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# First and Second Derivative Spectrophotometric Methods for Determination of Diacerein in Pharmaceutical Formulation

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**Abstract.:** Simple, fast and reliable derivative spectrophotometric methods were developed for determination of diacerein in bulk and pharmaceutical dosage forms. The solutions of standard and the sample were prepared in acetonitrile. The quantitative determination of the drug was carried out using the first derivative values measured at 243 nm and the second derivative values measured at 256 nm (n=6). Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of diacerein using 2-6 µg.mL$^{-1}$ ($r^2$ = 0.9948 and $r^2$ = 0.9921) for first and second derivative spectrophotometric method. All the proposed methods have been extensively validated as per ICH guidelines. There was no significant difference between the performance of the proposed methods regarding the mean values and standard deviations. Developed spectrophotometric methods in this study are simple, accurate, precise, specific, sensitive, reproducible and robust to assay diacerein in capsules.
**Keywords:** Diacerein, Derivative spectrophotometric, First derivative spectrum, Second derivative spectrum.

## 1. Introduction

Diacerein, a thienobenzodiazepine derivative with chemical name 1,8-diacetoxy-3-carboxy anthraquinone (Fig. 1) is a novel osteoarthritis drug which selectively inhibits the IL-1 [1].

It is semisynthetic anthraquinone derivative extracted from certain plants. It directly inhibits IL-1 synthesis and release which plays a fundamental role in osteoarthritis pathophysilogy and cartilage destruction. IL-1 promotes expression of inducible nitric oxide synthase, increase release of PGE, Stimulates matrix metalloproteinase, IL-6, IL-8 in human osteoarthritis chondrocytes, which promotes joint degradation. Hence, by inhibiting IL-1 diacerein retards all pathological prepossess initiated OA [2-5].

Diacerein also inhibits IL-1 induced expression of cartilage degrading enzymes. In contrast to NSAIDS, diacerein does not inhibit synthesis of prostaglandin hence no gastrodeodenal toxicity. It also involved in prevention of loss of hydroxyproline and proteoglycans in joint cartilage.

There are no derivative spectrophotometric methods reported for the analysis of diacerein in pharmaceutical formulation. Derivative spectrophotometry is an analytical technique of great utility for extracting both qualitative and quantitative information from spectra composed of unresolved bands, and for eliminating the effect of baseline shifts and baseline tilts. It consists of calculating and plotting one of the mathematical derivatives of a spectral curve. Derivative spectrophotometry is now a reasonably prized standard feature of modern micro-computerized UV spectrophotometry. The aim of the present research work was to develop simple, sensitive and validated as per the ICH guideline [5] derivative spectrophotometric methods for the determination of diacerein in pharmaceutical formulation.

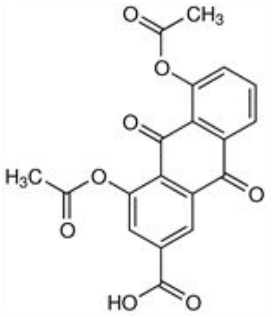

**Figure 1. Chemical structure of diacerin**

## 2. Experimental

### 2.1. Materials and methods

Diacerein pure compound was kindly supplied by Glenmark Pharmaceuticals, Kurkumbh, India and was used without further purification. All chemicals and reagents used were of analytical grade and were purchased from Merck Chemicals, India.

### 2.2. Instrumentation

UV and derivative spectra of the solutions were recorded on double beam UV–Vis spectrophotometer Jasco V-530 using 10mm path length quartz cells with fixed slit width of 2 nm at a scanning speed of 1000 nm.min$^{-1}$, scan range of 200–400 nm, data pitch 0.5 nm.

### 2.3. Preparation of standard and sample solutions:

Stock solution of 1000 µg.mL$^{-1}$ of diacerein was prepared in acetonitrile, for first and second derivative spectrophotometric analysis. The standard solutions were prepared by dilution of the stock solution with methanol in a concentration range of 2, 3, 4, 5 and 6 µg.mL$^{-1}$ with methanol for first and second derivative spectrophotometric methods. Methanol was used as a blank solution.

### 2.3. Assay procedure:

A total of 20 capsules of diacerein were opened and the contents were weighed and mixed.accurately weighed and powdered. An aliquot of powder equivalent to the weight of 1 capsule was accurately weighed and transferred to volumetric flask and was dissolved in 100 ml of acetonitrile and made up to the volume with HPLC grade acetonitrile. The solutions were filtered through a 0.45 µm nylon filter and sonicated for about 45 min and then volume made up with methanol. This solution was filtered to remove anyinsoluble matter. The filtrate was collected in a clean flask. Appropriate dilutions were made to obtain 10 µg.mL$^{-1}$ with acetonitrile from stock solution for both UV and derivative spectrophotometric methods.

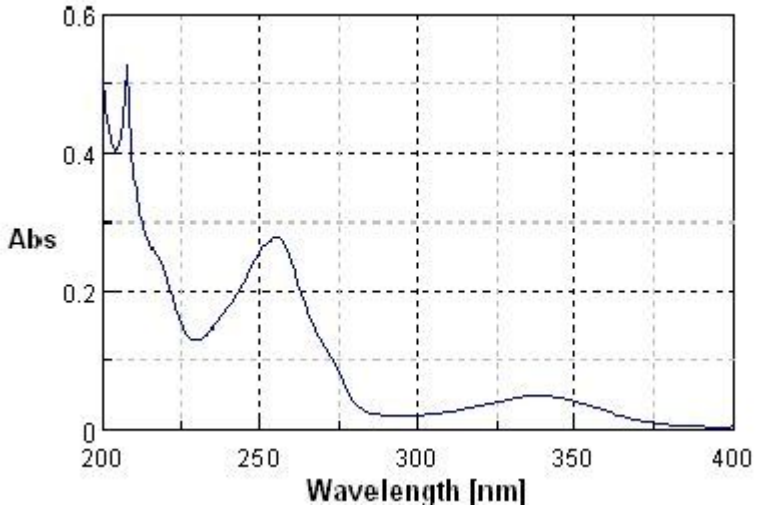


**Figure 2. UV spectrum of 10 µg.mL$^{-1}$ diacerein in acetonitrile**

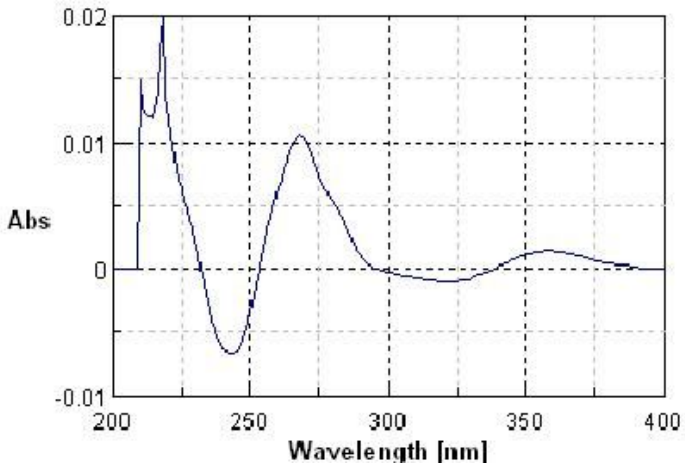


**Figure 2. First derivative spectrum of 10 µg.mL$^{-1}$ diacerein in acetonitrile**

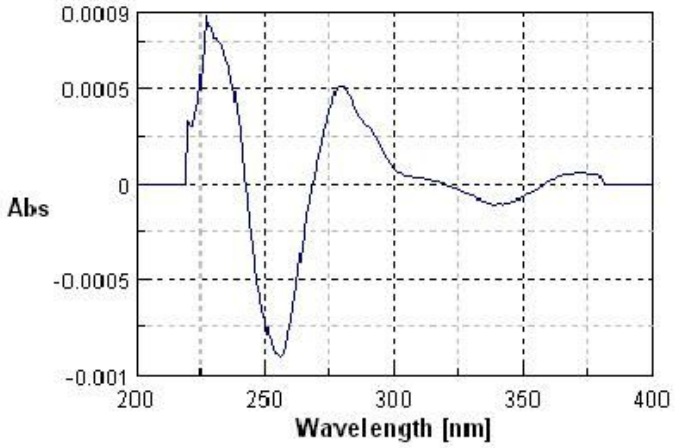


**Figure 3. Second derivative spectrum of 10 µg.mL$^{-1}$ diacerein in acetonitrile**

**Table I :Stastical data for the calibration graphs for determination of diacerein by proposed methods**

| Parameters | First derivative | Second derivative |
|---|---|---|
| Linearity range (2-6µg.mL$^{-1}$) | 2-6 | 2-6 |
| $r^2$ ± S.D. | 0.9948 | 0.9991 |

[a] n=6.

**Table II: Results of Intra and Inter Day Precision**

| Parameters | Intra Day Precision | | Inter Day Precision | |
|---|---|---|---|---|
| | S.D | % RSD | S.D | % RSD |
| First derivative | 0.039 | 0.47 | 0.1 | 0.58 |
| Second derivative | 0.056 | 0.98 | 0.6 | 0.88 |

[a] n = 6, [b] Average of three concentrations 2, 4, 6 µg.mL$^{-1}$.

**Table III:** Data of recovery studies

| Actual concentration ($\mu g.mL^{-1}$) | Observed concentration ($\mu g.mL^{-1}$) | Recovery (%) | % RSD |
|---|---|---|---|
| **First derivative spectrophotometric method** | | | |
| 6 | 5.91 | 99.50 | 0.82 |
| 6.6 | 6.62 | 100.303 | 1.20 |
| 7.6 | 7.58 | 99.73 | 0.96 |
| **Second derivative spectrophotometric method** | | | |
| 6 | 6.03 | 100.15 | 1.02 |
| 6.6 | 6.57 | 99.69 | 0.69 |
| 7.6 | 7.59 | 99.87 | 0.58 |

[a] n = 6, [b]Matrix containing 50 mg drug.

**Table IV :Assay results for the determination of diacerein in pharmaceutical formulation**

| Parameters | Tablet brand name | Drug Content (%) | %RSD |
|---|---|---|---|
| First derivative method | Artodar 50 mg | 99.59 | 0.75 |
| Second derivative method | Artodar 50 mg | 99.11 | 0.59 |

[a] n=6, Average of three concentrations 2, 4, 6 µg $ml^{-1}$

**Table V :Summary of validation parameters**

| Parameter | First derivative method | Second derivative method |
|---|---|---|
| Wavelength (nm) | 243 | 256 |
| Linearity range ($\mu g.mL^{-1}$) | 2-6 | 2-6 |
| Correlation coefficient | 0.9948 | 0.9991 |
| Limit of detection ($\mu g.mL^{-1}$) | 0.80 | 0.7 |
| Limit of quantitation ($\mu g.mL^{-1}$) | 2.5 | 2.0 |
| Mean recovery % | 99.51 | 99.90 |
| Precision (% ±S.D.) repeatability<br>Inter day | 0.47<br>0.98 | 058<br>0.88 |
| Robustness | Robust | Robust |

## 3. Results and discussion

The UV, first and second derivative spectra for diacerein were recorded at the
wavelength of 254 nm, 243 nm, 256 nm respectively [Fig. 2-4].

### 3.1. Linearity and range:

Under the experimental conditions described, the graph obtained for UV, first, second derivative spectra showed linear relationship. Regression analysis was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curves were $y = 0.1296x + 0.014$ ($r^2 = 0.9948$) at 243 nm for first derivative spectrophotometry and $y = 1.25x + 29$ ($r^2 = 0.9991$) for second derivative spectrophotometry. The range was found to be 2-6 $\mu g.mL^{-1}$ for both first and second derivative spectrophotometric methods. (Table I).

### 3.2. Precision:

To determine the precision of the method, diacerein solutions at a concentration of 2, 4, 6 $\mu g.mL^{-1}$ were analyzed each six times for both first and second derivative spectrophotometric methods. Solutions for the standard curves were prepared fresh everyday (Table II).

### 3.3. Robustness and ruggedness:

For robustness and ruggedness of analytical methods the tests mentioned below were carried out. The robustness of developed methods was tested by changing parameters such as degree of derivation, wavelength range and N value and the optimum

parameters were chosen for this study. The UV and derivative spectrophotometric determinations of diacerein were carried out by two different analysts on the same instrument with the same standard. The results showed no statistical differences suggesting that the developed methods were robust and rugged.

**3.4. Sensitivity:**

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equations LOD = 3 x σ / S and LOQ = 10 x σ /S, where σ is the standard deviation of intercept, S is the slope. The LOD and LOQ were found to be 0.80 $\mu g.mL^{-1}$ and 2.5 $\mu g.mL^{-1}$ respectively for first derivative and The LOD and LOQ were found to be 0.7 $\mu g.mL^{-1}$ and 2.0 $\mu g. mL^{-1}$ for second derivative respectively.

**3.5. Recovery study**

To study the accuracy of the proposed methods, and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method. This study was performed by addition of known amounts of diacerein to reanalyzed solutions of commercial capsules (Table III).

**3.6. Analysis of the marketed formulation**

There was no interference from the excipients commonly present in the capsules. The drug content was found to be 99.59± 0.92% with a % R.S.D. of 0.75 and 99.11± 1.92% with a % R.S.D. of 0.59 for first and second derivative spectrophotometric methods respectively. It may therefore be inferred that degradation of diacerein had not occurred in the marketed formulations that were analyzed by this method. The low % R.S.D. value indicated the suitability of this method for routine analysis of diacerein in pharmaceutical dosage form (Table IV).

The summary of the validation parameters is depicted in (Table V).

## 4. Conclusion

No UV or derivative spectrophotometric methods have been described for the determination of diacerein. Therefore simple, fast and reliable derivative spectrophotometric methods were developed for the routine determination of diacerein. The developed methods can be concluded as accurate, sensitive and precise and can be easily applied to the pharmaceutical formulation.

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