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UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF LULICONAZOLE IN MARKETED FORMULATION (LOTION)

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ABSTRACT

A new, simple, precise, accurate, reproducible and economical and sensitive UV - Spectrophotometric method has been developed for the estimation of luliconazole in marketed formulation. The determination was made at 296 nm for Luliconazole over the concentration range of 5-25 µg/ml with mean recovery of 99.97%. The LOD and LOQ were found to be 0.38µg/ml and 1.06µg/ml respectively. Methanol was used as solvent. The validation of method was carried out as per ICH Guidelines.

KEYWORDS: Luliconazole, UV Spectrophotometric method, Validation, LULIFIN Marketed formulation.

INTRODUCTION

Luliconazole (LCZ) belongs to imidazole class of drug that possesses a wide spectrum of antifungal activity and is very potent against dermatophytes. Luliconazole is chemically, (2E)-2-[(4R)-4-(2, 4-dichlorophenyl)-1, 3-dithiolan-2-ylidene]-2-imidazol-1-yl-acetonitrile. It is not official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United States Pharmacopoeia (USP). Till date no analytical method was reported for quantitative estimation of LCZ except stability indicating method. LCZ is a novel antifungal drug launched in India by Ranbaxy Laboratories Ltd. The compound was originally screened from active compounds related to lanoconazole, a potent antidermatophytic drug. Literature survey reveals that the simple and rapid stability-indicating liquid chromatographic method has been developed and validated for LCZ. The present manuscript describes simple, accurate, precise, reproducible, and economical UV Spectrophotometric method for the estimation of Luliconazole in marketed formulation.

MATERIAL AND METHODS

Instruments

Spectrophotometric measurements were performed on Shimadzu UV –visible double beam

spectrophotometer (Model- 1800). All weighing were done on electronic analytical balance (Wensar Dab220).

Chemicals and Reagents

LCZ bulk powder was obtained from India. The formulation Lulifin^{TM} was procured from the local market. All other chemicals used were of analytical grade. Calibrated glass wares were employed throughout the work.

Preparation of Standard Stock Solution

Standard stock solution A:-100mg of Luliconazole drug sample was weighed accurately and transferred to 100ml volumetric flask and diluted upto the mark with methanol (1000µg/ml).

Standard working solution:-From stock A 10 ml was pipetted out and was diluted upto100ml with methanol in 100ml volumetric flask (100µg/ml).

Preparation of Working Solutions

This series consisted of different concentrations of standard Luliconazole solution ranging from 5-25µg/ml. The solutions were prepared by pipetting out 0.5, 1, 1.5, 2.0, and 2.5 of theworking stock solution of Luliconazole (100µg/ml) into series of 10 ml volumetric flasks and the volume was adjusted to mark with methanol to make 5, 10, 15 ,20, and 25µg/ml solution of LCZ.

Selection of Analytical Wavelength

By appropriate dilution of standard drug working solution with methanol, solution containing 10 µg/ml of LCZ was scanned in the range of 200-800 nm. Overlain spectra show 296 nm as the λmax of LCZ.

Assay

The 10ml of the lotion equivalent to 100mg was taken into 100ml volumetric flask and was diluted upto the mark with methanol (1000µg/ml). The solution was filtered through whatmann filter paper no.42. 10ml of the above solution was pipetted out in 10ml volumetric flask and diluted to mark with methanol. From this 1.5ml of the solution was pipetted out and transferred into 10ml volumetric flask and diluted upto the mark with methanol (15µg/ml). Absorbance of the resulting solution was measured at 296 nm against methanol. The concentration of luliconazole can be obtained as,

$$y = mx + c \ldots\ldots\ldots - (1)$$

Method Validation

Method validation was performed following ICH guidelines. The proposed method has been extensively validated in terms of linearity, accuracy and precision, limit of detection and limit of

quantification.

Linearity (Calibration curve)

Calibration curve was plotted over a wide concentration range and the linear response was observed over a concentration range of 5-25 µg/ml for LCZ. Accurately measured standard working solutions of LCZ (0.5, 1.0, 1.5, 2.0, and 2.5ml) were transferred to a series of 10 ml of volumetric flasks and diluted to the mark with Methanol, and the absorbance was measured (n=3) at 296 nm. The calibration curve was constructed by plotting absorbance v/s. concentrations. The linear regression equation was y = 0.051x + 0.055 (R^2= 0.998)

Accuracy

Accuracy was assessed by determination of the recovery of the method by addition of standard drug to the prequantified sample preparation at three different concentration levels 80 %, 100 % and 120 %, taking in to consideration percentage purity of added drug sample. The amount of LCZ was estimated by applying obtained values to the respective regression line equations. Each concentration was analysed 3 times and average recovery was measured.

Precision

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. The precision of the method was verified as repeatability, intra-day, inter-day and reproducibility.

The precision of the method was checked by repeated measurement of absorbance of solution of (n = 6) of LCZ (15µg/ml) without changing the parameter of proposed method. %RSD was calculated.

Limit of Detection and Limit of Quantification

ICH guideline describes several approaches to determine the detection and quantification limits. These include visual evaluation, signal-to-noise ratio and the use of standard deviation of the response and the slope of the calibration curve. In the present study, the LOD and LOQ were based on the third approach and were calculated according to the 3.3 × (SD/Slope) and 10 × (SD/Slope) criteria, respectively; where SD is the standard deviation of y-intercept of regression line and S is the slop of the calibration curve.

RESULT AND DISCUSSION

A reliable method was developed for the estimation of the LCZ in marketed formulationby UV Spectrophotometry. Beers law was obeyed in concentration range of 5-25µg/ml for LCZ at 296 nm. The correlation coefficient was found to be R^2= 0.998. The mean % recoveries were found

to be in the range of 99.63-101.09%. Precision (% RSD) of LCZ was found to be 0.15-0.87 %. The LOD and LOQ were 0.38µg/ml and 1.06µg/ml of LCZ respectively. The proposed method was precise, accurate and reproducible and acceptable recovery of the analytes, which can be applied for the analysis of LCZ in marketed formulation.

CONCLUSION

The results of our study indicate that the proposed UV spectroscopic method is simple, rapid, precise and accurate. The developed UV spectroscopic method was found suitable for determination of Luliconazole in marketed formulation without any interference from the excipients. Statistical analysis proves that the method is repeatable and selective for the analysis of Luliconazole. It can therefore be conclude that use of the method can save time and money and it can be used in small laboratories with accurate and wide linear range.

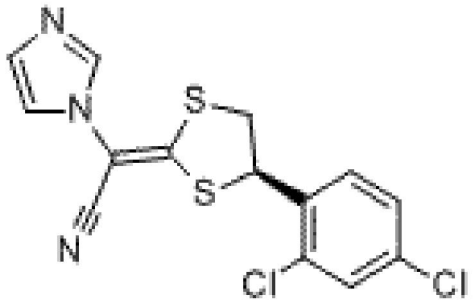

Figure 1: Structure of Luliconazole

Table 1: Regression analysis data and summary of validation parameters for the proposed method

SR.NO	PARAMETERS	RESULTS
1	Linearity and Range(µg/ml)	5-25
2	Correlation coefficient	0.998
3	Precision (%RSD) 1.Repeatability 2.Intraday 3.Interday	 0.7862 0.51-0.74 0.54-0.87
4	Accuracy (%Recovery)	99.2-101.09
5	LOD(µg/ml)	0.38
6	LOQ (µg/ml)	1.06
7	Assay	99.33

Table 2: Recovery data of proposed method

Drug	Level (%)	Test amount (µg/ml)	Spiked STD amount (µg/ml)	Total amount recovered (µg/ml)	% Mean recovery ± SD. (n=3)
Luliconazole	80	10	8	18.18	101.09 ± 0.0052
	100	10	10	19.84	99.20 ± 0.0037
	120	10	12	21.92	99.63 ± 0.0077

Table 3:Analysis of Marketed Formulation (Lotion)

Active ingredient	Label claim	Test Concentration (µg/ml)	Amount found (µg/ml)	% Assay
Luliconazole	100 mg	15.0	14.90	99.33

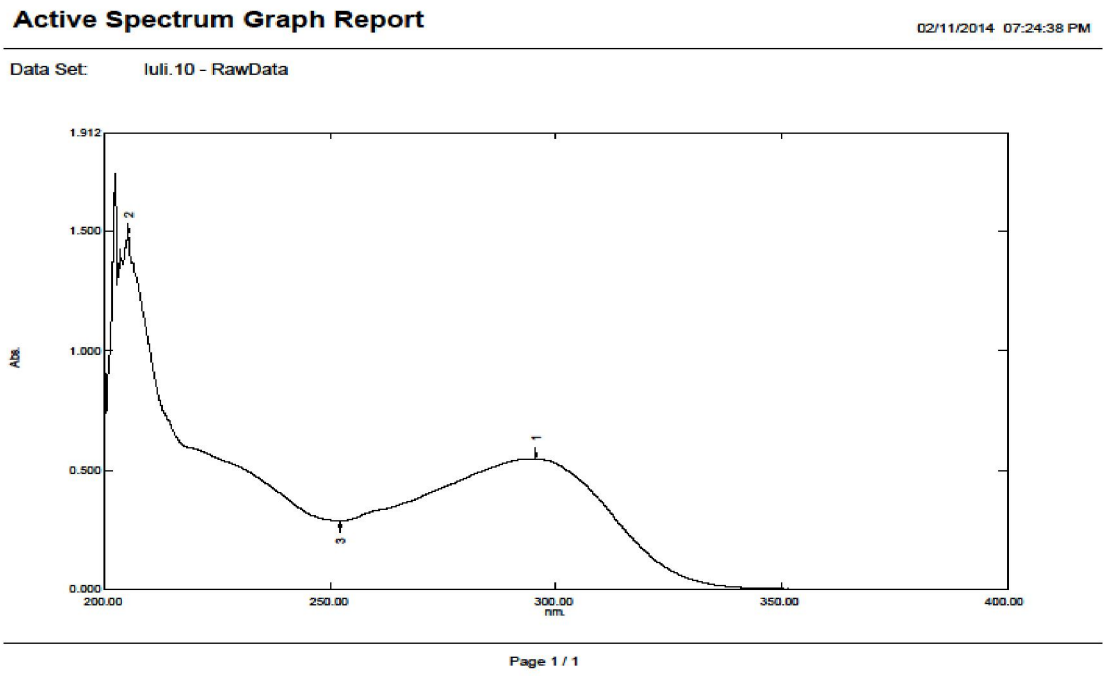

Figure 2: UV Spectrum for Luliconazole (10 µg/ml) at 296 nm in methanol

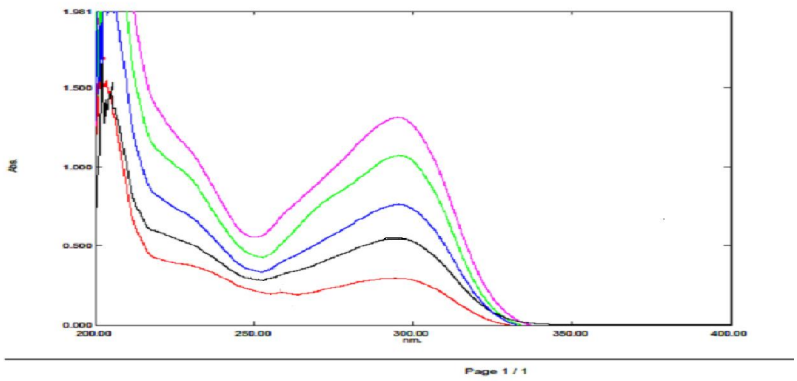

Figure 3: Overlain spectrum of Luliconazole (5-25 µg/ml) in methanol

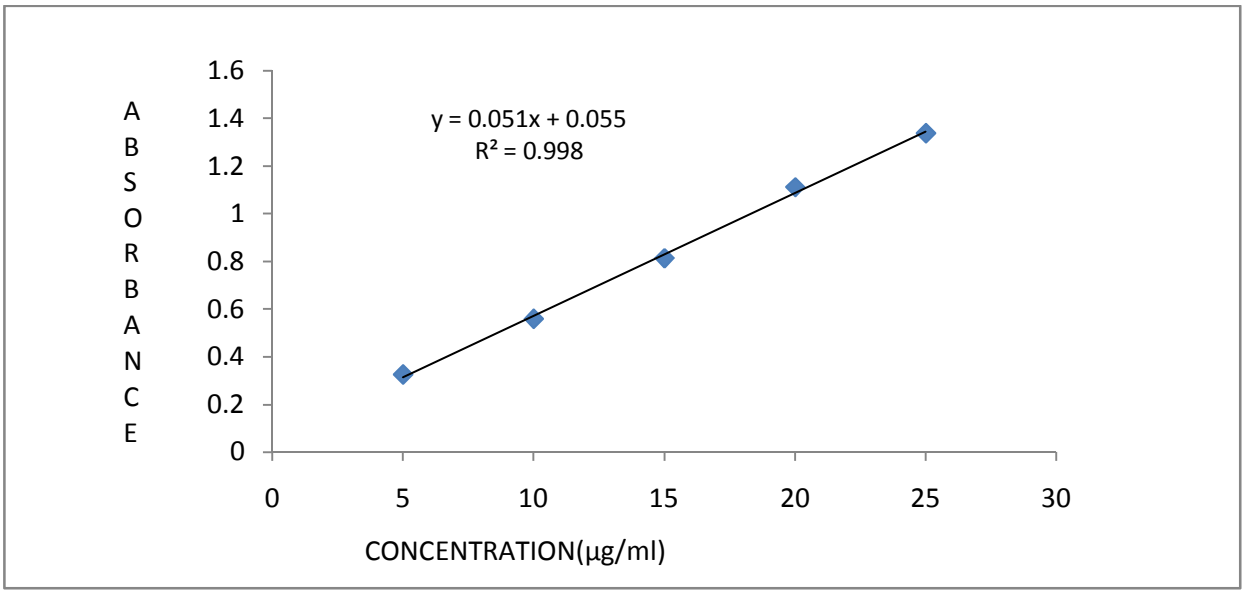

Figure 4: Calibration curve of Luliconazole at 296 nm in methanol

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