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Research Article

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF METAXALONE IN BULK AND ITS PHARMACEUTICAL FORMULATION BY UV SPECTROSCOPIC METHOD

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ABSTRACT

Metaxalone, a muscle relaxant used to relax muscles and relieve pain caused by strains, sprains and othermusculoskeletal conditions. A simple, accurate, precise, reproducible, highly sensitive, economic UV spectrophotometric method has been developed for the estimation of metaxalon in bulk and tablet dosage form. In this method metaxalon showed maximum absorbance at 280 nm in methanol. The developed spectrophotometric method was validated in accordance with ICH guidelines. Linearity of the method was found to be 5 - 160µg/ml. The method obeyed Beer's law in the concentration range of 5 -160 µg/ml. The LOD and LOQ were found to be 3.489µg/ml and 10.575µg/ml respectively. A mean recovery of metaxalon in tablet dosage form was found to be 99.69%.the method was found to be simple, accurate, precise, specific, sensitive, reproducible and can be directly and easily applied to tablet dosage form.

Keywords: Metaxalone, Method Validation, UV- Spectroscopy, ICH guidelines.

INTRODUCTION

Metaxalone is a muscle relaxant used to relax muscles and relieve pain caused by strains, sprains, and other musculoskeletal conditions. Chemically metaxalone is 5-[(3, 5-dimethylphenoxy) methyl]-1, 3-oxazolidin-2-one (Figure 1)[1]. It is a white to almost white, odorless crystalline powder freely soluble in chloroform, soluble in methanol, 96% ethanol and in propylene glycol, but practically insoluble in ether and water[2]. Metaxalone has no direct action on the contractile mechanism of striated muscle, the motor end plate, or the nerve fiber. There is very limited or inconsistent data regarding the effectiveness and safety of metaxalone[3]. Metaxalone is one of the commonly used muscle relaxant therapies for acute low back pain[4].

Literature survey carried out revealed that several methods have been reported for estimation of metaxalone by using,, RP-HPLC Method[5,6], HPLC[7], RP-UPLC Method[8], LC-MS Method[9], UV spectrophotometric method[10], UV Derivative spectrophotometric method[11], HPTLC Method[12] are available to determine metaxalone in tablet dosage form. However, there is no method reported for estimation of metaxalone in tablet dosage form by using UV spectroscopy.

MATERIALS AND METHODS

Instrumentation

A Shimadzu UV –Visible spectrophotometer model 1800 with 1cm matched quartz cells were used for measuring the absorbance.

Chemicals and reagents

Metaxalone pure drug was obtained as a gift sample from MSN Labs, Hyderabad. Tablets of 400mg strength (skelaxi) were purchased from the local market of Rajampet. All the chemicals used were of analytical grade.

Determination of maximum wavelength (λmax)

Preparation of stock solution

Standard stock solution of metaxalone was prepared by dissolving accurately weighed 100mg of metaxalone in methanol in a 100ml volumetric flask to give a concentration of 1000µg/ml. From this, 10ml of the solution was transferred to a 100ml volumetric flask and made up the volume with methanol to give aconcentration of 100µg/ml which is the standard stock solution.From the above stock solution, pipetted out 6ml and 8ml into 10ml volumetric flask and finally made up the volumewith methanol to produce a concentration of 60µg/ml and 80µg/ml respectively. The samples was then scanned inUV spectrophotometer from a range of 200- 400nm against methanol as blank and the wavelength corresponding tomaximum absorbance in methanol was recorded.

Preparation of sample solution (Assay of marketed formulation)

The proposed method was applied to analyze commercially available metaxalone tablet. Ten tablets were weighed and powdered. The amount of tablet powder equivalent to 250 mg of metaxalone was weighed accurately and transferred to 25ml volumetric flask then 10 ml of methanol was added and kept for 15-20 min with frequent shaking and volume was made up to mark with the same solvent. The solution was then filtered through Whattman filter paper. This filtrate was diluted suitably with solvent to get the solution of 80 µg/ml concentration.

RESULTS

Linearity and Range

Various concentrations were prepared from the secondary stock solution (500µg/ml) ranging from 5-130µg/ml. The samples were scanned in UV-VIS Spectrophotometer against methanol as blank. It was found that the selected drug shows linearity between the ranges of 5-130µg/ml. Absorbance values of these solutions were measured at λmax of 280 nm. The calibration curve of metaxalone (Figure 3) was plotted between concentration of metaxalone and respective measured absorbance values at 280nm. It was found to be linear in the specified range and the regression coefficient should not be less than 0.997.

Accuracy

Accuracy of the developed method was determined by the recovery study at 3 concentration levels by replicate analysis (n=3). Standard drug solutions were added to a pre-analysed sample solutionand percentage of total drug content was calculated. The results of accuracy studies were reported in Table 2.

Precision

Precision studies were carried out to ascertain the reproducibility of the proposed method. Repeatability was determined by preparing six replicates of same concentration of the sample and the absorbance was measured. Intraday precision study was carried out by preparing drug solution of same concentration and analyzing it at three different times in a day. The same procedure was followed for three different days to determine inter day precision. The results were reported as %RSD. The precision result showed a good reproducibility with percent relative standard deviation less than 2. The results of intraday and inter day precision studies are shown in (Table 3 and Table 4).

LOQ and LOD

Limit of detection (LOD) is the lowest amount of analyte in the sample that can be detected. Limit of quantification (LOQ) is the lowest amount of analyte in the sample that can be quantitatively determined by suitable precision and accuracy. LOQ and LOD was determined using the following equation LOQ – 10 S/m , LOD – 3 S/m where S is the standard deviation of the response and m is the slope of the related calibration curve. The values of LOD and LOQ was found to be 3.489µg/ml and 10.575µg/ml respectively

Assay of marketed formulation

The optimized concentration of the drug in dosage form, 80µg/ml was determined the absorbance at 280 nm and percentage purity of the metaxolan in tablets was calculated using the following formula:

$$\text{Percentage purity} = \frac{\text{Sample absorbance} \cdot \text{standard dilution} \cdot \text{Average weight} \cdot \text{potency}}{\text{Standard absorbance} \cdot \text{sample dilution} \cdot \text{table claim} \cdot 100} \text{ X } 100$$

Table 1: Optical characteristics of the proposed method for estimation of metaxalone

λmax (nm)	280
Beer's range (µg/ml)	5-135
Molar absorptivity (l/mol/cm)	5.62 x 103M
Sandell's sensitivity (mg/cm2/0.001AU)	0.0758
Correlation coefficient (r^2)	0.997
Regression equation	Y=0.0064+0.0088
Intercept (a)	0.0088
Slope (b)	0.0064
Limit of detection (µg/ml)	3.489
Limit of quantification(µg/ml)	10.575
Precision (% RSD)*	0.7580

** Indicates mean of six determinations (n=6); RSD: Relative standard deviation*

Table 2: Accuracy data of the proposed method for metaxolan

Amount of sample (µg)	Amount spiked (µg)	Absorbance	Amount found	%recovery	% Mean Recovery
40	80	0.255	40.02667	99.93333	99.69
80	80	0.475333	80.45	99.43667	
160	80	0.937667	160.46	99.70667	

Table 3: Intraday assay precision

Concentration(µg/ml)	Absorbance1	Absorbance2	Absorbance 3
80	0.477	0.463	0.463
80	0.475	0.458	0.466
80	0.470	0.469	0.460
80	0.476	0.468	0.469
80	0.482	0.466	0.465
80	0.478	0.462	0.462
% RSD	0.825634	0.889702	0.686935

Table 4: Interday assay precision

Concentrations (µg/ml)	Absorbance		
	Day1	**Day2**	Day3
80	0.8057	0.9114	0.9234
80	0.8110	0.9128	0.9200
80	0.8099	0.9100	0.9260
% RSD	0.345795	0.15361	0.325942

Table 5: Assay of marketed formulation

Assay	Absorbance	%Purity	Mean % Purity
Assay1	0.461	101.76	101.11
Assay2	0.459	100.60	
Assay3	0.460	100.98	

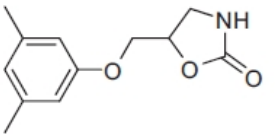

Figure 1: Chemical Structure of Metaxolan

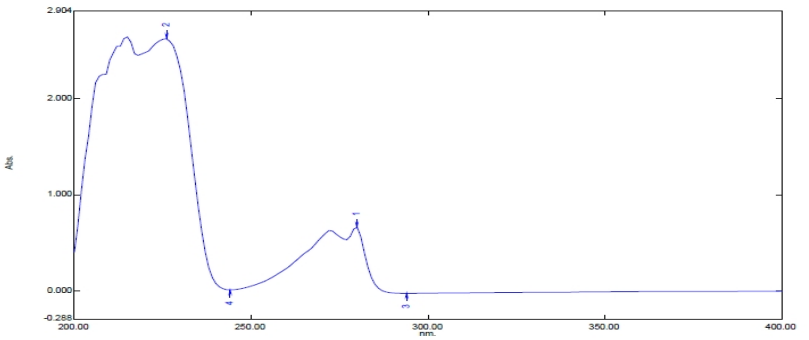

Figure 2: UV spectrum of Metaxalone, showing the λmax at 280 nm.

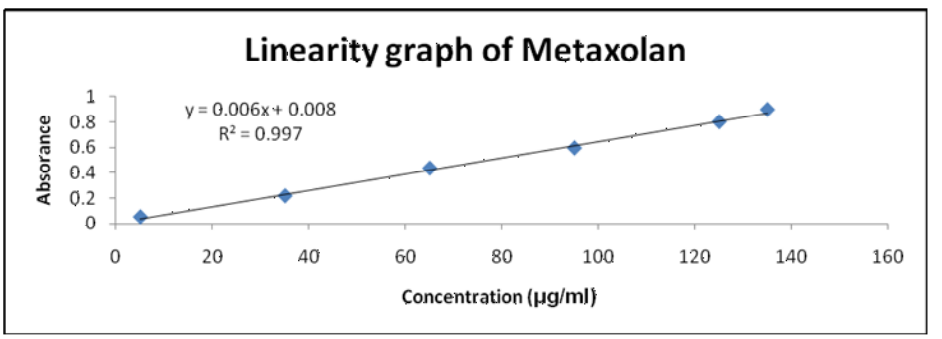

Figure 3: Linearity graph of Metaxalone

DISCUSSION

The optimized concentration of the drug 80µg/ml was scanned in UV spectrophotometer from a range of 200- 400 nm against methanol as blank and the wavelength corresponding to maximum absorbance in methanol was found to be 280 nm. The developed UV spectroscopic method was then validated according to ICH guidelines and found to be linear over the range of 5-135µg/ml concentration of metaxalone by using methanol as solvent. This method was proved to be accurate and precise as the percentage recovery values was between 99%-101% and the %RSD values for repeatability, intraday precision and inter day precision lie within the limits. LOD and LOQ values were found to be 3.489µg/ml and 10.575 µg/ml respectively. The developed method was highly specific, robust and can be used for routine analysis of metaxalone in tablet formulations.

CONCLUSION

The developed method was found to be sensitive, accurate, precise, reproducible and linear over the concentration range studied. The proposed method can be used for the routine quality control analysis of metaxalone in bulk and its tablet dosage form.

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