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METHOD DEVELOPMENT AND VALIDATION OF NEW HPLC METHOD FOR ATOMOXETINE IN PHARMACEUTICAL DOSAGE FORM.

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ABSTRACT

A simple and selective HPLC method is described for the determination of Atomoxetine.Chromatographic separation was achieved on a C18column using mobile phase consisting of a mixture of 40 volumes of Methanol, 40 volumes of Acetonitrile and 20 volumes of Water with detection of 253 nm. Linearity was observed in the range 50-150 µg /ml for Atomoxetine (r^2 =0.990) for the amount of drugs estimated by the proposed methods was in good agreement with the label claim. The proposed methods were validated. The accuracy of the methods was assessed by recovery studies at three different levels. Recovery experiments indicated the absence of interference from commonly encountered pharmaceutical additives. The method was found to be precise as indicated by the repeatability analysis, showing %RSD less than 2. All statistical data proves validity of the methods and can be used for routine analysis of pharmaceutical dosage form.

Key Words: Atomoxetine, HPLC method

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INTRODUCTION

Pharmaceutical analysis simply means analysis of pharmaceuticals. Webster' dictionary defines a pharmaceutical is a medical drug. A more appropriate term for a pharmaceutical is active pharmaceutical ingredient (API) or active ingredient to distinguish it from a formulated product or drug product is prepared by formulating a drug substance with inert ingredient (excipient) to prepare a drug product that is suitable for administration to patients. Research and development (R&D) play a very comprehensive role in new drug development and follow up activities to ensure that a new drug product meets the established standards is stable and continue to approved by regulatory authorities ,assuring that all batches of drug product are made to the specific standards utilization of approved ingredients and production method becomes the responsibility of pharmaceutical analysts in the quality control (QC) or quality assurance department . The methods are generally developed in an analytical R&D department and transferred to QC or other departments as needed. At times they are transferred to other divisions (1-3).Quality investigation plays a very important role in quality specification establishment of chemical drugs. The number of drugs introduced into the market every year .very often there is a time lag from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias. Hence, standards and

analytical procedures for these drugs may not be available in the pharmacopoeias. It becomes necessary, therefore to develop newer analytical methods for such drugs.Analytical method development provides the support to track the quality of the product from batch to batch. Method development involves considerable trial and error procedures. The most difficult problem usually is where to start, what type of column is worth trying with what kind of mobile phase (4). Aim is to develop and validate new HPLC method for Atomoxetine in pharmaceutical dosage form.

MATERIALS AND METHODS

Determination of Working Wavelength (λmax)

Preparation of standard stock solution ofAtomoxetine

10 mg of Atomoxetinewas weighed and transferred in to 100ml volumetric flask and dissolved in Methanol and then make up to the mark with methanol and prepare 10 µg /ml of solution by diluting 1ml to 10ml with Methanol.

Preparation of samples for Assay (5-8)

Preparation of standard solution

weigh accurately 10 mg of Atomoxetine in 25 ml of volumetric flask and dissolve in 25ml of mobile phase and make up the volume with mobile phase.From above stock solution 20 µg/ml ofAtomoxetineis prepared by diluting 0.5ml to 10ml with mobile phase. This solution is used for recording chromatogram.

Sample preparation:weigh accurately 10 Tablets **(Atomoxetine-60 mg)**weigh accurately 10 mg of Atomoxetine in 25 ml of volumetric flask and dissolve in 25ml of mobile phase and make up the volume with mobile phase.From above stock solution 20 µg/ml ofAtomoxetineis prepared by diluting 0.5ml to 10ml with mobile phase. This solution is used for recording chromatogram.

System Suitability& System precision

To verify that the analytical system is working properly and can give accurate and precise results were evaluated by 20µg/mLof atomoxetinewas injected six times and the chromatograms were recorded for the same.

Specificity

A study to establish & determine the interference of blank and placebo as conducted. Analysis was performed on placebo in triplicate equivalent to about the weight of placebo in portion of test preparation as per test method. Chromatograms of blank and placebo solutions had shown no peaks at the retention times of atomoxetine

RESULTS AND DISCUSSION

The wavelength of maximum absorption (λ_{max}) of the drug, 10 µg/ml solution of the drug in Methanol were scanned using UV-Visible spectrophotometer within the wavelength region of 200–400 nm against Methanol as blank. The resulting spectraand the absorption curve shows characteristic absorption maxima at 253 nm for Atomoxetine, selected as detector wavelength for the HPLC chromatographic method.The amount of Atomoxetine present in the taken dosage form was found to be 101.49% respectively (Table-1).

Table-1 Assay Results

Atomoxetine		
	Standard Area	**Sample Area**
Injection-1	3844.82	3906.83
Injection-2	3846.71	3905.34
Injection-3	3850.83	3907.13
Injection-4	3851.11	3908.74
Injection-5	3854.26	3907.29
Average Area	3849.546	3907.066
Standard deviation	3.76	
%RSD	0.1	
Assay(%purity)	101.49	

The %RSD ofdeterminations of Atomoxetinefound to be within the acceptance criteria (less than 2.0%). %Assay Also within the limits (95.0 to 105.0) hence method is precise (Table-2).

Table-2Method precision results for Atomoxetine

S. No.	RT	AREA
1	2.027	3855.52
2	2.026	3855.32
3	2.026	3855.67
4	2.026	3854.45
5	2.026	3856.67
AVG	2.0262	3855.526
SD	0.00045	0.795
%RSD	0.022	0.021

A graph was plotted for atomoxetineagainst the concentrations of the solutions and the peak areas (Table 7.9). The correlation coefficient R^2 was determined and was found to be 1.00 for atomoxetine(Fig-1).

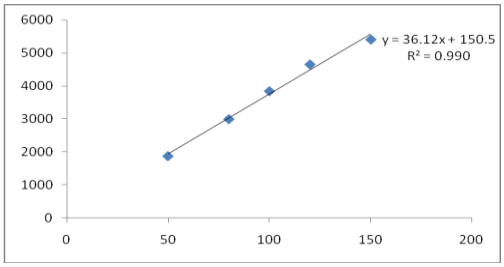

Fig-2 Graph for Linearity data of atomoxetine.

The Average % recovery of atomoxetinebetween 98% and 102% (Table-3).

Table-3 Results for Recovery of atomoxetine

Name of Sample	StdWt (mg)	Area	Conc Recovered	% Recovered	Average
50 % Recovery_1	50	1881.95	48.50	97.00	
50 % Recovery_2	50	1883.46	48.54	97.07	
50 % Recovery_3	50	1880.71	48.47	96.93	
100 % Recovery_1	100	3865.51	99.61	99.61	
100 % Recovery_2	100	3865.34	99.61	99.61	99.64
100 % Recovery_3	100	3868.15	99.68	99.68	
150 % Recovery_1	150	5816.27	149.89	99.92	
150 % Recovery_2	150	5815.82	149.87	99.92	
150 % Recovery_3	150	5815.96	149.88	99.92	

CONCLUSION

From the above experimental results and parameters it was concluded that, this newly developed method for the simultaneous estimation of Atomoxetine was found to be simple, precise, accurate and high resolution and shorter retention time makes this

method more acceptable and cost effective and it can be effectively applied for routine analysis in research institutions, quality control department in meant in industries, approved testing laboratories studies in near future.

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