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Uv-Visible Spectrophotometric Methoddevelopmentand Validation of Sertaconazole Nitrate

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ABSTRACT: A simple, reliable and accurate UV spectrophotometeric method has been developed for analysis of antifungal drug sertaconazole nitrate from drug samples as well as formulations. Method validation was performed with respect to accuracy, precision, linearity, sensitivity, range and robustness per the ICH guidelines. The method was found to be linear between the concentration ranging from2-150ug/ml. The sensitivity was 0.659 (LOD) and 1.998(LOQ), accuracy and precision were also within acceptable range.

KEYWORDS: Setaconazole nitrate, Analytical method validation, Roubstness, LOD, LOQ, Linearity, Range

I. INTRODUCTION

Sertaconazole is a drug which belongs to antifungal category belonging chemically to imidazole class with IUPAC name is (RS)-1-{2-[(7-chloro-1-benzothiophen-3-yl)methoxy]-2-(2,4-dichlorophenyl)ethyl}-1H-imidazole.Some of the details are mentioned in table-1.

Table-1:- Details of Sertaconazole Nitrate

Chemical formula	C20H15Cl3N2OS
Molecular mass	437.77g/mol
Route of administration	Topical, vaginal
log P	6.23
Pka	6.77(strongly basic)
log S	-4.8
Melting point	158-160°c
BCS Classification	

Fungal cells convert a chemical lansetrol to ergosterol via an enzyme 14-a demethylase. Sertaconazole selectively inhibits this enzyme by inhibiting cytochrome P-450 which in turn is responsible for production of this enzyme. Due to this, the cell wall synthesis of fungal cells is blocked and the contents of the cytoplasm leaks, and cell dies, therefore the growth of fungal cell in hindered. Mechanisms like endogenous respiration, impairment of triglycerides synthesis and purine uptake, in fungal cells are also affected.

The reported methods for ultraviolet-visible spectrophotometric analysis of sertaconazole nitrate was having a limited linearity range, it was between 5-25ug/ml[3],4-64ug/ml[4]4-16ug/ml[5]and 1-20ug/ml[6] Also,the experiment performed Amal Mahmoud About Alamein[3] shows linearity at different wavelengths of 290nm, 260nm 300nm and 304nm.

II. UV METHOD VALIDATION

As per ICH guidelines the analytical procedure refers to the way of performing the analysis. It should describe in detail the steps necessary to perform each analytical test. This may include but is not limited to: the sample, the reference standard and the reagents preparations, use of the apparatus, generation of the calibration curve, use of the formulae for the calculation, etc.

Validation is a confirmation of the documented evidences which demonstrates that the procedure, process, activity and method is maintaining compliance at every stage of its performance. It is based on the predetermined specifications and quality objectives related to the process. Parameters for validation are accuracy, precision, limit of detection, limit of quantification, robustness, ruggedness, linearity, specificity and range.

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The objective of this workwas to develop a UV-Visible spectroscopic method for analysis of sertaconazole nitrate with a broad linearity range and validate it as per ICH guidelines.

III. MATERIAL AND METHODS

A double beam UV-Visible spectro photometer, Shimadzu (1600) with matched quartz cell and equipped with UV probe software was used.

Sample of Sertaconazole nitrate (drug) was obtained as a gift sample from Ferrer healthtech Interquim SA.

Solvents methanol and ethanol used were of analytical grade Sertaconazole lotion and Sertaconazole Cream were purchased from local market.

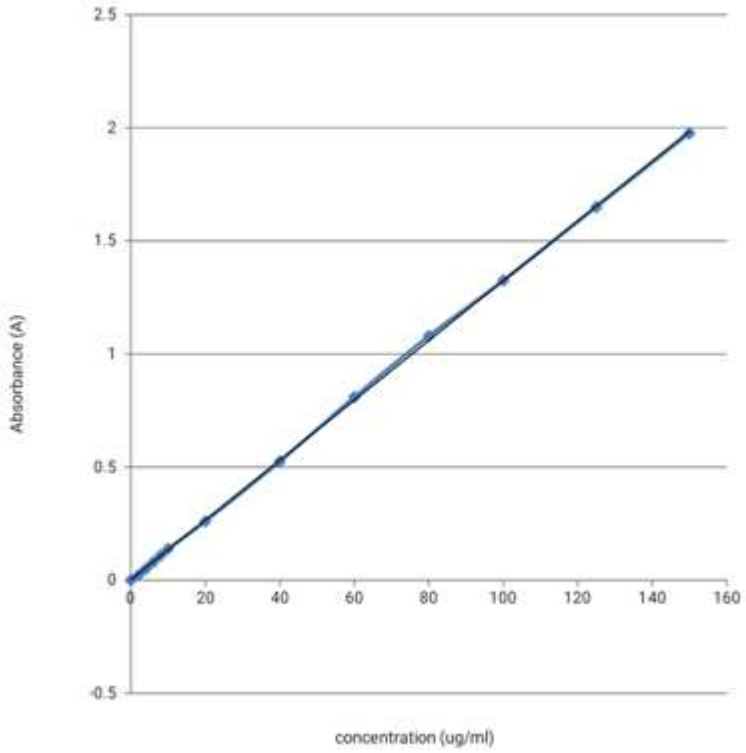

Figure 1: Calibration curve of sertaconazole nitrate

Method

Preparation of stock solution-

The stock solution was prepared by adding 100 mg of accurately weighed drug in a 100 ml volumetric flask. Methanol 50 ml was added and the drug was completely dissolved. The volume was then made upto 100 ml.

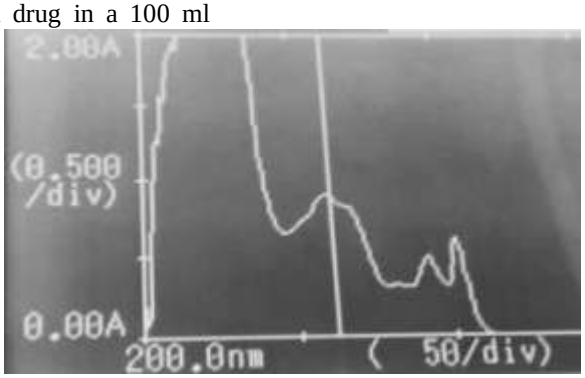

Fig 2- Spectrum of sertaconazole nitrate

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Selection of wavelength-

Sertaconazole nitrate drug solution in methanol was scanned over UV-visible spectrophotometer and was found to show peaks at 225,260,292 and 303nm.

In order to eliminate any possible interference 260nm was selected as the maximum wavelength for analysis.

Method Validation

Linearity indicates the ability to produce results that are directly proportional to the concentration of the analyte in samples. A series of samples should be prepared in which the analyte concentrations span the claimed range of the procedure. If there is a linear relationship, test results should be evaluated by appropriate statistical methods. A minimum of five concentrations should be used.

Preparation of calibration curve-

The stock solution was used to prepare the working solutions by dilution of the stock solution in various concentration in the range of 2-150ug/ml, viz, 2, 4, 6, 8, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150 ug/ml. Various solutions were analysed using UV- Visible spectrophotometer at 260nm and a calibration curve was plotted between concentration of 2-150 ug/ml.

Range is an expression of the lowest and highest levels of analyte that have been demonstrated to be determinable for the product. The specified range is normally derived from linearity studies.

Sensitivity

Detection limit (limit of detection) is the smallest quantity of an analyte that can be detected, and not necessarily determined, in a quantitative fashion. Approaches may include based on visual evaluation;signal to noise ratio;standard deviation of the response and the slope;standard deviation of the blank; calibration curve.

LOD= 3.3*Standard Deviation Of Intercept/Slope Of Calibration Curve Of Analyte

Quantitation limit (limit of quantitation) is the lowest concentration of an analyte in a sample that may be determined with acceptable accuracy and precision. Approaches may include instrumental or non-instrumental procedures and could include those based on:visual evaluation;signal to noise ratio;standard deviation of the response and the slope;standard deviation of the blank; calibration curve.

LOQ= 10*Standard Deviation Of Intercept/Slope Of Calibration Curve Of Analyte

Accuracy is the degree of agreement of test results with the true value, or the closeness of the results obtained by the procedure to the true value. It is normally established on samples of the material to be examined that have been prepared to quantitative accuracy. Accuracy should be established across the specified range of the analytical procedure.It is the degree of agreement among individual results. The complete procedure should be applied repeatedly to separate, identical samples drawn from the same homogeneous batch of material. It should be measured by the scatter of individual results from the mean (good grouping) and expressed as the relative standard deviation (RSD).The accuracy was determined by recovery method performed on 3 concentrations namely 4ug/ml, 40ug/ml and 150ug/ml.

Precision expresses within-laboratory variations (usually on different days, different analysts and different equipment). If reproducibility is assessed, a measure of intermediate precision is not required. Precision studies were performed by conducting interday and intraday studies of variations. In intraday 9 samples of different solutions of same concentration that is 4microgram/ml were prepared and analysed. Results of precision studies are represented by %RSD. For interday precision different samples of 4microgram/ml, 40 microgram/ml and 150microgram/ml were prepared and analysed for three consecutive days. The results were indicated by %RSD.

Robustness (or ruggedness) is the ability of the procedure to provide analytical results of acceptable accuracy and precision under a variety of conditions. The results from separate samples are influenced by changes in the operational or environmental conditions. Robustness should be considered during the development phase and should show the reliability of an analysis when deliberate variations are made in method parameters. The verification of stability of analytical solutions is of particular importance.

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IV. APPLICATION OF DEVELOPED METHOD TO DETERMINE CONCENTRATION OF SERTACONAZOLE NITRATE IN MARKETED FORMULATIONS

Marketed formulations of sertaconazole were analysed for checking the developed UV method.For this a lotion and a cream formulations were used.

For lotion- 100 mg of the lotion was dissolved in 10 ml ethanol which was further diluted by ethanol and analysed by the approximately developed method using reagent blank with the help of spectrophotometer.

For cream- 100 mg of the lotion was dissolved in 10 ml ethanol which was further diluted by ethanol and analysed by the approximately developed method using reagent blank with the help of spectrophotometer.

Table 2- Application of proposed procedure for determining concentration of sertaconazole nitrate in marketed formulation.

Formulation	claimed conc mg/ml	Found conc mg/ml	SD	SE
Cream	2	2.00	0.015	0.002
Lotion	2	1.99	0.005	0.007

V. RESULTS AND DISCUSSIONS

Beer's Lambarts law was obeyed at concentration range of 2-150 ppm.A linearity curve was calibrated by concentration Vs absorbane. The regression equation of curve was calculated asY=0.013x + 0.0019. Correlation Coefficient r^2=0.99. The accuracy was determined by recovery study and the overall percentage recovery was found to be 101.40%.The % RSDof precision was found to be 0-1.04 for interday precision and 0-.001for interday precision. The LOD and LOQ were calculated as 0.659 and 1.998 respectively. The developed method was validated in terms of linearity, accuracy, precision, limit of detection, limit of quantification, robustness as per ICH guidelines. The developed and validated method was applied for estimation of Sertaconazole in cream and lotion dosage form. Table 2 shows various parameters recorded for the UV-Visible spectroscopic method of sertaconazole nitrate.

Table 3- Various parameters of UV-Visible spectroscopic method of Sertaconazole Nitrate.

Parameters	UV-spectrophotometric method
Linearity (ug/ml)	2-150ug/ml
Regression equation	y= 0.013x + 0.0019
Regression coefficient	0.99
LOD	0.659
LOQ	1.998
% Recovery	101.4%
% RSD	0.0025
Intraday precision (%RSD)	0-0.011
Interday precision (%RSD)	0-1.04
Robustness	Robust
Specificity	Specific

The product claim with respect to the concentration of sertaconazole nitrate in the respective formulation was approximately satisfied.

The standard error was found to be of 0.01 for both the kind of dosage form.

VI.CONCLUSIONS

The UV-Visible spectroscopic method validation was developed for determination of sertaconazole nitrate . The method was found to be accurate,simple and reliablewith a broad linearity range of 2-150ug/ml. The obtained values of validation method can be used for analysis purpose.Also, the method has proved successful to analyze the formulation.

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