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ESTIMATION OF SERTRALIN BY CHROMATOGRAPHIC (RP-HPLC) TECHNIQUE UNDER VARIOUS STRESS CONDITIONS

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Abstract
A simple, sensitive, precise a RP-HPLC method was developed in order to study decomposition of sertraline (SRT) under the hydrolytic stress conditions (acid, alkaline and oxidative).Method was carried out on a Develosil ODS HG-5 RP C18, 5□ m, 15cmx4.6mm i.d. column. The mobile phase was composed of ACN: Buffer =70:30(stop time; 6mins) The detection wavelength was 235 nm. The method was validated and response was found to be linear in the drug concentration range of 0–100 µg ml–1 with correlation coefficient of 0.993.

Keywords: RP-HPLC, Sertraline, method development and validation.

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INTRODUCTION

Sertraline hydrochloride belongs to a class of antidepressant agents known as selective serotonin-reuptake inhibitors (SSRIs).Despite distinct structural differences between compounds in this class, SSRIs possess similar pharmacological activity [1]. (1S,4S)-4-(3,4-dichlorophenyl)-N-methyl-1,2,3,4-tetrahydronaphthalen-1-amine is used for the management of major depressive disorder, posttraumatic stress disorder, obsessive-compulsive disorder, panic disorder with or without agoraphobia, premenstrual dysphoric disorder, social phobia, premature ejaculation, and vascular headaches. According to the literature survey [2-8] it was found that few analytical methods such as (HPLC, UV-Visible analysis and LC-MS) were reported for the estimation of Sertraline .The objective of the proposed method is to develop simple and accurate methods for the determination of Sertraline by RP-HPLC method in pharmaceutical dosage forms & it's stability indicative studies.

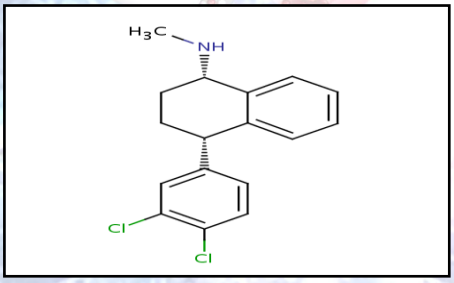

Fig.1: Strusture of Sertraline

MATERIALS AND METHOD

Instruments and Reagents

The chromatographic separation was performed on HITACHI L2130 with D Elite 2000 Software with UV-Visible Detector (L-2400), PUMP (LC-IOAT). C18 Develosil ODS HG-5 RP 150mm x 4.6mm 5µm particle has been used as a stationary phase. P^H Analyzer (ELICO), Electronic Balance (SHIMADZU ATY224), Ultra Sonicator (Wensar wuc-2L) has been used in the work. All chemicals purchased from Sd fine-Chem ltd; Mumbai & Loba Chem; Mumbai

Experimental, Result & Discussion

Method Development [9]

Mobile Phase

Mobile phase preparation:

The mobile phase used in this analysis consists of a mixture of Acetonitrile & Phosphate buffer (pH=3.95) in ratio 70:30.

Preparation of solutions:

Preparation of Standard solution:

Accurately weighed around 25mg of Sertraline working standard, taken into a 25 ml volumetric flask, then dissolved in mobile phase and diluted to volume with the mobile phase to obtain a solution having a known concentration of about 1000 mcg/ml.

Further dilutions has been made to get the final concentration of 10 µg/ml

Preparation of Test solution:

Diluted quantitatively an accurately measured volume of label claim solution with diluents to obtain a solution containing about a linear range.

Optimized Chromatographic Conditions:

Column	: C_{18}Develosil ODS HG-5 RP 150mm x 4.6mm 5µm particle size
Mobile Phase	: ACN : phosphate buffer = 70:30
Flow Rate	: 0.8ml/minute
Wave length	: 235 nm
Injection volume	: 20 µl
Run time	: 6 mins
Column temperature	: Ambient
Sampler cooler	: Ambient

Forced Degradation Studies [10]**:**

Following protocol was strictly adhered to for forced degradation of Sertraline Active Pharmaceutical Ingredient (API). The API (Sertraline) was subjected to stress conditions in various ways to observe the rate and extent of degradation that is likely to occur in the course of storage and/or after administration to body. The various degradation pathways studied are acid hydrolysis, basic hydrolysis, dry heat degradation , peroxide degradation.shortercoloum used.

Method Validation [11-13]

Accuracy

Recovery study:

To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (80%, 100%, and 120%) of pure drug of SERTRALINE were taken and added

to the pre-analyzed formulation of concentration 50µg/ml. From that percentage recovery values were calculated. The results were shown in table-3.

Precision

Repeatability

The precision of each method was ascertained separately from the peak areas & retention times obtained by actual determination of five replicates of a fixed amount of drug. Sertraline(API) The percent relative standard deviation were calculated for Sertraline are presented in the table-4.

Intra-assay & inter-assay

The intra & inter day variation of the method was carried out & the high values of mean assay & low values of standard deviation & % RSD (% RSD < 2%) within a day & day to day variations for Sertraline revealed that the proposed method is precise

Linearity& Range

The calibration curve showed good linearity in the range of 0-100 µg/ml, for Sertraline (API) with correlation coefficient (r^2) of 0.993. A typical calibration curve has the regression equation of y = 13865x - 39285 for Sertraline

Method Robustness

Influence of small changes in chromatographic conditions such as change in flow rate (± 0.1ml/min), Temperature (±2^0C), Wavelength of detection (±2nm) & acetonitrile content in mobile phase (±2%) studied to determine the robustness of the method are also in favour of (Table-4, % RSD < 2%) the developed RP-HPLC method for the analysis of Sertraline(API).

LOD & LOQ

The Minimum concentration level at which the analyte can be reliable detected (LOD) & quantified (LOQ) were found to be 0.03 & 0.09 µg/ml respectively.

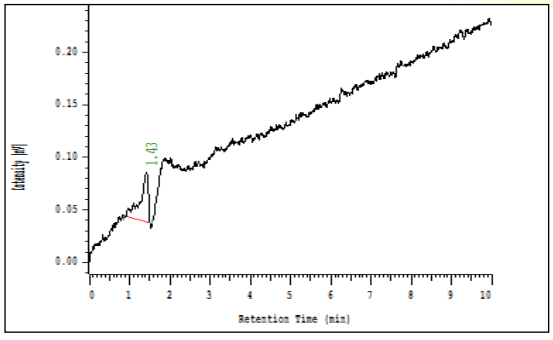

Fig. 2: Chromatogram of Blank

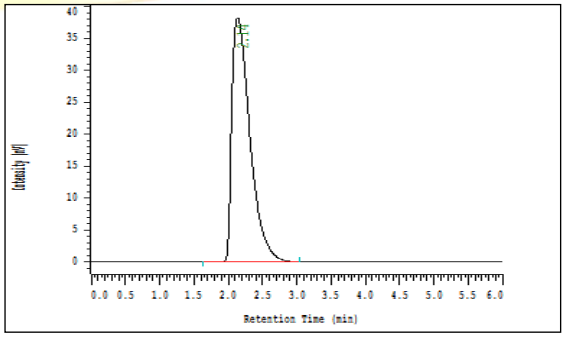

Fig. 3: Optimised method of sertraline.

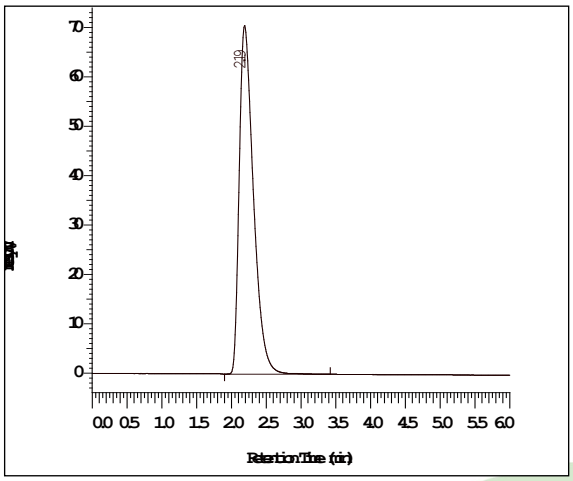

Fig. 4: Chromatogram showing acid Degradation

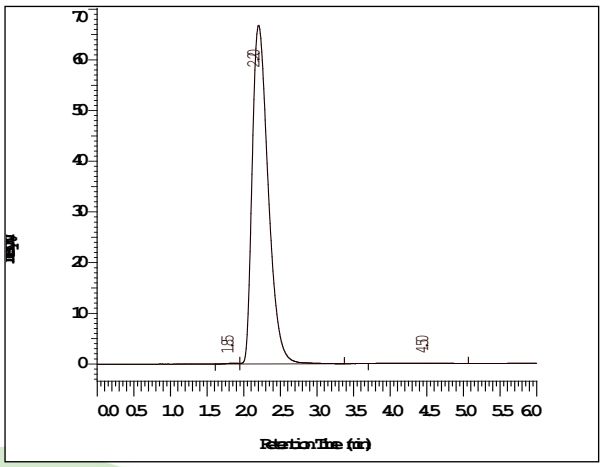

Fig. 5: Chromatogram showing Basic Degradation

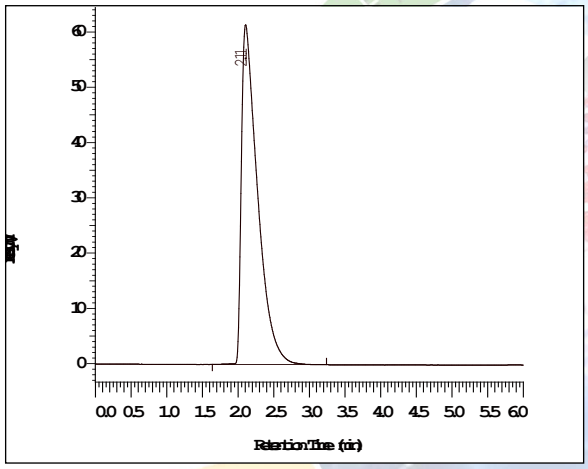

Fig. 6: Chromatogram showing Dry heat Degradation

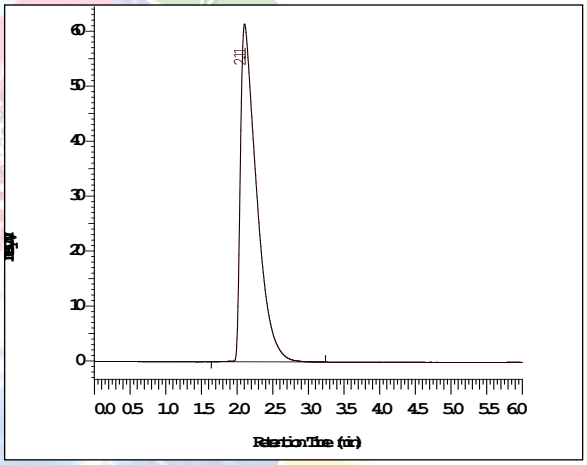

Fig.7: Chromatogram showing photolytic degradation

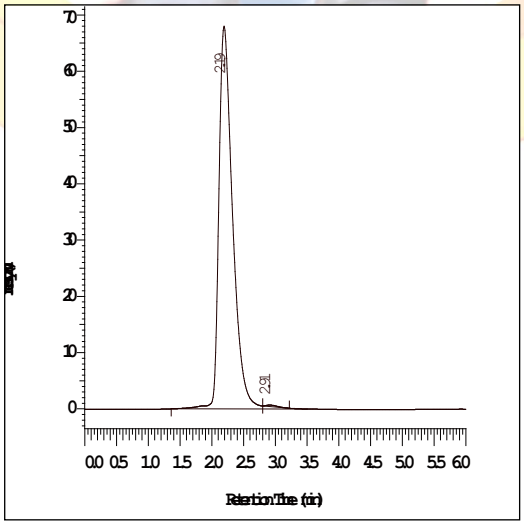

Fig. 8: Chromatogram showing oxidative degradation

Table 1: Results of force degradation studies of Sertraline API

Stress condition	Time	Assay of active substance	Assay of degraded products	Mass Balance (%)
Acid Hydrolysis (0.1 M HCl)	24Hrs.	4.41	95.59	95.59921
Basic Hydrolysis (0.I MNaOH)	24Hrs.	1.53	95.02	96.77748
Thermal Degradation (50 ^{0}C)	24Hrs.	98.13	--	98.43005
UV (254nm)	24Hrs.	67.92	43.76	99.53744
3 % Hydrogen peroxide	24Hrs.	70.40	30.14	95.49932

Table 2: Accuracy Readings

Sample ID	Concentration (µg/ml)		%Recovery of Pure drug	Statistical Analysis
	Pure drug	Formulation		
S_1 : 80 %	40	50	99.94147	Mean= 99.2444%
S_2 : 80 %	40	50	99.26508	S.D.=0.707639
S_3 : 80 %	40	50	98.52664	% R.S.D.= 0.713027
S_4 : 100 %	50	50	100.5094	Mean= 101.0075%
S_5 : 100 %	50	50	101.6957	S.D. = 0.615564
S_6 : 100 %	50	50	100.8175	% R.S.D.= 0.609424
S_7 : 120 %	60	50	101.1903	Mean= 100.7113%
S_8 : 120 %	60	50	99.59007	S.D. = 0.974407
S_9 : 120 %	60	50	101.3534	% R.S.D. = 0.967525

Table 3: Repeatability

HPLC Injection Replicates of Sertraline	Retention Time	Area
Replicate – 1	2.11	913131
Replicate – 2	2.12	918160
Replicate – 3	2.11	911367
Replicate – 4	2.12	880447
Replicate – 5	2.11	891995
Average	2.114	903020
Standard Deviation	0.005477	16064.05
% RSD	0.259093	1.778926

Table 4: Results of intra-assay & inter-assay

Conc. Of SERTRALINEE (API) (µg/ml)	Observed Conc. Of SERTRALINEE (µg/ml) by the proposed method			
	Intra-Day		Inter-Day	
	Mean (n=6)	% RSD	Mean (n=6)	% RSD
70	10.03	1.03	10.41	0.46
90	30.49	0.51	30.94	0.28
110	99.14	0.19	99.19	0.15

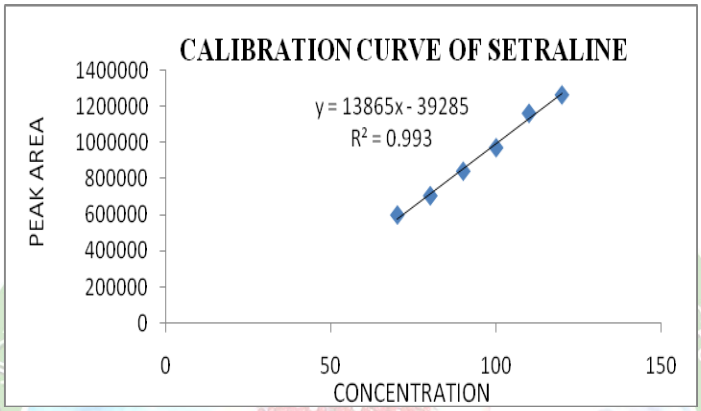

Fig. 1: Calibration curve of .Sertraline (API)

Table 5: Result of linearity

CONC.	AUC (n=6)
70	597425
80	704634
90	841499
100	972335
110	1163929
120	1266251

Table 6: Result of method robustness test

Change in parameter	% RSD
Flow (1.1 ml/min)	0.12
Flow (0.9 ml/min)	0.22
Temperature (27^0C)	0.09
Temperature (23^0C)	0.11
Wavelength of Detection (227 nm)	0.44
Wavelength of detection (223 nm)	0.54

Table7: Data of System Suitability Parameter

S.No.	Parameter	Limit	Result
1	Resolution	Rs> 2	5.98
2	Asymmetry	T ≤ 2	SERTRALINEE=0.56
3	Theoretical plate	N > 2000	SERTRALINEE=4292

Table 8: Recovery Data for estimation SERTRALINEE in serta

Brand name of tablet	Labelled amount of Drug (mg)	Mean (±SD) amount (mg) found by the proposed method (n=6)	Assay + % RSD
Serta (unichem laboratories ltd)	100	100.87(±0.498)	101.01(0.494)

Table 9: Data of System Suitability Parameter

S.No.	Parameter	Limit	Result
1	Resolution	Rs> 2	5.98
2	Asymmetry	T ≤ 2	SERTRALINEE=0.56
3	Theoretical plate	N > 2000	SERTRALINEE=4292

Table10: Recovery Data for estimation SERTRALINEE in serta

Brand name of tablet	Labelled amount of Drug (mg)	Mean (±SD) amount (mg) found by the proposed method (n=6)	Assay + % RSD
Serta (unichem laboratories ltd)	100	100.87(±0.498)	101.01(0.494)

CONCLUSION

The proposed method was found to be rapid, accurate, precise, specific, robust and economical. The mobile phase is simple to prepare and economical. The sample recoveries in all formulations were in good agreement with their respective label claims and they suggested non-interference of formulation excipients in the estimation. This method is also having an advantage than reported method that the retention time of the drugs is below 3 mins and the drug can be assayed with the short time. Thus the method is not time consuming and can be used in laboratories for the routine analysis.

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