Estimation of Lisinopril dihydrate in bulk and pharmaceutical preparations by visible spectrophotometry

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ABSTRACT

A Simple and sensitive visible spectrophotometric method is described for the determination of Lisinopril dihydrate in bulk and pharmaceutical preparations based on the formation of Blue color complex formed with cobalt thiocyanate exhibiting λ_{max} at 625nm. The Regression analysis of Beer's law plot showed good correlation in a general concentration range of 50-300µg/ml with correlation coefficient (r=0.999). 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 of Lisinopril dihydrate in tablet form without the interference of excipients.

Key words: Beer's Law, CTC, Nitrobenzene, Tablets, Spectrophotometry.
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INTRODUCTION

Lisinopril Tablets contain the active ingredient lisinopril. It acts by widening your blood vessels, which helps reduce your blood pressure and makes it easier for your heart to pump blood to all parts of the body .(2S)-1-[(2S)-6-amino-2-{[(1S)-1-carboxy-3-phenylpropyl] amino} hexanoyl] pyrrolidine-2-carboxylic acid Lisinopril dihydrate(LPH) is drug of angiotensin-converting enzyme(ACE)inhibitor. It is typically used for the treatment of hypertension, congestive heart failure, acute myocardial infarction, and diabetic nephropathy. It is assigned to pregnancy category D by the FDA for use during second and third trimesters and to category C during first trimester.It can also be used in conjuction with the diuretichydrochlorothiazide. Molecular formula: $C_{21}H_{31}N_3O_5 \cdot 2H_2O$ soluble in water and sparingly soluble in methanol and practically insoluble in ethanol. It can be estimated by HPLC methods but no spectrophotometric method was reported in literature till date. Hence an attempt has been made to develop and validate a simple,economic rapid and accurate method. Some analytical methods which include HPLC, LC-MS and visible spectrophometric have been reported in the literature or the determination of LSPD in pharmaceutical preparations. The main purpose of the present study was to establish a relatively simple, sensitive and validated visible spectrophotometric method for the determination of LSPDin pure form and in pharmaceutical dosage forms, since most of the previous methods have been found to be relatively complicated and tedious. The proposed method based on the formation of coordination complex between durg and CTC. This method can be extended for the routine assay of LSPDformulations.
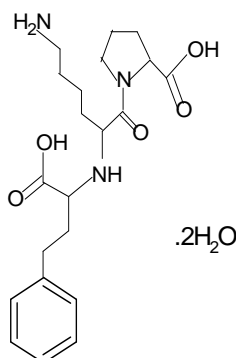
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Fig1:showing chemical structure of LSPD

EXPERIMENTAL SECTION

Apparatus and chemicals

A Shimadzu UV-Visible spectrophotometer 1601 with 1cm matched quartz cells was used for all spe4ctral measurements. All the chemicals use4d were of analytical grade Tablets were purchased from local market. CTC solution prepared by dissolving 7.25g of cobaltnitrate (BDH) and 3.8gm of ammonium thiocyanate (BDM) in 100m, of distilled water,nitrobenzene(Qualigens) used as it is. Buffer P^H 2.0 Solution prepared by mixing 25ml of potasiumchloride solution (0.2M) and 13ml of HCL(0.2M) and made upto 100ml of distilled water were prepared.

Standard drug solution

The stock solution of drug was prepared by dissolving 100 mg in 100 ml distilled water. A portion of this stock solution was diluted stepwise with the distilled water to obtain the working standard drug solution of concentrations of 100 µg/ml. from the stock solution, a series of standards were freshly prepared during the analysis day.

Preparation of sample solution.

Twenty tablets were weighed and finely powdered. A quantity of tablet powder equivalent to 100 mg of LPH taken in volumetric flask (100 ml) was shaken with methanol (10.0 ml) for 10 min and the volume was made upto the mark with distilled water. The solution was then filtered through whatman filter paper and the aliquot portion of the filtrate was diluted to 100.0 ml with distilled water to get sample solution.

Assay:

Aliquots of LPH solution (0.5-2.5ml, 200µg/ml) were delivered into a series of 125ml separating funnels. Then 3.0 ml of p^H 2.0 buffer solution and 7.0 ml of CTC solution were added and the total volume of aqueous phase in each funnel was adjusted to 15.0ml with distilled water. To each separating funnel, 10 ml of nitrobenzene was added and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the separated nitrobenzene layer was measured immediately at 625 nm against a similar reagent blank. The colored species was stable for 1 hr. The amount of LSPD present in simple solution was calculated from its calibration graph.
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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, temperature, volume and strength of (CTC, Nitrobenzene) reagents, order of addition of reagents on color development and solvent for final dilution of the colored species were studied and the optimum conditions were established. Other water miscible solvents like methanol, ethanol, propan-2-ol and acetonitrile were found to provide no additional advantage. 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 (S_b), standard deviation of intercept (S_a), standard error of estimation (S_e) and % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table-1.

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Commercial formulations containing LSPD were successfully analyzed by the proposed method. The values obtained by the proposed and reference method (reported UV method in methanol, λ_{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. These results are summarized in Table-2. The ingredients usually present in formulations of LSPD did not interfere with the proposed analytical method.

Chemistry of colored species:
In the present investigation of LSPD functions as a donor due to the presence of cyclic tertiary nitrogen in pipperidene portion. The method is based on the formation of coordination complex between drug and CTC. In order to establish optimum conditions for the formation of complex between drug (electron donor) and CTC, the author has studied the various parameters such as type of buffer, Ph and volume of the buffer, shaken time, concentration and volume of CTC, volume of aqueous phase, organic solvent for extraction, stability of colored complex formed by varying one and fixing the other parameters . The formation of colored species with these reagents may be assigned through above analogy as shown in Figure 2.
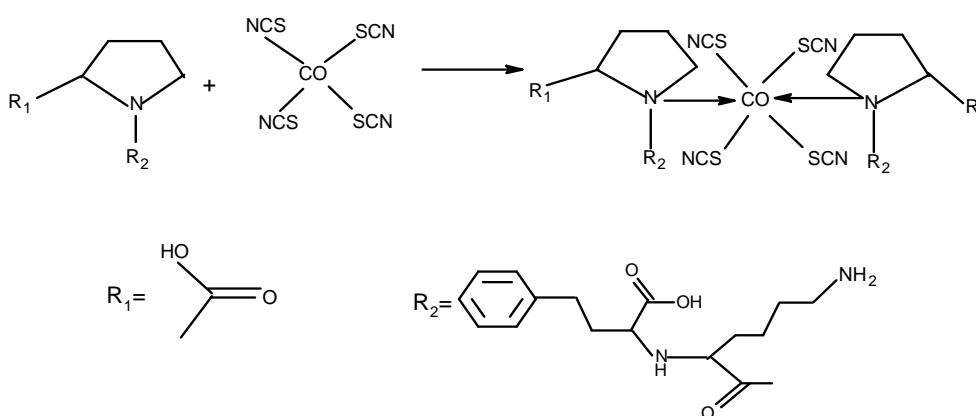

Fig 2: Probable scheme for proposed method

Table 1: optical characteristics, precision and accuracy of proposed method

Parameters	values
λ_{max} (nm)	625
Beer's law limit (μg/ml)	500-300
Sandell's sensitivity (μg/cm^2/0.001 abs. unit	1.1304
Molar absorptivity (Liter/mole/cm)	2.9791×10^4
Regression equation	
(Y)*= a+bc	
Intercept(a)	0.0002
Slope (b)	0.002
%RSD	0.342
%Range of errors (95% Confidence limits)	
0.05 significance level	0.394
0.01 significance level	0.716

$Y^*=a+bc$; where y=absorbance. C= concentration of LSPD inμg/ml.

Table 2: Analysis of LSPD in pharmaceutical formulations by proposed and reference methods

Method	*formulations	Labled Amount(mg)	Found by proposed Methods			Found by Reference Method ± SD		#% Recovery by proposed Method ± SD
			**Amount found ± SD	t	f			
CTC	Tablet-1	60	59.58±0.114	0.186	1.538	59.58±0.142	99.31±0.190	
	Tablet-2	60	59.65±0.219	0.287	1.316	59.65±0.191	99.43±0.364	

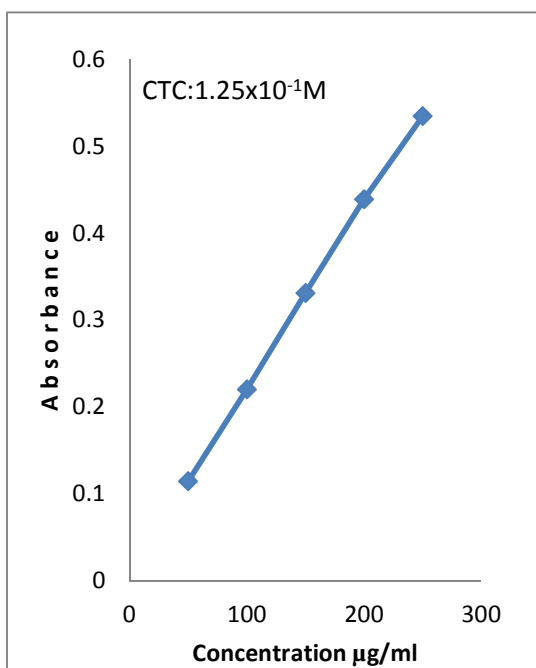*Tablet 1 and Tablet 2 from two different companies*

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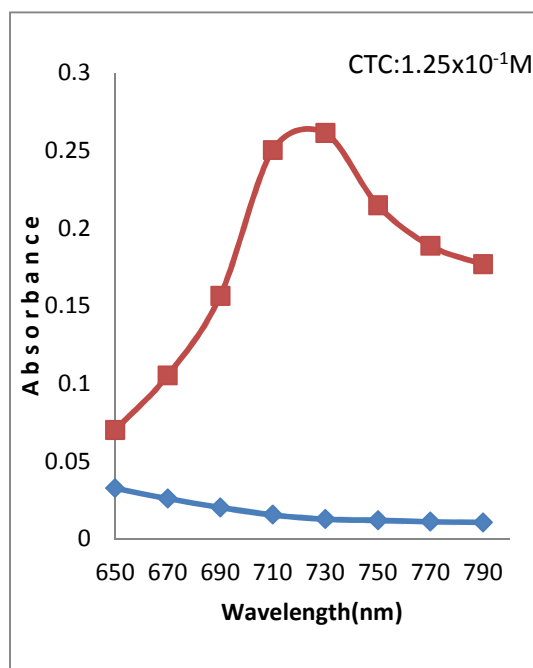**Fig3 Beers law plot of LSPD with CTC system**   **Fig 4: Absorption spectra of LSPD with CTC system and its reagent blank**

CONCLUSION

The reagents utilized in the proposed method are cheap and readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed analytical 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 LSPD depending on the need and situation.

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