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Visible Spectrophotometric Method for Estimation of Lurasidone Hydrochloride In Synthetic Mixture

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ABSTRACT

A simple, sensitive, accurate, precise and economical visible spectrophotometric method was developed and validated for the estimation of lurasidone Hydrochloride in synthetic mixture. The method is based on the reaction of lurasidone Hydrochloride with bromocresol green dye in dichloromethane giving yellow color chromogen, which shows maximum absorbance at 418 nm against reagent blank. The chromogen obeyed Beer's law in the concentration range of 4-12 µg/ml for lurasidone Hydrochloride. The results of the analysis have been validated statistically and by recovery studies.

Keywords: Lurasidone Hydrochloride, Chromogen, Bromocresol green, Visible spectrophotometric.

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INTRODUCTION

Lurasidone Hydrochloride (LSD) is chemically, (3a*R*,4*S*,7*R*,7a*S*)-2-[((1*R*,2*R*)-2-{[4-(1,2-benzisothiazol-3-yl)-piperazin-1yl]methyl} cyclohexyl) methyl] hexahydro-1*H*-4,7-methanisoindol-1,3-dione. Lurasidone Hydrochloride is a relatively new atypical antipsychotic for the treatment of schizophrenia.[1] Lurasidone Hydrochloride is not yet official in IP, USP, BP, JP and EP. Literature survey reveals spectrophotometric [2] and HPLC [3] methods for the estimation of lurasidone Hydrochloride in pharmaceutical formulations. The present communication describes simple, sensitive, accurate, precise and economical visible spectrophotometric method using bromocresol green for the estimation of lurasidone Hydrochloride in tablet dosage form.

MATERIALS AND METHOD

Apparatus

A Shimadzu model 1800 double beam UV/Vis. spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cells was used to measure absorbance of the resulting solutions. A Sartorius CP224S analytical balance (Germany) and an ultra sonic cleaner (Frontline FS 4, Mumbai, India) were used in the study.

Reagents and Materials

Lurasidone Hydrochloride powder was procured as a gift sample from Astron research limited, Ahmedabad, Gujarat, India. The synthetic mixture containing 20 mg LSD was prepared in the laboratory using pharmaceutical excipients. Bromocresol green dye and dichloromethane (AR Grade, Finar Chemicals Ltd., Ahmedabad) were used in the study.

Preparation of reagent and standard stock solution

Accurately weighed Bromocresol green dye powder (15 mg) was transferred to a 100 ml volumetric flask, dissolved in and diluted to the mark with dichloromethane (0.15% w/v). Accurately weighed LSD (10 mg) was transferred to a 100 ml volumetric flask, dissolved in and diluted to the mark with dichloromethane (100 µg/ml).

Methodology

Standard stock solution of LSD (0.8 ml) was transferred to a 10 ml corning volumetric flask. Bromocresol green dye solution (3.0 ml) was added and mixed. The volume was adjusted to 10 ml with dichloromethane. The absorbance of the colored solution was scanned in the range of 300 to 600 nm against reagent blank, prepared similarly in which volume of standard solution was replaced by an equal volume of dichloromethane. Maximum absorbance was obtained at 418 nm.

Optimization of different conditions

Choice of organic solvent

Few organic solvents such as methanol, dichloromethane, acetone and carbon tetrachloride were examined since LSD is soluble in these solvents. Among these solvents, dichloromethane was preferred as the most suitable solvent to carry out the experiments because in this medium, the reagent blank gave negligible blank absorbance and the ion-pair complex formed was found to exhibit higher sensitivity and stability. In other solvents, the reagent blank yielded high absorbance value.

Effect of concentration of bromocresol green dye

Standard stock solution of LSD (0.8 ml) was transferred to a series of 10 ml corning volumetric flasks. To each flask, different volumes of Bromocresol green dye (1, 2.0, 3.0, 4.0, and 5.0 ml) was added, mixed and volume in each flask was adjusted to 10 ml with dichloromethane. The absorbance of the resulting solutions was measured at 418 nm against reagent blank. Maximum absorbance was observed in the presence of 3 ml of 0.15% w/v bromocresol green dye solution, which remained constant with increase in the volume of the reagent solution.

Time for maximum color development

Standard stock solution of lurasidone Hydrochloride (0.8 ml) was transferred to a series of 10 ml corning volumetric flasks. To each flask, 3 ml of bromocresol green dye solution was added and mixed. The flasks were kept at room temperature for different time interval (0, 5, 10, 15, and 20 minutes) and the volume in each flask was adjusted to 10 ml with dichloromethane. The absorbance of the resulting solutions was measured at 418 nm against reagent blank. Maximum absorbance was obtained after 5 minutes.

Validation of the proposed method

The proposed method was validated according to the International Conference on Harmonization (ICH) guidelines.[4]

Linearity

Calibration curve was plotted over a concentration range of 4-12 µg/ml for LSD. Accurately measured standard stock solutions of LSD (0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, and 1.2 ml) were transferred to a series of 10 ml corning volumetric flasks. To each flask, 3 ml of bromocresol green dye solution(0.15%) was added and mixed. The flasks were kept at room temperature for 5 minutes and the volume in each flask was adjusted to 10 ml with dichloromethane. The absorbance of the resulting solutions was measured at 418 nm against reagent blank. Calibration

curve was constructed for LSD by plotting concentration versus absorbance at 418 nm. Each reading was an average of five determinations.

Method Precision (% Repeatability)

The precision of the instrument was checked by repeated scanning and measurement of the absorbance of solutions (n = 6) of LSD (8 µg/ml) without changing the parameters for the method. The repeatability was expressed in terms of relative standard deviation (%RSD).

Intermediate Precision (Reproducibility)

The intraday and interday precision of the proposed method was performed by analyzing the corresponding responses 3 times on the same day and on 3 different days over a period of 1 week for different concentrations of standard solutions of LSD (4-12 µg/ml). The results were reported in terms of relative standard deviation (%RSD).

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection (LOD) and the limit of quantification (LOQ) of the drug was derived by calculating the signal-to-noise ratio (S/N, i.e., 3.3 for LOD and 10 for LOQ) using the following equations as per International Conference on Harmonization (ICH) guidelines[4].

$$LOD = 3.3 \times \sigma/S$$

$$LOQ = 10 \times \sigma/S$$

Where σ = the standard deviation of the response and S = Slope of calibration curve.

Accuracy (% Recovery)

The accuracy of the method was performed by calculating recovery of LSD by the standard addition method. Known amounts of standard solutions of LSD were added at 50, 100 and 150% levels to prequantified sample solutions of LSD (4 µg/ml). Each sample was prepared in triplicate at each level. The amount of lurasidone Hydrochloride was estimated by applying obtained values to regression equation.

Estimation of lurasidone Hydrochloride from pharmaceutical synthetic mixture.

The synthetic mixture containing 20 mg LSD was prepared in the laboratory. A quantity of powder equivalent to 10 mg of LSD was transferred to a 100 ml volumetric flask and mixed with dichloromethane (50 ml) and sonicated for 20 minutes. The solution was filtered through Whatman filter paper No. 41 and the residue was washed thoroughly with dichloromethane. The filtrate and washings were combined in a 100 ml volumetric flask and diluted to the mark with dichloromethane. The solution (0.8 ml) was transferred to a 10 ml corning volumetric flask. Bromocresol green dye solution (3 ml) was added and mixed. The flask was kept at room temperature for 5 minutes and the volume was adjusted to 10 ml with dichloromethane. The

absorbance of the resulting solution was measured at 418 nm against reagent blank. The amount of LSD was determined by fitting the responses into the regression equation. The analysis procedure was repeated five times with synthetic mixture.

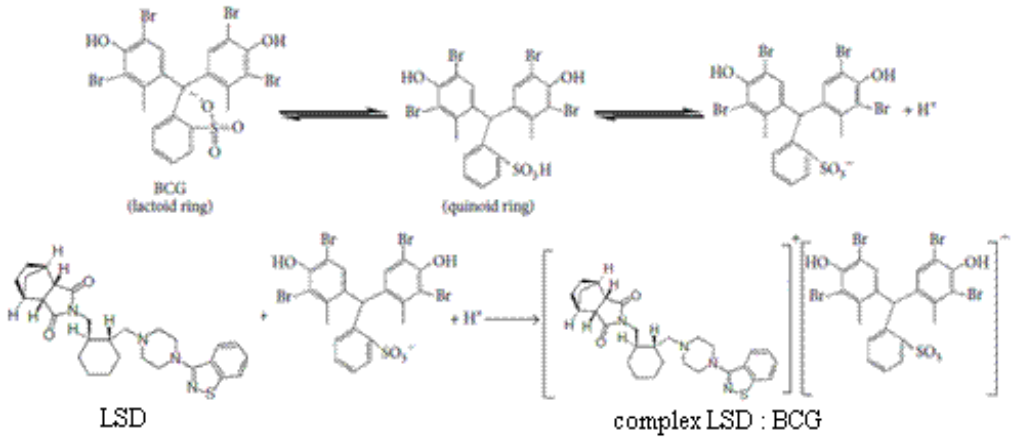
RESULTS AND DISCUSSION

The proposed procedures are based on the reaction between LSD and BCG, resulting in the formation of yellow ion-pair complexes which could be measured directly in dichloromethane.

LSD features a Piperazine ring. This structure suggests the possibility of utilizing anionic dyes as chromogenic agents. In dichloromethane, LSD does not absorb in the visible region. Also, the dyes used have almost negligible absorbance. In contrast, when a solution of BCG in dichloromethane is mixed with the drug solution also in dichloromethane, an intense yellow color is immediately produced with the absorption maximum at 418 nm (Figure 1). This is due to the conversion of the dye into an open quinoidal anionic derivative[4,5], which subsequently forms an ion pair with LSD as shown in Scheme 1.

Literature survey reveals spectrophotometric method for the determination of ofloxacin using bromocresol green[6]. Therefore it was thought of interest to extend the application of bromocresol green in the estimation of LSD.

In the proposed method, reagent solution and standard stock solutions of drugs were prepared in dichloromethane. Various reaction conditions were established by varying one parameter at a time and keeping the others fixed by observing the effect produced on the absorbance of the colored species. The parameters involved for maximum color development time and concentration of bromocresol green dye solution to yield chromogen of maximum color intensity and stability were optimized. In this method all these parameters were strictly followed.



Scheme 1: Possible reaction scheme of LSD:BCG

The yellow colored complex formed having wavelength of maximum absorbance at 418 nm (Figure 1). In proposed method, it was found that 1.5 ml of 0.1% w/v bromocresol green dye (Figure 2), and 5 minutes for color development (Figure 3) was sufficient for the development of maximum color intensity. Stability study of the developed chromogen was carried out by measuring the absorbance values at a time intervals of 15 minutes for 2 h and it was found to be stable for more than 2 h for the drugs at room temperature.

The linearity was found in the concentration range of 4 to 12 µg/ml ($r^2 = 0.9960$) (Figure 4). The reproducibility, repeatability and precision of method are very good as shown by the low values of standard deviation and relative standard deviation (%RSD). The % recovery value in the range of 98.47 to 102.82 % for synthetic mixture indicates non-interferences from the formulation excipients. The data of recovery studies and assay results are given in Table 1 and Table 2, respectively. Optical characteristics of method and summary of validation parameters for LSD was given in Table 3.

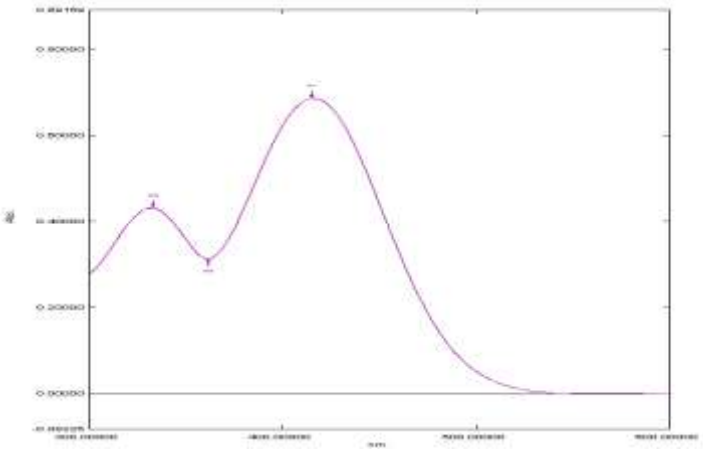


Figure 1: Spectra of LSD with bromocresol green dye at 418 nm in dichloromethane

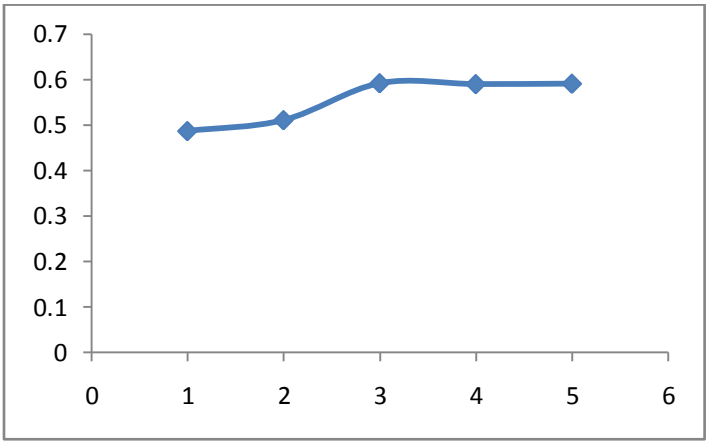


Figure 2: Optimization of volume of 0.1% w/v bromocresol green dye (ml)

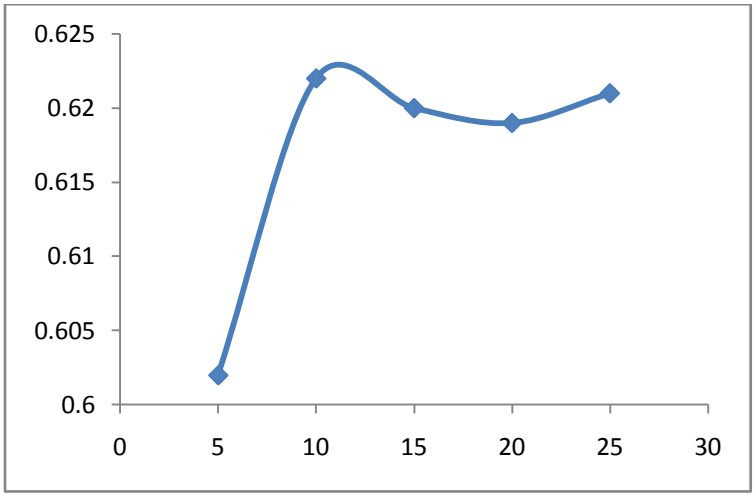


Figure 3: Optimization of reaction time (minutes)

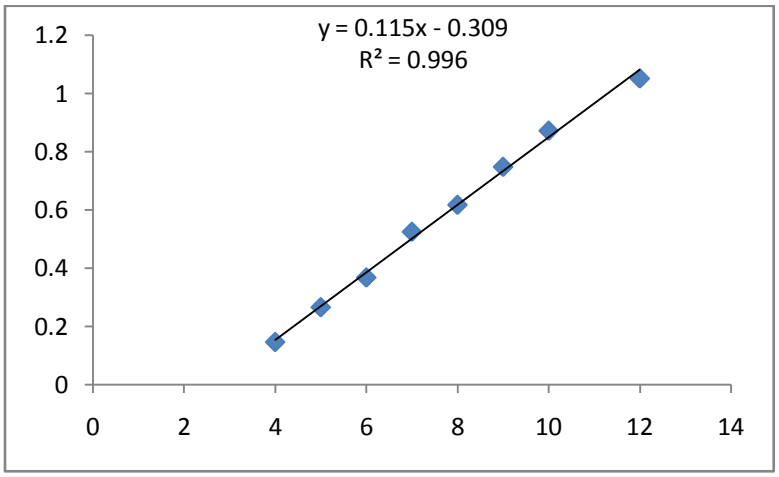


Figure 4: Linearity curve of Lurasidone HCl

Table 1: Results of Recovery Studies In Tablet Dosage Forms

Formulation	Level	Amount of sample taken (µg/ml)	Amount of standard spiked (%)	Mean % recovery ± S. D.*(n = 3)
Synthetic mixture	I	4	50	98.47 ± 1.20
	II	4	100	101.25 ± 0.494
	III	4	150	102.82 ± 0.472

S. D. is standard deviation and n is number of determinations

Table 2: Results of Analysis of Tablet Formulation

Formulation	Label claim (mg)	Amount found (mg)	% Label claim ± S. D.* (n = 5)
Synthetic mixture	20	20.085	100.43±0.460

S. D. is standard deviation n is number of determinations

Table 3: Optical Characteristics and Summary of Validation Parameters

Parameters	Results
λ max (nm)	418
Linearity range (µg/ml)	4-12
Sandell's sensitivity (µg/cm^2/0.001 A.U.)	0.014013
Molar extinction coefficient (l/mol.cm)	60950
Correlation coefficient (r^2)	0.9960
Regression equation (y* = b + ac)	
Slope (a)	0.115
Intercept (b)	0.309
Standard deviation (S. D.)	± 0.005303
% Relative standard deviation (% RSD)	± 0.6971
Standard error of mean (S.E.M)	± 0.003226
Repeatability (% RSD, n = 6).	1.05
Intermediate Precision (% RSD)	
Interday (n = 3)	0.536 - 1.6115
Intraday (n = 3)	0.247 – 0.617
Accuracy (% Recovery) (n = 5)	98.47 - 102.82
Limit of detection (LOD) (µg/ml)	0.154
Limit of quantification (LOQ) (µg/ml)	0.464

y* = b + ac where 'c' is the concentration and y is absorbance unit. n is the number of determinations, RSD is relative standard deviation and S.E.M is standard error of mean.

CONCLUSION

The proposed visible spectrophotometric method was found to be, simple, sensitive, accurate, precise and economic for determination of LSD in synthetic mixture. The most attractive feature of the methods is their relative freedom from interference by the usual tablet diluents and excipients in amounts far in excess of their normal occurrence in pharmaceutical formulations. Hence it can be conveniently adopted for routine quality analysis of the drug in pharmaceutical dosage form.

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