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Open Access Research Article

Simultaneous estimation of Doxofylline and Sertraline tablet dosage form by using RP-HPLC

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ABSTRACT

The present study was to develop a simple, accurate, rapid and precise isocratic stability indicating RP- high-performance liquid chromatographic method for simultaneous estimation of Doxofylline and Sertraline in tablet dosage form. The separation method was carried out using shimadzu- HPLC with empower software, UV detector and with BDS column (250mm x 4.6 mm, 5µ), an injection volume of 10µl is injected and eluted with the mobile phase of mixed buffer (0.01N sodium dihydrogen ortho phosphate): acetonitrile (30: 70), which was pumped at a flow rate of 1.1ml/min and detected by UV detector at 220nm. The peaks of Doxofylline and Sertraline were found well separated at 2.4 and 3.7 respectively. Assay studies, it was found that the formulation contains 99.93% of Doxofylline and 99.931% of Sertraline. System suitability studies, it was found that all the system suitability parameters were within the acceptance criteria. Linearity, it was found that the drug obeys linearity within the concentration range of 50 - 300µg/ml for Doxofylline, 6.25-37.5µg/ml for Sertraline. Accuracy, it was found that the percentage recovery values of pure drug from the pre- analysed solutions of formulations were in between 99.4% for Doxofylline, 99.5% for Sertraline, which indicates that the method was accurate. Precision, it was found that % RSD is less than 2%; which indicates that the proposed method has good reproducibility. Robustness, it was found that there is little change in the results with the change in the parameters like flow rate and temperature, indicating the robustness of the method. The developed chromatographic method for the determination of Doxofylline and Sertraline in tablet dosage forms was simple, rapid, accurate, precise, specific, robust and economical.

Keywords: Simultaneous estimation, Doxofylline, Sertraline, RP-HPLC

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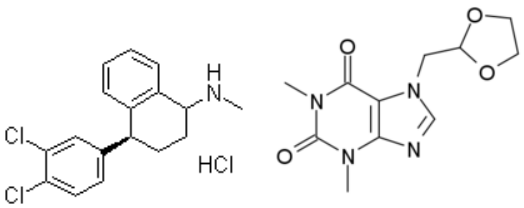
INTRODUCTION

For the treatment of asthma xanthine derivative Doxofylline was used. It is a phosphodiesterase inhibitor, and having bronchodilator, antitussive effects, Chemically, Doxofylline is 7-(1,3-dioxolan-2-methyl)-1,3-dimethyl purine-2,6-dione. Sertraline is a selective serotonin reuptake inhibitor, to treat panic, social anxiety disorder of both adults and children's Chemically, Sertraline is (1S, 4S)-4-(3, 4-dichlorophenyl)-N-methyl - 1, 2, 3, 4 tetrahydronaphthalen-1-amine. [1-8]

The literature survey reveals that there is no reported method on simultaneous estimation of Doxofylline and Sertraline in combined tablet dosage forms. Hence, it is necessary to develop a rapid, accurate and validated RP-HPLC method for the determination of Doxofylline and Sertraline from combined dosage form [10-14]. The method followed according to ICH guidelines.



MATERIALS &METHODS

Acetonitrile and water of HPLC grade were procured from Sigma-Aldrich, Doxofylline and Sertraline standards were received as gift samples from Glochem Laboratories, Hyderabad, India. O-phosphoric acid was purchased from E. Merck chemicals, Mumbai, India. Tablet DOXODER having combination of Sertraline (50mg), Doxofylline (400mg) was used.

Analytical Method Development

Development and optimization of liquid chromatography is interesting in research field**.** Among all, the liquid chromatographic methods, the RP systems based on modified silica offers the best results. However, many (system) variables (parameters) affect the selectivity and the resolution. [15-18]

RESULTS AND DISCUSSIONS

System suitability

All the system parameters are within range and satisfactory according to ICH guidelines.

Linearity: The linearity of analyte is its ability to obtain test results, which are directly proportional to the concentration (amount) of analyte in the sample.

Precision: Intraday precision (Repeatability):

Acceptance Criteria: The % RSD for the area of 5 standard injections results should be ≤2%. **Result:** The percentage relative standard deviation for the peak area of Doxofylline and Sertraline was 0.7 and 0.4 at the working concentrations. The result complies with the acceptance criteria and indicates acceptable precision of the system.

Assay: From formulation samples was prepared and from Active pharmaceutical ingredient standard solution was prepared. Both sample and standards are injected 5 samples. The Average %Assay was calculated and found to be 99.93% and 99.931% for Doxofylline and sertraline respectively.

Accuracy

Acceptance criteria: The percentage recovery should be in the range of 99.0 to 101.0 and the percentage relative standard deviation should not be more than 2.00.

Calculation:

$$\text{Assay} = \frac{\text{Spl area}}{\text{Std area}} \times \frac{\text{Std. Dil. Fac}}{\text{Spl. Dil. Fac}} \times \frac{\text{Avg. Wt of Tab}}{\text{L.C}} \times \text{Potency of Std.}$$

Spl area – Sample Peak area, Std area – Standard Peak area, Std. Dil. Fac- standard dilution factor, Spl. Dil. Fac- sample dilution factor, Avg. Wt of Tab- average weight of tablet, L.C – lable claim

Result: The percentage recovery values were in the range of 99.59 to 100.08 and the percentage relative standard deviation obtained in the range of 0.1 to 0.9, which is within the acceptance criteria.

Detection Limit: The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample, which can be detected but not necessarily quantities under stated experimental conditions.

LOD=3.3*standard deviation of Intercept/Average of Slope

Result: Limit of detection was calculated by intercept method and LOD for Doxofylline and Sertraline were found to be 0.1**µg/ml** and 0.1**µg/ml** respectively.

LOQ: Quantization Limit:

The quantization limit of an individual analytical procedure is defined as the lowest amount of analyte in a sample, which can be quantitatively determined with suitable precision and accuracy

LOQ=10*standard deviation of Intercept/Average of Slope

Result: limit of Quantification was calculated by intercept method and LOQ for Doxofylline and Sertraline were found to be 0.3µg/ml and 0.3 µg/ml respectively.

Robustness: Small deliberate changes in method like Flow rate, mobile phase ratio, and temperature are made but there were no recognized change in the result and are within range as per ICH Guide lines.

Acceptance Criteria: RSD < 2%. Robustness conditions like Flow minus (0.9ml/min), Flow plus (1.1ml/min), mobile phase minus, mobile phase plus, temperature minus (25°C) and temperature plus (35°C) was maintained and samples were injected in duplicate manner. System suitability parameters were not much affected and all the parameters were passed. %RSD was within the limit.

Table 1: System suitability of Doxofylline and Sertraline

S. No	Parameter	Doxofylline	Sertraline
1	RT(min)	2.492 ± 0.3 min _	3.705±
2	Tailing Factor	1.08±0.11	1.31±0.11
3	No. of theoretical plates	4683±162.	6416±162.23

Table 2: Linearity of Doxofylline & Sertraline

S.NO	Linearity level	Conc.	Rt time	Area	USP plate count	USP tailing	Conc.	Rt time	Area	USP plate count	USP tailing
1	25	50	2.490	770796	5016	1.05	6.25	3.670	154449	7014	1.27
2	50	100	2.489	1594917	5300	1.07	12.5	3.669	328004	7052	1.29
3	75	150	2.488	2301155	52535	1.06	18.75	3.663	450697	6786	1.31
4	100	200	2.489	3070554	5206	1.06	25	3.666	617173	6996	1.29
5	125	250	2.488	3835133	5271	1.01	31.25	3.662	771029	7062	1.31
6	150	300	2.489	4692566	5131	1.08	37.5	3.663	939384	6836	1.32

Table 3: Summary of peak area for intraday precision

Injection	Doxofylline peak Area	Sertraline peak area
Injection-1	2977222	543336
Injection-2	3001962	540098
Injection-3	2981860	541083
Injection-4	2954543	538291
Injection-5	2953234	538452
Average	2973764	540252
Standard Deviation	20393.3	20804
%RSD	0.7	0.4

Table 4: Summary of peak area for interday precision

Injection	Doxofylline peak Area	Sertraline peak area
Injection-1	2974382	541748
Injection-2	3000536	538165
Injection-3	2980028	539417
Injection-4	2952740	536535
Injection-5	2951750	537625
Average	2971887	538698
Standard Deviation	20404.3	19959
%RSD	0.7	0.4

Table 5: Assay of Tablet

S. No.	Doxofylline %Assay	Sertraline %Assay
1	100.5201	100.3867
2	99.25758	99.72267
3	100.0131	100.4712
4	100.5318	100.0537
5	99.75074	99.84915
6	99.48887	99.10043
AVG	99.93	99.931
STDEV	0.5284	0.50
%RSD	0.5	0.5

Table 6: Accuracy of Doxofylline and Sertraline

Sample	Amount Taken(µg/ml)	Amount Recovered (µg/ml)	Recovery (%)	% RSD
Doxofylline	100	99.60	99.62	0.6
	200	199.74	99.59	0.8
	300	299.80	99.75	0.9
Sertraline	12.5	12.48	99.90	0.5
	25	25.10	100.01	0.8
	37.5	37.53	100.08	0.1

Table 7: Retention time data of Doxofylline and Sertraline

	Peak Name	RT	Area	s/n
1	Doxofylline	2.487	18533	149.3
2	Sertraline	3.658	3634	27.7
3	Doxofylline	2.488	41107	306.0
4	Sertraline	3.661	6178	47.0

Table 8: Robustness data of Doxofylline and Sertraline

S.NO	Robustness condition	Doxofylline % RSD	Sertraline %RSD
1	Flow minus	0.1	0.1
2	Flow Plus	0.2	0.6
3	Temperature minus	0.3	0.6
4	Temperature Plus	0.7	0.9

SUMMARY

An attempt has been made to develop the RP-HPLC method for simultaneous estimation of Doxofylline and Sertraline in combined dosage form. As the literature survey revealed that few methods were available for their estimation individually, but there is a need of a simple, economical and proper method for estimation of above combination in combined dosage form.

CONCLUSION

The present study was validated as per the ICH guidelines. From the comparative study, it was inferred that the method is simple, specific, precise, linear, sensitive, and system suitability. The results obtained on the validation parameter met the respective acceptance criteria.

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