ARTICLE

Determination of Satranidazole through Ion-Associative Complex Reaction

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ABSTRACT

A simple, selective, accurate and low-cost spectrophotometric method has been described for determination of satranidazole in bulk and pharmaceutical formulations. The developed method involves the formation of chloroform extractable colored ion-association complex of satranidazole with Tropaeolin OOO (TPooo). The extracted colored complex showed absorbance maximum at wavelength 484 nm and obeying Beer's law in the concentration 4-20 μg mL^{-1} with the correlation coeffiecent of 0.9998. The results of statistical analysis of the proposed method reveals high accuracy and good precession. Thus, the proposed method can be used commercially for the determination of satranidazole in bulk and pharmaceutical formulations.

KEYWORDS

Satranidazole, Ion-Associative complex, Tropaeolin OOO, Validation, Visible spectrophotometry.

INTRODUCTION

Satranidazole {1-methylsulfonyl-3-(1-methyl-5-nitro-2-imidazolyl)-2-imidazolidinone} (Fig. 1) is a nitroimidazole derivative and widely used as antiprotozoal agent in the treatment of amoebiasis [1]. Literature survey revealed that few analytical methods have been developed for the determination of satranidazole in pharmaceutical formulations and biological materials include spectrophotometric [2-5], HPLC [6-11], HPTLC [12,13] and electron-capture gas chromatographic determination [14].

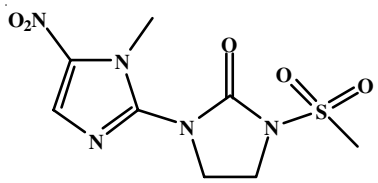

Fig. 1. Structure of satranidazole

Previously reported spectrophotometric methods [2,4] for the determination of satranidazole in pharmaceutical formulations and biological materials were complicated and not economical. The aim of the present study is to develop a relatively simple, sensitive, validated and low-cost visible spectrophotometric method for the determination of satranidazole in bulk drug and pharmaceutical dosage form.

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In quality control laboratories of the developing countries, the mostly adopted quantitative method for determination of pharmaceutical drugs is visible spectrophotometry. Among the different reactions engaged in visible spectrophotometric estimation of pharmaceutical drugs, ion association complex [15-20] formation and oxidation [21,22] methods are found to be acceptable and sensitive methods. In addition, the former is very easy to accomplish. Out of all the existing various techniques, formation of coloured ion association complex is a prevalent methodology for the determination of pharmaceutical drugs in a quantitative manner. Ion association complex formation method can be easily extended for all such pharmaceutical drugs holding at least one hetero atom (like nitrogen or oxygen) having lone pair of electrons. So, such compounds are protonated due to acceptance of proton(s) and yield cations. Acidic dyes undergo hydrolysis in aqueous medium to form anions and are capable to promote the generation of an ion association complex with the cationic form of the drug [18].

Tropaeolin OOO (TPooo) is an azo dye and its chemical name is 4-(4-hydroxy-1-naphthylazo)benzenesulfonic acid sodium salt. Other names of it are Orange I, α-naphthol orange and acid orange 20. The sodium sulfonate group of TPooo experiences ionization in acidic medium to result in a negatively charged anion. The so formed ion association complex is extractable in organic solvent and absorbance of organic phase can be measured spectrophotometrically [17]. The added gain of ion association complex is its application for precise determination of target compound in spite of the API′s existence with various formulation constituents. Driven by the advantages mentioned above, the present proposed study enlightens to establish a process, that is grounded on formation of a soluble ion-pair complex with the dissociated form of an acidic chromogenic dye like Tropaeolin OOO.

EXPERIMENTAL

An Elico, UV-visible digital spectrophotometer [SL-159] with 1 cm matched quartz cells was used for the spectral and absorbance measurements. For pH measurements, an Elico LI-120 digital pH meter was used. All the reagents used in this assay were of analytical grade and the reagent solutions were prepared using double distilled water.

Preparation of standard drug solutions: The pharmaceutical grade pure sample of satranidazole (99.56 %) was procured from Celon Laboratories Limited, India. The stock solution (1.0 mg mL^{-1}) of satranidazole was prepared by dissolving 100 mg of drug in 10 mL of methanol and made up to 100 mL with distilled water to get a clear solution. Appropriate volumes of this stock solution were diluted step wise to get the working standard solutions with concentrations of 80 µg/mL for method.

Preparation of tablets solution: About 10 tablets of SATROGYL (300 mg) were pulverized to fine powder and the powder equivalent to 100 mg of satranidazole was accurately weighed and transferred into a 100 mL calibrated flask, 60 mL of methanol was added and the contents shaken thoroughly for 15-20 min to extract the drug into the liquid phase. The volume was finally diluted to the mark with water, mixed well and filtered through Whatmann filter paper No. 41. The filtrate was made up to mark with distilled water in a 100 mL volumetric flask. A suitable volume of this filtrate was accurately diluted with water and this solution was used for the determination of satranidazole as per the recommended procedures.

Preparation of reagents

TPooo (0.1 % w/v): Aqueous solution of TPooo dye solution was prepared by dissolving 100 mg dye in 100 mL of double distilled water.

0.1 N HCl: Prepared by dissolving 8.6 mL of HCl in 100 mL of double distilled water.

Recommended procedures: Aliquots of standard satranidazole (80 µg mL^{-1}) solution ranging from 0.5-2.5 mL were transferred into a series of 125 mL separating funnels. To that 2 mL of TPooo (0.1 %) and 1.0 mL of 0.1 N HCl were added and the total volume of aqueous phase was made up to 10 mL with distilled water. To each funnel, about 10 mL of chloroform was added and the contents were shaken for 2 min. Later, the two phases were allowed to separate and the absorbance of chloroform layer was measured at 484 nm against the corresponding reagent blank. The amount of satranidazole present in the sample solution was computed from its calibration curve (Fig. 2).

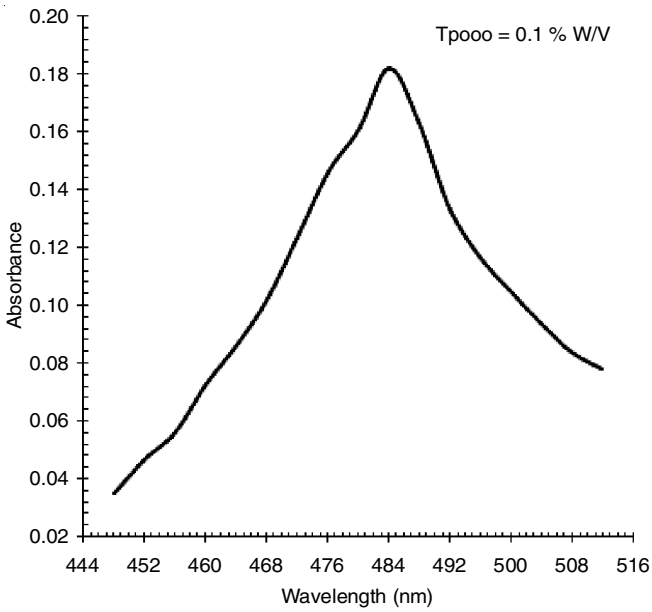

Fig. 2. Absorption spectra of satranidazole

RESULTS AND DISCUSSION

Optimization of experimental conditions: The optimum conditions were fixed based on the study of effects of various parameters *viz*., type of acid, conc. of acid, conc. of dye (TPooo), shaking time, temperature, choice of organic solvent, ratio of organic phase to aqueous phase, intensity and stability of the coloured species in organic phase. Controlled impediments were performed by varying one and fixing the other parameters. Then absorbance was measured at λ_{max} (484 nm) for a series of solutions and the results are incorporated in Table-1.

Optical characteristics: The proposed method is validated as per the existing ICH guidelines [23,24]. The Beer′s law and

TABLE-1
OPTIMUM CONDITIONS ESTABLISHED IN METHOD-TPooo FOR SATRANIDAZOLE

Parameter	Optimum range	Conditions in procedure	Remarks
λ_{max} (nm)	480-490	484	–
Effect of volume of dye TPooo	0.5-3.0 mL	2.0 mL	2.0 mL of TPooo of dye was necessary for covering the broad range of Beer's law limits.
Choice of organic solvent for extraction of colored complex	Chloroform	Chloroform	$CHCl_3$ was preferred for its selective extraction of the colored drug-dye complex from the aqueous phase.
Effect of shaking time (min)	1-5 min	2 min	Constant absorbance values were obtained for the shaking period of 1-5 min.
Effect of temperature (°C) on the colored species	Laboratory temperature (28 ± 5)	Laboratory temperature (28 ± 5)	At low temperature (< 20 °C) and at high temperature (>35 °C) the extraction of the colored species was found to be improper and the stability of the colored species was found to be very less.
Stability of the colored species	–	60 min	The colored species after separation from organic phase was stable for 60 min, after wards the absorbance gradually decreases.

Ringbom plots of the proposed methods were recorded graphically (Figs. 3 and 4). Regression analysis of the Beer′s law data using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (r^2) for this method and the values are presented in Table-2. The values of optical characteristics (Beer′s law limits, molar absorptivity and Sandell's sensitivity) for method are also given in Table-2.

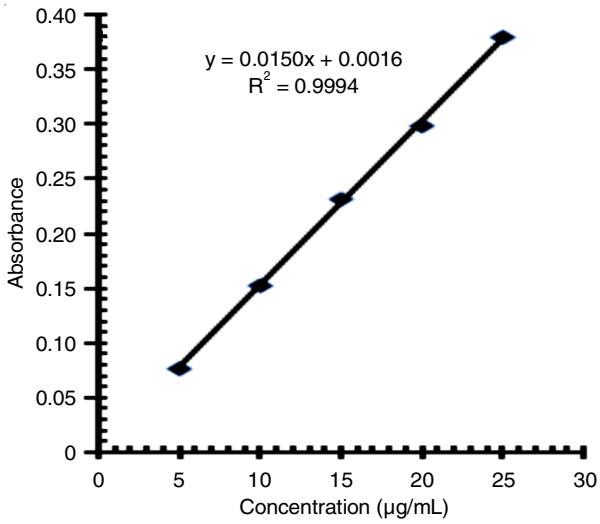

Fig. 3. Beer's law plot of satranidazole

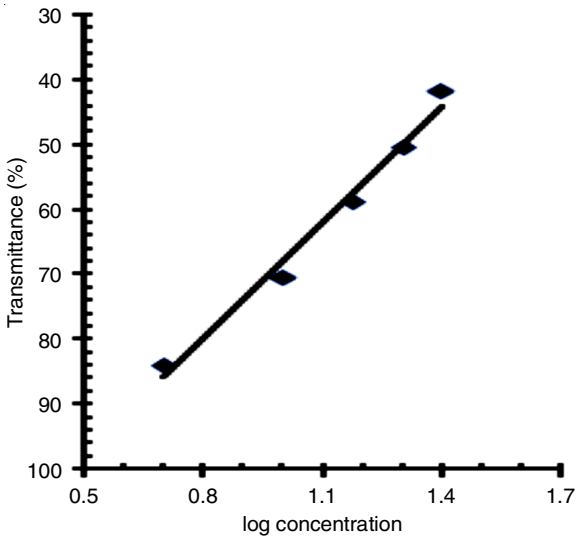

Fig. 4. Ringbom plot of satranidazole

TABLE-2
RESULTS OF OPTICAL, REGRESSION, PRECISION AND ACCURACY OF THE PROPOSED METHOD

Parameter	Tpooo
λ_{max} (nm)	484
Beer's law limits (µg/mL)	4.0-20.0
Molar absorptivity (1 mol^{-1} cm^{-1})	6.946×10^3
Sandell's sensitivity (µg cm^{-2}/0.001 absorbance unit)	0.12455
Optimum photometric range (µg/mL)	6.0 -18.0
Regression equation (Y = a + bc); slope (b)	0.0219
Intercept (a)	0.0066
Correlation coefficient (r)	0.9998
Standard deviation on intercept (S_a)	1.2792×10^{-4}
Standard deviation on slope (S_b)	2.2174×10^{-4}
Standard error on estimation (S_c)	2.8048×10^{-3}
LOD (µg/mL)	0.0173
LOQ (µg/mL)	0.0579
Relative standard deviation (%)*	1.278
% Range of error (confidence limits)	
0.05 level	1.069
0.01 level	1.581

*Average of six determinations considered

Precision: The precision of the proposed method was ascertained from the absorbance values obtained by actual determination of six replicates of a fixed amount of satranidazole. The % RSD (percent relative standard deviation) and percent range of error (at 0.05 and 0.01 confidence limits) was calculated for the proposed method (Table-2).

Accuracy: The accuracy was evaluated as percentage relative error between the measured concentrations and taken concentrations for satranidazole. The results obtained are compiled in Table-2.

Analysis of pharmaceutical formulations: The proposed method was applied to determine satranidazole in commercial brand (Satrogyl, 300 mg). The results were compared with those of the literature method. Statistical analysis of the results using Student's t-test for accuracy and F-test for precision revealed no significant difference between the proposed methods and the literature method at the 95 % confidence level with respect to accuracy and precision. The results of the proposed methods are summarized in Table-3.

Chemistry of the colored species: Satranidazole consists of different analytically useful functional groups such as nitro group in the imidazole system and tertiary nitrogen group of

TABLE-3
ASSAY AND RECOVERY OF SATRANIDAZOLE IN DOSAGE FORM

Pharmaceutical formulation	Labeled amount (mg)	Proposed method			Found by reference method** ± S.D (mg)	% Recovery by proposed method
		Amount found mean* ± S.D (mg)	T value	F value		
Satrogyl	300.00	299.95 ± 0.79	0.33	1.300	299.99 ± 0.204	99.96 ± 0.18

*Average ± standard deviation of six determinants the t and F- values refer to comparison of the proposed method.
Theoretical values at 95 % confidence limits t = 2.571 and F = 5.05.
*Average of six determinations. **Reference Method – [Ref. 2]

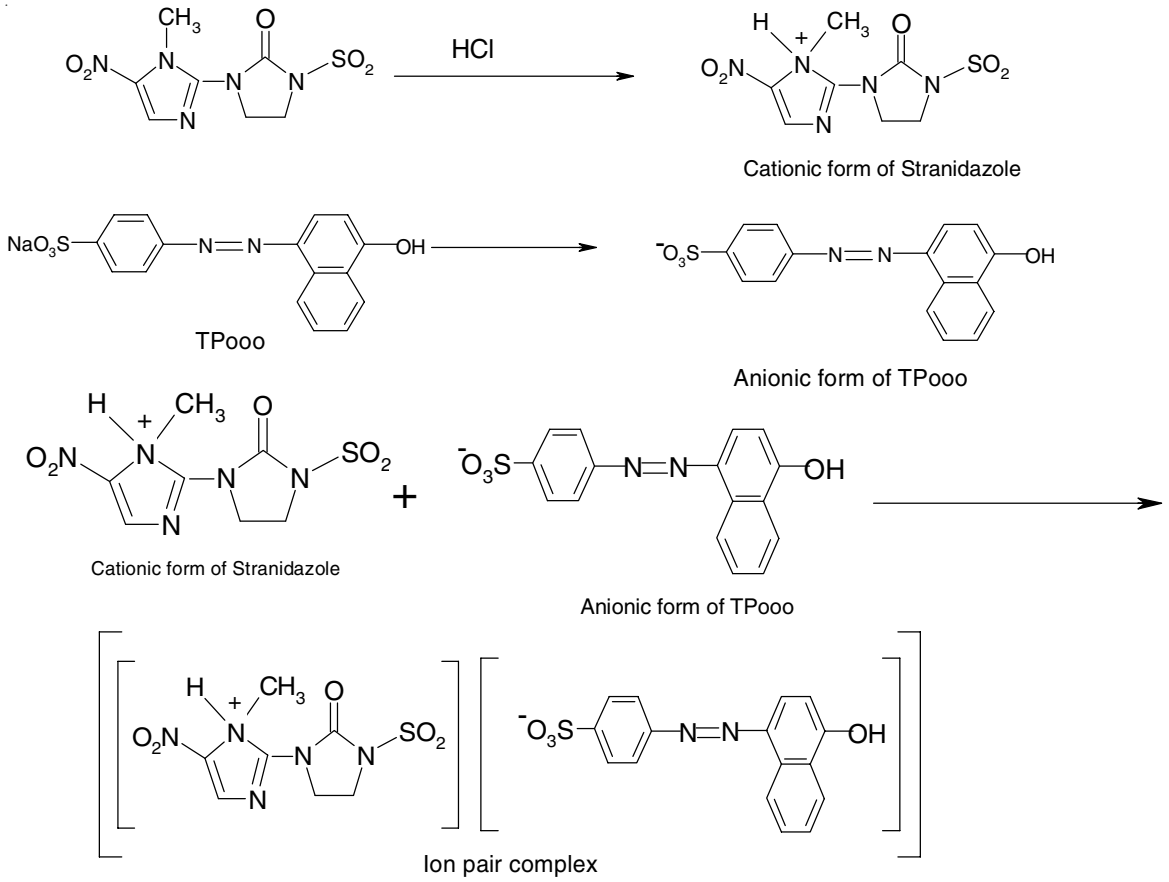

Fig. 5. Reaction of satranidazole with TPooo

varied reactivity and it is difficult to say the exact nature of the existing coloured species of reasonable stability in each one of the proposed method formed with the chromogenic reagents. Reaction involved is ion pair association complex with the positive charge of the basic drug (protonated amino group in satranidazole) with the negative charge of acidic dye TPooo. The chemistry of coloured species formed in proposed method for the assay of satranidazole has been presented in Fig. 5.

Conclusion

A new visible spectrophotometric method for determination of satranidazole has been developed using chromogenic dye reagent Tropaeolin OOO (TPooo). The method was found to be simple, cost effective, sensitive and reproducible. From the analytical data reported, the LOD and LOQ values reported by the proposed method indicating high sensitivity of the proposed method. The simplicity, selectivity and robustness achieved by the proposed methods advocate their applicability in routine quality control of satranidazole tablets.

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