Oriental Journal of Chemistry Vol. **26**(1), 239-242 (2010)

Determination of Mizolastine in pharmaceutical formulations

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(Received: January 17, 2010; Accepted: February 20, 2010)

ABSTRACT

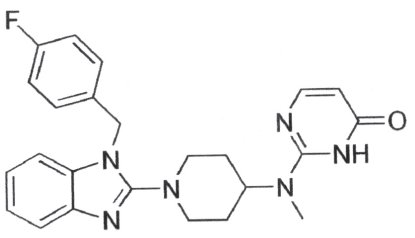
Mizolastine is an antihistamine drug. Two simple, sensitive and accurate spectrophotometric methods have been developed for the determination of Mizolastine in pure state and in its pharmaceutical formulations. The developed Method A is based on the formation of picrate salt between picric acid and free base of Mizolastine and it shows maximum absorption at λ_{max} 400 nm and Linearity in the range of 3-15 µg/mL. Method B involves reaction between free base of Mizolastine and chloranilic acid. The developed chromogen in Method B shows maximum absorption at λ_{max} 530 nm and Linearity in the range of 50-250 µg/mL. The results obtained were statistically evaluated and were found to be accurate and reproducible.

Key words: Mizolastine, Spectrophotometric, MZL.

INTRODUCTION

Mizolastine[1] 2-[[1-[1-[(4-fluorophenyl) methyl] benzimidazol-2yl] piperidin-4-yl]-methylamino]-1H-pyrimidin-6-one is a new benzimidazole derivative drug, which is a potent and selective antagonist of H_1 receptors. Mizolastine blocks histamine H_1 receptors and is commonly fast acting. It does not prevent the actual release of histamine from mast cells, just prevents it binding to receptors.

Literature survey reveals that the pharmacokinetic study of MZL by liquid-liquid extraction[2], LC-ESI-MS Method for the determination of Mizolastine in Human Plasma[3], Coupled liquid-liquid extraction and column switching LC for the determination of a new antihistaminic H_1 drug in human urine[4], development of a CZE method for the determination of Mizolastine and its impurities in pharmaceutical preparations using response surface methodology[5], spectrophotometric determination of Mizolastine in pharmaceutical formulations[6] were reported. In the present investigation two simple, sensitive and accurate visible spectrophotometric methods have been developed for the estimation of Mizolastine in pharmaceutical formulation and in bulk drug. Method A shows λ_{max} at 400 nm and Linearity in the range of 3-15 µg/mL. Method B exhibits λmax 530 nm and Linearity in the range of 50-250 µg/mL.



Structure of Mizolastine

EXPERIMENTAL

Spectral and absorbance measurements were made on systronics Double beam UV-Visible spectrophotometer model 2201 with 1cm matched quartz cells. Mizolastine was procured from a local pharmaceutical industry. All other reagents used were of analytical grade.

Reagents Preparation

For Method A, 400 mg of Picric acid was dissolved in 100 mL of chloroform.

For Method B, 100 mg of Chloranilic acid was dissolved in 20 mL of isopropyl alcohol, filtered and made upto 100 mL with chloroform.

Standard Preparation

For methods A and B, about 100 mg of the MZL was accurately weighted and dissolved is small amounts of chloroform in a 100 mL volumetric flask and then make up to volume with chloroform to give a stock of 1 mg/mL. From this 10 mL was taken and further diluted 10 100 mL with chloroform to get a working standard of 100 µg/mL.

Preparation of sample solution

Methods A and B: To a series 10 mL volumetric flasks, aliquots of standard chloroformic MZL solutions (freebase) containing 3-15 µg (0.3-1.5 mL) from 100 ìg/mL for Method A and 50-250 µg (0.5-2.5 mL) from 1 mg/mL for method B were transferred and make up to equal volume with chloroform. To this 1.0 mL of picric acid for Method A and 1.0 mL of Chloranilic acid for Method B were added drop wise to each volumetric flask. The final volume as made up to the mark with chloroform solution for Method A and B. The absorbances of the solutions were measured at 400 nm and 530 nm for Methods A and B respectively against its reagent blank. The amount of MZL was computed from its Beer's plot.

RESULTS AND DISCUSSION

The developed Method A is based on

Table 1:

Parameter	Method A	Method B
λ_{max} (nm)	400	530
Beer's law limits (µg/mL)	3.-15	50-250
Molar absorptivity (Lit. $mole^{-1}.cm^{-1}$)	1.46×10^4	1.04×10^3
Detection limits (µg/mL)	0.336	5.496
Sandell's Sensitivity (µg/cm^2/0.001 abs. unit)	0.02955	0.4149
Optimum photometric range	2.5 -16.5	45.5 -249.5
Regression equation (Y = a+bc): Slope (b)	0.031167	0.002404
Standard deviation of slope (Sb)	3.19×10^{-4}	2.4×10^{-5}
Intercept (a)	0.0135	0.0047
Standard error of estimation (Se)	3×10^{-3}	5.53×10^{-3}
Correlation coefficient (r)	0.9996	0.9995
% Relative standard deviation*	0.5985	0.6087
% Range of Error* (Confidence limits)		
0.05 level	0.0969	0.1177
0.01 level	0.1274	0.1547
% Error in bulk samples**	0.11	-0.25

* Average of six determinations
** Average of three determinations

Table 2: Array and recovery of Mizolastine in dosage forms

Method	Pharmaceutical Formulation	Labeled Amount (mg)	Proposed Method Amount found* (mg)	Proposed Method t (value)	Proposed Method F (value)	Found by reference method ± S.D. (mg) ± S.D.	% recovery by Proposed methods** ± S.D.
A	Tablet - I	10	9.93 ± 0.012	0.572	1.210	9.42 ± 0.009	99.97 ± 0.09
	Tablet – II	10	10.06 ± 0.013	0.457	2.065	10.01 ± 0.010	99.26 ± 0.55
B	Tablet - I	10	10.01 ± 0.010	0.541	1.893	9.42 ± 0.009	100.04 ± 0.12
	Tablet – II	10	9.42 ± 0.009	0.683	2.193	10.07 ± 0.010	100.29 ± 0.13

* Average ± Standard deviation of six determinations, the t and F values refer to comparison of the proposed method with reference method. Theoretical values at 95% confidence limits t = 2.571 and F = 5.05

** Average of five determinations.

the quantitative yellow colored complex formation of drug with picric acid reagent. Picric acid in chloroform solution will have very little or no color. When chloroform solution of drug is added to this picric acid reagent it develops intense yellow color. The yellow colored salt formed between Mizolastine and picric acid can be attributed to presence of cyclic tertiary nitrogen in Mizolastine.

The proposed Method B is based on the drug which possesses cyclic tertiary nitrogen of aliphatic nature and function as electron donor and participates in charge transfer interaction with substituted quinones (chloranilic acid). The colored species formed due to the formation of radical cation.

The interference studies revealed that the common excipients usually present in the dosage forms do not interfere in the proposed method.

The optical characteristics and validation parameters were given in Table 1. To evaluate the accuracy and reproducibility of the method, known amounts of the pure drug was added to the previously analyzed pharmaceutical formulations and the mixture were reanalyzed by the proposed methods and the recoveries (average of six determinations) were given in Table 2.

The values obtained for the determination of Mizolastine in several pharmaceutical formulations (tablets) and bulk drug by the proposed and reference methods were compared (Table 2). The results indicate that the proposed methods are simple, sensitive, accurate and reproducible and can be used for the routine determination of Mizolastine in bulk and pharmaceutical formulations.

ACKNOWLEDGEMENTS

The authors are grateful to Montessori Mahila Kalasala, Vijaywada for their continuous support and encouragement and for providing the necessary facilities.

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