



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

N. V. Mahipal Reddy, B. Mohammed Ishaq*, V. S. Thiruvengada Rajan, C. Gopinath

Department of Pharmaceutical Analysis and QA, Annamacharya College of Pharmacy, New Boyanapalli, Rajampet, A.P., India

Email: bmdishaq@yahoo.com

Article Received on: 18/01/13 Revised on: 09/02/13 Approved for publication: 01/03/13

DOI: 10.7897/2230-8407.04329

IRJP is an official publication of Moksha Publishing House. Website: www.mokshaph.com

© All rights reserved.

ABSTRACT

Metaxalone, a muscle relaxant used to relax muscles and relieve pain caused by strains, sprains and other musculoskeletal conditions. A simple, accurate, precise, reproducible, highly sensitive, economic UV spectrophotometric method has been developed for the estimation of metaxalone in bulk and tablet dosage form. In this method metaxalone 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 - 160 µg/ml. The method obeyed Beer's law in the concentration range of 5 - 160 µg/ml. The LOD and LOQ were found to be 3.489 µg/ml and 10.575 µg/ml respectively. A mean recovery of metaxalone 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 water². 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 metaxalone³. Metaxalone is one of the commonly used muscle relaxant therapies for acute low back pain⁴.

Literature survey carried out revealed that several methods have been reported for estimation of metaxalone by using, RP-HPLC Method^{5,6}, HPLC⁷, RP-UPLC Method⁸, LC-MS Method⁹, UV spectrophotometric method¹⁰, UV Derivative spectrophotometric method¹¹, HPTLC Method¹² 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 (λ_{max})

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 1000 µg/ml. From this, 10ml of the solution was transferred to a 100ml volumetric flask and made up the volume with methanol to give a concentration of 100 µg/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 volume with methanol to produce a concentration of 60 µg/ml and 80 µg/ml respectively. The samples were then scanned in UV spectrophotometer from a range of 200- 400nm against methanol as blank and the wavelength corresponding to maximum 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 Whatman 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 (500 µg/ml) ranging from 5-130 µg/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 5-130 µg/ml. Absorbance values of these solutions were measured at λ_{max} 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 solution and 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 3.489 µg/ml and 10.575 µg/ml respectively

Assay of marketed formulation

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

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

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

λ_{max} (nm)	280
Beer's range (µg/ml)	5-135
Molar absorptivity (l/mol/cm)	5.62 x 10 ³ M
Sandell's sensitivity (mg/cm ² /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	

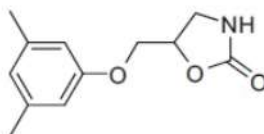


Figure 1: Chemical Structure of Metaxolone

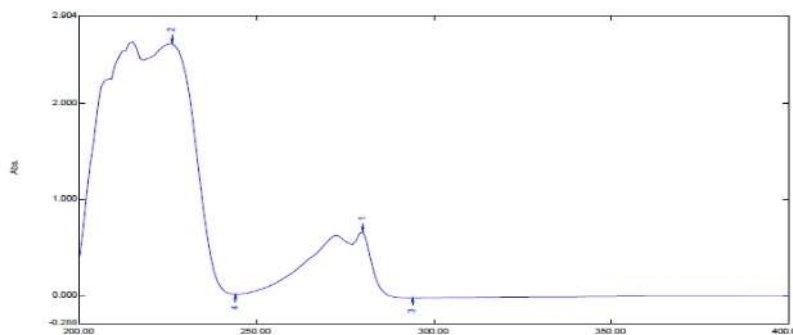
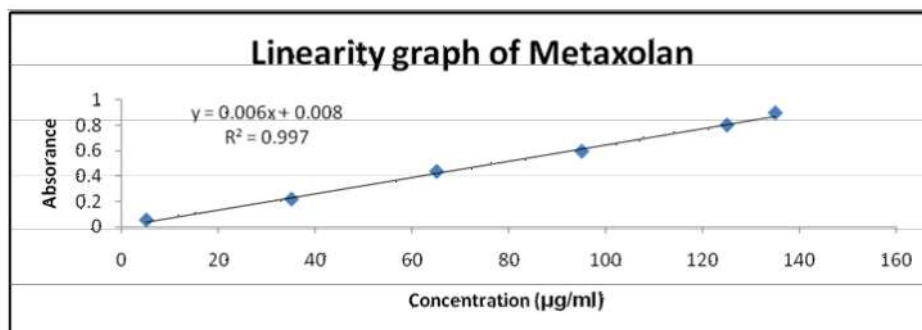
Figure 2: UV spectrum of Metaxolone, showing the $\lambda_{\max}$ at 280 nm.

Figure 3: Linearity graph of Metaxolone

DISCUSSION

The optimized concentration of the drug 80 µg/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 5-135 µg/ml concentration of metaxolone 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 3.489 µg/ml and 10.575 µg/ml respectively. The developed method was highly specific, robust and can be used for routine analysis of metaxolone 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 metaxolone in bulk and its tablet dosage form.

ACKNOWLEDGEMENTS

Authors are very much thankful to MSN labs, Hyderabad for providing the gift sample of metaxolone. Authors are also thankful to Management and Principal Dr. C. Gopinath, for providing the necessary facilities to carry out the research work.

REFERENCES

1. M.N. Carrol Jr., W.R. Luten, R.W. Southward, The pharmacology of a new oxazolindione with anticonvulsant, analgesic and muscle relaxant properties, Arch. Int. Pharmacodyn. Ther. 130 (1961) 280-298
2. <http://www.medicinenet.com/metaxolone/article.htm> Searched on Feb 1st 2013.
3. Chou R, Peterson K and Helfand M, J Pain Symptom Manage., 2004, 28(2), 140-175. <http://dx.doi.org/10.1016/j.jpainsymman.2004.05.002> PMID:15276195
4. Toth P E and Urtis J, Clinical Therapeutics, 2004, 26(9), 1355-1367. <http://dx.doi.org/10.1016/j.clinthera.2004.09.008> PMID:15530999
5. Prafulla Kumar Sahu, M. Mathrusri Annapurna and Sahoo Dillip Kumar; Development and Validation of Stability Indicating RP-HPLC Method for the determination of Metaxolone in Bulk and its Pharmaceutical Formulations; E-Journal of Chemistry 2011, 8(S1), S439-S447. <http://dx.doi.org/10.1155/2011/645710>

6. Sagar Suman Panda , Debasis Patanaik, Bera V. V. Ravi Kumar; New Stability-Indicating RP-HPLC Method for Determination of Diclofenac Potassium and Metaxalone from their Combined Dosage Form; *Sci Pharm.* 2012; 80: 127–137. <http://dx.doi.org/10.3797/scipharm.1109-16> PMID:22396909 PMCID:3293350
7. Vamsi Krishna Marothu et al; Kinetics study of metaxalone degradation under hydrolytic, oxidative and thermal stress conditions using stability-indicating HPLC method; *Journal of Pharmaceutical Analysis* 2012;2(6):431–436. <http://dx.doi.org/10.1016/j.jpha.2012.08.004>
8. Rakshit Kanubhai Trivedi , Mukesh C. Patel; Development of a Stability-Indicating RP-UPLC Method for rapid determination of Metaxalone and its degradation products in solid oral dosage form; *sci pharm.* 2012; 80: 353–366.
9. Kandasamy et al., Bioanalytical Method Development, Validation and Quantification of Metaxalone in Rat Plasma by Liquid Chromatography Tandem Mass Spectrometry; *J Bioanal Biomed* 2012, S6.
10. Patel et al, Spectrophotometric Estimation of Metaxalone and Diclofenac Potassium by Multicomponent Analytical Method from Tablet Dosage Form; *J Anal Bioanal Techniques* 2012, 3:3 <http://dx.doi.org/10.4172/2155-9872.1000137>
11. Ramya et al., UV Derivative spectrophotometric method for simultaneous estimation of Metaxalone And Diclofenac Potassium In combined dosage form *Ijpsr*, 2012; Vol. 3(11): 4301-4305.
12. Milindkumar P Rajput, Vishal V Bharekar, Savita S Yadav, Toufik S Mulla and Janhavi R Rao; Validated HPTLC Method for simultaneous estimation of Diclofenac Potassium And Metaxalone in bulk drug and formulation; *Pharmacie Globale (IUCP)* 2011, 12 (04)

Cite this article as:

N. V. Mahipal Reddy, B. Mohammed Ishaq, V. S. Thiruvengada Rajan, C. Gopinath. Analytical method development and validation of Metaxalone in bulk and its pharmaceutical formulation by UV spectroscopic method. *Int. Res. J. Pharm.* 2013; 4(3):149-152

Source of support: Nil, Conflict of interest: None Declared