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UV Spectrophotometric Method For The Estimation of Seratrodast in Bulk and Pharmaceutical Dosage Form

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Abstract

A simple, specific, accurate and precise U.V Spectroscopy method was developed and validated for the estimation of Seratrodast in pharmaceutical dosage forms. The stock solution was prepared by weighing 100 mg of Standard Seratrodast in 100ml volumetric flask containing distilled water. The final stock solution was made to produce 1000µg/ml with Methanol. Further dilutions were prepared as per procedure. The linearity was found in the concentration range of 2.5-25µg/ml. The Correlation coefficient was 0.999. The regression equation was found to be Y = 0.039x + 0.018. The method was validated for linearity, accuracy, precision, limit of detection, limit of quantitation, and ruggedness. The limit of detection and limit of quantitation for estimation of Seratrodast was found to be 0.169µg/ml and 0.717µgml respectively. Recovery of Seratrodast was found to be in the range of 99.1-100.5%. Proposed method was successfully applied for the quantitative determination of Seratrodast in pharmaceutical dosage forms.

Keywords: Seratrodast, U.V-Spectroscopy, Method validation, ICH guidelines.

1. Introduction

Seratrodast is a thromboxane A_2 (TXA_2) receptor (TP) antagonist used primarily in the treatment of Asthma. TXA_2 and other bronchoconstrictor prostanoids, like PGD_2 and $PGF_{2\alpha}$, are generated in asthma and participate in acute and chronic inflammatory processes. Seratrodast, being a TP receptor antagonist, inhibits the pathophysiological processes in asthma. Chemically it is known as 7-Phenly-7(2, 4, 5-trimethyl-3, 6-dioxocyclohexa-1, 4-dien-1-yl) hepatonic acid. Seratrodast is an orally active Quinone derivative and a potent TXA_2 receptor antagonist used in the prophylactic management of asthma and treatment of allergic rhinitis.[1-4]The survey of literature reveals that good analytical methods are not available for drugs like Seratrodast. Even though very few methods are available, many of them suffer from one disadvantage or the other such as low sensitivity, lack of selectivity, and simplicity. In the present work, an attempt was made to provide novel, simple, accurate and economic UV Specrophotometric method for the effective quantitative determination of Seratrodast, in bulk as well as in pharmaceutical Dosage forms. The developed methods can successfully be applied to estimate the amount of Seratrodast in formulations and bulk drugs. The proposed method to be validated as per ICH guidelines.

1.1 Seratrodast:

Structure:

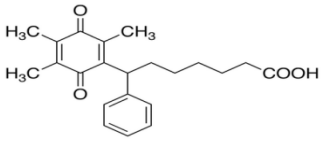

Figure 1: Chemical Structure of Seratrodast

2. Materials and methods:

2.1 Apparatus and chromatographic parameters:

Precision balance CA123 Contech, UV-Spectrophotometer UV-3000 Lab India, UV-Spectrophotometer UV-1800 Shimadzu and pH Meter3 Star Global

2.2 Preparation of Standard stock solution of Seratrodast

An accurately weighed quantity of Seratrodast100mg was transferred to 100ml volumetric flask, dissolved in Methanol, the final volume (100ml) was made with Methanol to obtain standard solution having concentration of 1000µg/mL. 1ml of this solution was transferred to 10ml volumetric flask, volume was made with Methanol. It gives 100µg/ml. These stock solutions were used to prepare further dilutions.

2.3 Preparation of working standard solutions

Six working standard solutions of Seratrodast were prepared by pipetting 0.25, 0.5, 1, 1.5, 2, 2.5mL of stock solution in 10mL of volumetric flasks and the volume was adjusted up to mark by Methanol to make the concentrations 2.5, 5, 10, 15, 20, 25µg/ml.

2.4 Selection of Analytical wavelength

For selection of analytical wavelength the standard solution was further diluted and then scanned in UV spectrophotometer from a range of 200-400nm against Methanol as blank and the wavelength corresponding to maximum absorbance (λmax) was found at 267ηm.

2.5 Preparation of sample solution

Seratrodast is available as tablets of extended release containing 80mg of Seratrodast. Seratrodast is available in the local market with brand name SERETRA 80.

Twenty tablets of Seratrodast were taken and into a fine powder of the tablets and the powder equivalent to 100mg of Seratrodast was weighed accurately and transferred into a 100ml standard volumetric flask. The contents were dissolved in Methanol and sonicated for 30 Minutes. This entire solution was filtered through 0.45 micron Whatmann filter paper (No. 41) and the final solution was made with Methanol to get the solution of 1000µg/ ml. 1ml of this solution was transferred to 10ml volumetric flask, volume was made with Methanol. It gives 100µg/ml.1ml of the solutions were pipetted out separately into 10 ml volumetric flask to give 10µg/ml concentration. The sample solution absorbance was measured at 267ηmηm against blank solution of Methanol.

2.6 Estimation of drug content in tablet formulation

Assay procedure

Sample solution of10µg/mL of Seratrodast was scanned and the absorbance of sample solutions was measured. The amount of Seratrodast in tablet dosage form was determined and the results obtained were comparable with the corresponding label claim to obtain % recoveries.

3. Results and Discussion

3.1 Assay of commercial formulations

Table 1: Summary of Assay of commercial formulation

Conc. (µg/ml)	Formulation (SERETRA 80)	Label claim (mg)	Amount found (mg)	% Recovery
10	Tablets	80	80.24	100.30

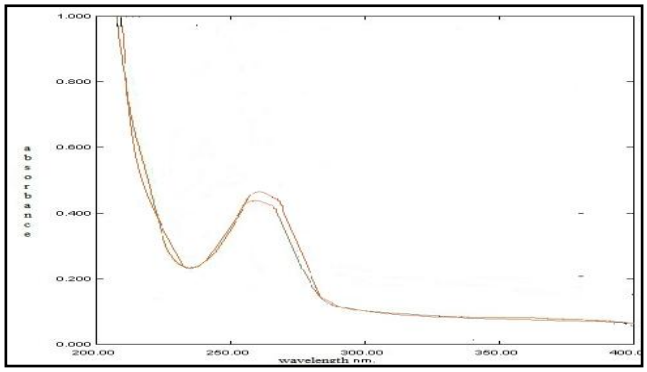

Figure 2: Overlay spectrum of Standard and sample drug (20µg/ml)

3.2 Specificity:

The analyte was assessed in the presence of the components and it was found that there was no interaction with the analyte.

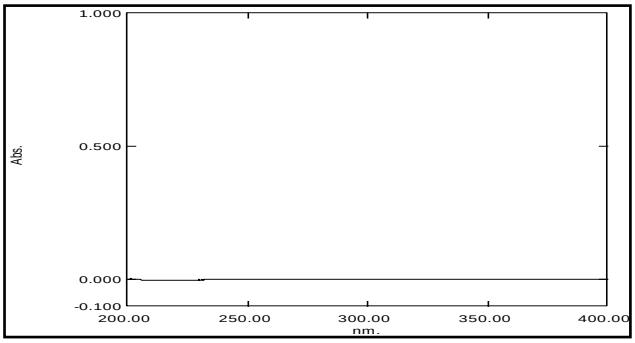

Figure 3: Spectrum of Specificity

3.3 Linearity:

Various standards in the range 2.5-25µg/ml of Seratrodast were observed in to UV system. A graph of absorbance (on Y-axis) versus concentration (on X-axis) is plotted and the correlation coefficient was calculated as shown in Fig No-10 and the Fig No-11 gives the linearity overlain spectra for Seratrodast.

Table 2: Summary of linearity of Seratrodast

Concentration (µg/ml)	Absorbance 267ηm
0	0
2.5	0.131
5	0.220
10	0.420
15	0.596
20	0.808
25	0.995

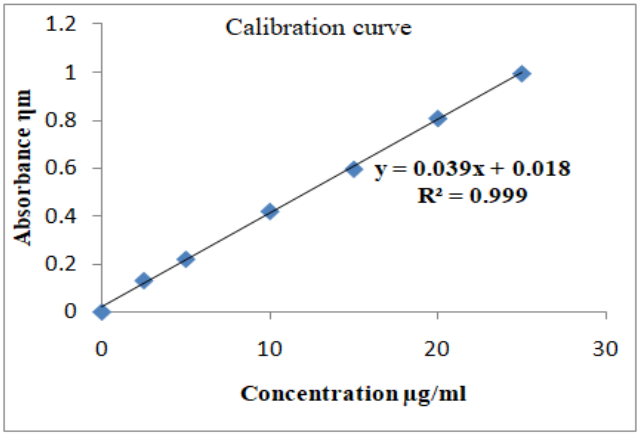

Figure 4: Linearity graph of Seratrodast

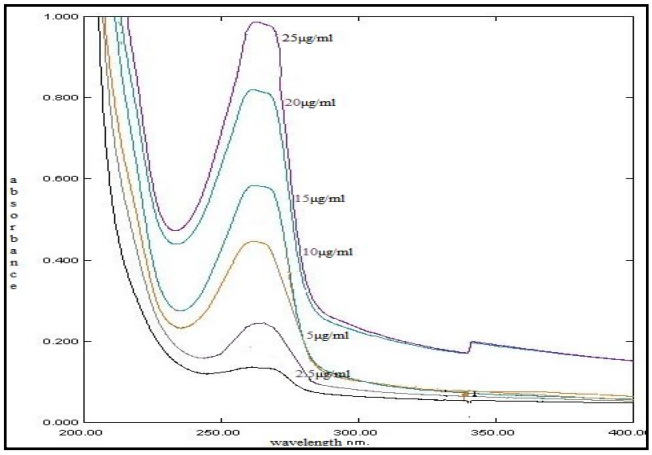

Figure 5: Overlay of Linearity graph of Seratrodast

3.4 Precision:

Precision of an analytical method is usually expressed as standard deviation or relative standard deviation. The standard deviation and % relative standard deviation are calculated from statistical formula. The standard deviation and relative standard deviation for the absorbance values were calculated from statistical formula.

3.4.1 Repeatability:

Table 3: Summary of system precision

Concentration (µg/ml)	Absorbance
10	0.421
10	0.422
10	0.424
10	0.423
10	0.424
10	0.427
Mean	**0.423**
S.D	**0.002**
%R.S.D	**0.47**

Table 4: Summary of method precision

Concentration (µg/ml)	%Assay
10	100.75
10	100
10	99.6
10	100.3
10	99.8
10	99.3
Mean	**99.95**
S.D	**0.5161**
%R.S.D	**0.5162**

3.4.2 Intermediate Precision:

Table 5: Summary of Intermediate precision

Concentration (µg/ml)	Laboratory-1 (%Assay)				Laboratory-2 (%Assay)			
	Analyst-1		Analyst-2		Analyst-1		Analyst-2	
	Day-1	Day-2	Day-1	Day-2	Day-1	Day-2	Day-1	Day-2
10	100.3	99.3	100	100.3	100.5	100	99.8	99.8
10	100.5	100.3	100.3	100.07	99.8	99.8	99.6	99.6
10	99.1	99.1	99.8	99.6	99.6	99.8	100.07	99.6
10	100.3	100	100.7	99.3	100.06	99.3	99.6	99.8
10	100.07	100.5	100.3	99.8	100.07	100.07	100.3	100.3
10	100	100.3	100.3	99.6	100.06	100.6	100.3	100.3
Mean	**100.04**	**99.91**	**100.23**	**99.77**	**100.01**	**99.92**	**99.94**	**99.9**
S.D	**0.496**	**0.581**	**0.307**	**0.360**	**0.303**	**0.425**	**0.324**	**0.322**
%RSD	**0.496**	**0.581**	**0.306**	**0.36**	**0.3**	**0.42**	**0.32**	**0.322**

3.5 Reproducibility:

Table 6: Summary of Reproducibility

	Laboratory-1	Laboratory-2
Over All Mean	99.96	99.88
Mean S.D	0.436	0.343
Mean %R.S.D	0.435	0.340

Over All Mean	99.96
Mean S.D	0.389
Mean %R.S.D	0.388

3.5 Accuracy studies:

The accuracy of the method, recovery studies were carried out by adding different amounts (50%, 100% and 150%) of bulk samples of Seratrodast within the linearity range were taken and added to the pre-analyzed formulation of concentration 10µg/ml. From that percentage recovery values were calculated. The results were within the range and were found to be highly accurate this was shown in table 7.

Table 7: Summary of Accuracy studies

Spiked level (%)	Formulation Conc (µg/ml)	Pure Drug Conc (µg/ml)	Amount Found	% Recovery	% Mean recovery	SD	%RSD
50	10	5	4.97	99.5	100.1	0.66	0.664
	10	5	79.9	100.0			
	10	5	80.0	100.9			
100	10	10	79.68	99.6	100.3	0.62	0.622
	10	10	79.68	100.8			
	10	10	80.4	100.5			
150	10	15	79.4	99.2	99.5	0.305	0.306
	10	15	79.68	99.6			
	10	15	79.82	99.8			

3.6 Limit of Detection and Limit of Quantification

The LOD and LOQ were calculated based on the standard deviation of the response and the slope of the constructed calibration curve, as described in International Conference on Harmonization guidelines Q2 (R1) was shown in table 9.

Table 8: Summary of LOD and LOQ

Parameter	Conc.(µg/ml)
LOD (Limit of Detection)	0.169
LOQ (Limit of Quantification)	0.717

3.7 Robustness:

The Robustness of the method was determined by making slight changes in the experimental conditions such as the temperature and scanning the samples maintained at room temperature, cooled to 23°C and heated to 27°C (i.e., 25°C±2°C) as shown in table 9.

Table 9: Summary of Robustness data

Sample no.	Temperature [23˚C (Abs)]	Room temperature [25˚C (Abs)]	Temperature [27˚C(Abs)]
1	0.434	0.423	0.454
2	0.431	0.42	0.456
3	0.43	0.427	0.455
4	0.43	0.427	0.456
5	0.43	0.424	0.457
6	0.431	0.427	0.458
Mean	**0.431**	**0.424**	**0.456**
S.D	**0.0015**	**0.0028**	**0.0014**
%R.S.D	**0.232**	**0.204**	**0.219**

3.8 Forced Degradation Study

Drug samples were subjected to alkaline hydrolysis using 0.1N NaOH, Acid hydrolysis using 0.1N HCl, peroxide oxidation using 3% H_2O_2, thermal and photolysis, treated samples were scanned and their respective spectra were recorded and the Changes in absorbance value were recorded and the results were shown in table 10 and the absorption spectra were shown in figures 6-10.

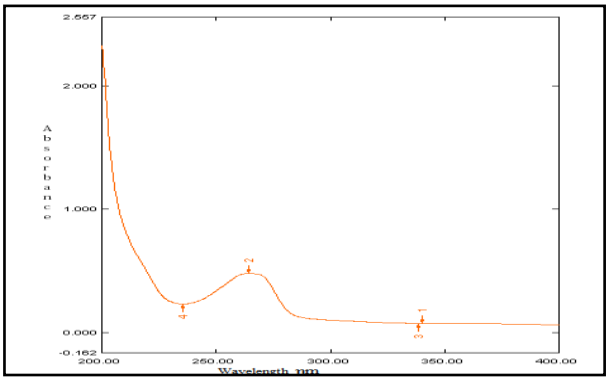

Figure 6: Spectrum of Seratrodastin 0.1N HCl (Acidic condition)

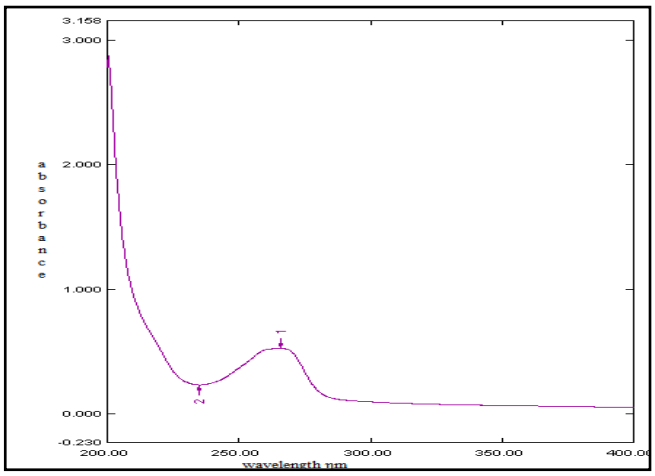

Figure 7: Spectrum of Seratrodast in 0.1N NaOH (Basic condition)

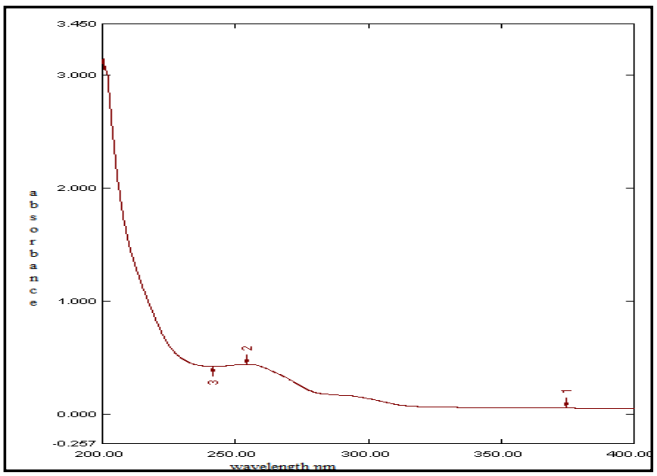

Fig.9: Spectrum of Seratrodast in Photolysis condition

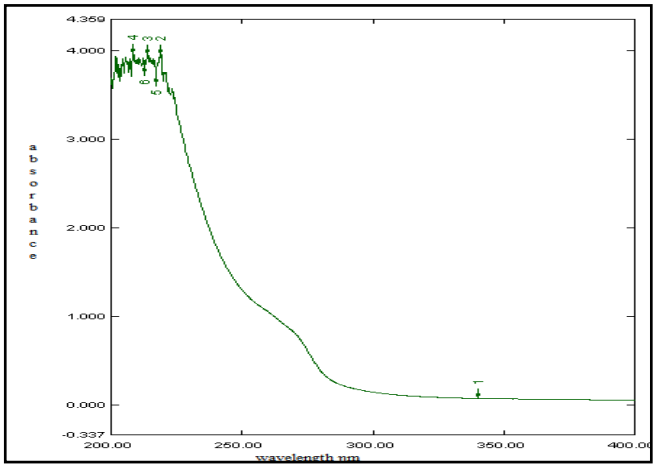

Fig.8: Spectrum of Seratrodast in 3% H_2O_2 (Oxidation condition)

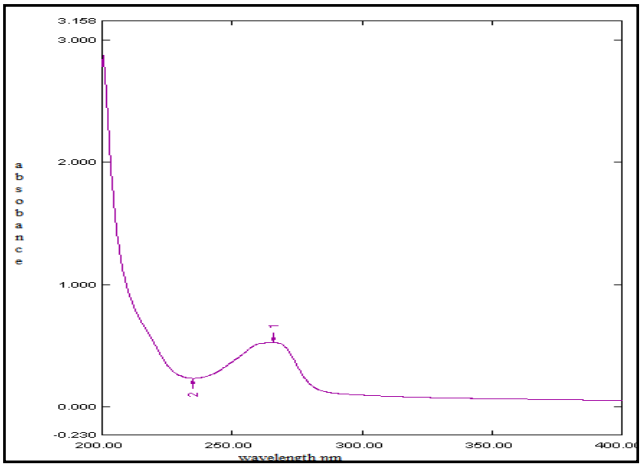

Fig.10: Spectrum of Seratrodast in thermal Condition

Table 10: Summary of Forced Degradation analysis

Degradation Parameters	Absorbance	Concentration (µg/ml)	%Drug Recovered	% Drug Decomposed	Degradation time
Normal condition (Water)	0.421	10	100	0	90mins
Acidic degradation (0.1N HCl)	0.388	9.21	92.1	7.9	90mins
Basic degradation (0.1N NaOH)	0.422	10.02	100.2	0	90mins
Peroxide degradation (3% H_2O_2)	1.009	23.96	0	100	90mins
Photolysis Condition	0.282	6.69	66.98	33.02	90mins
Thermal condition	0.423	10.04	100.4	0	90mins

4. Conclusion

A simple method was developed for the determination of Seratrodast in pure and its pharmaceutical formulations. Seratrodast exhibited maximum absorption at 267ηm in distilled water and obeyed linearity in the concentration range of 2.5-25µg/ml. The proposed method was statistically validated. This study presents a simple stability-indicating UV spectroscopic method for estimation of Seratrodast in the presence of degradation products. By the forced degradation studies, it was found that the drug Seratrodast is degraded in the thermal condition as per the studies performed. So it was concluded that the drug should

be stored in cool and dark place, away from air. The proposed study describes a new UV-Spectrophotometric method for the Estimation of Seratrodast in bulk and combined dosage form. A UV-Spectrophotometric method was developed using distilled water as solvent. The developed methods were validated in accordance with ICH guidelines and all of the results were within the limits.

The UV method for the Estimation of Seratrodast in tablet dosage form was also found to be simple, rapid, precise, accurate and sensitive. A good agreement was observed in UV method. The validated UV method can be used for the routine analysis of quality control samples. Since the developed methods have been applied only to a single brand (SERETRA 80), the same methods are applicable to different brands.

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