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Development and Validation of UV Spectrophotometric Method For Estimation of Desvenlafaxine Succinate ER-Tablets Forms

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ABSTRACT

A simple, precise and accurate method has been described for the estimation of Desvenlafaxine in formulation of Desvenlafaxine Succinate ER-Tablets using Agilent 1200 series HPLC and Column-Zorbax SB CN (250 x 4.6 mm) 5µ or equivalent in isocratic mode consisting of quaternary pump and UV detector with mobile phase 4.0 ml of Trifluoroacetic acid and 7.0 ml of Triethylamine to 1000 ml of water (pH to 3.0 with Triethylamine): Acetonitrile (80:20 %v/v) at flow rate of 1 ml/min. The effluent is monitored at 225nm. The retention time of Desvenlafaxine was 7.0 min. The linearity range for Desvenlafaxine was found to 48.066 µg/ml to 72.099 µg/ml. The correlation co-efficient were closed to 1 proving the good linearity between concentration of drug and response. The %RSD values of precision were less than 2, which indicate that the method has good reproducibility. The method validation parameters like theoretical plates, resolution, tailing factor, LOD and LOQ were found to be within the USP standards. As the chromatogram for Desvenlafaxine in formulation is free from any other peaks except at the retention time corresponding to drugs, it was revealed that excipients used in the formulation were not interfering in the method. Thus the proposed method is suitable for routine analysis, formulations containing Desvenlafaxine.

INTRODUCTION

Desvenlafaxine is a synthetic form of the isolated major active metabolite of venlafaxine, and is categorized as a serotonin-norepinephrine reuptake inhibitor (SNRI). It works by blocking the transporter "reuptake" proteins for key neurotransmitters affecting mood, thereby leaving more active neurotransmitters in the synapse.[1-3]. Literature survey reveals, there are HPLC method reported for the estimation of Desvenlafaxine in Pharmaceutical formulations[4-9].Aim of present work was to develop simple, precise, accurate and economical HPLC methods for Desvenlafaxine Succinate ER-Tablets formulation[16].

The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines[17]

MATERIALS & METHODS

Apparatus: Agilent 1200 series HIGH PERFORMANCE LIQUID CHROMATOGRAPHY, Rhenodyne valve with 20µl fixed loop, quaternary pump, column Zorbax SB CN (250 X 4.6 mm), 5µ. Reagent: Trifluoroacetic acid, Triethylamine, Acetonitrile, Methanol, Desvenlafaxine Succinate API.

EXPERIMENTAL SECTION

Chromatographic Condition

Preparation of Buffer solution:

Add 4.0 ml of Trifluoroacetic acid and 7.0 ml of Triethylamine to 1000 ml of Water. Adjust the pH to 3.0 with Triethylamine.

Preparation of Mobile phase:

Prepared a degassed mixture of 800 ml of Buffer and 200 ml of Acetonitrile.

Diluent: Mobile Phase

Standard preparation:

Transfer an accurately weighed quantity of about 29 mg Desvenlafaxine succinate standard in to 100 ml volumetric flask. Add about 40 ml of diluent and sonicate to dissolve. (During sonication necessary care should be taken to control the temperature between 20-25°C using ice). Dissolve and dilute to volume with diluent and mix well. Dilute 3.0 ml of this solution into 10mL volumetric flask with diluent and mix well.

System suitability:

Equilibrate the column with mobile phase at the prescribed conditions until a stable baseline is achieved. Separately inject six replicate injections of standard preparation in to liquid chromatography and record the chromatograms.

In the chromatogram obtained with standard preparation:

- %Relative standard deviation for Desvenlafaxine peak area of replicate injections should not be more than 2.00.
- Tailing factor for Desvenlafaxine peak should be between 0.80 to 2.00.
- The theoretical plates (by tangent method) for Desvenlafaxine peak should not be less than 2000.

Procedure

Separately inject single injection of diluent and duplicate injections of assay preparation into liquid chromatography and record the chromatograms. Calculate the Desvenlafaxine Succinate eq. to Desvenlafaxine content in percentage of label claim from the Desvenlafaxine peak areas of standard preparation, assay preparation and percentage potency of working standard used.

$$\frac{Au}{As} \times \frac{W_1}{50} \times \frac{3}{20} \times \frac{250}{W2} \times \frac{100}{3} \times \frac{W_3}{L.C} \times \frac{263.375}{381.463} \times \frac{P}{100} \times 100$$

Calculation:

Where;

Au = Mean peak area due to Desvenlafaxine Succinate obtained with assay preparation.

As = Mean peak area due to Desvenlafaxine Succinate obtained with standard preparation

W1 = Weight of Desvenlafaxine Succinate working standard taken in mg.

W2 = Weight of substance being examined taken in mg

W3 = An average weight of tablet in mg.

L.C. = Label claim of Desvenlafaxine Succinate in mg per tablet.

263.38 = Molecular weight of Desvenlafaxine.

381.48 = Molecular weight of Desvenlafaxine Succinate.

P = Potency of Desvenlafaxine Succinate working standard in percentage on as is basis.

Study of overlain spectra and selection of wavelength

Transfer an accurately weighed quantity of about 29.3 mg Desvenlafaxine succinate standard in to 50 ml volumetric flask. Add about 20 ml of methanol and sonicate to dissolve. (During sonication necessary care should be taken to control the temperature between 20-25°C using ice). Dissolve and dilute to volume with methanol and mix well. Prepare different linearity concentration solutions 48.066 µg/ml to 72.099 µg/ml by diluting accurately measured volume of linearity stock solution in to specified volumetric flask with diluent and mix. Results of Linearity of Desvenlafaxine were determined (Table 1). Calibration curve were plotted of Desvenlafaxine (Fig 1). From the spectra (Fig 2) of wave lengths 225.0 nm was selected.

Analysis of Formulation

Preparation of standard solution

Transfer an accurately weighed quantity of about 29 mg Desvenlafaxine succinate standard in to 100 ml volumetric flask.

Table No.2: Analysis of formulation

Drug	Amount (mg/tablet)		% label claim	% RSD*
	Labeled	Estimated		
Desvenlafaxine	50	50	99.5%	0.215
	100	100	98.2%	0.347

RSD* of six observations

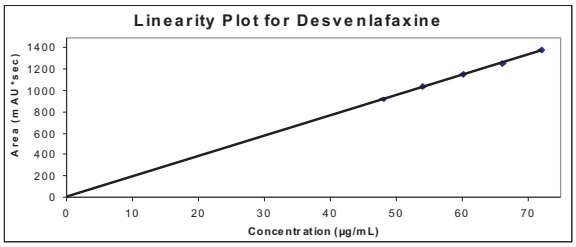

Fig. 1: Linearity Graph for Desvenlafaxine

Table No.1: Results of Linearity of Desvenlafaxine

Linearity of Desvenlafaxine			
Linearity levels(%)	Conc. of Desvenlafaxine (µg/ml)	Mean area	Response factor
80	48.066	919.47642	19.129
90	54.074	1039.62410	19.226
100	60.082	1149.41751	19.131
110	66.090	1261.66825	19.090
120	72.099	1382.46655	19.175
Correlation co-efficient			0.99986
Y-intercept			2.50195
Slope of regression line			19.10763
R^2 Value			0.99972
%Y-intercept bias at 100% Level			0.2
% RSD of response factor			0.27

Add about 40 ml of diluent and sonicate to dissolve. (During sonication necessary care should be taken to control the temperature between 20-25°C using ice). Dissolve and dilute to volume with diluent and mix well. Dilute 3.0 ml of this solution into 10mL volumetric flask with diluent and mix well.

Preparation of sample solution

Weigh and transfer 10 intact tablets in to 250 ml volumetric flask. Add about 150 ml of methanol and sonicate for 30 min. (During sonication necessary care should be taken to control the temperature between 20-25°C using ice). Dilute to volume with methanol and mix well. Filter the solution through 0.45 µ nylon filter. Discard first few ml of the filtrate. Dilute 3.0 ml of this solution to 100 ml with diluent and mix well.

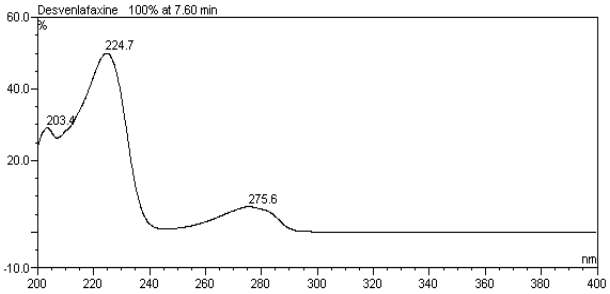

Figure 2: UV- spectra of Desvenlafaxine (10 µg/ml)

Table 3: Recovery studies

Set No.	Accuracy levels (%)	Expected amount of Desvenlafaxine (mg /tablet)	Recovered amount of Desvenlafaxine (mg /tablet)	% Recovery
1	80	40.000	39.858	99.6
2			40.202	100.5
3			40.107	100.3
			Mean	100.1
			%RSD	0.47
1	100	50.000	50.093	100.2
2			50.187	100.4
3			50.246	100.5
			Mean	100.4
			%RSD	0.15
1	120	60.000	60.172	100.3
2			60.188	100.3
3			60.251	100.4
			Mean	100.3
			%RSD	0.06

Over all Mean: 100.3 Over all % RSD: 0.27

Separately inject single injection of diluent and duplicate injections of assay preparation into liquid chromatography and record the chromatograms. Calculate the Desvenlafaxine Succinate eq. to Desvenlafaxine content in percentage of label claim from the Desvenlafaxine peak areas of standard preparation, assay preparation and percentage potency of working standard used. [Table: 2].

PRECISION

System precision:

Prepare standard preparation as mentioned in method of analysis 4.0. Inject six replicate injections in to the liquid chromatography and record the chromatograms.

Determine the mean and relative standard deviation for replicate injections with respect to peak area of Desvenlafaxine peak. Record tailing factor and theoretical plates for the

Table 4 : Results of System precision

System Suitability Parameters	Observation	Acceptance Criteria
%RSD of area of six replicate injections	0.14	NMT 2.00
Mean tailing factor	1.02	Between 0.80 to 2.00
Mean theoretical plates	14688	NLT 2000
Difference in retention time	0.0	NMT ± 0.2 min.
Mean area	1139.00206	NA
Mean retention time	7.146	NA

Table 5: Results of Method precision strength

Set No.	Mean area of assay preparation	% Assay
1	1148.48123	99.7
2	1150.93843	99.5
3	1156.24640	99.7
4	1154.87579	99.8
5	1151.17930	99.6
6	1157.78240	99.7
	Mean	99.7
	% RSD	0.10

Desvenlafaxine peak. Also record difference in retention time with respect to mean retention time of Desvenlafaxine peak. and 288 nm. Low %RSD shows that the method has good precision. [Table 4].

Method precision: (Repeatability)

Prepare six assay preparations for both strengths as mentioned in method but different serial number), different make of chromatographic system by different analyst on a different day as that of method precision study. Determine the mean and relative standard deviation of test results.

Also calculate the percentage difference against mean of method precision result and similarity factor between method precision and intermediate precision results. [Table 6]

SOLUTION STABILITY

Bench top (23 to 27^{0}C) stability studies of standard preparation and assay preparation. Prepare single set of standard preparation and assay preparation for both strengths as mentioned in method of analysis 4.0. Inject in duplicate of standard preparation and assay preparation of both strengths in to the liquid chromatography and record the initial peak area of Desvenlafaxine peak. Store these solutions in tight flask at 23-27°C/ not protected from light. [Table 7].

RESULTS AND DISCUSSION

To develop a precise, accurate and suitable RP- HPLC method for the devlopment and validation of the Desvenlafaxine tablets, different temperature and the column were tried and the proposed chromatographic conditions were found to be appropriate for the quantitative determination of the Desvenlafaxine. So by performing different trials of Temperature and column for Desvenlafaxine we concluded final method with desire tailing and the temperature. Also concluded separation of the different impurity from main peak of Desvenlafaxine.

CONCLUSION

The proposed method is simple, precise, and accurate for the rapid for simultaneous determination of Desvenlafaxine tablet dosage forms and this method may be successfully applied in control laboratories for their determination in combined dosage form.

Table 6: Results of Intermediate Precision Strength

Set No.	Mean area of assay preparation	% Assay
1	1197218	100.3
2	1192374	99.9
3	1192391	99.9
4	1195071	100.1
5	1194709	100.2
6	1201445	100.3
	Mean	100.1
	% RSD	0.18

Table 7: Stability studies

For assay preparation		
Time in Hrs.	Mean area	% Difference
Initial	1136.54473	NA
6	1138.38270	0.16
12	1135.43297	0.10
18	1130.77251	0.51
24	1129.32615	0.64

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