REPORT

Dissolution studies and quantification of meloxicam in tablet dosage form by spectrophotometry

Madhusudhanareddy Induri*, Bhagavan Raju Mantripragada[2], Rajendra Prasad Yejella[3], Pavankumar Reddy Kunda[2], Dharma Theja Nannapaneni[1] and Rajkumar Boddu[1]

[1]Department of Pharmaceutical Chemistry, Malla Reddy College of Pharmacy, Maisammaguda, Dhulapally, Secunderabad, Andhra Pradesh, India

[2]Department of Pharmaceutical Chemistry, CM College of Pharmacy, Maisammaguda, Dhulapally, Secunderabad, Andhra Pradesh, India

[3]Department of Pharmaceutical Chemistry, AU College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, Andhra Pradesh, India

Abstract: Two simple and inexpensive UV spectrophotometric methods were developed for the quantification and dissolution studies of meloxicam in tablet dosage forms. Meloxicam was estimated at 365nm and 360nm in Method I and Method II, respectively. The calibration curve was linear over a concentration range from 2.0 to 12.0µg/mL for both methods. The limit of detection and limit of quantitation were found to be 0.12µg/mL and 0.38µg/mL, 0.09µg/mL and 0.27µg/mL for Method I and Method II, respectively. The percentage recoveries of meloxicam were found to be 99.68 to 100.61% and 99.11 to 100.96% for Method I and Method II, respectively. It was concluded that the developed methods are precise, accurate and were successfully applied for the estimation of meloxicam in pharmaceutical formulations and *in vitro* dissolution studies.

Keywords: Meloxicam, dissolution, spectrophometry, tablet dosage form.

INTRODUCTION

Meloxicam, chemically, 4-hydroxy-2-methyl-N-(5-methyl-1,3-thiazol-2-yl)-2H-1,2-benzothaizine-3-carboxamide 1,1-dioxide (Martindale, 1999) (fig. 1), is a non-steroidal anti-inflammatory drug, which is known to preferentially inhibit the enzyme cyclooxygenase-2 (COX-2). It is used for treatment of osteoarthritis, rheumatoid arthritis and polyarticular course juvenile rheumatoid arthritis. It has analgesic, antipyretic, and anti-inflammatory activity as a result of inhibition of COX-2 (Noble, Balfour, 1996; Davies, Skjodt, 1999; Turck *et al*, 1996).

A detailed literature survey for meloxicam revealed that several analytical methods are reported for the determination of meloxicam by pulse polarography (Altiokka *et al*, 2000), electrochemical oxidation (Radi *et al*, 2001), electrochemical reduction (Beltagi *et al*, 2002), voltametry (Radi *et al*, 2001), flourimetry (Hassan, 2002), capillary electrophoresis (Nemutlu, Kir, 2003), HPLC (Joseph-Charies, Bertucat, 1999; Velpandian *et al*, 2000; Dasandi *et al*, 2002; Zawilla *et al*, 2003; Arayne *et al*, 2005; Vignaduzzo *et al*, 2008), LC/MS (Wiesner *et al*, 2003) and spectrophotometric (Bebewy, 1998; You *et al*, 1999; Garcia *et al*, 2000; Nemutlu, Kir, 2004) methods.

Dissolution test has emerged in the pharmaceutical field as a very important tool based on the fact that for a drug to be absorbed and available to the systemic circulation, it must previously be solubilized. Therefore the dissolution studies are used not only to assess batch-to-batch consistency of drug release from solid dosage forms, but they are also essential in several stages of formulation development, for screening and proper assessment of different formulations. Moreover, the *in vitro* dissolution profile obtained from dissolution rate studies has been used for the successful characterization of the *in vivo* behavior of drugs (Furlanetto *et al*, 2003). So far, to our present knowledge, no spectrophotometric method has been reported for the dissolution studies of meloxicam in tablet dosage forms. The aim of the present work is to develop and validate simple spectrophotometric methods to be applied for the quantification and dissolution rate studies of meloxicam in tablets, which therefore serves as a tool for the quality control and safety of this type of pharmaceutical preparations.

EXPERIMENTAL

Materials

The meloxicam reference standard (assigned purity 99.89%) was kindly donated by Aurobindo Pharma Ltd, Hyderabad, India and used without further purification. The commercially available tablet dosage forms (Label claim: 15mg) were procured from local market. All the

**Corresponding author:* msreddyinduri@yahoo.com

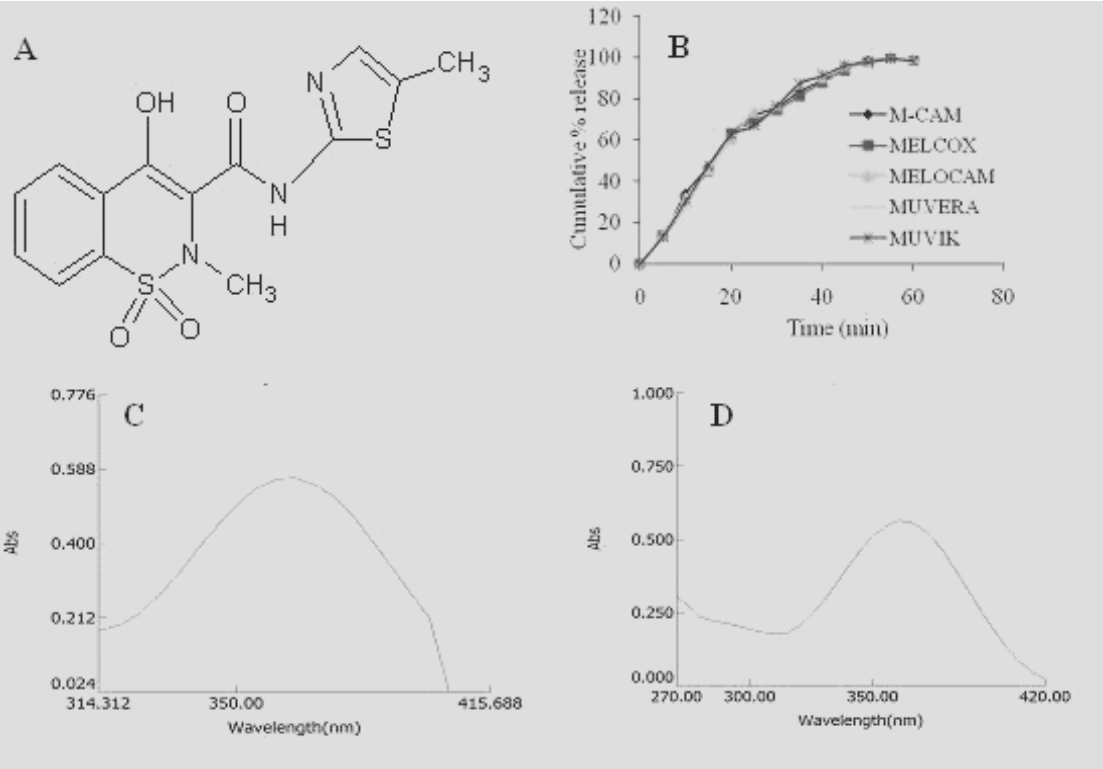

Fig. 1: A) Chemical structure of meloxicam, B) Dissolution profile of different brands of meloxicam, C) UV-spectra of meloxicam against methanol as blank (Method I), D) UV-spectra of meloxicam against 0.05M phosphate buffer as blank (Method II).

chemicals used in the spectrophotometric analysis were of analytical reagent grade.

Apparatus

A Labindia 3000$^+$ UV-Visible Spectrophotometer with 10mm quartz cell was used for the absorbance measurements connected with UVWIN software. An ELICO digital pH meter C-212 is used for making pH measurements. The dissolution rate studies of meloxicam from tablets were performed on an Electro Lab, TDT-08L USP dissolution apparatus.

Methods

Preparation of standard stock solutions of meloxicam

A standard stock solution (100µg/mL) was prepared by accurately weighed 10 mg of standard meloxicam in a 100 mL volumetric flask containing 20 mL of 0.1 M sodium hydroxide and final volume adjusted with methanol (Method I) and 0.05M phosphate buffer (Adjusted pH 7.5 with 0.1N sodium hydroxide) (Method II), respectively, and sonicated for about 15 min and the volume was made up to the mark with respective solvents.

Determination of maximum absorption (λ_{max})

Spectral scan of standard solution (10µg/mL) against respective blanks (Method I & Method II) was in the range of 270 to 420 nm and 320 to 420 nm, respectively, where maxima were observed at 365nm and 360nm, respectively (figs. 2-3).

Calibration curve

The calibration curve was constructed by analyzing six different concentrations of standard solution, prepared on the same day. The range of solution varied from 2.0 to 12.0µg/mL for both the methods. Absorbance of each concentration was measured in triplicate.

Method validation

Different parameters in the method validation like linearity, accuracy, precision and limit of detection (LOD) & limit of quantitation (LOQ) were analyzed according to ICH guidelines (ICH- Q 2B; 1996)

Analysis of tablet dosage forms

To quantify the strength of meloxicam in tablet dosage forms, 20 tablets of each were individually weighed and powdered to obtain homogeneous mixture. Powder equivalent to 15 mg of meloxicam was transferred to 100 mL volumetric flask containing 20 mL of 0.1M sodium hydroxide, sonicated for about 15 min. The above solutions were filtered through whatmann filter paper and the volume was made up to the mark with respective solvents to obtain final concentration of 6.0µg/mL. All determinations were conducted with triplicate.

Dissolution studies

The dissolution rate studies of meloxicam from tablets were performed on a paddle-stirrer type of apparatus. The dissolution studies were performed according to dissolution procedure recommended for single-entity products (FDA, 1997a) in 900 mL of pH 7.5 phosphate buffer (75 rpm). The temperature of the cell was maintained at 37 ± 0.5°C by using a thermostatic bath. At each sample time interval, an exact volume of the sample was withdrawn from each flask and immediately replaced with an identical volume of fresh medium to maintain a dissolution sink condition. At predetermined time intervals (0, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 and 60 min) for the dissolution studies, and the proposed method (Method II) was used to determine the concentration of meloxicam in dissolution medium. In order to obtain the dissolution profile, the cumulative percentage of drug released was plotted against time (min).

RESULTS

The developed UV spectrophotometric methods were used to quantify the meloxicam in tablet dosage forms. The calibration curves shows that, the developed methods were linear in the concentration range of 2.0 to 12.0µg/mL. The correlation coefficients, intercepts and slopes of the calibration data were tabulated (table 1). Regression equation values of Method I and Method II were found to be y=0.0548x+0.0022 and y=0.0538x+0.0061, respectively, and correlation coefficients were found to be 0.9993 and 0.9995, respectively. The LOD of meloxicam for Method I and Method II were found to be 0.12µg/mL and 0.09µg/mL, respectively, LOQ values were found to be 0.38µg/mL and 0.27µg/mL, respectively.

Table 1: Calibration data of the proposed methods

Parameters	Results	
	Method I	Method II
λ_{max} (nm)	365	360
Beer's law range (µg/mL)	2.0-12.0	2.0-12.0
Molar extinction coefficient (1/mol/cm)	0.05521	0.05528
Sandell's sensitivity (µg/cm^2)	0.018116	0.018109
Limit of detection (µg/mL)	0.12	0.09
Limit of quantitation (µg/mL)	0.38	0.27
Regression equation		
Intercept (a)	0.0548	0.0538
Slope (b)	0.0022	0.0061
Correlation coefficient (r^2)	0.9993	0.9995

The precision of the method was checked by subjecting known amounts of standard drug into proposed methods and %RSD was calculated. The lower %RSD values shows that the proposed methods were more precise (table 2). For the determination of accuracy, pre-analyzed tablet

Table 2: Precision data of the proposed methods

Methods	Intra-day and inter-day precision						
	Conc. (µg/mL)	Intra-day precision			Inter-day precision		
		Mean Abs±SD*	RSD (%)	SEM	Mean Abs±SD*	RSD (%)	SEM
Method I	6	0.336±0.003	0.893	0.00173	0.343±0.0046	1.336	0.00265
	8	0.444±0.0046	1.032	0.00265	0.452±0.006	1.327	0.00346
	10	0.557±0.005	0.903	0.00291	0.573±0.005	0.879	0.00291
Method II	6	0.326±0.0035	1.078	0.00203	0.332±0.0031	0.921	0.00176
	8	0.422±0.0045	1.019	0.0026	0.442±0.003	0.679	0.00173
	10	0.549±0.0025	0.459	0.00145	0.545±0.0051	0.942	0.00296

* Average of three determinations; SEM- Standard error of mean

Table 3: Recovery data of standard solutions added to the samples analyzed by using the proposed methods

Method	Amount (%) of drug added to analyte	Theoretical content (µg/mL)	Conc. found µg/mL±SD*	Recovery (%)	RSD (%)	SEM
Method I	50	4.5	4.4854±0.0516	99.68	1.151	0.0298
	100	6	6.0365±0.0645	100.61	1.069	0.03725
	150	7.5	7.5207±0.0129	100.28	0.172	0.00745
Method II	50	4.5	4.5149±0.0174	100.33	0.385	0.01004
	100	6	6.0576±0.0255	100.96	0.42	0.0147
	150	7.5	7.3587±0.1235	99.11	1.661	0.0713

*Average of three determinations

Table 4: Assay results of meloxicam in tablet dosage forms

Tablet Dosage form (15mg)	Theoretical concentration (µg/mL)	Method I			Method II		
		Found* (mean±SD)	RSD (%)	Content (%)	Found* (mean±SD)	RSD (%)	Content (%)
M-CAM	6.0	5.9518±0.077	1.295	99.18	5.9412±0.0372	0.627	99.02
MELCOX	6.0	5.9628±0.0687	1.153	99.38	5.9484±0.0445	0.747	99.54
MELOCAM	6.0	5.9555±0.1103	1.852	99.26	5.9996±0.0435	0.726	99.99
MUVERA	6.0	6.0394±0.0941	1.559	100.66	5.9704±0.0394	0.659	99.51
MUVIK	6.0	6.0066±0.0845	1.406	100.11	6.0145±0.0599	0.995	100.24

*Average of five determinations

powder was spiked with pure meloxicam at three concentration levels (50, 100, and 150 % of that in tablet powder) and the total was found by the proposed methods. The percentage recovery values were found to be 99.68-100.61 and 99.11-100.96 with %RSD of <2% for Method I and Method II, respectively (table 3), which indicates that the proposed methods were accurate.

The developed methods were applied to the quantification of meloxicam in tablet dosage forms available in local market. The results are tabulated in table 4. Dissolution studies of different brands of meloxicam tablets by Method II reveal that more than 70% of labeled amount is dissolved in 30min, which is correlating with USP method.

DISCUSSIONS

Generally, assay methods are relatively time consuming and involve expensive instrumentation not readily accessible to many groups. Therefore, our goal was to develop a relative rapid and economical assay that would be performed at any laboratory with adequate spectrophotometer. The spectrophotometric methods, as described, were validated and successfully employed for the quantification and dissolution studies of meloxicam in tablet dosage forms.

It can be seen that, the results obtained by proposed methods are very much similar to that of established methods. As per USP the assay of meloxicam was done by using liquid chromatography and dissolution studies were performed by spectrophotometry where as the advantage of these methods can be used for both assay and dissolution studies of meloxicam in tablet dosage form

CONCLUSION

It is concluded that, the proposed methods were found to be simple, accurate and inexpensive for the quantification of meloxicam in tablet dosage forms. The recovery studies were in good agreement with their respective label claim. The excipients usually present in the formulations do not interfere in the proposed method. These advantages encourage that; these methods can be routinely employed in quality control for analysis of meloxicam in tablet dosage forms and dissolution studies.

ACKNOWLEDGEMENT

The authors are grateful acknowledge the receipt of pure meloxicam from Aurobindo Pharma Ltd., Hyderabad, India. One of the authors thanks to Ch. Malla Reddy, chairman (Malla Reddy Group of Institutions) and Dr. M. Sudhakar, Principal (Malla Reddy College of Pharmacy), Secunderabad, Andhra Pradesh for providing the necessary facilities.

REFERENCES

Altiokka G, Atkosar Z and Tuncel M (2000). Pulse polarographic determination of meloxicam. *Die Pharmazie*, **56**: 184-203.

Arayne MS, Sultana N and Siddiqui FA (2005). A new RP-HPLC method for analysis of meloxicam in tablets. *Pak. J. Pharm. Sci*, **18**: 58-62.

Bebewy LI (1998). Stability-indicating method for the determination of meloxicam and tetracaine hydrochloride in presence of their degradation products. *Spectrosc. Lett*, **31**: 797-820.

Beltagi AM, Ghoneim MM and Radi A (2002). Electrochemical reduction of meloxicam at mercury electrode and its determination in tablets. *J. Pharm. Biomed. Anal.*, **27**: 795-809.

Dasandi B, Saroj SH and Bhat KM (2002). LC determination and pharmacokinetics of meloxicam. *J. Pharm. Biomed. Anal.*, **28**: 999-1008.

Davies NM and Skjodt NM (1999). Clinical pharmacokinetics of Meloxicam. *Clin. Pharmacokinet.*, **36**: 115-122.

FDA (1997a). Center for Drug Evaluation and Research, Guidance for Industry: Dissolution Testing of Immediate Release Solid Oral Dosage Forms.

Furlanetto S, Maestrelli F, Orlandini S, Pinzauti S and Mura P (2002). Optimization of dissolution test precision test for a ketoprofen oral extended-release product, *J. Pharm. Biomed. Anal*, **32**: 159-165.

Garcia MS, Pedreno CS, Albero MI and Marti A (2000). Spectrophotometric method for determining meloxicam in pharmaceutical using batch and flow-injection procedures. *Eur. J. Pharm. Sci.*, **9**: 311-316.

Hassan EM (2002). Spectrophotometric and fluorimetric methods for the determination of meloxicam in dosage forms. *J. Pharm. Biomed. Anal.*, **27**: 771-793.

International Conference on Harmonization (ICH) of Technical Requirements for the Registration of Pharmaceuticals for Human Use (1996). Validation of Analytical Procedure: Methodology (ICH–Q 2B), pp. 1-8.

Joseph-Charies J and Bertucat M (1999). Determination of meloxicam in tablet formulations by ultraviolet spectrophotometry and high-performance liquid chromatography. *Anal. Lett*, **32**: 2051-2059.

Martindale (1999). The Extra Pharmacopoeia, 32nd ed., The Pharmaceutical Press, London, England, p.52.

Nemutlu E and Kir S (2004). Validated determination of meloxicam in tablets by using UV spectrophotometry. *Hecettepe University Journal of The Faculty of Pharmacy*, **24**: 13-24.

Nemutlu E and Kir S (2003). Method development and validation for the analysis of meloxicam in tablets by CZE. *J. Pharm. Biomed. Anal*, **31**: 393-405.

Noble S and Balfour JA (1996). Meloxicam. *Drugs*, **51**: 424-431.

Radi AE, El-Ries MA, El-Anwar F and El-Sherif Z (2001). Electrochemical oxidation of meloxicam and its determination in tablet dosage form. *Anal. Lett*, **34**: 739-746.

Radi AE, Ghoneim M and Ghoneim MM (2001). Cathodic adsorptive stripping square-wave voltametry of the anti-inflammatory drug, meloxicam. *Chem. Pharm. Bull*, **49**: 1257-1261.

Turck D, Roth W and Busch U (1996). A review of the clinical pharmacokinetics of Meloxicam. *Brit. J. Rheumatol*, **35**: 13-19.

Velpandian T, Jaiswal J, Bhardwaj RK and Gupta SK (2000). Development and validation of a new high-performance liquid chromatographic estimation method of meloxicam in biological samples. *J. Chromatogr. B*, **738**: 431-436.

Vignaduzzo SE, Castellano PM and Kaufman TS (2008). Method development and validation for the simultaneous determination of meloxicam and pridinol mesylate using RP-HPLC and its application in drug formulations. *J. Pharm. Biomed. Anal.*, **46**: 219-225.

Wiesner JL, De Jager AD, Sutherland FCW, Hundt HKL, Swart KJ, Hundt AF and Els J (2003). Sensitive and rapid liquid chromatography-tandem mass spectrometry method for the determination of meloxicam in human plasma. *J. Chromatogr. B*, **785**: 115-121.

You WW, Liu Y and Wang ZB (1999). Determination of meloxicam by ultraviolet spectrophotometry, *Chinese. J. Anal. Chem.*, **27**: 841-845.

Zawilla NH, Abdul-Azim Mohammad M, El-Kousy NM and El-Moghazy Aly SM (2003). Determination of meloxicam in bulk and pharmaceutical formulations. *J. Pharm. Biomed. Anal.*, **32**: 1135-1142.