)	0.9999
%RSD	0.38883

Table 2
Analysis of diacerein in capsule dosage form

Capsule formulation	Label Claim (mg)	Amount found (mg/cap)	% Label Claim found ±SD
Brand A	50	50.12 50.30 50.25 49.80 50.10	100.28±0.194

Table 3
Recovery Studies

Concentration of drug added to the formulation (mcg/ml)	% Recovery ±SD*	Coefficient of variance
10	99.08±0.1768	0.1784
20	99.84±0.1767	0.1769
30	99.6258±0.257	0.2579

*SD standards for standard deviation, the results are mean of five readings (n=5)

DISCUSSION

The spectrum of Diacerein in colour complex showed the absorbance maxima at 514 nm. No effect of dilution was observed at maxima, which confirmed the maxima at 514 nm. The statistical analysis of data obtained for the calibration curve of Diacerein in pure solution indicates a high level of precision for

the proposed method. The coefficient of correlation was highly significant. The linearity range was observed between 10 -50 µg/ml. The plot clearly showed a straight line passing through origin (Y=0.0157x+.0046). The assay method was validated by low value of % RSD and standard error, indicating accuracy and precision of the methods. Excellent recovery studies further proves the accuracy of the method. The robustness of method was studied by varying the instrument time of study and analyst. Reproducibility of the result confirmed the robustness of the method.

CONCLUSIONS

From the result and discussion the method described in this paper for the determination of Diacerein from capsule formulation is simple, accurate, sensitive and reproducible. The proposed method utilizes inexpensive solvents. The proposed method could be applied for routine analysis in quality control laboratories.

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