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Development and Validation of Visible Spectrophotometric methods for the Estimation of Metolazone in Pharmaceutical Dosage Forms

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ABSTRACT

Two simple and sensitive spectrophotometric methods (A and B) have been developed for the quantitative determination of Metolazone in bulk drug and pharmaceutical Formulations. Method A is based on the oxidative coupling reaction of Metolazone with MBTH to yield a green colored chromogen exhibiting absorption maxima at 623nm and Method B is based on the reaction of Metolazone with Folin-Ciocalteu (Fc) reagent in alkaline media to yield a blue colored chromogen exhibiting absorption maximum at 725nm. Beer's law was obeyed in the concentration range of 10-50µg/ml for methodA and 50-250µg/ml for methodB. These methods were extended to pharmaceutical formulations and there was no interference from any common excepients. The results of analysis have been validated statistically and by recovery methods.

Key words: Spectrophotometry, MBTH, FC reagent.

INTRODUCTION

Metolazone is chemically known as 7-chloro-1,2,3,4-tetrahydro-2-methyl-3-(2-methyl phenyl)-4-oxo-6-quinazoline Sulfonamide [1-2], is an anti-hypertensive drug and primarily used to treat congestive heart failure and high blood pressure. Metolazone indirectly decreases the amount of water reabsorbed into the blood streams by the kidney, so that blood volume decreases and urine volume increases. This lowers blood pressure and prevents excess fluid accumulation in heart failure [2-4]. The literature survey reveals that few analytical methods for this drug are reported, which include chromatographic [5-7],and spectrophotometric methods[8-9]. The present investigation has been undertaken to develop two simple and accurate spectrophotometric methods using MBTH and Folin-Ciocalteu reagent,which are essential for routine quality control analysis of pharmaceutical products containing Metolazone as active constituent.

MATERIALS AND METHODS

Apparatus

All spectral measurements were made on Shimadzu 1800 UV-Visible spectrophotometer with 1cm matched quartz cells were used.

Materials

Pure drug of Metolazone was obtained as gift sample from Centaur pharmaceutical Pvt Ltd, Goa and commercial formulations were procured from local market. All the chemicals used were of analytical grade.

Preparation of Standard solution:

Weigh accurately 100 mg of Metolazone and transferred in to 100 ml volumetric flask and dissolve in 100 ml of distilled water to obtain a concentration of 1mg /ml. From this suitable dilutions were made to obtain the working standard concentration of 100µg/ml (MethodA).For MethodB 1mg /ml solution was prepared in ethanol same as above.

Preparation of sample solution:

Two brands of commercially available tablets were taken, twenty tablets each weighing 5mg were weighed and powered. A tablet powder equivalent to 100mg was weighed accurately and transferred in to 100ml volumetric flask containing 50ml of distilled water, the flask was sonicated for 5min, the volume was made up to mark with distilled water, and the solution was filtered through whatmann filter paper 41, from the above stock solution, working standard solution of 100mg/ml were prepared by further dilution with distilled water, the above procedure was applied for analysis (methodA). For MethodB 1mg /ml solution was prepared in ethanol same as above.

Assay Procedure:

Fresh aliquots of Metolazone ranging from 1-.5ml was transferred into a series of 10ml volumetric flasks. To each flask add 0.2ml of $FeCl_3$ (1%) and 0.2ml MBTH (0.5%) were prepared. The solutions were kept aside for 10mins. The solution in each flask were made upto the mark with distilled water. The absorbance of green colored chromogen was measured at 623nm against the reagent blank (Fig 1). The amount of Metolazone present in the sample was computed from calibration curve (Fig 2).

Method:-

Fresh aliquots of Metolazone ranging from 0.5-2.5ml were transferred into a series of 10ml volumetric flasks. To each flask 2ml of Na_2Co_3 (20%) and 1 ml (1:2) of FC reagent were added and kept aside for 10min. The volume was made upto the mark with distilled alcohol. Then the solutions were centrifuged for 10min at 1000rpm. The absorbance of the solutions were measured at 725nm against solvent blank (Fig 3). The amount of Metolazone present in the sample was computed from calibration curve (Fig 4).

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, Molar absorptivity, and relative standard deviation were calculated and the results are summarized in Table 1.Regression characteristics like slope, intercept and correlation coefficient were calculated and are presented in Table 1.Commercial tablets of Metolazone were successfully analyzed by the proposed methods and the results are presented in Table 2.

Table 1 Optical characteristic and precision

Parameters	Method A	Method B
λmax (nm)	623	725
Beer's law limits (µg/ml)	10-50	50-250
Molar absorptivity (lit. mol^{-1} cm^{-1})	5.560 x 10^3	10.268 x 10^3
Limit of Detection (LOD/ µgml^{-1})	0.0382	0.7362
Limit of Quantification (LOQ/ µgml^{-1})	1.1604	2.2312
Sandell's sensitivity (µg/ml 0.001 abs unit)	0.0011	0.0022
Regression equation (Y*) Slope (b)	 0.0162	 0.0029
Intercept (a)	0.03	0.0223
Correlation coefficient (r)	1.018	0.9998
% RSD	0.4140	0.1554
Range of Errors** Confidence limits with 0.05 level Confidence limits with 0.01 level	 0.0019 0.0029	 0.0006 0.0010

**Y=bC+a, where C is the concentration of Metolazone in µg/ml and Y is the absorbance. **Average of eight determination*

Table-2 Evaluation of Metolazone in Tablet Dosage formulations

	Label Claim (mg)	Methods		Reference method UV	% Recovery*		% Recovery UV**
		A	B		A	B	
M_1	5	4.99	4.89	4.93	99.49	99.37	99.37
M_2	5	5.01	4.96	4.97	100.36	99.54	99.28

**mean of six determinations, M_1= Metoz (Centaur pharma), M_2= Zytanix (Zydus Cadila)*
********UV Method developed in our laboratory*

Comparison of the results obtained with the proposed and UV methods for dosage forms (Table 2) confirms the suitability of these methods for Pharmaceutical dosage forms. To evaluate validity and reproducibility of the methods recovery experiments were conducted and the results are summarized in Table 2. The other active ingradients and excipients usally present in pharmaceutical dosage forms did not interfere.

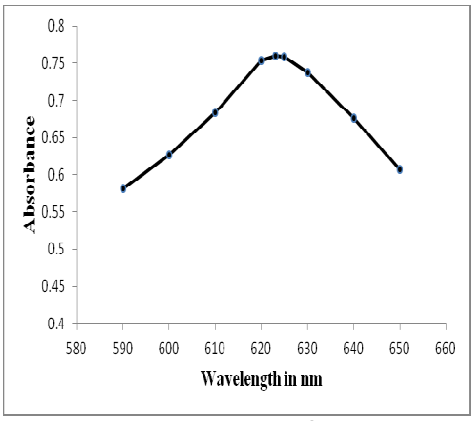

Fig 1 Absorption Spectrum of Metolazone with MBTH

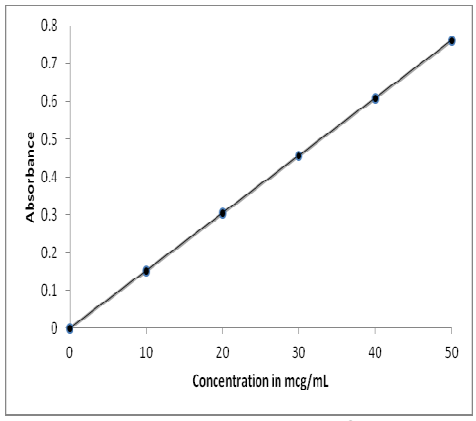

Fig 2 Calidration Curve Of Metolazone with MBTH

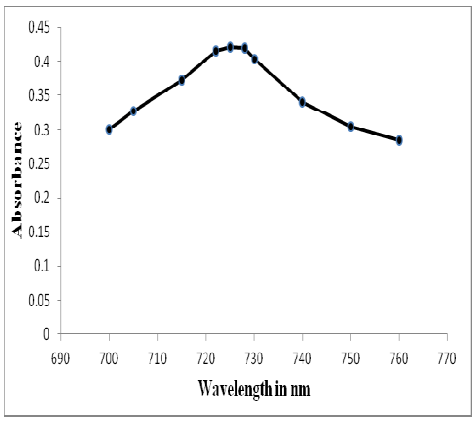

Fig 3 Absorption Spectrum of Metolazone with FC

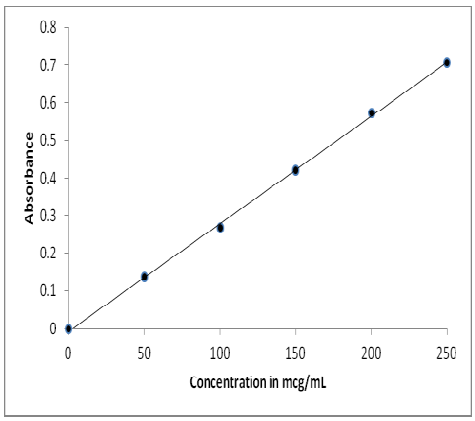

Fig 4 Calidration Curve Of Metolazone with FC

CONCLUSION

The proposed visible spectrophotometric methods for the estimation of Metolazone are simple, Sensitive, accurate and can be used for the routine quality control of the drug in bulk as well as in Pharmaceutical formulations.

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