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A Quantitative Assay for Olmesartan medoxomil in Bulk and Pharmaceutical preparations by Visible Spectrophotometry

K.Sandhyarani*

Pydah engineering and Technology, Visakhapatnam, Andhrapradesh(India)

Abstract : A simple, sensitive and cost effective visible spectrophotometric method has been developed for the determination of Olmesartan medoximil from bulk and tablet dosage forms. The method is based on the formation of green colored coordination complex by the drug with cobalt thiocyanate which is quantitatively extractable into nitro benzene with an absorption maximum of 627nm.The Regression analysis of Beer's Law plot showed good correlation in a general concentration range of 10-60µg/ml with correlation coefficient (r= 0.992). The proposed method is validated with respect to accuracy, precision, linearity and limit of detection. The suggested procedure is successfully applied to the determination of the drug in pharmaceutical preparation, with high percentage of recovery, good accuracy and precision. The results of analysis have been validated statistically by repeatability and recovery studies. The results are found satisfactory and reproducible. The method is applied successfully for the estimation Olmesartan medoxoml in tablet form without the interference of excipients.
Key Words: Beer's Law, Cobalt thiocyanate, Extractive Spectrophotometry, Nitrobenzene, Olmesartan medoxomil.

Introduction

Olmesartan medoxomil was approved by the US Food and Drug Administration (FDA) in April 2002 (Benicar, Daiichi Sankyo) for the treatment of hypertension. Chemically it is known as 2,3-dihydroxy-2-butyl 4-[1-hydroxy-1-methylethy]-2-propyl-1-[p(o-1H-tetrazol-5-ylphenyl) benzyl] imida-zole-5-carboxylate, cyclic 2,3-carboxylatate[1] and its structure (fig. 1). It belongs to the category of Angiotensin II receptor blockers. It is a prodrug and is rapidly de-esterifies during absorption to form olmesartan, the active metabolite[2-3]. Olmesartan is more effective than other angiotensin II receptor blockers (candesartan, irbesartan, losartan and valsartan) tested at their recommended doses, in terms of reduction in cuff or 24-h ambulatory blood pressure, in patients with essential hypertension. These differences in blood pressure reduction may be clinically relevant and have important long-term implication[4]

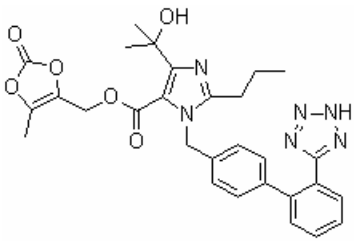

Figure1: Structure of Olmesartan medoxomil

Some analytical methods which include HPLC [5-10], LC- MS-MS [11-12], Capillary electrophoresis [13], Resonance Rayleigh Scattering (RRS) [14], UV [15-16] and visible spectrophotometric [17-21] have been reported in the literature for the determination of OLS in pharmaceutical preparations. The main purpose of the present study was to establish a relatively simple, sensitive, validated and inexpensive visible spectrophotometric method for the determination of OLS in pure form and in pharmaceutical dosage forms, since most of the previous methods have been found to be relatively complicated and expensive. So the authors have made some attempts in this direction and succeeded in developing a method based on the reaction between the drug and cobalt thiocyanate [22]. The method can be extended for the routine assay of OLS formulations.

Experimental Section

A Systronics UV/Visible spectrophotometer model -2203 with10mm matched quartz cells was used for all spectral measurements. A Systronics µ- pH meter model-362 was used for pH measurements. All the chemicals used were of analytical grade.CTC (2.50x10-1M, solution prepared by dissolving 7.25 g of cobalt nitrate and 3.8 g of ammonium thiocyanate in 100ml distilled water), Citrate buffer pH(2.0) (prepared by mixing 306ml of 0.1M trisodium citrate with 694ml of 0.1M HCl and pH was adjusted to 2.0) were prepared.

Preparation of standard solution:

Standard stock solution of Olmesartan medoxomil was prepared by dissolving 10 mg of drug in 10mL volumetric flask using methanol as solvent. Stock solutions of 1000 µg/ml were obtained in this manner. From this stock solution, working standard solution of concentration 500µg/ml was prepared by appropriate dilutions.

Sample preparation for tablet formulations

Twenty tablets each claimed to 10 mg of Olmesartan Medoxomil were weighed accurately and powdered. A quantity equivalent to 10mg of Olmesartan Medoxomil was weighed accurately and transferred to a 100 mL volumetric flask. Then 40mL methanol was added to it and the mixture was sonicated for 5 minutes for a complete solution of drug and then the volume was diluted up to the mark with the same solvent. The resulting solution was filtered through What man filter paper.

.Assay: Aliquots of standard OLS solution (0.5ml-3.0ml, 400µg/ml) were delivered into a series of 125ml separating funnels. Then 2.0ml of buffer solution (pH2.0) and 5.0 ml CTC solution were added. The total volume of aqueous phase in each separating funnel was adjusted to 15.0 ml with distilled water. To each separating funnel 10.0 ml of nitrobenzene was added and contents were shaken for 2 minutes. The two phases were allowed to separate and absorbance of nitrobenzene layer was measured at 627nm against a similar reagent blank (Fig-2 showing absorption spectra).The colored product was stable for 1 hour. The amount of OLS in the sample solution was computed from its calibration graph (Fig.3 showing Beer's Law plot).

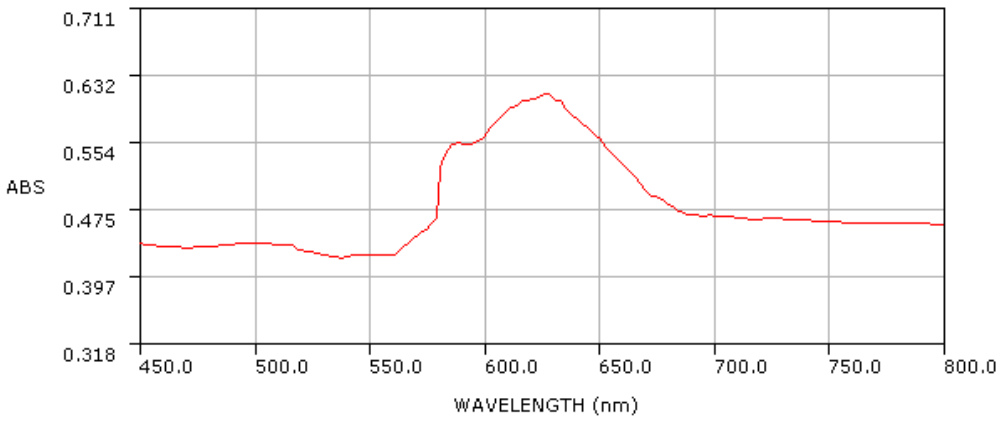

Fig.2.Showing Absorption Spectra of OLS vs. CTC

Results and Discussion

In developing this method, a systematic study of the effects of various parameters were Undertaken by varying one parameter at a time and controlling all others fixed. The effect of various parameters such as time, volume and strength of CTC reagent and pH buffer solution and solvent for final dilution of the colored species were studied and the optimum conditions were established. Among the various water immiscible organic solvents(C6H6, CHCl3, di chloro methane, nitro benzene, chlorobenzene and CCl4)tested for the extraction of colored coordinate complex into organic layer, nitrobenzene was preferred for selective extraction of colored complex from organic phase. The optical characteristics such as Beer's law limit, Sandell's sensitivity, molar absorptivity, percent relative standard deviation (calculated from the six measurements containing 3/4th of the amount of the upper Beer's law limits), Regression characteristics like standard deviation of slope (Sb), standard deviation of intercept (Sa), standard error of estimation (Se) and % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table-1. Commercial formulations containing OLS were successfully analyzed by the proposed method. The values obtained by the proposed and reference method (reported UV method in methanolλ max 289nm) for formulations were compared statistically by the t-and f-test and found not to differ significantly. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the preanalyzed formulations at three different concentration levels (50%, 75% and 100%). These results are summarized in Table-2. The ingredients usually present in formulations of OLS did not interfere with the proposed analytical method.

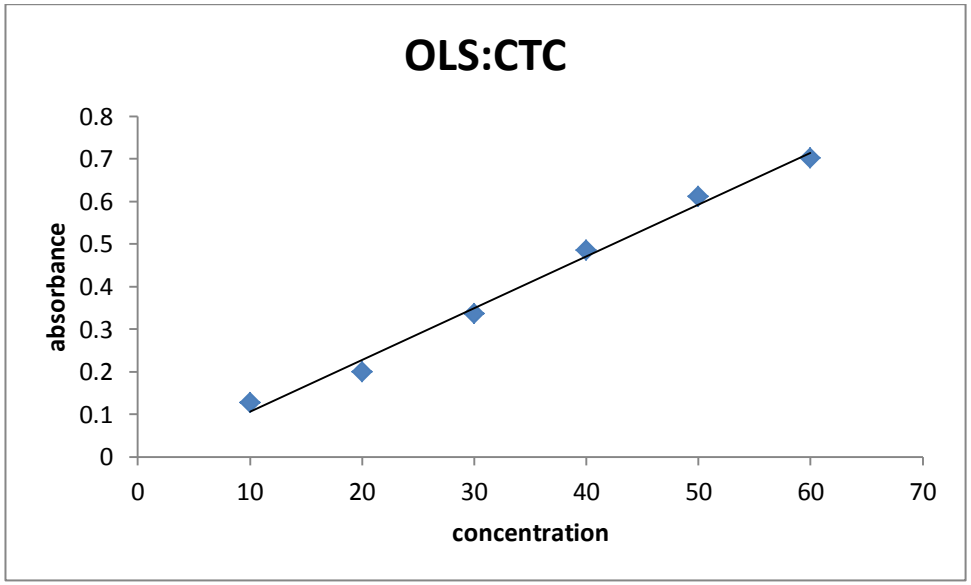

Fig.3. Showing Beer's Law Plot

Chemistry of colored species:

The colored species formed is the coordination complex of the drug (electron donor) and the central metal of cobalt thiocyanate, which is extractable into nitro benzene from aqueous solution. Formation of the green colored complex when OLS was treated with CTC is due to the presence of the cyclic tertiary amino group in it. It is based on the analogy of tertiary amine as given in the scheme (Fig-4).

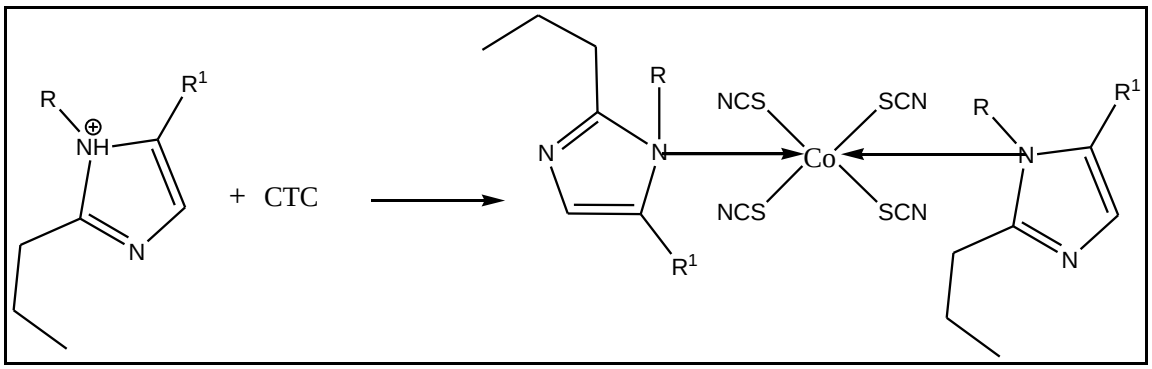

Fig.4 Showing the Scheme

Table 1: Optical characteristics, precision and accuracy of proposed analytical method

PARAMETER	**VALUES**
ƛmax (nm)	627nm
Beer's law limit(µg/ml)	10-60
Sandell's sensitivity (µg/cm2/0.001 abs. unit	0.00654
Molar absorptivity (Litre/mole/cm)	$1.6981*10^4$
Correlation Coefficient	0.992
Regression equation (Y)*	
Intercept (a)	0.014
Slope(b)	0.012
%RSD	0.52209
% Range of errors(95% Confidence limits)	
0.05 significance level	0.5479
0.01 significance level	0.8593

*Y = a+bx, where Y is the absorbance and x is the concentration of

OLSM in µg/ml

Table-2 analysis Olmesartan medoxomil by proposed and reference methods

Method	**Formulations**	**Labeled Amount (mg)**	**Found by Proposed Methods**	**t**	**f**	**Recovery by Proposed**
CTC	Tablet-1	20	19.923±0.061	0.35	0.49	99.78%

Average ± Standard deviation of six determinations, the t- and f-values refer to comparison of the proposed method with UV reference method. Theoretical values at 95% confidence limits t =2.57 and f = 5.05.

Conclusion

The reagents utilized in the proposed method are cheap, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed extractive colorimetric method is validated as per ICH guide lines and possess reasonable precision, accuracy, simple, sensitive and can be used as alternative method to the reported ones for the routine determination of OLS depending on the need and situation.

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