

Research Article



SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF METAXALONE AND DICLOFENAC POTASSIUM FROM TABLET DOSAGE FORM

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ABSTRACT

In the present research work, absorbance correction method and first order derivative spectrophotometric method have been developed for the simultaneous estimation of Metaxalone and Diclofenac potassium in tablet dosage form. Methanol was used as a solvent in both the methods. The wavelengths of absorption of Metaxalone and Diclofenac potassium were found to be 279 nm and 300 nm respectively and absorbencies at these wavelengths were used for absorption correction method, while in the first order derivative spectrophotometric method, amplitudes were measured at 302.42nm for Metaxalone (zero cross for Diclofenac potassium) and 282.08 nm for Diclofenac potassium (zero cross for Metaxalone). Metaxalone was found to be linear in the concentration range of 20 to 180 µg/ml at 279nm while Diclofenac potassium was found to be linear in the concentration range 5 to 35 µg/ml at 300nm and 3 to 24 µg/ml at 279nm. The marketed formulation was analysed using these methods and the results were obtained in the range of 98.26% to 100.97% for Metaxalone and 98.43.39% to 101.49% for Diclofenac potassium, which was found satisfactory. These methods allow rapid analysis of binary pharmaceutical formulation of Metaxalone and Diclofenac potassium with accuracy.

Keywords: Metaxalone and Diclofenac Potassium, Absorption Correction Method, First Order Derivative Spectrophotometric Method.

INTRODUCTION

Chemically Metaxalone (MET) is 5-[(3, 5-dimethylphenoxy) methyl]-1, 3-oxazolidin-2-one with molecular formula $C_{12}H_{15}NO_3$ and molecular weight 221.252 g/mol. It is a white to almost white, odorless crystalline powder freely soluble in chloroform, soluble in methanol and in 96% ethanol, deionized water and in propylene glycol, but practically insoluble in ether and water¹.

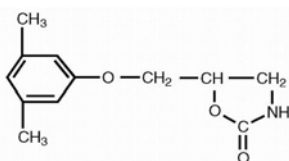


Figure 1: Chemical Structure of Metaxalone (MET)

Chemically Diclofenac potassium (DP) is 2-[(2,6-dichlorophenyl) amino] benzene acetic acid, monopotassium salt. Its molecular formula is $C_{14}H_{10}Cl_2NKO_2$. The molecular weight is 334.25. It is a faintly yellowish white to light beige, virtually odorless, slightly hygroscopic crystalline powder. It is freely soluble in methanol, soluble in ethanol, sparingly soluble in water and practically insoluble in chloroform and in dilute acid².

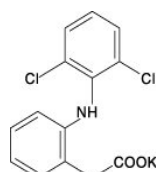


Figure 2: Chemical Structural of Diclofenac Potassium

Literature survey revealed that few analytical methods like Spectrophotometric methods³⁻⁷ chromatographic methods⁸⁻¹² and spectrofluorometry¹³ are available to determine Metaxalone and Diclofenac potassium individually or in combination with other drugs. An attempt has been made to develop and validate new UV-visible spectrophotometric methods for simultaneous estimation of Metaxalone and Diclofenac potassium in tablet dosage form.

MATERIALS AND METHODS

Instrument

A Shimadzu UV- Visible double beam spectrophotometer model 1700 (Japan) with 1cm matched quartz cells connected to a computer running UV- Probe 2.32 software for absorbance measurements and treatment of data was used along with Sartorius digital balance for weighing.

Chemicals and Reagents

The drug samples of Metaxalone and Diclofenac potassium were obtained from Ra chem Pharma Ltd, Hyderabad and Wexford Laboratories Pvt Ltd, Bangalore respectively. Tablets containing MET and DP (MyospasTM D Win-Medicare Pvt.Ltd. New Delhi.) were purchased from local pharmacy. Methanol (AR grade) and Whatmann filter paper (no.41) was used throughout the experiment.

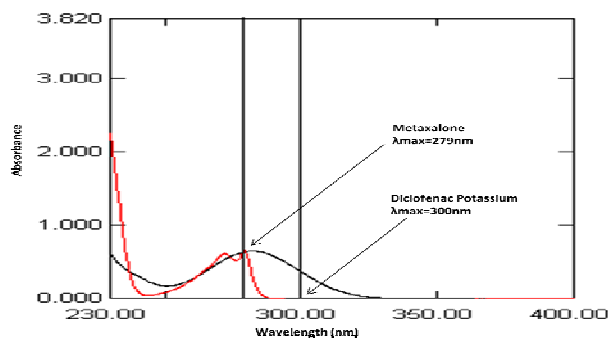


Preparation of Standard Solution

The stock solution (1000µg/ml) of MET and DP were prepared separately by dissolving accurately weighed 50mg of drug in 50ml of methanol.

Determination of Wavelength of Absorbance Maxima

The above stock solution was further diluted with methanol to get concentration of 120µg/ml for MET and 15µg/ml for DP. These solutions were scanned in the range 200-400nm against methanol as a blank. The absorbance maxima of MET and DP were found to be at 279nm and 282nm.



λ_{max} for Metaxalone (MET) and Diclofenac potassium (DP) is 279nm and 300nm, respectively.

Figure 3: Overlain spectra of MET and DP

Calibration Curves for MET and DP

The stock solution of drugs were appropriately diluted to obtain concentration range of 20 to 180µg/ml for MET and 5 to 35µg/ml and 3 to 24 µg/ml for DP. The absorption of the solution were measured at 279nm for MET and 300nm, 279nm for DP respectively for absorption correction method. The Calibration curves of MET and DP were plotted and are showing in fig. 4,5,6.

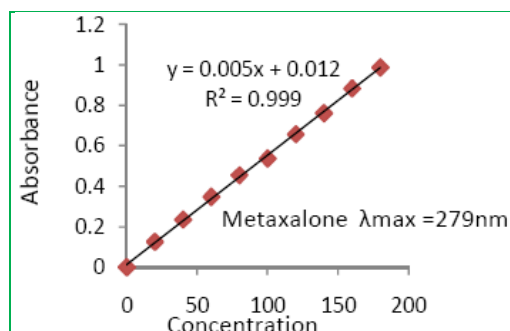


Figure 4: Calibration Curve of MET at 279 nm

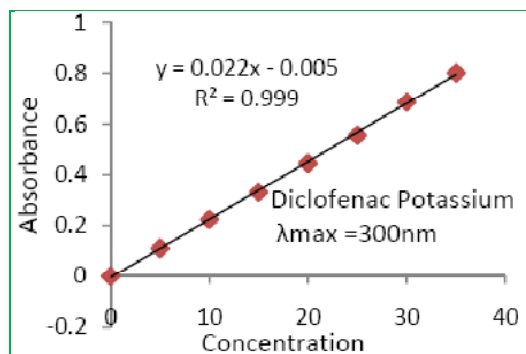


Figure 5: Calibration Curve of DP at 300 nm

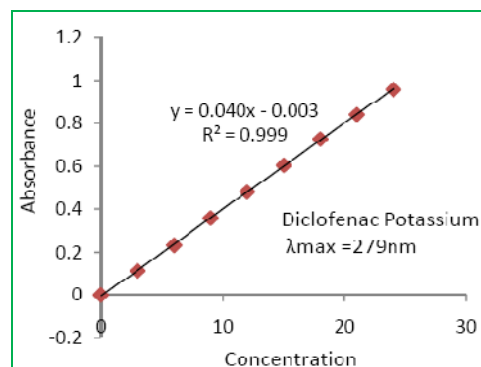


Figure 6: Calibration Curve of DP at 279 nm

The stock solution of drugs were appropriately diluted to obtain concentration range of 20 to 180µg/ml for MET and 5 to 40 µg/ml for DP. The absorption of the solution were measured at 282.08nm for MET and 302.40nm for DP for first order derivatives. The Calibration curves of MET and DP were plotted and are showing in fig. 7,8,9.

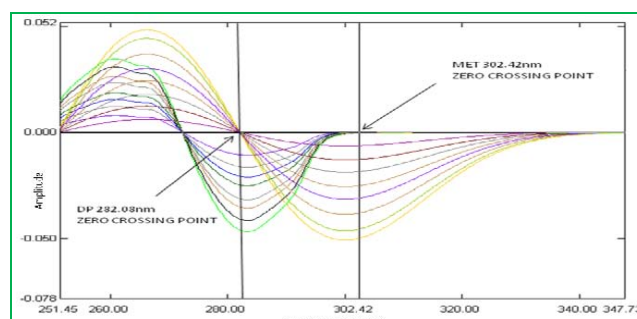


Figure 7: Zero Cross Point for MET and DP in First Order Derivative Method

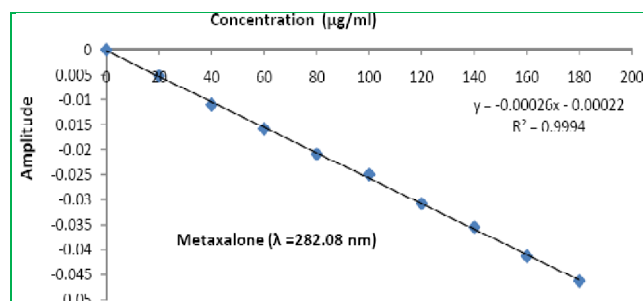


Figure 8: Calibration Curve of MET at 282.08 nm

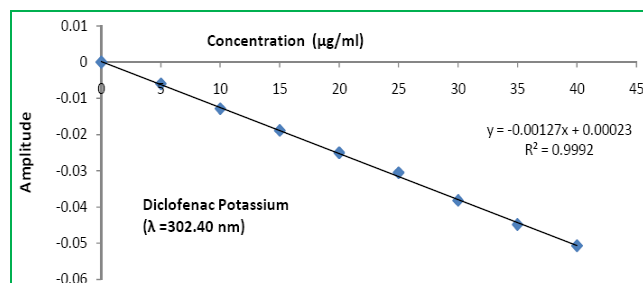


Figure 9: Calibration Curve of DP at 304.40 nm

Absorption correction method (Method I)

In this method, two wavelengths, 279nm (λ_1) and 300 nm (λ_2) were selected in such way that an absorbance of MET was nearly zero at the absorbance maximum of DP(300nm). The concentration of two drugs in mixture was calculated by using following equations:

$$C_{DP} = \frac{A_1}{ax_1} \quad (1)$$

$$C_{MET} = \frac{A_2 - ax_2 C_{DP}}{ay_2} \quad (2)$$

A_1 and A_2 are the absorbencies of mixture at 300 nm and 279 nm; ax_1 , and ax_2 are the Absorptivities of DP at 300 nm and 279 nm, respectively; whereas ay_2 is the absorptivity of MET at 279 nm.

First Order Derivative Spectroscopy (Method II)

In this method, the sample solution was scanned in the spectrum mode from 190 nm to 400 nm. The absorption spectrum obtained was transformed to its first order derivative ($\Delta = 16$ nm, and scaling factor 1). Amplitudes of first order derivative spectrum were measured at 302.40 nm for DP (zero cross for MET) and 282.08 nm for MET (zero cross for DP). The concentration of the individual drug present in the mixture was determined by putting the amplitude values of first derivative in respective regression equations.

$$C_{MET} = \frac{D'_1 - 0.00023}{-0.00026} \quad (a)$$

$$C_{DP} = \frac{D'_2 - (-0.00022)}{-0.00127} \quad (b)$$

Where, C_{DP} and C_{MET} are the concentration of DP and MET respectively, D'_1 is the amplitude of DP at 302.42 nm and D'_2 is the amplitude of MET at 282.08 nm.

Analysis of Marketed Formulation

Twenty tablets of MET and DP were weighed and crushed to obtain fine powder. An accurately weighed tablet powder equivalent to about 50mg of MET and 6.25mg of DP was transferred to 100 ml volumetric flask and sonicated for 10 minutes in 25ml in Methanol and made up the volume with methanol. The resulting solution was filtered through whatman filter paper no. 41. Filtrate was appropriately diluted to get concentration of 64 $\mu\text{g/ml}$ for MET and 8 $\mu\text{g/ml}$ for DP with methanol. The solution was scanned in range of 190-400 nm and the absorbance of solution was measured at 279 nm and 300 nm. The amount of MET and DP present in the tablets were calculated by putting the values of absorbance in the equations given in method I. For method II, the spectrum was transformed to first order derivative ($\Delta\lambda = 16\text{nm}$, and scaling factor 1) and the amplitudes were measured at 302.42 nm for DP and 282.08 nm for MET. The amount of MET and DP present in the tablets were calculated using regression equations and results are reported in table 2.

Method Validation

The proposed methods of analysis for MET and DP in combination were validated as per the recommendations of ICH guidelines¹⁴ for the parameters like accuracy, linearity, precision, detection limit and quantitation limit.

To study the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). A known amount of MET and DP were added separately to preanalysed tablet powder and percent recoveries were calculated. The results of recovery studies were satisfactory and are presented in table 3.

Table 1: Linear regression analysis of calibration curves with their respective absorptivity values.

	Method-I			Method-II	
	MET	DP		MET	DP
Beer's law limit ($\mu\text{g/ml}$)	20 to 180	5 to 35	3 to 24	20 to 180	5 to 40
Wavelength (nm)	279	300	279	282.08	302.40
R^2	0.9992	0.9995	0.9999	0.9994	0.9992
Slope	0.0054	0.0229	0.0403	-0.00026	-0.00127
Intercept	0.0127	-0.0054	0.0039	-0.00022	0.00023
LOD ($\mu\text{g/ml}$)	1.8292	0.2962	0.3015	1.3924	0.1771
LOQ ($\mu\text{g/ml}$)	5.5431	0.8978	0.9137	4.2194	0.5368

Table 2: Results of Marketed Formulation

Method	Tablet content	Label claim (mg/tablet)	Amount Found in mg (n=6)	$\pm\text{SD}$	% RSD
I	MET	400	395.83	3.3115	0.8366
	DP	50	50.29	0.2663	0.5296
II	MET	400	402.27	1.2445	0.3093
	DP	50	49.62	0.4865	0.9804



Table 3: Level of Recovery Study

Level of recovery	Drug	Method - I		Method -II	
		Recovery (%)	±SD	Recovery (%)	±SD
80%	MET	97.92	0.3600	97.76	0.4330
	DP	100.05	0.7063	102.11	0.7101
100%	MET	102.07	0.4429	99.85	0.7044
	DP	99.33	0.3637	100.78	0.1154
120%	MET	101.57	0.1443	99.89	0.2886
	DP	99.16	0.9248	102.27	0.4734

Table 4: Results of intermediate precisions

Day	Method I (% RSD)		Method II (% RSD)	
	MET	DP	MET	DP
Intra day	1.1696	1.015	1.1841	1.4226
Inter day	0.9270	0.9786	2.0141	2.0828

RESULTS AND DISCUSSION

MET and DP being freely soluble compounds in methanol, the stock solution of MET and DP were prepared in methanol. Further dilutions were made in methanol, 0.1 N hydrochloric acid, 0.1N sodium hydroxide and water. Since hyperchromic effect was observed in methanol, further study was continued in the methanol. In absorption correction method, the Beer-Lambert's concentration ranges were found to be 5-35 µg/ml for DP at 300 nm where as 20-180 µg/ml for MET at 279 nm. In first order derivative method, linearity was observed in the concentration ranges of 5-40 µg/ml for DP at 302.40 nm (Zero cross point for MET) where as 20-180 µg/ml for MET at 282.08 nm (Zero cross point for DP).

Precision of both the methods were calculated by interday and intraday variation study and % RSD of the observations were found to be less than 3%. When the marketed formulation was analysed using the proposed methods, the amount of MET and DP were found in the range from 98.26% to 100.97% and 98.43% to 100.95%, respectively. The accuracy of both the methods were determined at 80%, 100% and 120% levels and the percent recovery and results were found in the range from 97.51% to 102.56% for MET and 98.12% to 102.55% for DP.

CONCLUSION

The results of validation studies were found to be satisfactory for both methods hence, the proposed methods were found to be simple, accurate and rapid for the routine determination of MET and DP simultaneously in tablet dosage form.

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