ejpmr, 2017,4(9), 137-141

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

DPP METHOD FOR THE STUDY OF MELOXICAM IN PHARMACEUTICALS

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Article Received on 17/07/2017 **Article Revised on 07/08/2017** **Article Accepted on 27/08/2017**

ABSTRACT

A planned method has been tested for Meloxicam estimation in dosage forms. This method based on using DPP with a DME versus Ag/AgCl as reference electrode. The best peak response was obtained at applied potential -1.2V in 0.1M acetate buffer at pH 4 and 0.01M KCl as supporting electrolyte. Calibration curve was suitable at a concentration variety between 0.1 and 0.8 µg.ml^{-1} with a correlation coefficient: r of 0.9995. The LOD and LOQ is found to be 0.024 and 0.079 µg.ml^{-1} respectively, RSD and overall mean recovery were 0.2 to 0.67% and 99.11% (n=5) respectively. The improvement method shows good sensitivity, selectivity; also it was applied to the determination of Meloxicam in pharmaceuticals.

KEYWORDS: Meloxicam; DPP; Analysis.

1. INTRODUCTION

Meloxicam, $C_{14}H_{13}N_3O_4S_2$, 351.403 g.mol^{-1}, the product name Mobic; known as [4 – hydroxyl - 2-methyl - N (5 – methyl – 2 – thiazolyl) – 2 – H - 1, 2 – benzothiazine -3 carboxamide -1,1-dioxide], Fig. 1, is a new non-steroidal anti-inflammatory drug (NSAID). Like other NSAIDs, the primary mechanism of action of Meloxicam is via inhibition of the cyclooxygenase enzyme system resulting in decreased prostaglandin synthesis.[1,2]

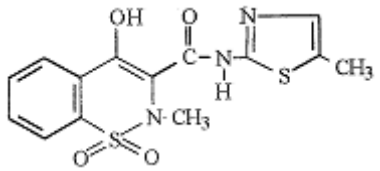

Fig. 1: Chemical structure of Meloxicam.

Several methods have been reported for the estimation of Meloxicam, like spectrophotometry.[3,4], HPLC[5,6] and mass Spectrometer.[9,10] Voltammetric behavior of Meloxicam was study in tablet and plasma samples using DC, DPP and CV techniques. The finest peak response was get at -1.49 V with DPP, SMDE mode versus Ag/AgCl in acetate buffer at pH 4.88. The calibration curve for was linear at a concentration range between 0.38 to 15.0 µg ml^{-1} with mean recovery of 99.20±0.37%.[7]

The electrochemical oxidation of L-cysteine was completed by cycling potential in cysteine solution, using glassy carbon electrode with anionic layer of cysteic acid providing electrostatic accumulation of the analyte on to the electrode surface. The peak current obtained at + 1.088 V versus Ag/AgCl. Calibration graph was linear at the concentration ranging from 4.3 x10^{-8} to 8.5 x10^{-6} M in 0.04M B-R buffer solution at pH 1.86 with r= 0.999 and LOD of 1.5 x10^{-9} M.[8]

The objective of this work is to confirmed the voltametric behaviour of Meloxicam also improve a simple and sensitive polarographic process for its determination in pharmaceuticals.

2. EXPERIMENTAL

2.1. Apparatus

Polarographic analysis were done by a 797VA Computrace Metrohm, Herisau, Switzerland polarographic analyser equipped with DME as working electrode and Ag/AgCl as a reference electrode also Pt wire as auxiliary electrode. All experiments were performed at 25 ± 5°C.

2.2. Materials and reagents

All experiments were performed with analytical grade reagent, chemicals and solvents. Deionised water was use for preparation the standard and samples. Meloxicamwas purchased from Sigma–Aldrich. Mobic tablets contain 7.5 mg Meloxicam per tablet was obtained from local pharmacies.

A 250 µg.ml^{-1} Meloxicam standard solution was prepared by disolved 12.5 mg of standard Meloxicam in 50 ml dimethyl formamid, DMF. This solution was stored at +4°C through two months. Diluted 50 µg.ml^{-1} Meloxicam solution was prepared by diluted 10 ml from 250 µg.ml^{-1} standard solution in 50 ml volumetric flask

with deionised water. Diluted 5µg.ml^{-1} solution was ready by diluted 5 ml of 50 µg.ml^{-1} solution in 50 ml volumetric flask with deionised water.

Acetate buffer, 0.1 M was prepared by mixing 41 ml of 0.1M acetic acid with 9 ml of 0.1 M sodium acetate in 100 ml volumetric flask and complete the volume with deionized water.[11] KCl, 1M was prepared by dissolved 7.45 g in 100 ml deionized water.

2.3. Universal Meloxicam DPP Procedure

An aliquot volume of Meloxicam samples was transferred to 25ml volumetric flask, then 2 ml of 0.1M acetate buffer at pH 4 was adding with 0.2 ml of 1M KCl as supporting electrolyte and complete the volume to the mark with deionized water. All samples was transfered to a polarographic device and purged the oxygen with 99.999% purity nitrogen gas for 300 sec and check at scan rate 5 mV s^{-1} with pulse amplitude 50.

2.4. Preparation the calibration curve of Meloxicam

A series of eigth standard solutions in the extent of 0.1 - 0.8 µg.ml^{-1} newly prepared by diluted volumes 0.5 - 4 ml from 5 µg.ml^{-1} Meloxicam standard solution solution in 25 ml volumetric flask; 2 ml of 0.1M acetate buffer at pH 4 was added, also 0.2 ml of 1M KCl as supporting electrolyte and diluted to the mark with deionized water. Every stansard solution was analysis using optional DPP method, paragraph 2-3, in the best conditions. A standard calibration graph were prepared between id find for Meloxicam against the concentration using the Least Squares Method.[12]

2.5. Analysis of Meloxicam tablets

A 10 tablets were weighed and milled, an 25 µg weight was transferred to a 25 ml volumetric flask then added 10 ml of DMF with shakikg for 5 min to complete liquefy and completed to the mark with deionized water. Appropriate solutions were prepared by taking suitable volumes of the clear layer and diluted with deionized water. Each one tablet sample were analysed as a same in paragraph 2-3.

3. RESULTS AND DISCUSSION

Meloxicam analysis using DPP technique gained sensitive and high peak current signal. The pH effect was examine in acidic and alkali media with acetate, phosphate and B-R buffer solutions at pH values from 2 to 9. In 0.1M acetate buffer solution, Meloxicam gained high signal that prepared at pH 4 in water, also 0.01M KCL was choose as a supporting electrolyte instead of KNO3 or LiCl. Meloxicam shows a large peak at -1.2 V versus Ag/AgCl, Table 1, Figure 2.

Table 1: Suitable conditions for Meloxicam analysis.

Experimental condition	Variable	Appropriate condition
Solvents	Water, Methanol, DMF, Acetonitrile	DMF
pH	2, 4, 7, 9	4
Buffers	Acetate, Phosphate, B-R	Acetate buffer
Supporting Electrolytes	KNO3 , KCl , LiCl	KCl

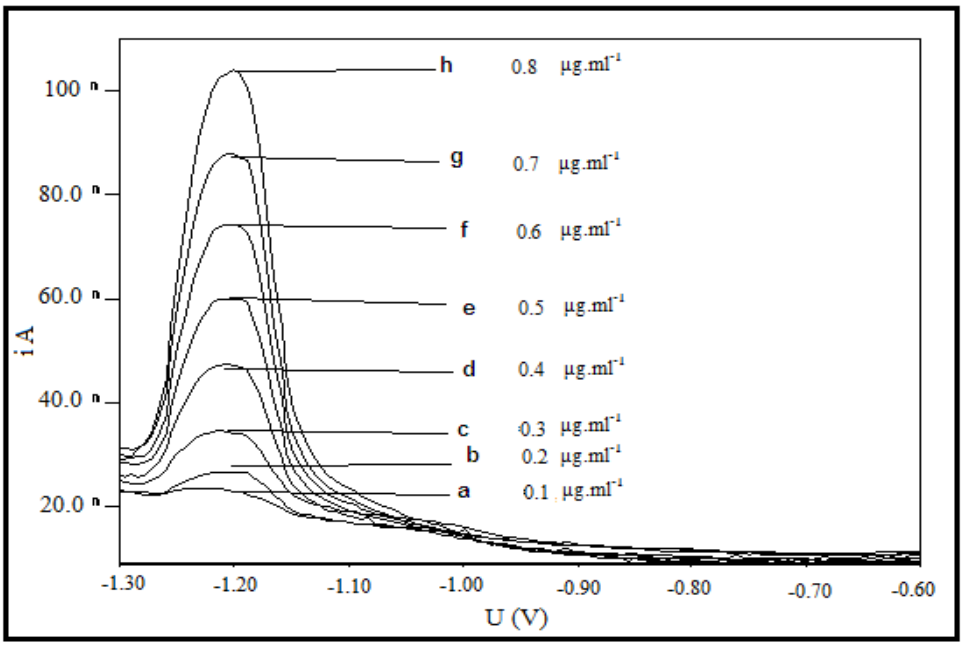

Figure 2: Meloxicam polarograms at special concentrations.

3.3. Method validation

At the optimal setting, The statistical treatments of the peak current determined for Meloxicam was complete by plotting the peak current against the related concentration of analyte solutions, Figure 3. The arithmetical inspection for the calibration curve showed that the linear regression equation for meloxicam is quietly appropriate. This regression line is used to calculate the analyte concentration in a various samples, Table 2.

The Limit of detection (LOD) and the limit of quantification (LOQ) for Meloxicam was calculated using signal to noise ratio (S/N) of 3.3 and 10 respectively.[12] The results show that the LOD and LOQ for Meloxicam was found as 0.024 and 0.079 µg.ml^{-1} respectively.

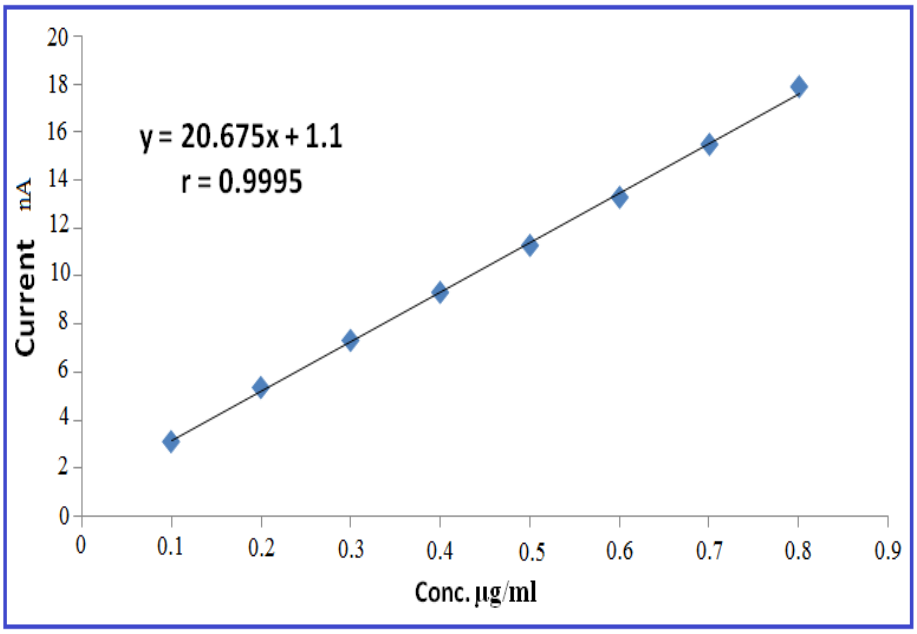

Figure 3: Standard calibration graph for Meloxicam.

Table 2: Analytical numbers of the Meloxicam analysis using DPP method.

Parameter	Values
Peak potential, E_p(V)	-1.2
Concentration range (µg.ml^{-1})	0.1 - 0.8
Regression equation y=bx-a	Y=20.675 X+1.1
Correlation coefficient (r)	0.9995
Linearity (R^2)	0.9990
Slop (b)	20.675
Intercept (a)	1.1
Standard deviation of regression line (S **y/x**)	0.1639
Standard deviation of intercept (S_a)	0.1277
Standard deviation of slope (S_b)	0.2529
C.L. for the intercept ($a \pm ts_a$) at 95%	1.1 ± 0.31
C.L. for the slope ($b \pm ts_b$) at 95%	20.675 ± 0.619
Limit of Detection- LOD, (µg.ml^{-1})	0.024
Limit of Quantitation - LOQ, (µg.ml^{-1})	0.079

The accuracy and precision of the proposed method was established. different standard samples were prepared and analysis(n=5), Table 3.

Table 3. Analysis of standard sample.

Initial Conc. µg.ml^{-1}	Found conc. µg.ml^{-1}	Absolute Error	%RE	%Rec	SD	$\frac{SD}{\sqrt{n}}$	C.L of the mean	%RSD
0.3	0.296	-0.004	-1.33	98.66	0.002	0.0009	0.296±0.002	0.67
0.5	0.496	-0.004	-0.80	99.54	0.001	0.0004	0.496±0.001	0.20
0.7	0.694	-0.006	-0.86	99.14	0.003	0.0013	0.694±0.003	0.41

*n=5, t= 2.57.

The suggested DPP method was apply to the inspection of Meloxicam in commercial mobic tablet, 7.5 mg. Every one sample was treated according to paragraph 2.3, explained in experimental part by recommended DPP procedure, the real Meloxicam amount in marketable mobic tablet, 7.5 mg was found in the extent of 7.429 to 7.436 mg which are really the same to the amounts fixed in the original products. The results are depicts in Table 4.

Table 4. Analysis of commercial Mobic 7.5 mg tablets sample.

Mobic tablets, 7.5 mg Meloxicam				
Initial Conc. µg.ml^{-1}	Measured Conc. µg.ml^{-1}	Amount Found (mg)	%Rec	%RSD
0.5	0.495	7.436	99.10	0.11
	0.495	7.436	99.10	
	0.496	7.443	99.20	
	0.495	7.429	99.10	
	0.496	7.443	99.20	
	av.=0.495	av=7.437	99.14	

3.4. Number of moved electrons and the value of E½

The real number of shared electrons in electrode process and the actual value of E½ was calculated using Heyrovsky–Ilkovic equation.[13]

E applied = E1/2 - (0.0591 / n) Log (i / id – i)

This equation give details about the relationship between diffusion current and applied voltage. Number of electrons (n) can be establish from the plot of log (i / id – i) versus applied voltage (E) at an suitable concentrations. For a reversible process, (n) appear to be a correct number, while an incomplete number for (n) appeared an irreversible process.[14,15] The calculated E½ was -1.205 V and the number of required electrons (n) for the Meloxicam reduction was equal to 2 electron, Figure 4. The choicest planned reduction mechanism recommended that the alkenes bond get reduce via 2e / 2H^{+} process closely required for the reduction, Figure 5.

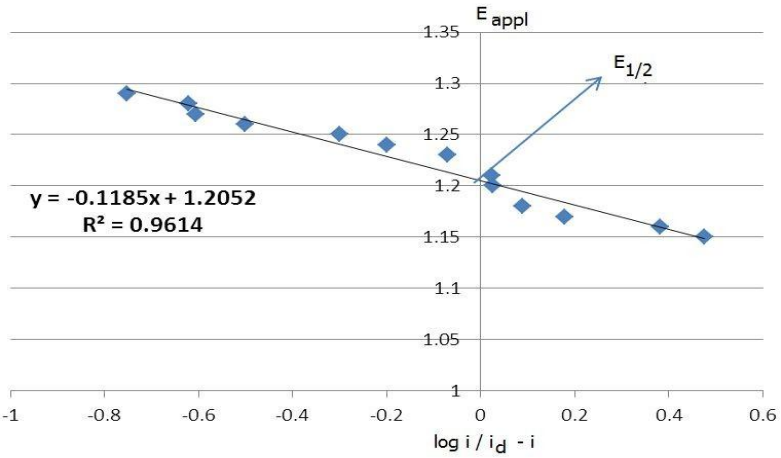

Figure 4: Effect of E applied on the log (i/id- i) variation using Heyrovsky-Ilkovic equation at 0.8µg.ml^{-1} Meloxicam concentration.

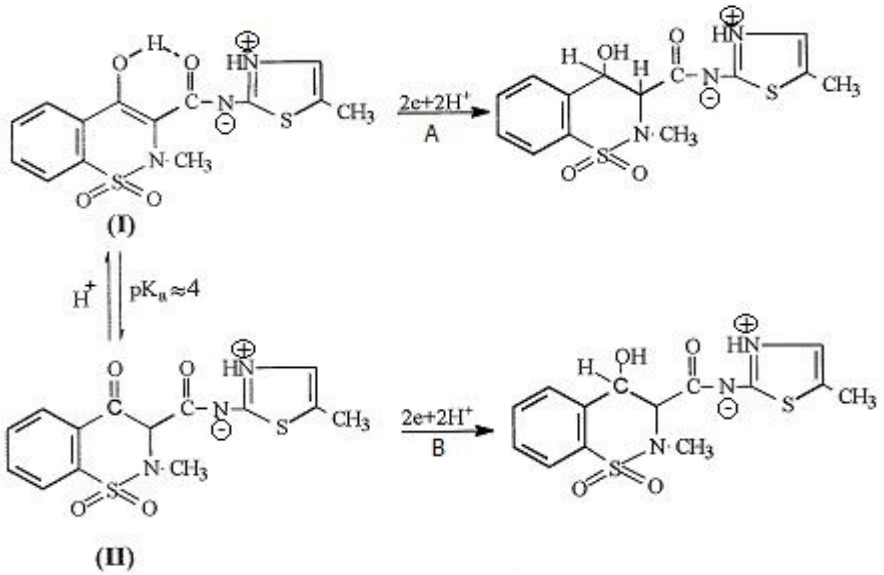

Figure 5: Suggested reduction mechanism for Meloxicam reduction.

CONCLUSION

This study has demonstrated that DPP method has several advantage found suitable for the check of Meloxicam in the pharmaceutical tablets. The method is rapid, cheap, accurate, sensitive and selective according to the evaluation of the validation factors.

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