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Development and Validation of Method for Simultaneous Estimation of Trifluoperazine Hydrochloride from Capsule Dosage Form Using Citric Acid

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Abstract: Simple, sensitive, selective and accurate Spectrophotometric methods for the determination of Trifluoperazine Hydrochloride in bulk drug and pharmaceutical formulations have been described. The individual method is based on the charge transfer complex formation (citric acid), of drug. The method employed first order derivative spectroscopy. For determination of sampling wavelength 10 µg/ml of each of were scanned in 200-400 nm range and sampling wavelengths were 277 nm and 269 showed zero crossing point in first order derivative spectroscopy. For this method linearity observed in 5-35 µg/ml. The recovery studies confirmed accuracy of proposed method and low values of standard deviation confirmed precision of method. The method is validated as per ICH guidelines.

Key words: Trifluoperazine Hydrochloride · Spectrophotometric methods · Citric acid

INTRODUCTION

Trifluoperazine Hydrochloride, 10-[3-(4-methylpiperazin-1-yl) propyl]-2 trifluoro methyl phenothiazine dihydrochloride used as antipsychotic. MOA includes inhibiting dopamine D_2 receptors in the brain possessing α-adrenergic blocking, antiemetic and some anticholinergic activity [1]. Literature review shows that there are developed methods for including UV [2-4], Fluorometric [5, 6], HPTLC [7, 8], GC-MS [9] methods. The author has developed a simple and sensitive UV Spectrophotometric method by dissolving the drug in isopropyl alcohol for the determination of Trifluoperazine Hydrochloride in pure or pharmaceutical formulations (tablets) and adopted it as a reference method to compare the results obtained by proposed methods. Author of the article and his research team has developed a UV Method development different pharmaceutical dosage form [10-21]. However no Spectrophotometric method is reported till date for simultaneous determination of these drugs. In this communication we report a new UV Spectrophotometric method using derivative spectroscopy. The methods based on different chemical reactions have been developed by using reagents such as Citric acid.

MATERIALS AND METHODS

UV Visible spectrophotometer was employed with spectral bandwidth of 1 cm and wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 1 cm matched quartz cells). All chemicals and reagents used were of AR/HPLC grade, Chloroform, ammonia (SD'S) and methanol (A.R., Ranbaxy Ltd., New Delhi) were used for mobile phase preparation and as solvent. All chemicals used in this study were of analytical grade and used without further purification. Formulations for the estimation were purchased from local market.

Preparation of Stock Solution: Trifluoperazine Hydrochloride was accurately weighed and dissolved in minimum amount of 1N HCl followed by dilution to 100 ml with distilled water in standard flask and this stock solution was diluted step wise with distilled water to get the working standard solutions of concentration of 25 µg/ml Citric acid. Citric acid - glacial acetic acid reagents was added and the flasks were immersed in a boiling water bath for 30 min. The tubes were cooled to room temperature and made up to the mark with glacial acetic acid. The absorbance of the colored solutions was

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measured after 15 minutes at 360 nm against a reagent blank. The content of the drug was computed from the calibration graph.

Preparation of Working Solution: From the above stock solution 25 ml was transferred into 100 ml volumetric flask and volume was made up to the mark with methanol to make 10µg/ml. Then the sample was scanned with UV Spectrophotometer in the range 200-400nm against absolute ethanol as blank and the wavelength corresponding to maximum absorbance was noted which is its λ max i.e. at 246 nm.

Preparation of Sample Solutions: Twenty capsules of Trifluoperazine hydrochloride were weighed and powdered in glass mortar. Powder equivalent to 10 mg of the drug was weighed accurately and transferred to 100 ml volumetric flask, dissolved in about 50ml of phosphate buffer pH 7.8 with frequent shaking and made up the volume to the mark with phosphate buffer pH 7.8 to obtain the concentration of 10 µg/ml. The solution was filtered through Whatmann filter paper No.41. The absorbance of sample solution was measured at 290 nm and the amount of Trifluoperazine Hydrochloride present in tablet formulation was determined by extrapolating from the calibration curve.

Method- Simultaneous Equation Method: Simultaneous equation method of analysis is based on the absorption of drug (Trifluoperazine Hydrochloride) at the wavelength maximum of the each other. Wavelengths were selected for the developments of the simultaneous equations were 277 nm, λmax of Trifluoperazine Hydrochloride respectively. The absorptivity values E (1%, 1cm) determined for Trifluoperazine Hydrochloride at 290 nm. These values were means of six estimations. The absorbances and absorptivity at these wavelengths were substituted in following equations to obtain the concentration of both drugs.

$$CTH = \frac{(A_2 \times 277 - A_1 \times 290)}{18532}$$

Where C_{TH} are concentrations of Trifluoperazine Hydrochloride in g /10mL. A_1 and A_2 are the absorbance of the mixture at 277 and 290 nm respectively.

First Order Derivative Spectroscopy Method: Stock solutions were prepared separately in Ether: water (80:20) to obtain 10 µg/ml of drugs. The nine working standard were prepared by dilution of stock solution in same solvent system in concentration range 5-35 µg/ml of Trifluoperazine Hydrochloride. Trifluoperazine Hydrochloride initially canned for determining sampling wavelength in range 200-400 nm. Sampling wavelengths were 269 nm for Trifluoperazine Hydrochloride showed zero crossing point. Calibration graphs were constructed from the absorbances at respective wavelength.

Analytical Method Development: UV-Spectrophotometric method for the analysis of Trifluoperazine hydrochloride in formulations. For selection of media the criteria employed were sensitivity of the method, ease of sample preparation, solubility of the drug and cost of solvents and applicability of method to various purposes. An UV spectroscopic scanning run (400 - 200 nm) was carried out to select the best UV wavelength (λ max = 258 nm) for detection of Trifluoperazine hydrochloride in an aqueous solution. The analyses were carried out using distilled water as blank. Absorbance of Trifluoperazine hydrochloride was determined and apparent molar absorptivity was calculated according to standard formula.

RESULTS AND DISCUSSION

Trifluoperazine hydrochloride solutions (10µg/ml) were prepared in media along with and without common excipients separately. All solutions were scanned from 400 to 200 nm and checked for change in absorbance. In separate study, drug concentration of 10µg/ml was prepared independently from pure drug stock and commercial sample stock and analysed (N=6). Paired t-test at 95% confidence limit of significance was performed to compare the means of absorbance. As a part of determining accuracy of the proposed method, different levels of drug concentrations were prepared from independent stock solution and analysed (N=6). Accuracy was assessed as the percentage relative error and mean percentage recovery. Repeatability was determined by using different levels of drug concentrations (same concentration levels taken in accuracy study), prepared from independent stock solution and analysed (N=6). Inter-day and intra-day variation and instrument variation were taken to determine intermediate precision of the proposed methods. Different levels of drug concentrations in triplicates were prepared three different times in a day and studied for intra-day variation. Same protocol was followed for three different days to study inter-day variation. The relative standard

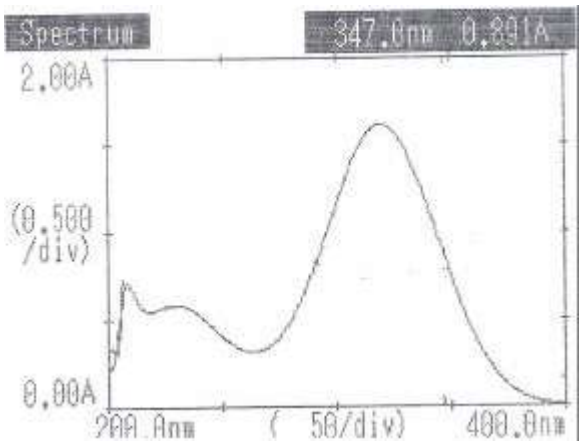

Fig. 1: Overlain spectra of Trifluoperazine Hydrochloride

deviation (in %) of the predicted concentrations from the regression equation was taken as precision. To establish linearity of the proposed method six separate series of solutions of the drug was prepared from stock solution and analysed. Least square regression analysis was done for the obtained data. The UV-spectrum of Trifluoperazine hydrochloride was not changed in the presence of common excipients in media. The calculated t-values were found to be less than the critical t-value, indicating that statistically there was no significant difference between mean absorbance of solutions prepared from pure drug sample and one with excipients. Sampling wavelengths were determined from scanning individual drug samples in 200-400 nm range. Sampling wavelengths were 277 nm and 290 nm for Trifluoperazine Hydrochloride in

Table 1: Optical Characteristics Data for Method

	Trifluoperazine Hydrochloride	
Parameters / Working λ	277 nm [I]	269 nm[II]
Beer's law limit (µg/ml)	5-35	5-35
Absorptive E (1%,1cm)*	284	278
Molar absorptivity (l/mol.cm)*	21654	4332
Correlation coefficient*	0.9992	0.9996
Intercept*	0.0374	0.0518
Slope*	0.0532	0.0821

[I] Simultaneous equation method [II] First Order Derivative Spectroscopy

Table 2: Analysis Data of Tablet Formulation, Statistical Validation and Recovery Studies

			Amt.found*					Amt. Added		
Method	Drug	Lab. Claim (mg/tab)	mg/tab.	%	S.D.*	% COV	S.E*.	At (%)	mg/ml	% Rec.#
I	TH	10	10.06	100.05	0.532	0.498	0.16	80	9.94	99.97
								100	10.11	100.05
								120	10.54	100.43
II	TH	10	9.99	99.99	0.298	0.376	0.47	80	10.03	101.02
								100	10.24	100.22
								120	9.98	99.97

TH- Trifluoperazine Hydrochloride, S.D.: Standard deviation, COV: Coefficient of variation, S.E.: Standard error, *Average of six estimation of tablet formulation, # Average of three estimation at each level of recovery

Table 3: Validation Parameters

				Precision (% COV)			
					Interday*		
Method	Drug	LOD*µg/ml	LOQ*µg/ml	Intraday n=6	First day	Second day	Third day
I	TH	1.376	0.967	0.764	0.569	0.472	0.365
II	TH	1.113	0.903	0.812	0.641	0.543	0.426

TH- Trifluoperazine Hydrochloride, S.D.: Standard deviation, COV: Coefficient of variation, S.E.: Standard error, *Average of six estimation of tablet formulation

Simultaneous equation method and 269 nm first order derivative mode. For this method equations generated were Y=0.54432+0.0029x (r^2=0.9992) Trifluoperazine Hydrochloride. Linearity of proposed method was found to be 5-35 µg/ml. Limits of detection were found to be 0.1765 and Limits of quantitation were found to be 0.3275. An attempt has been made to indicate the nature of coloured species in each proposed method for Trifluoperazine Hydrochloride tentatively based on analogy (reactive functional moiety in drug, reagents nature) and probability relative reactivates impact of functional moieties one over the other). The optical characteristics such as Beer's law limits, absorption maxima, molar absorptivity, Sandell's sensitivity are presented in Table 1. The assay and relative standard deviation (RSD) values are 99.32%.

CONCLUSIONS

The developed UV Spectrophotometric methods for the estimation of Trifluoperazine Hydrochloride were found to be simple and useful with high accuracy, precision and reproducible. Sample recoveries in all formulations using the above methods were in good agreement with their respective label claim.

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