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Development and validation of analytical methods for estimation of desvenlafaxine succinate in bulk and solid dosage forms by UV spectroscopy

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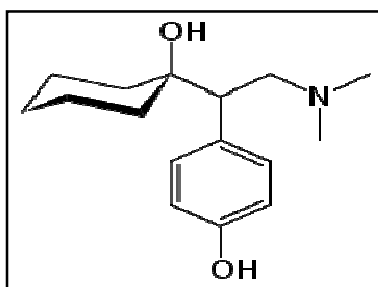
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ABSTRACT

Desvenlafaxine succinate is a serotonin-nor epinephrine reuptake inhibitor. The drug is commercially available as tablets for oral administration. In the present work, an attempt has been made to develop two rapid, precise and accurate spectrophotometric methods for the estimation of Desvenlafaxine succinate in bulk and dosage form. Method A is first order derivative spectroscopy where derivative amplitudes were calculated by considering minima and maxima of the curve. Method B is area under the curve in which wavelength range 215-230nm was selected for estimation of Desvenlafaxine succinate. Linearity was observed in the concentration range 10-50 μ g/ml for both the methods ($r^2=0.9996$ for method A and $r^2=0.9995$ for method B). The results of analysis have been validated statistically, which confirm the accuracy and reproducibility of the methods. All the methods were found to be simple, precise and accurate and can be employed for routine quality control analysis of Desvenlafaxine succinate in bulk as well as in its solid dosage form.

Keywords: Desvenlafaxine succinate, UV-spectrophometry, first order derivative spectroscopy, area under the curve.

INTRODUCTION



IUPAC name: RS-4-[2-dimethylamino-1-(1-hydroxycyclohexyl) ethyl] phenol succinate monohydrate.

Desvenlafaxine Succinate (DVS) is synthetic form of the major active metabolite of venlafaxine, and acts as a serotonin and nor epinephrine reuptake inhibitor (SNRI).[1] blocks the transporter "reuptake" proteins for key neurotransmitters affecting mood, thereby leaving more active neurotransmitters in the synapse. The desvenlafaxine succinate in solid dosage form is used as an antidepressant drug.

Literature survey reveals that only two spectrophotometric methods [2], [3] and one HPLC method [4] is reported in single dosage form of Desvenlafaxine succinate. However no derivative method and area under curve method is

reported so far for Desvenlafaxine succinate in single dosage form. The present work aims at developing UV method (derivative method and area under curve method) for analysis of drug in bulk and solid dosage form.

MATERIALS AND METHODS

Instrumentation: For the present study JASCO double beam UV/Visible spectrophotometer (Model V-630) was used with slit width fixed at 1.5nm, equipped with spectra manager software (Version 1.5), a pair of 1-cm matched quartz cells was used to measure the absorbance of solution. The samples were weighed on electronic analytical balance (Contech Model CB-50).

Materials: Gift samples of desvenlafaxine succinate were provided by Emcure Pharmaceuticals Limited, Pune, India. The pharmaceutical dosage form used in this study was VENTAB DXT 100 tablets (Intas Pharmaceuticals Pvt. Ltd). Each uncoated extended release tablet contains 100mg of desvenlafaxine succinate.

Solvent : distilled water

Preparation of Standard Stock Solution

Standard stock solution of desvenlafaxine succinate was prepared by dissolving 100mg of desvenlafaxine succinate in 100ml volumetric flask with distilled water and final volume was made upto 100ml with distilled water to get working standard stock solution containing 1000 μ g/ml of desvenlafaxine succinate and further dilutions were made with distilled water.

METHOD A -FIRST ORDER DERIVATIVE SPECTROSCOPY

1. Calibration curve for desvenlafaxine succinate

From the standard stock solution, appropriate dilutions were made to obtain concentration in range of 10-50 μ g/ml. Absorbance measured at first order derivative spectrum is characterized by a maximum and minimum and a cross over point at λ_{max} of absorption band. Further the absorbance difference at $n=1$ ($dA/d\lambda$) was calculated by the inbuilt software of the instrument which was directly proportional to the concentration of the standard solution. The calibration curve of $dA/d\lambda$ versus concentration was plotted. (Figure 1)

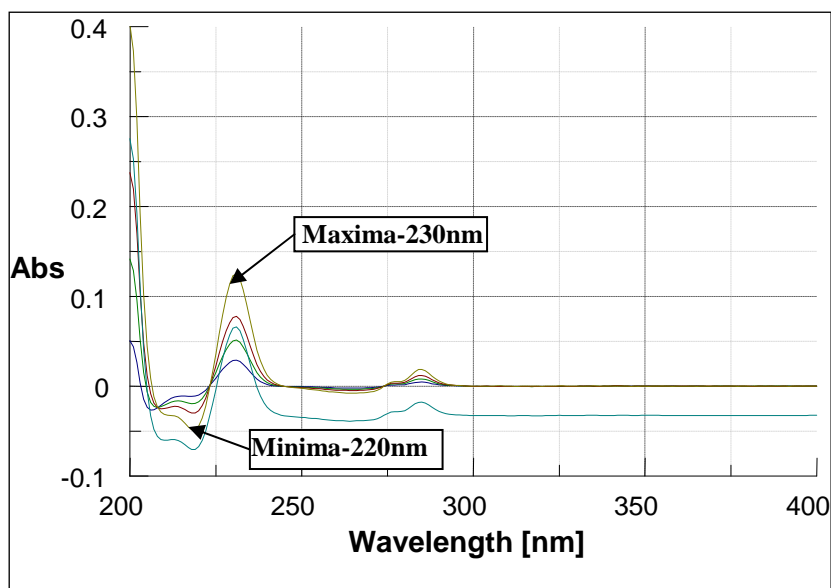


Figure 1: Overlay spectra of desvenlafaxine succinate for first order derivative method.

2. Analysis of marketed formulation

Tablets were procured from local market and average weight was determined. The tablets were crushed and powdered in glass mortar. For the analysis of drugs, quantity of powder equivalent to 100mg of desvenlafaxine succinate was transferred to 100ml volumetric flasks and dissolved in sufficient quantity of distilled water. It was sonicated for 45 minutes and then filtered through whatmann filter paper # 42. The filtrate was appropriately diluted with distilled water to give standard stock solution of 1000 μ g/ml. Further dilutions were made using distilled water to get required concentration. In first order derivative spectroscopy, derivative amplitude was determined directly from calibration plot by measuring difference between absorbance maxima at 230 nm and minima at 220 nm (i.e. $dA/d\lambda$) (table no. 1).

METHOD B -AREA UNDER CURVE**1) Calibration curve for desvenlafaxine succinate**

For the selection of analytical wavelength standard solutions of desvenlafaxine succinate were prepared and series of dilutions of standard solutions of desvenlafaxine succinate were prepared by using distilled water and were scanned from 200 to 400nm. From the spectra of drug obtained after scanning of standard solution of desvenlafaxine succinate area under the curve in the range of 215 nm-230nm was selected for the analysis, the calibration curve was plotted with concentration versus area under the curve and regression equation was calculated. (Figure.2)

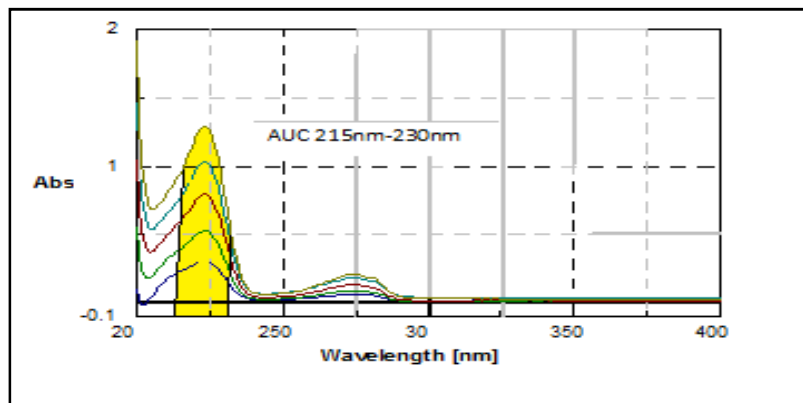


Figure 2: Overlay spectra of desvenlafaxine succinate for area under the curve method.

2. Analysis of marketed formulation

Tablets were procured from local market and average weight was determined. For the analysis of drugs, quantity of powder equivalent to 100mg of desvenlafaxine succinate was transferred to 100ml volumetric flasks and dissolved in sufficient quantity of distilled water. It was sonicated for 45 minutes and then filtered through whatmann filter paper # 42. The filtrate was appropriately diluted with distilled water to give standard stock solution of 1000 µg/ml. Further dilutions were made using distilled water to get required concentration. Area in the range of 215 nm-230nm was measured and content was calculated (table no. 1)

Table No. 1: Result of marketed formulation analysis

Method	Label claim(mg)	%Label Claim*(Mean±SD)	%RSD*
First order derivative	10	101.4±0.7874	0.78
Area under curve	10	101.95±0.9565	0.94

* Average of three determinations

Accuracy studies:

Accuracy studies were carried out by standard addition method. Pure Desvenlafaxine succinate was added at different levels i.e. 80%, 100% and 120% to pre analyzed sample solution. 100mg of Desvenlafaxine succinate was accurately weighed and transferred into a 100ml volumetric flask. This was dissolved in distilled water and volume was made up to 100ml to give standard stock solution of 1000µg/ml. To 1ml tablet stock solution in 3 different volumetric flask, aliquots of 0.8 ml, 1ml and 1.2ml of standard stock solution were added, volume was made up to 100ml with distilled water to give concentration of 18µg/ml (80%), 20µg/ml (100%) and 22µg/ml (120%). These were analyzed by first order derivative and area under the curve method. Procedure was repeated 3 times for 80%, 100% and 120% of level for recovery studies. The results are discussed in (table no. 2).

Table No.2: Results of recovery studies

Level Recovery	Conc. Of Drug in µg/ml		Method A *			Method B*		
	Drug taken	Std drug added	% recovery	SD	% RSD	% Recovery	SD	% RSD
80	10	8	99.95	0.4330	0.43	101.10	0.1960	0.19
100	10	10	102.0	0.148	0.99	100.70	0.4445	0.44
120	10	12	101.48	0.4858	0.83	102.17	1.5545	1.52

* Average of three determinations

Validation:

The developed method was validated as per ICH (ICH Q2B) guidelines [5]

Linearity:

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of desvenlafaxine succinate. The Beer's law was obeyed in the concentration range 10-50 µg/ml. The correlation coefficient was found to be 0.9996 and 0.99956 for method A and method B respectively.

Precision:

100mg of Desvenlafaxine succinate was weighed accurately and dissolved in 100ml of distilled water to give concentration of 1000µg/ml. From the standard stock solution appropriate quantity of solution was taken further dilutions were made with distilled water to give 10µg/ml. This procedure was repeated six times for each method individually. (Table No.3 & 4)

Table No.3: Inter-day and intra-day precision studies for first order derivative method

Parameter	%Mean *	± S.D.	%RSD	±S.E.
Interday	100.45	1.3111	1.31	0.5352
Intraday	99.82	0.7637	0.77	0.3118

*Average of six determinations

Table No.4: Inter-day and intra-day precision studies for area under the curve method

Parameter	% Mean *	± S.D.	%RSD	±S.E.
Interday	99.69	0.3443	0.3453	0.1407
Intraday	99.33	0.2953	0.2972	0.1206

*Average of six determinations

RESULTS AND DISCUSSION

The present work describes the first order derivative method and area under curve method for the estimation of desvenlafaxine succinate in bulk and dosage form. For both the methods linearity was observed in the concentration range of 10-50 µg/ml for desvenlafaxine succinate and correlation coefficient was found to be greater than 0.999. Accuracy of proposed method was assessed by recovery studies. The results of marketed formulation analysis are found in range of 99-101%. Percent recovery for desvenlafaxine succinate by both the methods was found in the range of 98.20% to 102 % (Table No. 2). The % RSD for six determinations of tablet sample by both the methods was found to be less than 2.0 indicating the good precision of both the methods. Hence, it can be concluded that the developed spectrophotometric methods are accurate, precise and can be employed successfully for the estimation of desvenlafaxine Succinate in bulk and formulation

CONCLUSION

The two spectrophotometric methods were developed for desvenlafaxine succinate and validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed methods are within limits, indicating high degree of precision of the methods. The results of the recovery studies performed indicate the methods to be accurate. Hence, it can be concluded that the developed spectrophotometric methods are accurate, precise and can be employed successfully for the estimation of desvenlafaxine succinate in bulk and dosage form.

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