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Spectrophotometric method for estimation of desvenlafaxine succinate in tablet dosage form

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ABSTRACT

Two simple and sensitive spectrophotometric methods (A and B) for the determination of desvenlafaxine succinate in tablet dosage form are described. In the method A - Simple UV Spectrophotometric method, distilled water was used as solvent and shows absorption maxima at 224.5 nm. In the method B - Difference Spectrophotometric method, the proposed method is based on the principle that desvenlafaxine succinate can exhibit two different chemical form in basic and acidic medium that differ in the absorption spectra in basic and acidic medium. The difference spectrum of desvenlafaxine succinate in 0.01 M Sodium hydroxide was recorded by taking desvenlafaxine succinate in 0.1 M Hydrochloric acid solution as blank. The difference spectrum showed that the maxima at 240 nm and minima at 224.5 nm. The Beer's law range for method A is 5 - 40 µg/mL and 8 - 40 µg/mL for method B. The linear regression for method A and B are found to be 0.99992 and 0.99994 respectively. When tablet dosage form where analyzed, the results are obtained by the proposed methods are in good agreement with the labeled amount and the results were validated statistically.

Keywords: Desvenlafaxine succinate, difference spectrophotometry, estimation, tablet dosage form.

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INTRODUCTION

Desvenlafaxine succinate is a newer antidepressant drug, which is chemically 1-[(1RS)-2-(dimethylamino)-1-(4-hydroxyphenyl) ethyl]cyclohexanol succinate monohydrate. Desvenlafaxine succinate is a structurally novel SNRI (serotonin - norepinephrine reuptake inhibitor) useful for the treatment of MDD (major depressive disorder). Desvenlafaxine (O-desmethyl venlafaxine) is the major active metabolite of the antidepressant venlafaxine, a medication used to treat major depressive, generalized anxiety and panic disorders. Desvenlafaxine succinate is not official in any pharmacopoeia. Literature survey revealed that LC-MS [1-3] methods were reported for the estimation of desvenlafaxine succinate in human plasma. But there is no spectrophotometric method was reported for the estimation of desvenlafaxine succinate in tablet dosage form. In the present report, the paper describes two simple and sensitive spectrophotometric methods for the determination of desvenlafaxine succinate in tablet dosage form.

MATERIALS AND METHODS

Materials

Pharmaceutical grade of desvenlafaxine succinate was kindly gifted from Orchid Pharma, Chennai. The commercially available marketed tablet, Ventab Dxt 50 (Intas Pharmaceuticals Ltd., Ahmadabad) containing 50 mg of desvenlafaxine was used and it was procured from the local market.

All the solvents and chemicals used were distilled water, freshly prepared 0.01 M Sodium hydroxide and 0.1 M Hydrochloric acid are of analytical reagent grade were used in the present investigation.

Instruments

Shimadzu UV - 1700 UV/VISIBLE spectrophotometer with 1 cm matched quartz cells was used for spectral an absorbance measurements, Shimadzu AUX - 220 electronic balance was used for weighing the sample.

METHOD A - SIMPLE UV - SPECTROPHOTOMETRIC METHOD

Selection of Solvent

The solubility of desvenlafaxine succinate was determined in a variety of solvents ranging from non - polar to polar using essentially a method of Schefter and Higuchi [4]. The drug was found to be freely soluble in methanol and dimethyl formamide, soluble in water, 0.1 M hydrochloric acid, 0.1 M sodium hydroxide, 0.01 M sodium hydroxide, 10 % glacial acetic acid and acetate buffer pH 4, slightly soluble in chloroform, sparingly soluble in ethanol, very slightly soluble in n-hexane and n-butane. Considering the economic factor and since the drug

was stable in distilled water for 5 hours and 10 minutes, distilled water was selected as the solvent for final dilution.

Preparation of standard stock solution

10 mg of desvenlafaxine succinate working standard was accurately weighed and transferred into a 10 mL standard flask and dissolved with minimum quantity of distilled water and made up to 10 mL with more distilled water. The solution was observed to contain 1000 µg/mL.

Selection of λmax and stability studies

The standard stock solution was further diluted with distilled water to get a 10 µg/mL of concentration (1 mL to 100 mL). The solution was scanned between 200 and 400 nm using distilled water as blank. From the spectrum obtained, 224.5 nm was selected as λmax for the analysis of desvenlafaxine succinate (Figure 1). Stability studies were performed and desvenlafaxine succinate was found to be stable for 5 hours and 10 minutes.

Preparation of working standard solution

25 mg of desvenlafaxine succinate working standard was accurately weighed and transferred into a 100 mL standard flask and dissolved with minimum quantity of distilled water and made up to the mark with distilled water and obtained a concentration of 250 µg/mL.

Calibration graph and linearity

To series of eight 50 mL volumetric flasks, different aliquots (1 to 8 mL) were taken from the above working standard solution and made up to the mark using distilled water. The absorbances were measured at 224.5 nm against distilled water as blank. The calibration curve was plotted between concentration and absorbance in the concentration range from 5 to 40 µg/mL.

Quantification of formulation

Twenty tablets of formulation (Ventab Dxt 50) containing 50 mg of desvenlafaxine were accurately weighed to find out the average weight and powdered. Transferred the powdered tablets equivalent to 25 mg of desvenlafaxine succinate into a 100 mL standard flask, extracted with distilled water for three times (3 x 25 mL), sonicated for 15 minutes and produced to 100 mL with distilled water. The solution was filtered through Whatman filter paper No. 41. From this solution, 4 mL was transferred to a 50 mL standard flask and produced to obtain 20 µg/mL of solution with distilled water. The absorbance was measured at 224.5 nm using distilled water as blank. This procedure was repeated for six times. The amount of desvenlafaxine succinate present in formulation was calculated from the slope and intercept of respective calibration curve [5].

Recovery studies

To determine the accuracy of the method, recovery study was performed by standard addition method. To the pre-analyzed tablet powder equivalent to 25 mg (labeled claim of tablet), known quantities of standard drug (80,100 and 120 % of test concentration as per ICH guidelines) were spiked separately and the total drug contents were described as per the formulation. The contents were mixed well, finally made up to the mark and filtered. The absorbances were measured at 224.5 nm using distilled water as blank and the amount of drug recovered from the formulation was calculated by the mathematical relation followed by Sane et al [6].

METHOD B - DIFFERENCE SPECTROPHOTOMETRIC METHOD

Selection of Solvent

The solubility of desvenlafaxine succinate was determined in a variety of solvents ranging from non - polar to polar using essentially a method of Schefter and Higuchi. The drug was found to be freely soluble in methanol and dimethyl formamide, soluble in water, 0.1 M hydrochloric acid, 0.1 M sodium hydroxide, 0.01 M Sodium hydroxide, 10 % glacial acetic acid and acetate buffer pH 4, slightly soluble in chloroform, sparingly soluble in ethanol, very slightly soluble in n-hexane and n-butane. Since the drug was stable in 0.01 M Sodium hydroxide and 0.1 M Hydrochloric acid were found to be stable for 5 hours and 5 hours 30 minutes respectively. Freshly prepared 0.01 M Sodium hydroxide and 0.1 M Hydrochloric acid were selected as the solvents for final dilution.

Preparation of standard stock solution

10 mg of desvenlafaxine succinate was weighed separately and dissolved in 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide separately. The solutions were made up the volume to 10 mL in a volumetric flasks with 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide separately to get the concentration of 1000 µg/mL.

Selection of λmax and stability studies

The standard stock solution were further diluted with 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide separately to get 10 µg/mL of concentration (1 mL to 100 mL). The solution was scanned between 200 and 400 nm. The difference spectrum of desvenlafaxine succinate in 0.01 M Sodium hydroxide was recorded by taking desvenlafaxine succinate in 0.1 M Hydrochloric acid solution as blank. The difference spectrum was showed that the maxima at 240 nm and minima at 224.5 nm (Figure 2). Stability studies were performed and desvenlafaxine succinate in 0.01 M Sodium hydroxide and 0.1 M Hydrochloric acid were found to be stable for 5 hours and 5 hours 30 minutes respectively.

Preparation of working standard solution

20 mg of desvenlafaxine succinate was weighed separately and dissolved in 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide separately. The solutions were made up the volume to 50 mL in a volumetric flasks with 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide separately to get the concentration of 400 µg/mL.

Calibration graph and linearity

In this method, different aliquots (1 - 5 mL) were taken separately from their working standard solutions and diluted with 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide separately to prepare a series of concentrations from 8 - 40 µg/mL as reference and test solutions respectively. Difference in absorbance between 224.5 nm and 240 nm was calculated to find out the amplitude. The calibration curve was prepared by plotting amplitude versus concentration.

Quantification of formulation

Twenty tablets of formulation (Ventab Dxt 50) containing 50 mg of desvenlafaxine were accurately weighed to find out the average weight and powdered. The powdered tablets equivalent to 20 mg of desvenlafaxine succinate was weighed separately and transferred into two 50 mL volumetric flasks, extracted with 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide separately and made up to the volume with 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide respectively. The solutions were filtered separately through Whatman filter paper No. 41. From the stock solutions, 24 µg/mL of solutions were prepared separately by using 0.1 M Hydrochloric acid and 0.01 M Sodium hydroxide. The amplitude was calculated by measuring the absorbances at 224.5 nm and 240 nm in the difference spectrum. This procedure was repeated for six times. The amount of desvenlafaxine succinate present in formulation was calculated from the slope and intercept of respective calibration curve.

Recovery studies

To determine the accuracy of the method, recovery study was performed by standard addition method. To the pre-analyzed tablet powder equivalent to 15 mg (labeled claim of tablet), known quantities of standard drug (80,100 and 120 % of test concentration as per ICH guidelines) were spiked separately and the total drug contents were described as per the formulation. The contents were mixed well, finally made up to the mark and filtered. The amplitude was calculated by measuring the absorbances at 224.5 nm and 240 nm in the difference spectrum and the amount of drug recovered from the formulation was calculated by the mathematical relation followed by Sane et al.

Statistical Validation [7]

The obtained results were treated for statistical validation parameters like Standard Deviation (S.D.) and Percentage Relative Standard Deviation (% R.S.D.).

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RESULTS AND DISCUSSION

The proposed methods for the estimation of desvenlafaxine succinate in tablet dosage form were found to be simple and sensitive. In the UV spectrophotometric method, the solvent used was distilled water and showed λmax at 224.5 nm. This is shown in Figure 1, with linearity range of 5 - 40 µg/mL. In the difference spectrophotometric method, the measured value is the difference in absorbance (ΔA) between two molar solutions of the analyte in different chemical forms which exhibit different spectral characteristics. The difference spectrum of desvenlafaxine succinate in 0.01 M Sodium hydroxide was recorded by taking desvenlafaxine succinate in 0.1 M Hydrochloric acid solution as blank. The difference spectrum showed that the maxima at 240 nm and minima at 224.5 nm. This is shown in Figure 2, with linearity range of 8 - 40 µg/mL. Beer's law limits, Sandell's sensitivity [8], Molar extinction coefficient, Correlation coefficient, Regression equation, Slope, Intercept, Limit of Detection and Quantification [9], Standard error of mean were performed for the methods A and B and results are shown in Table 1.

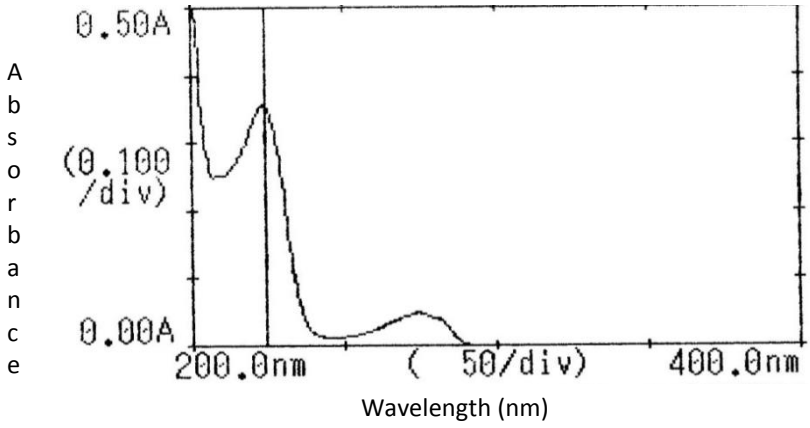

Figure 1: UV Spectrum of desvenlafaxine succinate

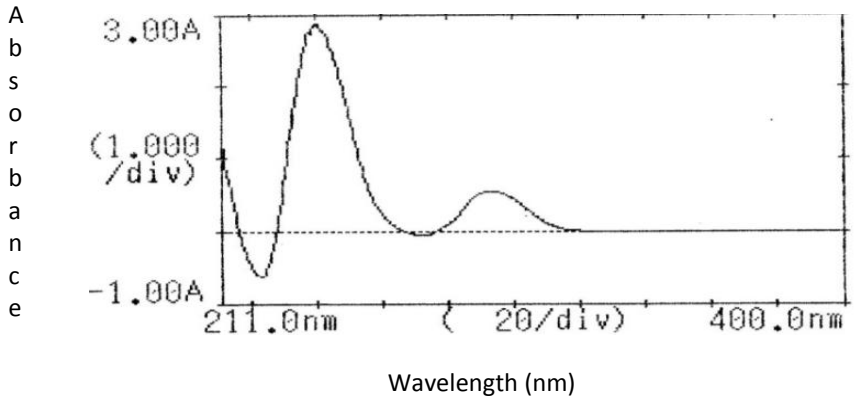

Figure 2: Difference Spectrum of desvenlafaxine succinate

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Table 1: Optical characteristics of Desvenlafaxine succinate

S.No.	Parameters	Method A	Method B
1.	λmax (nm)	224.5	240 and 224.5
2.	Beer's law limits (µg/mL)	5 - 40	8 - 40
2.	Sandell's sensitivity (µg/cm^2/0.001 A.U.)	0.045036462	0.030266719
3.	Molar extinction coefficient (l mol^{-1} cm^{-1})	12463.9698	18652.0931
4.	Correlation coefficient (r)	0.99992	0.99994
5.	Regression equation (Y = mx + c)	Y = 0.0222x + 0.0015	Y= 0.0330x + 0.0034
6.	Slope (m)	0.0222	0.0330
7.	Intercept (c)	0.0015	0.0034
8.	Limit of Detection (µg/mL)	0.524356882	0.19578768
9.	Limit of Quantification (µg/mL)	1.588960247	0.59329602
10.	Standard error of mean	0.000656536	0.00082405

The assay for brand of desvenlafaxine succinate by UV - spectrophotometric method for Ventab Dxt 50 was found to be 99.54 ± 0.64574 and by difference spectrophotometric method for Ventab Dxt 50 was found to be 100.58 ± 0.59607. The results are shown in Table 2.

Table 2: Results of analysis of commercial formulation

Drug	Method	Sample No.	Labelled Amount (mg/tab)	Amount found (mg/tab)	Percentage obtained (%)	Average	S. D.	% R. S. D.	S. E.
Ventab Dxt 50	Method A	1	50	49.520	99.04	99.54 %	0.64574	0.6486	0.01793
		2	50	50.155	100.31				
		3	50	49.436	98.87				
		4	50	49.500	99.00				
		5	50	50.078	100.15				
		6	50	49.951	99.10				
	Method B	1	50	49.997	99.99	100.58 %	0.59607	0.5926	0.01655
		2	50	50.138	100.27				
		3	50	50.796	101.59				
		4	50	50.069	100.13				
		5	50	50.457	100.91				
		6	50	50.305	100.61				

The recovery studies results by UV - spectrophotometric method for Ventab Dxt 50 was found to be 99.71 % and by difference spectrophotometric method for Ventab Dxt 50 was

found to be 101.17 %. The results are shown in Table 3. The values of co-efficient of variance were satisfactorily low and recovery was close to 100 % indicating reproducibility of the methods. The excipients in the formulation did not interfere in the accurate estimation of desvenlafaxine succinate in tablet dosage form.

Table 3: Results of Recovery studies

Method	Percentage recovery (%)	Average	S. D.	% R. S. D.	S. E.
Method A	99.12	99.71 %	0.52548	0.52699	0.05838
	99.90				
	100.12				
Method B	101.30	101.17 %	0.10692	0.10568	0.01188
	101.12				
	101.11				

From the results, both the methods is economical, rapid and do not require any sophisticated instruments contrast to chromatographic method. Hence it can be effectively applied for the routine analysis of desvenlafaxine succinate in bulk and in tablet dosage form. The methods were validated in terms of intraday and interday precision. The validation data are given in Table 4.

Table 4: Validation data of Intraday and Interday precision

Method	Intraday				Interday			
	% labeled claim*	S. D.	% R.S.D.	S. E.	% labeled claim*	S. D.	% R.S.D.	S. E.
Method A	99.06	0.50350	0.50828	0.05594	99.40	0.42895	0.43154	0.04766
Method B	100.30	0.47217	0.47074	0.05246	100.15	0.49974	0.49896	0.05552

* - Mean of six observations

CONCLUSION

The Standard Deviation, % R.S.D. and Standard Error were calculated for both the methods are low, it indicating high degree of precision of the methods. The % R.S.D. is also less than 2 % as required by ICH guidelines. The results of the recovery studies were performed at three levels (80,100 and 120 % of the test concentration as per ICH guidelines) shows the high degree of accuracy of the proposed methods. Hence the developed methods are simple, rapid, precise, accurate, cost effective and can be employed for the routine analysis of desvenlafaxine succinate in both bulk and tablet dosage form.

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