**IJPSR (2012), Vol. 3, Issue 11** **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 16 July, 2012; received in revised form 15 September, 2012; accepted 29 October, 2012

# UV DERIVATIVE SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF METAXALONE AND DICLOFENAC POTASSIUM IN COMBINED DOSAGE FORM

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**Keywords**:
Metaxalone,
Diclofenac potassium,
Method validation,
UV Derivative,
Spectrophotometric

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## ABSTRACT

A Simple, Fast and Reliable UV Derivative Spectrophotometric Method was developed and Quantitative Estimation of Metaxalone and Diclofenac potassium in Pharmaceutical Dosage Form was carried out using the First Derivative values measured at 276 nm for Metaxalone and 270 nm for Diclofenac potassium. Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of Metaxalone using 80-800 µg/ml and 10-100 µg/ml of Diclofenac potassium for First Derivative Spectrophotometric Method and the correlation coefficient was found to be 0.9986 and 0.9982 respectively. Precision study showed that the % RSD was within the range of acceptable limits (< 2), and the % Recovery was found to be in the range of 99-100% for Metaxalone and 100-101% for Diclofenac potassium. Developed Spectrophotometric Method in this study was Simple, Accurate, Precise, Specific, Sensitive, Reproducable and can be directly and easily applied to Pharmaceutical Dosage Form.

**INTRODUCTION: Derivative spectra:** If a spectrum is expressed as absorbance (A) as a function of wavelength (λ), the derivative spectra are:

1. Zero order: A= f (λ)
2. First order dA/ dλ= $f^1$ (λ)
3. Second order $d^2A/ d\lambda^2$= $f^{11}$ (λ)

The first derivative is the rate of change of absorbance against wavelength. It starts and finishes at zero, passing through zero at the same wavelength as λmax of the absorbance band. This derivative has a positive and a negative band with maximum and minimum at the same wavelengths as the inflection points in the absorbance band. This bipolar function is characteristic of all odd-order derivatives.

The most distinctive feature of the second-order derivative is a negative band with minimum at the same wavelength as the maximum on the zero-order band. This derivative also shows two positive satellite bands on either side of the main band.

The fourth order derivative shows a positive band with a maximum at the same wavelength as the maximum on the zero order band. Even-order derivatives show a negative or positive band with minimum or maximum at the same wavelength as $\lambda_{max}$ on the absorbance band.

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ICV (2011)- 5.07

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Note that the number of bands observed is equal to the derivative order plus one.

**Advantages of Derivative Spectroscopy:**

(1) Precise determination of the wavelength of peak maxima can be obtained from the zero crossing of the first derivative.

(2) Improved spectral resolution is obtained, especially with the second derivative. Spectral features which appear as barely noticeable shoulders in the original spectrum become much more prominent.

(3) Quantitative analysis can be performed in the presence of turbidity.

Metaxalone is chemically 5-[(3, 5-dimethylphenoxy) methyl]-1, 3-oxazolidin-2-one. It is a muscle relaxant used to relax muscles and relieve pain caused by strains, sprains, and other musculoskeletal conditions. Its Molecular formula is $C_{12}H_{15}NO_3$. It is freely soluble in chloroform, soluble in methanol and in 96% ethanol, soluble in ionized water and in propylene glycol. Its pKa is 12.24. The mechanism of action of metaxalone is central nervous system depression.

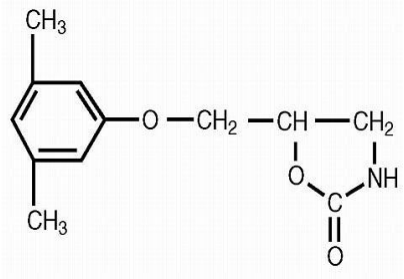


**FIG. 1: METAXALONE**

Diclofenac potassium is 2-[(2, 6-dichlorophenyl) amino] benzeneacetic acid, monopotassium salt. It is a Non-Steroidal Anti-Inflammatory Drug (NSAID) taken to reduce inflammation. Its Chemical formula is $C_{14}H_{10}Cl_2NKO_2$. It is freely soluble in methanol, soluble in ethanol, sparingly soluble in water. Its pKa is 4.15.

The anti-inflammatory effects (MOA) of Diclofenac are believed to be due to inhibition of leukocyte migration and the enzyme cyclooxygenase (COX-1 and COX-2), leading to the peripheral inhibition of prostaglandin synthesis.

Metaxalone (400 mg) and Diclofenac potassium (50 mg) is available in combination as tablet dosage form used successfully as muscle relaxant.


**FIG. 2: DICLOFENAC POTASSIUM**

The review of the literature revealed that no UV Derivative Spectrophotometric method was developed so far for the Simultaneous Estimation of these two drugs. So there is a need to develop an easy, sensitive, specific, reliable and cost effective UV Derivative Spectrophotometric Method.

**MATERIALS AND METHODS:**

**UV Spectrophotometer Instrument details:** UV and derivative spectra of the solutions were recorded on double beam UV–Vis spectrophotometer LABINDIA $3000^+$ using UV win software.

**Chemicals and reagents:** Metaxalone was provided by Rachem pharma and Diclofenac potassium was provided by Dr. Reddy's Laboratory, Hyderabad. Methanol and water of HPLC grade were purchased from Merck, Mumbai (India). Commercial formulation of Metaxalone is 400 mg and Diclofenac potassium is 50 mg label claim was purchased from a local medical store.

**Method development:**

1. **Selection of Wavelength:** UV Spectra of Metaxalone and Diclofenac potassium were converted into first derivative spectra and the two derivative spectra were overlapped and the zero crossing points of Metaxalone and Diclofenac potassium were selected.

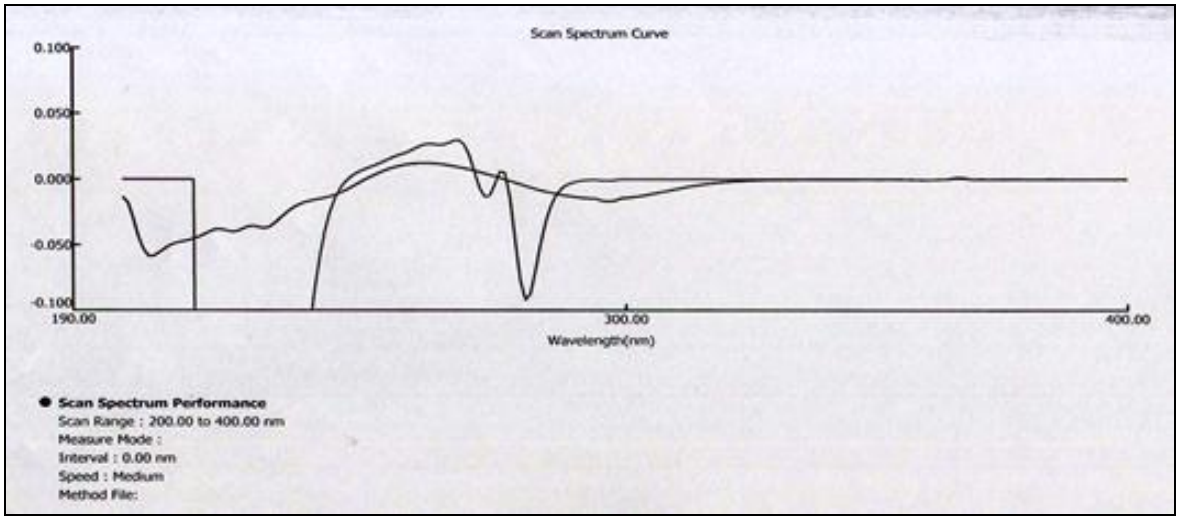


**FIG 3: OVERLAPPED FIRST DERIVATIVE SPECTRA OF METAXALONE AND DICLOFENAC POTASSIUM**

2. **Preparation of Standard and Sample solutions:** Stock solutions of 1000 µg/ml of Metaxalone and Diclofenac potassium were prepared in methanol, for First Derivative Spectrophotometric analysis. The standard solutions were prepared by dilution of the stock solution with water in a concentration range of 80-800 µg/ml for Metaxalone and 10-100 µg/ml for Diclofenac potassium. Water was used as a blank solution.

**Method validation:** The developed method was validated as per ICH guidelines**.** The validation parameters are Linearity, Accuracy, Precision, Assay, Limit of Detection (LOD), and Limit of Quantification (LOQ).

1. **Linearity:** The linearity of calibration curves in pure solution was checked over the ranges of 80-800 µg/ml for Metaxalone and 10-100 µg/ml for Diclofenac potassium. Slope, intercept, and correlation coefficient of standard curves (N=3) were calculated.

2. **Precision:** The system precision was studied by six replicate measurements of single concentration or three replicate measurements of three different concentrations. To assess the precision of the method, the intraday (3 times) and interday (3 days) measurements of two drugs were completed with computation of % RSD for replicate samples (n=3) using concentrations of 160, 320, 480 µg/ml of Metaxalone and 20, 40, 60 µg/ml for Diclofenac potassium. Both intraday and inter day results were calibrated with standard curve concurrently prepared on the day of analysis.

3. **Accuracy:** Accuracy of the method was determined by recovery experiments. To the formulation, the reference standards of the drug were added at the level of 50%, 100%, 150%. The recovery studies were carried out 3 times and the % Recovery and % RSD of the recovery of Metaxalone and Diclofenac potassium were calculated.

4. **Limit of Detection (LOD) and Limit of Quantification (LOQ):** LOD and LOQ were performed on samples containing very low concentrations of analyte under ICH guidelines. By applying the visual evaluation method, LOD was expressed by establishing the minimum level at which the analyte can be reliably detected. LOQ was considered as the lowest concentration of analyte in standards that can be reproducibly measured with acceptable precision.

5. **Assay of Mobiswift-D Tablets:** Ten tablets were weighed, finely powdered and an accurately weighed sample of powdered tablets of Metaxalone and Diclofenac potassium was extracted with methanol in a 100 ml volumetric flask and 50 ml of methanol was added to the same. The flask was sonicated for 10 min and volume was made up to the mark with methanol. The above solution was filtered using Whatman filter paper 0.8 ml was transferred into a 10 ml volumetric flask and the volume was made upto the mark with water to obtain 32 µg/ml of Metaxalone and 4 µg/ml of Diclofenac potassium. The solution was kept in instrument and absorbance was measured.

The assay procedure was made replicate (n=3) and weight of sample taken for assay was calculated. The percentage of drug found in formulation, mean and standard deviation in formulation were calculated.

## RESULTS AND DISCUSSIONS:

**Validation of the Developed method:** The method was validated with respect to parameters like linearity, precision, accuracy, and assay.

**Linearity:** The response for the drugs was strictly linear in the studied concentration range. The slope and correlation coefficient values were 0.0002 and 0.9986 for Metaxalone and 0.0009 and 0.9982 for Diclofenac potassium.

**Precision:** Intra-day and inter-day precision experiments were performed. The % RSD values for precision were < 2, there by indicating that the method was sufficiently precise.

**Accuracy:** The values of % Recovery were in between 98-102 % and % Relative Standard Deviations was < 2 indicating that the method is accurate.

**TABLE 1: LINEARITY DATA**

| S. No. | Concentration of Metaxalone (µg/ml) | Absorbance of Metaxalone | Concentration of Diclofenac potassium (µg/ml) | Absorbance of Diclofenac potassium |
|---|---|---|---|---|
| 1 | 80 | 0.021 | 10 | 0.003 |
| 2 | 160 | 0.034 | 20 | 0.009 |
| 3 | 240 | 0.051 | 30 | 0.018 |
| 4 | 320 | 0.065 | 40 | 0.027 |
| 5 | 400 | 0.082 | 50 | 0.038 |
| 6 | 480 | 0.094 | 60 | 0.047 |
| 7 | 560 | 0.105 | 70 | 0.056 |
| 8 | 640 | 0.122 | 80 | 0.067 |
| 9 | 720 | 0.135 | 90 | 0.076 |
| 10 | 800 | 0.149 | 100 | 0.085 |
| | Regression equation | Y= 0.0002x+ 0.0076 | | Y= 0.0009x- 0.009 |
| | Correlation coefficient | 0.9986 | | 0.9982 |
| | Slope | 0.0002 | | 0.0009 |
| | Intercept | 0.0076 | | 0.009 |

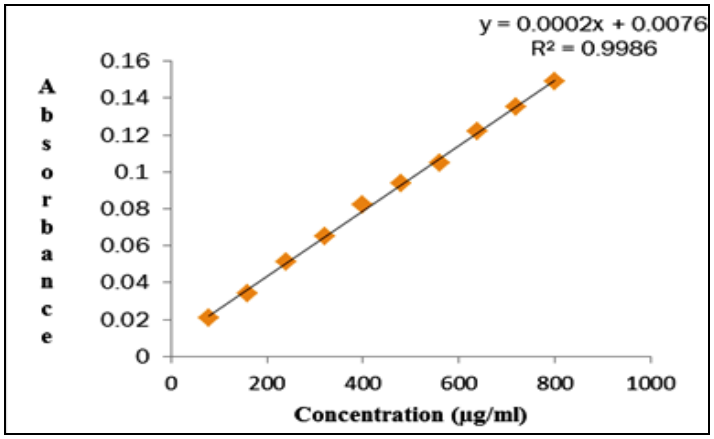


**FIG. 4: LINEARITY PLOT OF METAXALONE**

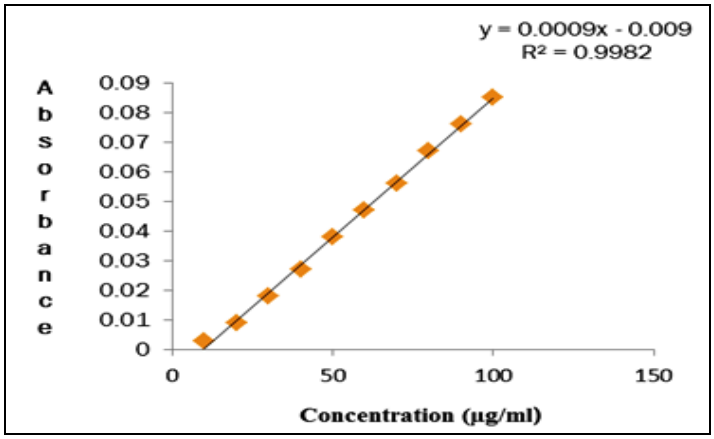


**FIG. 5: LINEARITY PLOT OF DICLOFENAC POTASSIUM**

**TABLE 2: PRECISION**

| Drug | Concentration (µg/ml) | % RSD | |
|---|---|---|---|
| | | Intraday | Interday |
| Metaxalone | 320 | 0.78 | 0.81 |
| | 480 | 0.52 | 0.53 |
| | 640 | 0.40 | 0.41 |
| Diclofenac potassium | 40 | 1.78 | 1.85 |
| | 60 | 1.04 | 1.08 |
| | 80 | 0.75 | 0.76 |

**TABLE 3: ACCURACY**

| Concentration of standard Drug | Recovery level | Amount of drug added (µg/ml) | Total amount of drug added (µg/ml) | Amount of drug found Mean± SD (n=3) | % Recovery | % RSD |
|---|---|---|---|---|---|---|
| Metaxalone 320 µg/ml | 50 % | 160 | 480 | 480.34± 4.62 | 100.06± 0.96 | 0.96 |
| | 100 % | 320 | 640 | 641.05± 3.33 | 100.16± 0.52 | 0.51 |
| | 150 % | 480 | 800 | 799.53± 4.22 | 99.93± 0.52 | 0.52 |
| Diclofenac potassium 40 µg/ml | 50 % | 20 | 60 | 60.73± 0.54 | 101.22± 0.90 | 0.88 |
| | 100 % | 40 | 80 | 80.32± 0.46 | 100.40± 0.57 | 0.57 |
| | 150 % | 60 | 100 | 101.07± 0.48 | 101.07± 0.48 | 0.47 |

**Assay:**

**TABLE 4: ASSAY**

| Drug | Labelled claim (mg) | Amount found (mg) mean ± SD, N=3 | Assay value | % RSD |
|---|---|---|---|---|
| Metaxalone | 400 | 400.60± 4.84 | 100.98 % | 0.92 |
| Diclofenac potassium | 50 | 50.35± 0.45 | 101.53 % | 1.25 |

**DISCUSSION:** A validated UV Derivative Spectrophotometric method was developed for the determination of Metaxalone and Diclofenac potassium in marketed formulation. Linearity was performed using Metaxalone of 80-800 µg/ml and 10-100 µg/ml of Diclofenac potassium for First Derivative Spectrophotometric Method and the correlation coefficient was found to be 0.9986 and 0.9982 respectively. Precision study showed that the % RSD was within the range of acceptable limits (< 2), and the % Recovery was found to be in the range of 99-100% for Metaxalone and 100-101% for Diclofenac potassium.

**CONCLUSION:** A validated UV Derivative Spectrophotometric method for the determination of Metaxalone and Diclofenac potassium in marketed formulation was developed. The developed method is simple, accurate, precise, and specific. It is suggested for routine analysis of Metaxalone and Diclofenac potassium in its marketed formulation.

**ACKNOWLEDGEMENT:** The authors thank Dr. Y. Padmanabha Reddy, Principal, Dr. J. Ravindra Reddy, Correspondent, and members of Pharmaceutical Analysis and Quality Assurance division, Raghavendra Institute of Pharmaceutical Education and Research (RIPER), Anantapur for providing necessary facilities, encouragement and guidance during dissertation work.

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**How to cite this article**:
Ramya B, Kumar KV, Ramalingam P and J Reddy JR: UV Derivative Spectrophotometric Method for Simultaneous Estimation of Metaxalone and Diclofenac Potassium in Combined Dosage Form. *Int J Pharm Sci Res*. 3(11); 4301-4305.