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Development and validation for Estimation of Levosulpiride by Area Under Curve and Difference Spectrophotometric Method

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Abstract : Two simple, precise and economical UV spectrophotometric methods have been developed for the estimation of Levosulpiride in bulk and pharmaceutical dosage form. Method A - AUC in which area under curve was integrated in the wavelength range of 284–294 nm using methanol as solvent. Method B – Difference Spectroscopic method, the proposed method is based on the principle that Levosulpiride can exhibit two different chemical form in basic and acidic medium that differ in the absorption spectra in basic and acidic medium. The difference spectrum of Levosulpiride in 0.01N Sodium Hydroxide was recorded by taking Levosulpiride in 0.01N Hydrochloric acid solution as blank. The difference spectrum showed that the maxima at 227nm and minima at 246nm. Linearity for the detector response was observed in the concentration range of 5-25 µg/ml for both the methods. The linear regression for Method A and B were found to be 0.999 and 0.999 respectively. The methods were validated and can be successfully applied to estimate levosulpiride in pharmaceutical dosage forms.

Key words: Levosulpiride, Area under curve, difference spectroscopy, validation.

INTRODUCTION

Levosulpiride, a purified levo-isomer of sulpiride is chemically 5- (aminosulfonyl)-N-[(1-ethyl-2-pyrrolidinyl) methyl]-2-methoxy benzamide. It is not official in any pharmacopoeia. It is listed in The Merck Index [1] and Martindale, The Complete Drug Reference [2]. Levosulpiride having D_2-dopamine receptor antagonistic activity which gives antidepressive and antiulcer effects [3]. Compared with racemic and dextro-forms, the levo-form of sulpiride has greater central antidopaminergic activity [4], antiemetic and antidyspeptic effects and lower acute toxicity [5]. A survey of literature has revealed simple UV-Spectrophotometry[6], derivative spectroscopy[6], visible spectrophotometry[7], spectro- fluorimetry[8], RP-HPLC[9] method for estimation of Levosulpiride in bulk drug and formulation. The objective of the present study is to develop simple, precise, accurate and economic spectrometric methods for estimation of Levosulpiride.

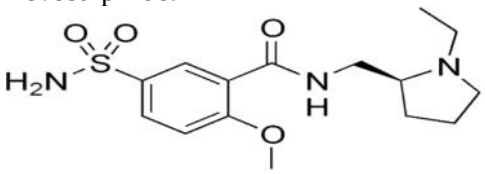

Figure 1: Structure of Levosulpiride

MATERIALS AND METHODS

Appratus

Spectroscopic measurements were carried out on a computerized UV - 1800 Double beam spectrophotometer with 1 cm matched quartz cells and Shimadzu electronic balance from Uni Bloc was used for weighing the sample. The ultrasonicator used for dissolving the market formulation from Life care equipment Pvt. Ltd., Mumbai.

Chemicals

Working stanadard of Levosulpiride was kindly gifted from Torrent Pharmaceutical Ltd., Ahmedabad. The commercially available marketed tablet, Lesuride (Sun Phrma) containing 25 mg of Levosulpiride was used and it was procured from the local market. Distilled water was obtained by in house distillation, AR grade Methanol was obtained from Astron Chemicals, India and AR grade Sodium Hydroxide was obtained from RFCL Ltd., India. AR grade Hydrochloric acid was obtained from Astron, Ahmedabad, India. Freshly prepared 0.01 N sodium hydroxide and 0.01 N hydrochloric acid is of analytical grade were used in the present investigation.

PROCEDURE

Preparation of standard stock solution

Standard stock solution of Levosulpiride was prepared by dissolving 10 mg in 10 ml (1000 mcg/ml) volumetric flask using methanol as solvent. From resulting stock solution prepare 100 mcg/ml with methanol for both the methods.

Preparation of working standard solution

For Method A, the prepared stock solution was further diluted with methanol in 10 ml volumetric flask to get working standard solution of 5-25 mcg/ml to construct Beer's law plot. The absorbance of each solution was measured at the area between 284-294 nm For Method B, the prepared stock solution was further diluted with 0.01 N sodium hydroxide and 0.01N hydrochloric acid in 25ml volumetric flask to get working standard solution of 5-25 mcg/ml. The difference spectrum for Levosulpiride was recorded by placing drug in 0.01N hydrochloric acid in reference cell and 0.01N sodium hydroxide in sample cell. The difference in absorbance between 227nm (maxima) and 246nm (minima) was calculated to find out the amplitude.

Analysis of commercial dosage form

Twenty tablets were weighed and powdered finely. A quantity of tablet powder equivalent to 25 mg of Levosulpiride was accurately weighed and transferred to 25 ml volumetric flask containing methanol and sonicated for 5 min. The solution was filtered through whatman filter paper. The resultant solution was diluted with methanol to get concentration of 10 mcg/ml for Method A and the solution was further diluted with 0.01N sodium hydroxide and 0.01N hydrochloric acid to get the concentration of 10 mcg/ml. The amount of drug present in the sample solution was determined using the calibration curve of standard drug.

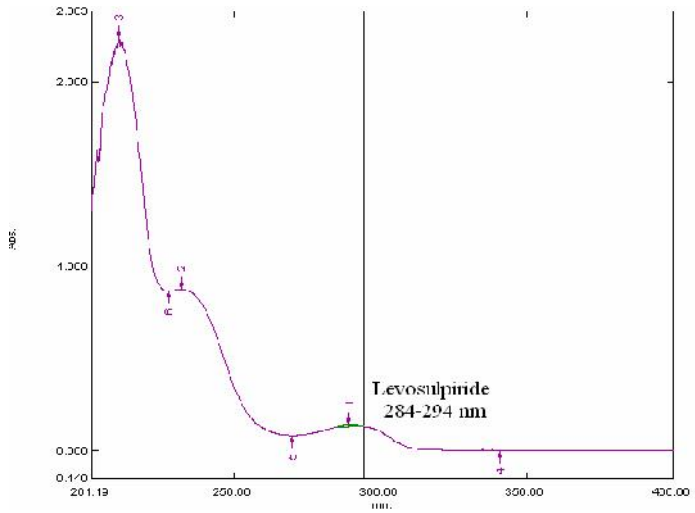

Figure 2: UV curve of Levosulpiride in wavelength region of 284-294 nm

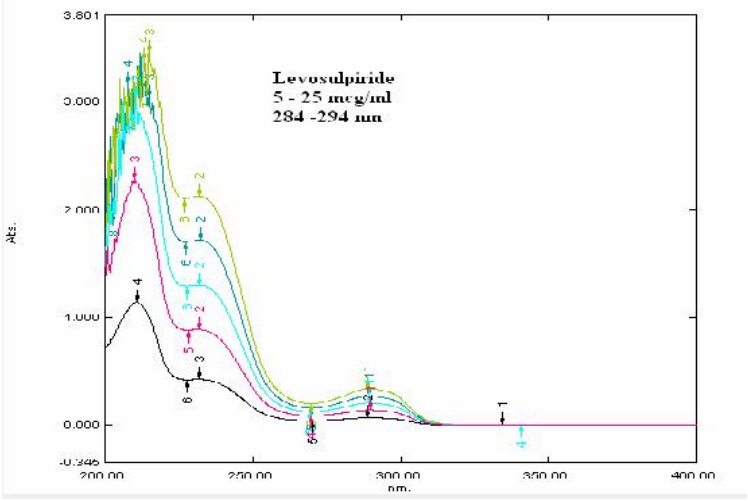

Figure 3: Overlay UV Curve of Levosulpiride

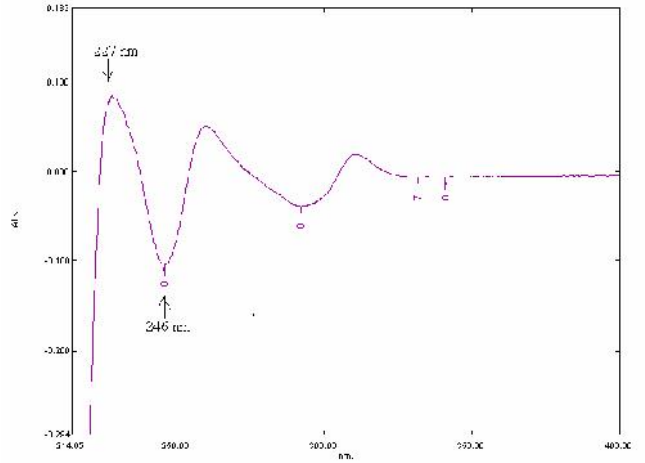

Figure 4: Difference spectrum of Levosulpiride in 0.01N NaOH w.r. to 0.01N HCl

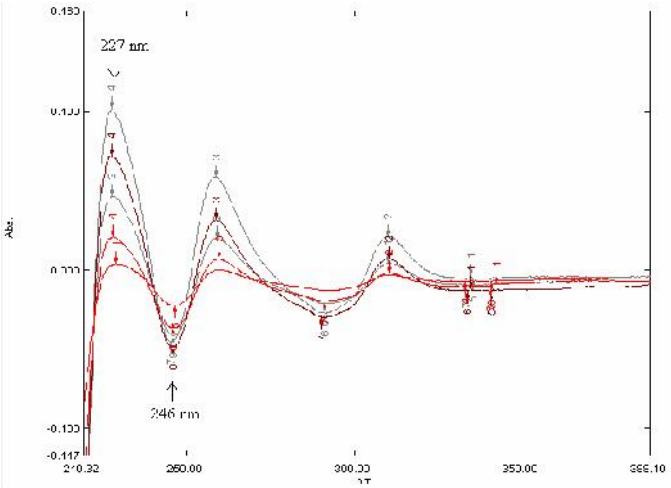

Figure 5: overlay Difference spectrum of Levosulpiride

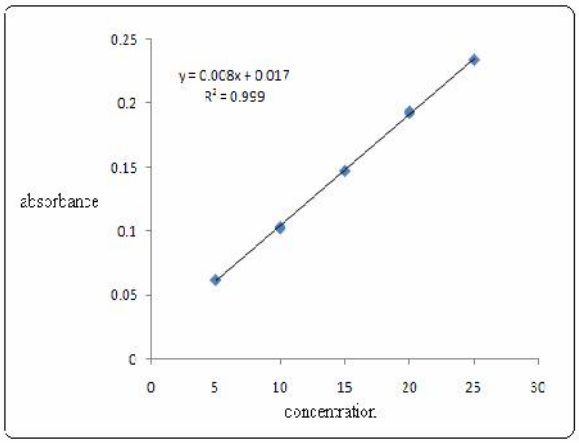

Figure 6: Calibration curve of Levosulpiride for Method A

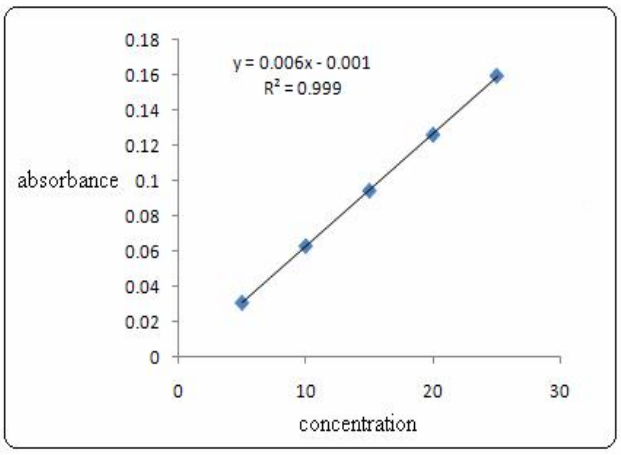

Figure 7: Calibration curve of Levosulpiride for Method B

RESULT AND DISCUSSION

METHOD VALIDATION

Linearity and range

Linearity of the concentration was taken in range of 5-25 mcg/ml for tablet formulation.

Precision

The interday precision was determined on three different days at three different levels 10, 15, 20mcg/ml and the intraday precision was determined at three different levels 10, 15, 20 mcg/ml by same analyst for both the methods. The %RSD values were found to be less than 2% indicating that the method is more precise.

Accuracy

Recovery studies were carried out by adding different amounts 80%, 100%, 120% of bulk sample of Levosulpiride within the linearity range. For Method A % Recovery was found to be 99.23-99.58% and for Method B % Recovery was found to be 99.14-99.68%. The %RSD values were found to be less than 2% indicating that the method is more accurate.

Table 1: Optical characteristics of Levosulpiride

Parameters	Method A	Method B
Beer's range (mcg/ml)	5-25	5-25
Wavelength	284-294 nm	227nm maxima 246 nm minima
Regression Equation	y = 0.006x - 0.001	y = 0.008x + 0.017
Correlation coefficient	0.999	0.999
Slope	0.006	0.008
Intercept	0.001	0.0017
Limit of Detection (mcg/ml)	0.317543	0.310519
Limit of Quantification (mcg/ml)	0.96225	0.940966
Intra day precision (n=3) (%RSD)	0.425833	0.5565
Inter day precision (n=3) (%RSD)	0.4216	0.5599

Table 2: Recovery study of Levosulpiride for Method A

Level of % Recovery (n=3)	Tablet concentration (mcg/ml)	Standard concentration spiked (mcg/ml)	% Mean Recovery	% SD	% RSD
80	10	8	99.23	0.7524	0.7582
100	10	10	98.78	1.2291	0.7641
120	10	12	99.59	0.7503	0.7533

Table 3: Recovery study of Levosulpiride for Method B

Level of % Recovery (n=3)	Tablet concentration (mcg/ml)	Standard concentration spiked (mcg/ml)	% Mean Recovery	% SD	% RSD
80	10	8	99.59	0.0757	0.0760
100	10	10	99.14	0.1662	0.1676
120	10	12	99.68	0.1625	0.1630

Table 4: Analysis of tablet dosage form

Method	Label amount	Amount found	% Label claim	SD	% RSD (n =3)
A	25 mg	24.87 mg	99.48	0.44	0.4422
B	25 mg	24.74 mg	98.97	0.2203	0.2225

CONCLUSION

The validated two spectroscopic methods are simple, precise, accurate and can be used for determination of Levosulpiride in bulk and tablet formulation

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