Research Article

Development and Validation of Stability Indicating Spectroscopic Method for Sartaconazole Nitrate in Bulk and Marketed Formulation

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ABSTRACT

The simple, rapid, precise, accurate and cost effective UV-Spectroscopic method has been developed for sartaconazole nitrate in bulk and pharmaceutical formulation. The drug was subjected to various stress condition to determine the stability for the drug in bulk and marketed formulation. Wavelength (λmax) selected for scanning of sartaconazole nitrate was 235 nm. Linearity of sartconazole was observed in the range of 4-14 µg/ml with regression coefficient 0.999 at 235 nm. To determine the reliability of method the proposed method was validated as per ICH [International Conference for Harmonization] guidelines. Sartaconazole Nitrate was subjected to force degradation study under different conditions such as acidic, alkaline, oxidative, photolytic and dry heat degradation. The stability study showed that sartaconazole shows the degradation in acidic, alkaline, oxidative and photolytic and dry heat. The propose method can be applied successfully for routine quality control analysis of sartaconazole in bulk and pharmaceutical formulation without interference of excipients.

Keywords: Sartaconazole nitrate, UV-spectroscopic, ICH-guideline, Stability study, degradation.

INTRODUCTION

Sartaconazole nitrate is chemically 1-(2-[(7-cholro-1-benzothiophen-3-yl) methoxy] -2-(2,4dichlorophenyl) ethyl-1-imidazole [1]. It is used as an antifungal agent of imidazole class[2].It is available in cream formulation to treat the skin infection Sartaconazole blocks the synthesis ergo sterol by inhibiting the 14α –demethylase enzyme. Ergosterol is critical components of fungal cell membrane. Inhibition of ergosterol synthesis prevents the fungal cell multiplication and impaired a hyphae growth[3].

Literature survey reveals that simple validation methods was reported but no any degradation method were reported by UV-Spectrophotometry for bulk and marketed formulation.

MATERIALS AND METHODS

Material

Reagents

1. Methanol
2. NaOH
3. HCL
4. H_2O_2

Instruments

Shimadzu UV 1800 with matched quard cell and equipped with UV probe software was used for this work. Single pan electronic balance was used for weighing. Sanitation is carried out by using an ultrasonicator. Calibrated glassware was used for this study.

METHOD

Preparation of stock solution

Stock solution is prepared by transferring accurately weighed 10 mg of sartaconazole nitrate in 100 ml volumetric form and dissolved in 50 ml methanol and sonicate it for 15 min by using ultrasonicator. Then volume was make up to the 100 ml to get the concentration of 100 µg/ml.

Selection of wavelength

The standard solution of 10 µg/ ml was prepared by taking 1ml of solution from 100 ppm stock solution and diluted up to the 10 ml. This solution was scanned between the range 200-400 nm in up spectrophotometer against the methanol as blank after base line correction. The optimum wavelength for sartaconazole nitrate was found to be 235 nm shown in Fig.1.

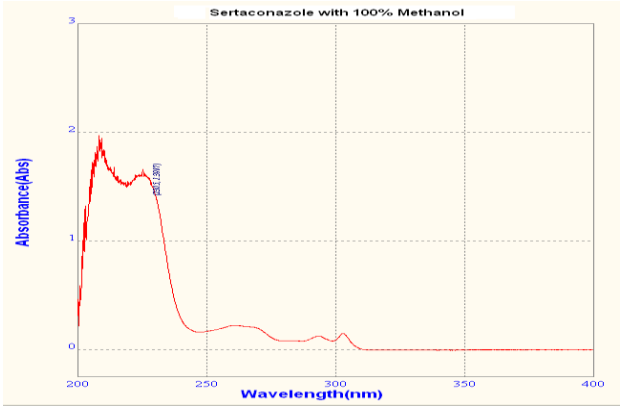

Figure 1: Spectra of Sartaconazole nitrate

Preparation of calibration curve

Working solution was prepared from stock solution by further dilution with methanol to obtained a concentration range 4, 6, 8, 10 12, 14 µg/ml, respectively. These solutions were scanned from the range 235nm and calibration curve was obtained between concentrations of 4-14 µg/ml.

Assay

A quantity of cream weighed equivalent to (10) mg of sartaconazole was dissolved in 50 ml of methanol and sonicates it for 20 min. The volume was made upto 100 ml, and then filtered through the whatman filter paper. The dilutions were made to obtain the final solution of 14 µg/ml of sartaconazole. Absorbance recorded at 235 nm. The % content was found to be 99.60%

Method validation [5, 6]

As per the guidance provided by ICH guideline the developed method was validated for the limit of detection and limit of quantitation, precision, (Intraday a and Interday), recovery (50%, 100%,150%), specificity, robustness, ruggedness, limit of detection(LOD), limit of quantitation(LOQ).

Linearity

Various aliquots were prepared form the standard stock solution (100µg/ml) ranging from 4- 14µg/ml. The samples were scanned in UV-VIS Spectrophotometer using methanol as blank. It was found that the selected drug shows linearity between the 4-14µg/ml.

Accuracy

The accuracy of the method was determined by preparing solutions of different concentrations that is 50%, 100% and 150% in which the amount of marketed formulation(SARTACONAZOLE Mg) was kept constant (8 µg/ml) and the amount of pure drug was varied that is 4 µg/ml, 8 µg/ml and 12 µg/ml for 50%, 100% and 150% respectively. The solutions were prepared in triplicates and the accuracy was indicated by % recovery.% recovery was found to be in range 98.5-101.43% and %RSD was to be in range 0.210-0.285.

Precision

Precision of the method was demonstrated by intraday and inter day variation studies. In intraday variation study, 6 different solutions of same concentration that is 8µg/ml were prepared and analyzed three times in a day i.e. morning, afternoon and evening and the absorbance were noted. The result was indicated by % RSD. For the inter day study, different solutions of 8 µg/ml concentration were prepared and analyzed for three times per day and for three consecutive days and the absorbance for same were noted. The result was indicated by % RSD (Table 1).

Table 1: Intraday and inter day Precision

Drug	Amount taken (µg/ml)	Intra-day (n =6)		Inter-day (n = 6)	
		SD	% R.S.D.	SD	% R.S.D.
Sartaconazole nitrate	8	2.0×10^{-3}	0.864	4.0×10^{-3}	0.942

Specificity

10 mg of sartaconazole was spiked with the excipient mix and the sample was analyzed for specificity.

Robustness

Two different temperatures were selected for to determine the robustness. Robustness study was performed at two different temperatures i.e. at room temperature and at 20 °c. The respective absorbance was noted and the result was indicated by % RSD.

Ruggedness

Ruggedness of the method was determined by carrying out the analysis by two different analysts. The result was found to be 98.86%and 99.60% respectively. The % RSD less than 2 indicates the method is rugged.

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

The LOQ is the concentration that can be quantitated reliably with a specified level of accuracy and precision. The LOQ was calculated using the formula involving standard deviation of response and slope of calibration curve.

$$LOD = \frac{3.3\,\sigma}{S}$$

Where, σ = The standard deviation of the response, S = Slope of calibration curve of analyte.

$$LOQ = \frac{10\,\sigma}{S}$$

Where, σ = The standard deviation of the respons, S = Slope of calibration curve of analyte

The summary of validation parameter is as shown in Table no. 2

Forced Degradation study [5, 6]

The International Conference for Harmonization (ICH) guideline was to perform the stress degradation studies on the sartaconazole using the method developed.

Table 2: Summary of Validation Parameters

Parameters	UV-Spectrophotometric
Linearity (µg/mL)	4-14 µg/ml
Regression equation	y = 0.0597x + 0.0131
Regression coefficient(r^2)	0.999
LOD	0.255
LOQ	1.138
% Recovery*	98.5-101.43
(%RSD)	0.210-0.285
Precision (%RSD)	
Intra-day (n = 6)	0.864
Inter-day (n = 6)	0.942
Robustness	Robust
Specificity	Specific
Ruggedness (%RSD)	
Analyst I (%RSD)	0.229
Analyst II(%RSD)	0.278

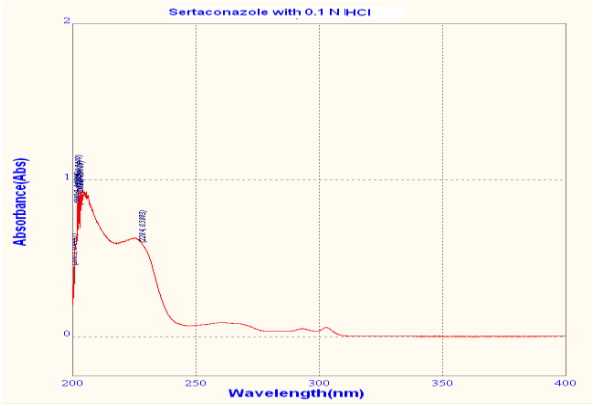

Figure 2a: Stress degradation by hydrolysis under acidic condition:

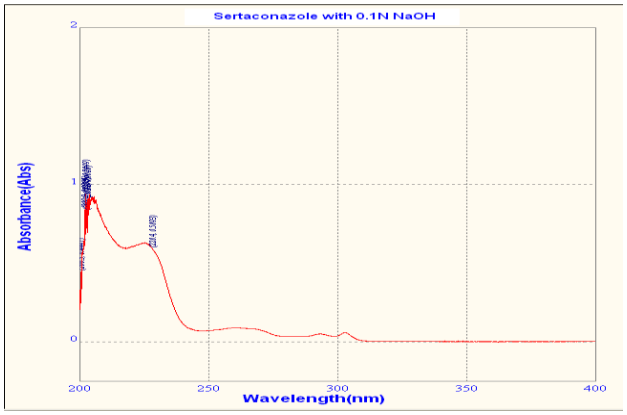

Figure 2b: Stress degradation by hydrolysis under alkaline condition

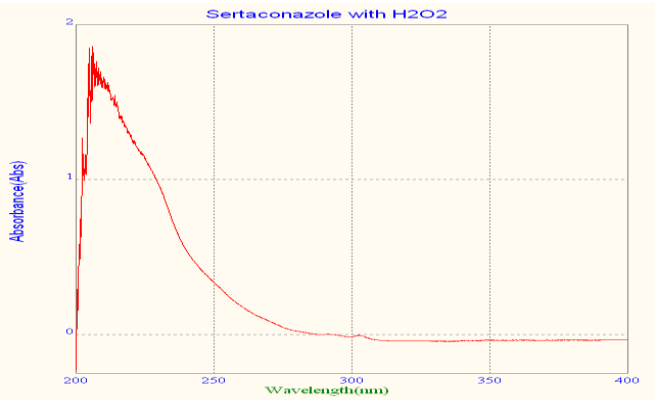

Figure 2c: Oxidative Degradation

Stress degradation by hydrolysis under acidic condition

To 1 ml of stock solution (100µg/ml) of sartaconazole, 1 ml of 0. 1 N HCl was added in 10 ml of volumetric flask and the volume was made up to the mark with methanol. Then, the volumetric flask was kept at normal condition for 90 minutes. After 60 min. time interval, this solution was taken in cuvette. Solution was analyzed by UV spectrophotometer. Results are shown in Fig. 2a.

Stress degradation by hydrolysis under alkaline condition

To 1 ml of stock solution of sartaconazole and 1 ml of 0.1 N NaOH was added in 10 ml of volumetric flask and made up the volume to the mark with methanol. Volumetric flask was kept at normal condition for 1 hr. After 1hr, 1 ml of solution was pipette out from this flask, neutralized and diluted with methanol in order to make the volume up to 10 ml and the dilutions were carried out to achieve the appropriate concentration (10µg/ml). The solution was then taken in cuvette. Solution was analysed by UV spectrophotometer. Results are shown in Fig. 2b

Dry heat induced degradation

Sartaconazole sample was taken in a petri plate and exposed to a temperature of 55 °c for 2 hours in an oven. After 2 hours, 10 mg of the sample was diluted with methanol in order to make the volume up to 10 ml. From this solution, dilutions were made to achieve the appropriate concentration (10µg/ml) and the solution was taken in cuvette for the UV-VIS analysis.

Oxidative Degradation

To 1 ml of the stock solution of sartaconazole , 1 ml of 30 % w/v of hydrogen peroxide added in 10 ml of volumetric flask and the volume was made up to the mark with methanol. The volumetric flask was then kept at room temperature for 15 min. Solution was heated on boiling water bath to remove the excess of hydrogen peroxide. Finally, after 15 minutes dilutions were made from the stock solution to achieve the required concentration (10 µg/ml). The solution was then taken in a cuvette and analysed. Results are shown in Fig. 2c

Photolytic Degradation

Sample of sartaconazole was exposed to ultraviolet light in photo stability chamber for 1 hour. Ten milligrams sample was dissolved in methanol and volume made up to 10 ml. From this solution appropriate dilution (10µg/ml) was made using methanol and taken in cuvette for the U.V. analysis. Results are shown in Fig. 2d.

Summary of the results of stress degradation studies of sartaconazole are given in Table 3.

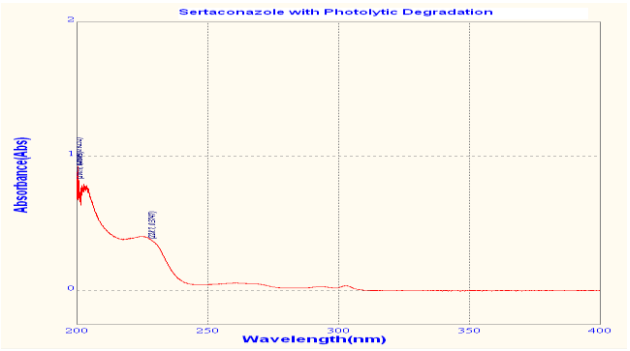

Figure 2d: Photolytic Degradation

Table 3: Summary of the results of stress degradation studies of sartaconazole

Condition	Time	% Degradation
Hydrolytic degradation Acidic degradation (0.1 N HCL)	90 min	86.29%
Alkaline degradation(0.1NaOH)	60 min	88.66%
Dry heat degradation(55^{o}c)	120 min	93.02%
Oxidative Degradation (30% H2O2)	15 min	69.66%
Photolytic degradation (by using photolytic chamber)	60 min	92.37%

RESULT AND DISCUSSION

The developed method was found to be precise as the %RSD values for intra-day and inter-day were found to be less than 2%. The method was also found to be accurate indicated by the % recoveries ranging from 98.5%-101.43%. The LOD and LOQ were found to be 0.255 and 1. 138 respectively, indicating the sensitivity of the method. The method was found to be robust and rugged and it is indicated by the % RSD with less than 2%. The results of assay show that the amount of drug was in good agreement with the label claim of the formulation as indicated by 98.60%. The drug was subjected to forced degradation study under the acidic, alkaline, dry heat, photo light and oxidation condition. The stress degradation studies showed that sartaconazole under goes degradation in acidic, alkaline, dry heat, oxidation and photolytic conditions.

CONCLUSION

All the above factors lead to the conclusion that the proposed method is accurate, precise, simple, sensitive, robust and cost effective and can be applied successfully for the estimation of sartaconazole nitrate in bulk and pharmaceutical formulation. The proposed method is also useful for determination of sartaconazole stability in sample of pharmaceutical dosage forms.

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