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DEVELOPMENT AND VALIDATION OF UV SPECTROSCOPIC METHOD FOR ESTIMATION OF TRIFLUOPERAZINE IN BULK AND TABLET PHARMACEUTICAL FORMULATION

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ABSTRACT

The aim of present research work was to develop and validate UV spectroscopic method for estimation of Trifluoperazine in bulk and tablet pharmaceutical formulation. The method employed simple spectroscopy based on the solubility of Trifluoperazine in water. For determination of wavelength different concentration samples were scanned in 200-400 nm range and the maximum absorbance was found at 257 nm wavelength. Lambert–Beer's law for trifluoperazine were followed in theconcentration range of 1-16 µg/ml (r^2 = 0.9999) respectively. The method is validated as per ICH guidelines. Accuracy was assessed by the standard addition method. The recoveries were obtained in range of 98.03-101.64%. The repeatability was determined by RSD for Trifluoperazine and were found to be 0.58% respectively. The intraday precision and interday precision was determined by RSD and were found to be 0.54-0.77% and 0.28-1.00% respectively. The LOD and LOQ value for Trifluoperazine was found to be 0.29 and 0.89 µg/ml.The newly developed method can be used or routine analysis in laboratories and it is suitable for the quality control of the raw material, formulations, and dissolution studies.

Keywords: Trifluoperazine, UV spectrophotometry, Method optimization, Validation.

INTRODUCTION

Trifluoperazine is a phenothiazine class containing antipsychotic drug. It have been widely used as antipsychotic drug for many years. It produce antipsychotic effect by blocking central dopamine D1 and D2 receptors in the brain. These drug have high protein binding, metabolize by hepaticenzymes, half-life is 10-20 hours and excreted in the urine. It produced severe side effect like fast or irregularheartbeat, Vision loss, yellowing of the skin or eyes and flu-likesymptoms. Therefore, there need to minimize this type of side effect by simple, sensitive, accurate and reproducible method for screening of these drugs in dosage and bulk foam [1].

Trifluoperazine is a white to pale yellow, odourless, crystalline powder; Freely soluble in water, soluble in chloroform, insoluble in ether and benzene; molecular mass is a 407.496gm/mole; melting point is a 240-243°C; and protected from light. Chemical name of Trifluoperazine is 10-[3-(4-methylpiperazin-1-yl)propyl]-2-(trifluoromethyl)- 10H-phenothiazine [2, 3].

In literature review several analytical methods are described for the determination of trifluoperazine in single and combination dosage foam. In analytical methods included UV spectroscopic [4, 5, 19, 20], HPLC [6, 11, 13, 16], RP-HPLC [8, 9, 10, 12, 14, 15], GC [18], GC-MS [17], HPLC-MS/MS.

So the purpose of the present study was to develop simple, sensitive, accurate and reproducible UV spectroscopic method and develop method is validate according to ICH guideline.

MATERIALS AND METHODS

UV-Visible double beam spectrophotometer (UV-1800, Shimadzu corporation), Trans-O-Sonic (Sonicator), Volumetric flask (10, 100 ml),

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Pipette (1, 2, 5 ml), Beaker (250, 500 ml), Measuring cylinder (50, 100ml), Whatman filter paper no.41.

Spectrophotometric System

UV Probe 2.42, Mode:Spectrum, Scan speed:Fast, Wavelength range: 400-200 nm, Absorbance scale: 0.000–4.000, Initial base line correction: Distilled Water. All the reagents used in the method were of HPLC grade. The standard Trifluoperazine was kindly provided by La Pharmaceuticals, Ahemdabad Gujarat. Formulations for the estimation were purchased from local market of Trazine 5mg (Sun Pharma).

Preparation of standard stock solution and diluted solutions of Trifluoperazine for determination of λ_{max}

Trifluoperazine powder (5 mg) was weighed accurately and transferred to a 100ml volumetric flask and dissolved insufficient quantity of distill water. The flask was sonicated for 5min. and volume was make up to the mark with distill water to give a solution containing 50 µg/ml of Trifluoperazine. Overlain spectra for Trifluoperazine were taken in range of 1-16µg/ml (1, 3, 5, 8, 12, 16 µg/ml). The solutions were scanned between 200-400 nm and λ_{max} observed were at 257 nm shown in (Figure 2).

Preparation of calibration curve for Trifluoperazine:

From the above stock solutions aliquots of 0.2, 0.6, 1.0, 1.6,2.4 and 3.2 ml were transferred in a series of 10 ml volumetric flasks and the volume was adjusted to the mark with distill water to give the concentrations of 1, 3, 5, 8, 12, 16 µg/ml for Trifluoperazine. All the solutions were scanned from 200-400nm and the spectra obtained in UV probe 2.42 software. Response of each solution of Trifluoperazine (1-16µg/ml) was measured at 257nm using spectra.

Calibration curves of absorbance versus respective concentration were plotted for Trifluoperazine shown in (Figure3).

Lambert – Beer's law for Trifluoperazine were followed in theconcentration range of 1-16 µg/ml respectively. The equations for straight lines and correlation coefficients for Trifluoperazine were determined. Shown in (Table 2).

Preparation of test solution of Trifluoperazine for the estimation in tablet Pharmaceutical formulation

Twenty tablets were weighed and average weigh 118.3mg was determined than finely powdered. The powder 118.3 mg equivalent to 5 mg of Trifluoperazine was weighed accurately and transferred to a100ml volumetric flask and dissolved insufficient quantity of distill water. The flask was sonicated for 5 min. and volume was make up to the mark with distill water to give a solution containing 50 µg/ml of Trifluoperazine. The solution was filtered using Whatman filter paper no. 41 and first few drops of filtrate were discarded.

Validation of Proposed Method

The developed method was validated for Trifluoperazine tablet formulation in accordance with ICH guidelines [3].

Linearity and range (n=5)

The linearity response was determined by analyzing 6 independent levelsof calibration curve in range of 1-16 µg/ml (1, 3, 5, 8, 12, 16 µg/ml) of Trifluoperazine solution. The calibration curve of absorbance against concentration was plotted. Correlation coefficient and regression line equations for Trifluoperazine were calculated and shown in (Figure 3 and Table 1 & 2).

Precision

Repeatability (n=6)

For the repeatability study, the above stock solution, wasutilized. From the aliquot of 1.0 ml was transferred to a separate 10 mlvolumetric flask and diluted up to mark with distilled water such that it gives the concentration of 5 µg/ml of Trifluoperazine. Theresulting solution was scanned from 200-400 nm and the absorbance wasrecorded at 257 nm. The procedure was repeated six times andRSD was calculated. Data shown in (Table3).

Intraday precision (n=3)

Intraday precision study was performed by analyzing 3, 5, 8 µg/ml of Trifluoperazine thrice on the same day using spectrophotometric method and RSD were calculated. Data show in (Table 4).

Interday precision (n=3)

Interday precision study was performed by analyzing 3, 5, 8 µg/ml of Trifluoperazine and thrice on different days using spectrophotometric method and RSD were calculated. Data shown in (Table 4).

Accuracy (n=3)

In order to ensure the suitability and reliability of proposed method, recovery studies were carried out. It was determined by calculating the % recovery of Trifluoperazine from tablet formulation by standard addition methodat three levels that is multi-level recovery studies.

To a fixedtarget concentration (5 µg/ml of Trifluoperazine respectively) from tablet formulation, a known quantity of standard Trifluoperazine were added at 80 %, 100 % and 120 % level and the contents were analyzed bythe proposedmethod. Each solution was scanned between 200 nm to 400 nm against distill water as a blank. The spectrum of each was obtained. The amount of Trifluoperazine was calculated at each level and % Recoveries were noted. Data Shown in (Table 5).

Specificity Study(n=6)

Interference of the excipients was checked by comparing the results of the standard solution 5 µg/ml and that of test with same concentration. The data of comparison shown in (table6)

LOD and LOQ

The LOD was estimated from the calibration curves. The LODwas calculated as,

LOD = 3.3 ×(SD/Slope)

Where,

SD = Standard deviation of the Y-intercepts of the 5 calibrationcurves.

Slope = Mean slope of the 5 calibrationcurves.

The LOQ was estimated from the calibration curves usedto determine method linearity. The LOQ was calculatedas,

LOQ = 10 ×(SD/Slope)

Where,

SD = Standard deviation of the Y- intercepts of the 5 calibrationcurves.

Slope = slope of the 5 calibrationcurves.

RESULTS AND DISCUSSION

Selection of Wavelength

From the overlain spectra Trifluoperazine λ_{max} was foundtobe 257 nm as shown in (Figure 2)

Linearity andRange

The linearity range for Trifluoperazine was found to be 1-16µg/ml respectively. The calibration curve and regression line equations were computed in (Figure 3 Table 1 and 2).

Precision

Repeatability was carried out and RSD was found to be 0.58% for Trifluoperazine (table3). RSD in Intraday precision was found to be 0.54-0.77% for Trifluoperazine. RSD in Interday precision was found to be 0.028-1.0%for Trifluoperazine. The results of Intraday and Interday precision are expressed in (Table 4)

Accuracy

% Recovery of Trifluoperazine was found to be 98.03-101.64%. The results of accuracy is expressed in (Table 5)

Specificitystudy

Interference of excipients in the formulation was checked by comparison of the amount obtained in the standard solution and that ofmarketed formulation. The difference should not be more than 0.5 %. The results of comparison are shownin (Table 6).

Limit of detection (LOD)

Trifluoperazine calibration curve were plotted (Absorbanceversus concentration). Linear equations were computedfor curves and intercept and slopes were noted down. From the data, Standard deviation of intercept and slope were calculated and LODwas calculated. Data shown in (Table 7)

Limit of quantification (LOQ)

Trifluoperazine calibration curve were plotted (Absorbance versus concentration). Linear equations were computedfor curves and intercept and slopes were noted down. From the data, standard deviation of intercept and slope were calculated and LOQ was calculated. Data shown in (Table 8).

Table 1. Linearity data for Trifluoperazine

Conc.(µg/ml)	Mean Response ±SD	RSD(%)
1	0.051 ± 0.0008	1.61
3	0.174 ±0.003	1.81
5	0.292 ±0.002	0.70
8	0.476 ±0.002	0.56
12	0.722 ±0.013	1.82
16	0.952 ±0.010	1.08

*(n=5)

Table 2. Data of Regression Analysis of Trifluoperazine

Drug	Wavelength of Measurement	Regression Equation	Correlation coefficient (r^2)
Trifluoperazine	257nm	Y = 0.0603x - 0.0076	0.9999

Table 3. Repeatability Data of Trifluoperazine

Trifluoperazine	
Conc. (µg/ml)	**Response at 257nm**
5	0.294
	0.290
	0.292
	0.295
	0.293
	0.291
Mean abs± SD	0.292 ± 0.001
RSD (%)	0.58

***(n=6)**

Table 4. Intra and Inter Day Precision data ofTrifluoperazine

Conc. (µg/ml)	IntradayPrecision		InterdayPrecision	
	Mean Absorbance ±SD		Mean	
3	0.174 ± 0.001	0.77	0.175 ±0.001	1.00
5	0.293 ±0.002	0.75	0.292 ± 0.0008	0.28
8	0.475 ± 0.002	0.54	0.475 ± 0.003	0.75

***(n=3)**

Table 5. Recovery data for Trifluoperazine

Level (%)	Target conc. (µg/ml)	Std. added (µg/ml)	Total amount (µg/ml)	Amount found mean± SD	% Recovery	RSD(%)
80	5	4	9	8.94 ± 0.072	98.87	0.80
100		5	10	10.07 ± 0.016	101.64	0.16
120		6	11	10.87 ± 0.131	98.03	1.21

***(n=3)**

Table 6. Specificity data of Trifluoperazine

Standard		Sample		Difference
Mean Abs. ±SD	RSD(%)	Mean Abs. ±SD	RSD(%)	
0.292 ± 0.001	0.58	0.291 ± 0.001	0.58	0.33%

***(n=6)**

Table 7. LOD data of Trifluoperazine

Parameters	Trifluoperazine
SD of Y intercept of the 5calibrationcurve curve	0.005
Mean Slope of 5 calibrationcurve	0.0602
LOD(µg/ml)	0.29

Table 8. LOQ data of Trifluoperazine

	Trifluoperazine
SD of Y intercept of the 5 calibration curve	0.005
Mean slope of 5 calibrationcurve	0.0602
LOQ(µg/ml)	0.89

Table 9. Summary of ValidationParameters

Parameters	Trifluoperazine
LinearityRange	1-16µg/ml
RegressionEquation	Y = 0.0603x -0.0076
	0.9999
Repeatability	0.58%
IntradayPrecision	0.54-0.77%
InterdayPrecision	0.28-1.00%
Accuracy	
LOD(µg/ml)	0.29
LOQ(µg/ml)	0.89

Fig 1.Structure of Trifluoperazine

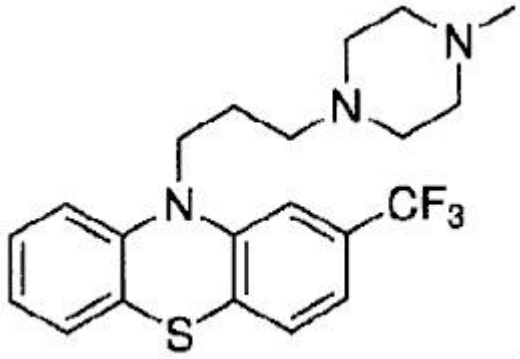


Fig 2. Overlain spectra of Trifluoperazine (1-16µg/ml)

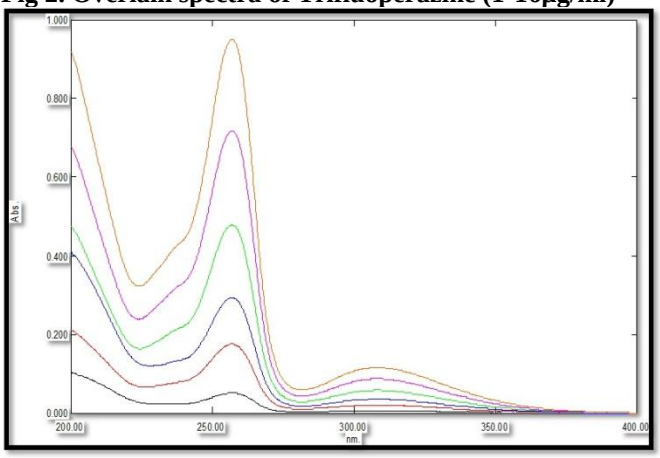
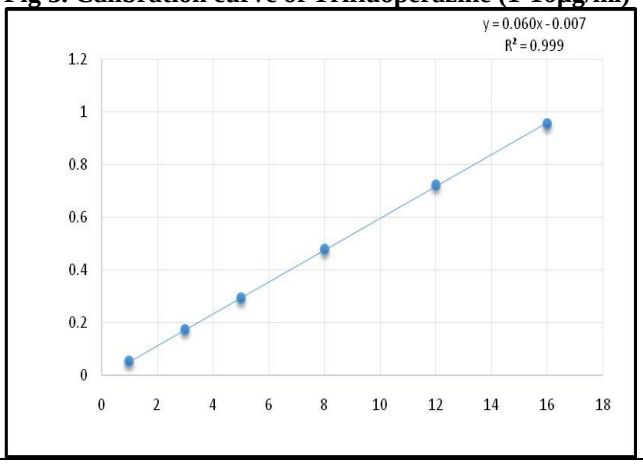


Fig 3. Calibration curve of Trifluoperazine (1-16µg/ml)



CONCLUSION

The suitability of the UV Spectroscopic method for determination of Trifluoperazine has been studied. It is reveal from this study that the method is simple, precise, specific and accurate. The newly developed method can be used for routine analysis in laboratories and it is suitable for the quality control of the raw material, formulations, and dissolution studies because the sample recoveries in formulation show good agreement with their respective label claim and all validation parameters are within the acceptance criteria of ICH guideline.

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None

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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