Development and Validation of a UV-Spectrophotometric Method for Determination of Meloxicam in Bulk and in TabletFormulations

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Abstract

A simple, accurate, precise and rapid UV-spectrophotometric method with good sensitivity was developedfor determination of meloxicam (MX) in bulk and in tablet. Meloxicam exhibit absorption maximum in 0.1 M of methanol-hydrochloric acid at 346.0 nm and the calibration curve was linear for a range of (5.0-150) µg/ml with a determination coefficient of 0.999. The validation of the present method was done by carrying out precision and accuracy studies. The limit of detection and limit of quantification for meloxicam was found to be 0.13and0.411µg/ml, respectively.The proposed method can be successfully used for routine quality control analysis of meloxicam in bulk and marketed formulations.

Keywords: Meloxicam, UV-spectrophotometry, Validation, Tablet formulations.

1. Introduction

Meloxicam, chemically named 4-hydroxy-2-methyl-N (5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide- 1,1-dioxide with chemical formula ($C_{14}H_{13}N_3O_4S$) and molecular weight 351.4 g/mol (Fig.1), is a non-steroidal anti-inflammatory drug (NSAID) used to relieve the symptoms of arthritis[1,2]. In contrast with other NSAIDs currently available, meloxicam appears to have greater inhibitory activity against the inducible isomer of cyclo-oxigenase, which is involved in the inflammatory response, than against the constitutive isomer, inhibition of which is associated with adverse gastrointestinal and renal events [3]. Various methods reported for the determination ofmeloxicam in pharmaceuticals and biological samples that include spectrophotometric and fluorimetry [4-8], polarography [9,10], turbidimetry [11], voltammetry [12], capillary zone electrophoresis [13], HPTLC [14], and high performance liquid chromatography [15, 16] and a UV-spectrophotometric method for the simultaneous estimation of meloxicam and paracetamol have been developed in tablet by simultaneous equation, absorbance ratio and absorbance correction method [17]. The UV spectrophotometric analyses are often preferred in quality control testing and ordinary laboratories due to its broad availability and suitability.The objective of this studywas to develop and validate a simple, accurate, precise and specific UV-spectrophotometric method for the estimation of MXin bulk drug and in tablets.

2. Experimental

2.1. Apparatus

All spectral and absorbance measurements were performed on a (Cecil CE3021-England) UV-VIS spectrophotometer was used for all spectral and absorbance measurements with matched 1 cm quartz cells.

2.2. Reagents

All chemicals were of analytical reagents grade and double distilled water was used throughout the experiments**.** Meloxicam (99% purity) was a gift from, Awamedica Company for Drug Industries and Medical Applications Awa, Erbil, Iraq. Methanol used was of analytical gradepurchased from (Hayman, England). Hydrochloric acid analytical grade purchased from (Merck, Darmstadt, Germany, 37%).

2.2.1. Preparation of (500 µg/ml)standard stock solutions of meloxicam

A stock solution, 500 µg/ml, of the drug under investigation was preparedby dissolving 50 mg of meloxicam (MX) in 0.1 M methanol-hydrochloric acid mixture [18]and made up to the mark in 100 ml-volumetric flask with the same solvent to obtain final concentration of 500 µg/ml.This solution was further diluted to get various working solutions.

2.3. General procedure (determination of λ_{max})

From the standard stock solution further diluted with 0.1 M methanol-hydrochloric acid to obtain the concentration of 120 µg/ ml, the solution was scanned in UV range (200-450 nm) in 1.0 cm quartz cell against solvent blank which showed an absorption maximum at 346.0 nm (Fig. 2).

2.4.Preparation of calibration curve for meloxicam

For linearity study, dilutions were made for meloxicam in the concentration range of 5.0 to 150 µg/ml by diluting thestock solution with 0.1M methanol -hydrochloric acid. The calibration curve was established at 346.0 nm by plotting graph between absorbance and concentration. Regression analysis of Beer's law plot revealed a good correlation (Fig.3).

2.5.Preparation of pharmaceutical tablets solution

The contents of 10 finely ground tablets were weighed and mixed. An accurately weighed portion of the tablet powder equivalent to 50 mg of the drug under investigation was weighed, and dissolved in about 50 ml of 0.1 M methanol-hydrochloric acid mixture. The solution was diluted to 100 ml in volumetric flask with the same solvent. From this solution, various diluted solutions were prepared by dilution with same solvent.

3. Results and discussion

3.1.Method development

The development of a simple, rapid, sensitive, and accurate analytical UV- spectrophotometric method for the quantitative determination of meloxicam in bulk and in tablet carried out to evaluate the optimum parameters.

3.1.1Selection of an appropriate solvent system

It has reported that, meloxicam practically insoluble in water [19]. Thus, various solvent systems as, 0.1 M HCl:phosphate buffer pH 6.0 (1:1), methanol, distilledwater: methanol (1:1), 0.1 M HCl: methanol (1:1), 0.1 MHCl: methanol(1:10),phosphate buffer pH 6.0: methanol (1:1) and phosphatebuffer pH 8.0: methanol (1:1) were tried to select anappropriate solvent with good suitability and stability. Asolvent system, 0.1 Mhydrochloric acid: methanol (1:10) was selectedfor the determination of meloxicam.

3.2.Validation of proposed method

The method discussed in the proposed method provides a simple, accurate, specific and economical method for the estimation of meloxicam using UV-spectrophotometry. The λ_{max} selected for quantitation was 346 nm and the solvent system, 0.1 M hydrochloric acid: methanol (1:10) was selected for the determination of meloxicam. In the developed method, the linearity was observed in the concentration range of 5-150 µg/ml. The slope, intercept, determination coefficient and optical characteristics were illustrated in Table 1.

3.2.1. Limit of detection (LOD) and limit of quantification (LOQ)

The LOD and LOQ of MX were calculated according to the International Union of Pure and Applied Chemistry (IUPAC) definition[20]using the formula:

$$LOD = 3\,\sigma / S \text{ and } LOQ = 10\,\sigma / S$$

Where: σ is the standard deviation of blank absorbance values and S is the slope of the calibration plot. The high values of molar absorptivity and low values of Sandell's sensitivity and LOD indicated the high sensitivity of the proposed method.

3.2.2. Accuracy

The accuracy of the proposed method was studied by calculating mean recovery % of the experimentally determined concentration compared to the theoretical one that performed at three different levels 30, 60, 120 µg/ml of MX. The results were expressed as percent recovery which was in the range between 97.1- 100.46 % (limit 95% to 105%) that indicating high degree of accuracy and absence of interference from the commonly encountered pharmaceutical additives and excipients that indicated the specificity of the proposed method. The results of the recovery study were shown in Table 2.

3.2.3. Repeatability

Repeatability of proposed method was determined by analyzing 40 µg/ml concentration of MX solution for six times and the absorbance were observed and the RSD% was calculated as shown in Table 3. The acceptable limit should be within 2%.

3.2.4.Precision

Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 30, 60, 120 µg/ml of MX solutions for present method; three times in the same day. Inter-day precision was determined by analyzing daily for three different days in the same conditions.Precision data (intraday and interday) were well below the specified limit of 1% and 2%, respectively that indicating a good precision of the proposed method that illustrated in Table 4.

3.2.5.Stability

The stability of the sample solution of MX under the proposed procedure was examined and responses which found to be stable for at least 20 days at room temperature.Indicated that meloxicam was highly stable in the mentioned conditions. This allows the processing of a large number of samples and their comfortable measurements with convenience.

3.3.Application of the method

The proposed UV- spectrophotometric method was applied for meloxicam determination in tablets. The results of tablet analysis by the present method were shown in Table 5.

3.4.Comparison of the proposed method with other reported spectroscopic methods

A comparison of solvent used, wave length selected, linear range and detection limit of the proposed method with those ofother spectroscopic methods have been described (Table 6). It was clear that thedeveloped investigated method has a clear edge overdescribed methods.

4. Conclusion

It can be concluded from the results that the proposed method for the determination of MX in tablets was specific, rapid, precise and simple with sufficient sensitivity and sample solution of MX under the proposed procedure found to be stable for at least 20 days at room temperature. This analytical method was also being adopted for quality control tests for the drug in tablets.

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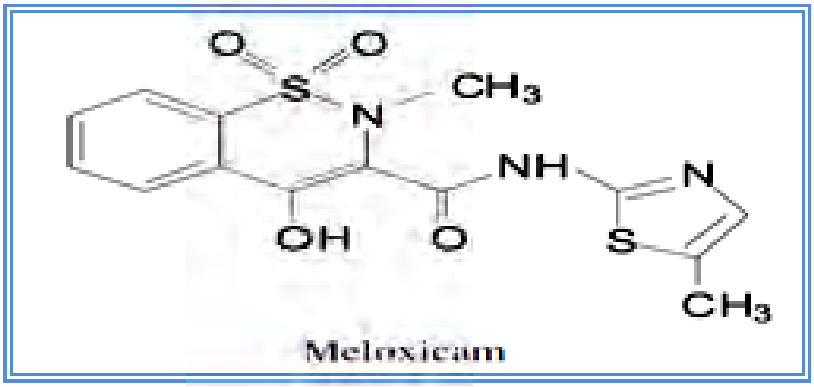

Fig.1:Chemical structure of MX

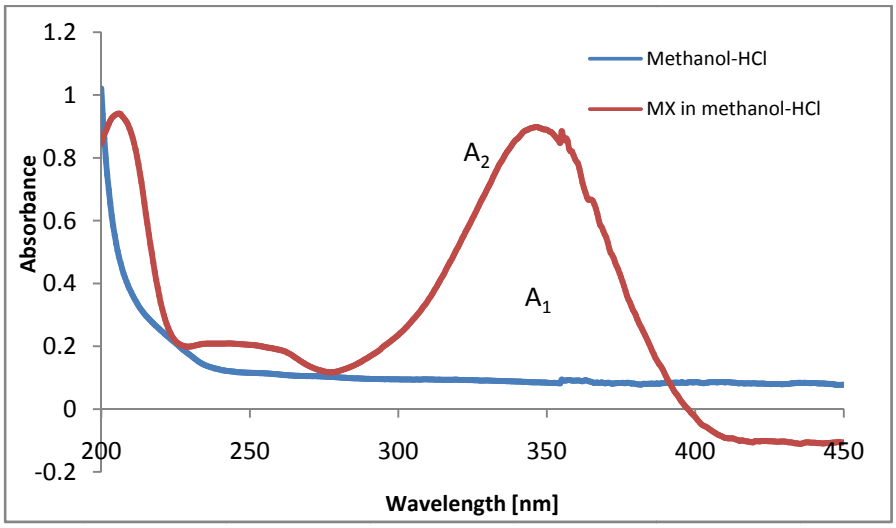

Fig. 2: UV Spectrum of meloxicam (120 µg/ ml) in 0.1M methanol- HCl(A_2) treated according to the recommended procedure and measured against reagent blank (A_1).

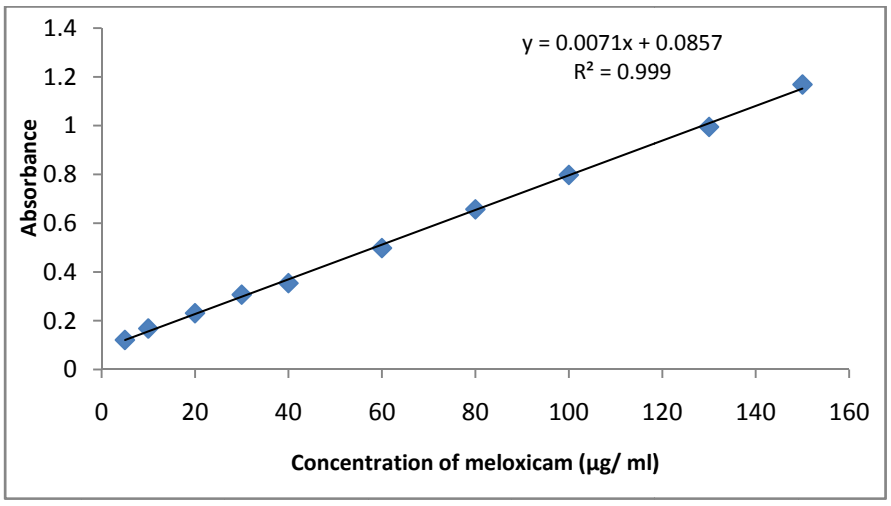

Fig. 3: Calibration curve of meloxicam.

Table 1.Quantitative parameters for the proposed method.

Parameters	The proposed method
λ_{max}, nm	346.0
Beer's law range (µg /ml)	5.0-150
Detection limits (µg / ml)	0.13
Quantitation limit (µg/ ml)	0.411
Molar absorptivity (L/mole.cm)	2.4949×10^4
Sandell's sensitivity (µg/cm^2)	0.014
Regression equation	y = 0.0071x + 0.0857*
Intercept (a)	0.0857
Slope (b)	0.0071
Determination coefficient (R^2)	0.999

* In Y = a + b x, Y is absorbance and x is concentration.

Table 2. Results of recovery study

Tablet, MX sample	Label value (mg /tablet)	Amount added (µg/ml)	Amount found (µg/ml)	Recovery%*, SD**
Awamedica-Meloxicam Awa, Erbil- Iraq.	7.5	30	29.71	99.0±0.24
		60	59.46	99.1±0.14
		120	120.18	100.15±0.54
BoehringerIngelhe-Mobic, Germany.	7.5	30	29.13	97.1±0.11
		60	60.28	100.46±0.71
		120	119.58	99.65±0.46

* Mean of 3 determinations, **SD: Standard deviation

Table 3. Repeatability of the proposed method

No. of determination	Concentration of MX (µg/ml)	Absorbance	Mean ± SD**	RSD%
1	40	0.3547	0.3549±0.0002	0.056
2	40	0.3550		
3	40	0.3542		
4	40	0.3553		
5	40	0.3552		
6	40	0.3550		

Table 4. Precision study of meloxicam by the proposed method

Tablet	Conc. (µg/ml)	Intra-day Absorbance			Inter-day Absorbance		
		Mean absorbance*	± SD**	RSD%**	Mean absorbance*	±SD**	RSD%**
Meloxicam Awa Erbil- Iraq.	30	0.3091	0.00013	0.042	0.3089	0.00123	0.0039
	60	0.5022	0.00022	0.043	0.4999	0.00146	0.2920
	120	0.9233	0.00016	0.017	0.9231	0.00111	0.2607
Mobic -Germany.	30	0.3111	0.00034	0.109	0.3107	0.00081	0.2607
	60	0.5013	0.00040	0.079	0.5006	0.00260	0.5193
	120	0.9202	0.00067	0.073	0.9198	0.00123	0.1337

* Mean of 3 determinations; **SD: Standard deviation, RSD: Relative standard deviation.

Table 5. Results of tablet analysis by the proposed method

Tablet, MX sample	Label value (mg /tablet)	Obtained value (mg)	Recovery%*,SD**
Awamedica-Awa, Meloxicam Erbil- Iraq.	7.5	7.47	99.6±0.19
BoehringerIngelheim-Mobic, Germany.	7.5	7.49	99.8±0.15

* Mean of 3 determinations; **SD: Standard deviation.

Table 6.Comparison between the proposed method and literature methods for determination of MX.

Method	λ_{max} (nm)	Solvent used	Linear range (µg/ml)	LOD (µg/ml)	Ref.
UV- Spectroscopy	360	0.1N NaOH	5.0– 25	0.026	21
UV- Spectroscopy	257.6	0.1N NaOH	1.0- 5.0	……	17
UV- Spectroscopy	363	100 mM borate buffer (pH 8.5)	1.0 – 150	0.05	22
FI- spectroscopy	362	0.1 N NaOH	0.5–20	0.04	23
Present method	346	Methanolic -0.1 M HCl	5.0–150	0.13	….