International Journal of Pharmacy and Industrial Research (IJPIR)

ISSN:2231-6567

IJPIR |Volume 12 | Issue 4 | Oct - Dec - 2022
Available online at: www.ijpir.com

Research article *Industrial Research*

Analytical method development and validation for Desvenlafaxine Succinate by UV-Visible Spectroscopy Method

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ABSTRACT

An inhibitor of serotonin-nor-epinephrine reuptake is desvenlafaxine succinate. The medication is marketed as pills to be taken orally. In the current work, an effort has been made to establish two spectrophotometric procedures that are quick, exact, and accurate for estimating desvenlafaxine succinate in bulk and dose form. First order derivative spectroscopy method A involved calculating derivative amplitudes by taking the curve's minima and maxima into account. The wavelength range 200-400nm was used for Method B's area under the curve estimation of Desvenlafaxine succinate. For both approaches, linearity was seen in the concentration range of 160 to 240µg/ml & 60-140 µg/ml (r2 = 0.9986 for method A and r2 = 0.9996 for method B). The statistical validation of the analysis' findings attests to the reliability and repeatability of the techniques. All of the procedures were determined to be easy to use, exact, and accurate, and they may all be used for routine quality control testing of desvenlafaxine succinate both in bulk and in its solid dosage form.

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

INTRODUCTION

Desvenlafaxine succinate (DVS) is a synthetic version of the main active metabolite of venlafaxine, and it functions as a serotonin and nor-epinephrine reuptake inhibitor (SNRI). It does this by blocking the transporter "reuptake" proteins for important neurotransmitters that affect mood, which results in more active neurotransmitters remaining in the synapse. Desvenlafaxine succinate is an antidepressant medication that comes in solid dose form. According to a review of the literature, only two spectrophotometric methods [2], [3], and one HPLC method [4] have been published for desvenlafaxine succinate in single dosage form. Area under the curve and no derivative methods, however, Desvenlafaxine succinate in a single dosage form has not been documented using either a derivative technique or an area under the curve method. The current work intends to create

UV methods (area under the curve and derivative methods) for drug analysis in solid dose form and bulk form.

MATERIALS AND INSTRUMENTS

Preparation of Standard solution

Precisely weigh and transfer 10mg of DESVENLAFAXINE SUCCINATE working standard into 10 ml calibrated clean and dry volumetric flask, add around 10ml of dissolvable ethanol, shake it well, for better dissolvability sonicate it. (primary stock arrangement 1000µg/ml) From the above arrangement (1^0 stock) pipette out 1ml and move it into

another 10ml volumetric flask and make up to the volume, it represents secondary stock arrangement (100µg/ml). From the 2^0 pipette out 0.1ml and make up to the volume with help of solvent it represents 1µg/ml.

MATERIALS AND INSTRUMENTS FOR FIRST ORDER DERIVATIVESPECTROSCOPY

Method Development

Preparation of Standard solution

Precisely weigh and transfer 10mg of DESVENLAFAXINE SUCCINATE working standard into 10 ml calibrated clean and dry volumetric flask, add about 10ml of solvent ethanol, shake it well, for better dissolvability sonicate it. (primary stock arrangement 1000µg/ml) From the above arrangement (1^0 stock) pipette out 2 ml and move it into another 10 ml volumetric flask and make up to the volume it gives 2^0stock arrangement (200µg/ml).

MATERIALS AND INSTRUMENTS FOR SECOND ORDER DERIVATIVESPECTROSCOPY

Method Development

Preparation of Standard solution

Precisely weigh and transfer 10mg of DESVENLAFAXINE SUCCINATE working standard into 10 ml calibrated clean and dry volumetric flask, add about 10ml of solvent ethanol, shake it well, for better dissolvability sonicate it. (primary stock arrangement 1000µg/ml) From the above arrangement (1^0 stock) pipette out 1 ml and move it into another 10 ml volumetric flask and make up to the volume it gives 2^0stock arrangement (100µg/ml).

Preparation of sample solution

Weigh 10 tablets and find the normal weight of every tablet and powder it with the help of clean motor and pestle. Measure the powder 39.498mg of Desvenlafaxine succinate and move it into a 10ml volumetric flask. Add about 10ml of the dissolvableand sonicate it to break down totally and filter if necessary and make up to the last volume. (1000µg/ml).
From the above arrangement (10 stock) pipette out 1ml move it into another 10 ml volumetric flask and make up to the volume it gives 2^0stock arrangement (100µg/ml).

Determination of maximum wavelength

A Standard concentration of the Desvenlafaxine succinate is checked in the UV region between 200-400nm for the absorption of maximum wavelength. The range of the Desvenlafaxine succinate was recorded and it has demonstrated a most wavelength of absorption at 236.40nm.

Method Trials

Based on Drug solubility different trails were finished by using distinctive solvents and concentration. Choice of appropriate solvent is conveyed as a blank arrangement.

Determination of λ max

By proper dilutions of standard arrangements with ethanol, arrangements containing 60/80/100/120/140µg/ml of desvenlafaxine succinate were filtered in the range of 200-400 nm to decide the wavelength of greatest absorbance for the drug.

Validation of analytical Method

The proposed method was validated for different parameters like linearity, precision, accuracy, specificity, robustness, Stability studies, LOD, LOQ and assay, and are discussed below.

Linearity

Preparation of standard stock solution

Prepare primary stock arrangement as above talked about way (1000µg/ml), from thisarrangement pipette out 1ml and make up to the volume with solvent, it represents 100µg/ml. From the above standard arrangement, a few working standard arrangements are set up by serial dilution technique. Correlation coefficient should not be < 0.999.

Precision

Weigh 39.498mg of tablet powder which is comparable to 10 mg of desvenlafaxine succinate, and move it into a 10ml volumetric flask. Add about 10ml of the solvent and sonicate it to disintegrate totally and filter if necessary and make upto the last volume. (1000µg/ml). From the above arrangement (1^0 stock) pipette out 1ml move it into another 10 ml volumetric flask and make up to the volume it gives 2^0stock arrangement (100µg/ml). The grouping of the arrangement was 100µg/ml (working solution). The absorbance is calculated for six examples at most wavelength.The %RSD is calculated forintraday accuracy and inter day exactness and the intra day and inter day accuracywere calculated. The %RSD responses of six samples should not be > 2.

Accuracy

Preparation of 50% solution

From the secondary stock arrangement pipette out 0.5ml of the arrangement into a 10 ml volumetric flask and make up to the last volume. Also, make 6 tests of a similar concentration.

Preparation of 100% solution

From the secondary stock arrangement pipette out 1ml of the arrangement into a 10 ml volumetric flask and make up to the last volume. Also, make 3 tests of a similar concentration.

Preparation of 150% solution

From the secondary stock arrangement pipette out 1.5ml of the arrangement into a 10 ml volumetric flask and make up to the last volume. Also, make 6 tests of a similar concentration, and the results were tabulated in table.
The % Mean recovery and its %RSD were calculated.

Amount Recovered = Amount found – Amount added
% Recovery = Amount recovered ÷ Amount added × 100

Acceptance criteria

The %Recovery and the mean %Recovery should be in the range from 99.0 – 102.0%
%RSD should not be > 2.

Limit of Detection

It is figured by ICH suggestions where the approach depends on the standard Deviation/Slope. Incline is gotten from the linearity chart. The standard Deviation/Slope esteem 1.88µg/ml for Desvenlafaxine succinate considered for figuring LOD.

Limit of Quantification

It is figured by ICH proposals where the approach depends on the Standard Deviation/Slope. Incline is acquired from the linearity chart. The standard Deviation/Slope esteem 6.26µg/ml for Desvenlafaxine succinate is considered for figuring LOQ.

RESULTS AND DISCUSSION

The present work is aimed at the analytical method development and validation for the selected drug by UV-VISIBLE SPECTROSCOPIC METHOD.

Selection of absorption maximum

The sensitivity of the UV-Visible method depends upon the proper selection ofabsorption maximum.

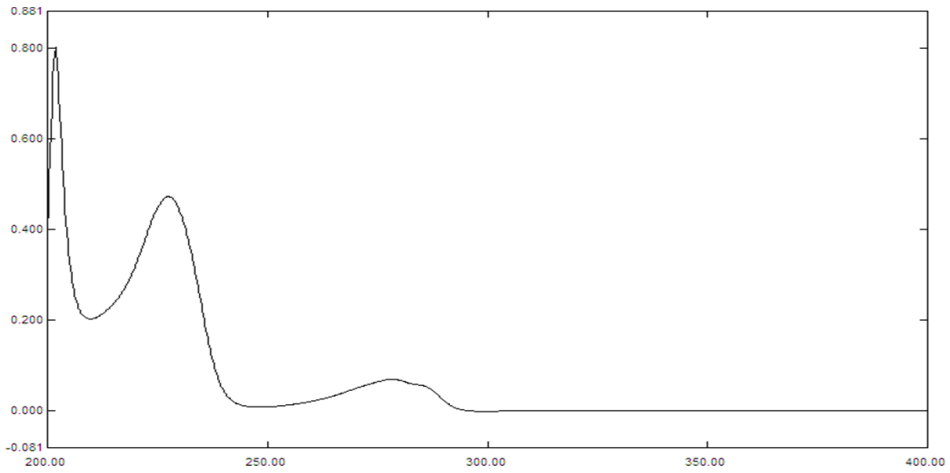

Fig 1: API spectrum of DS

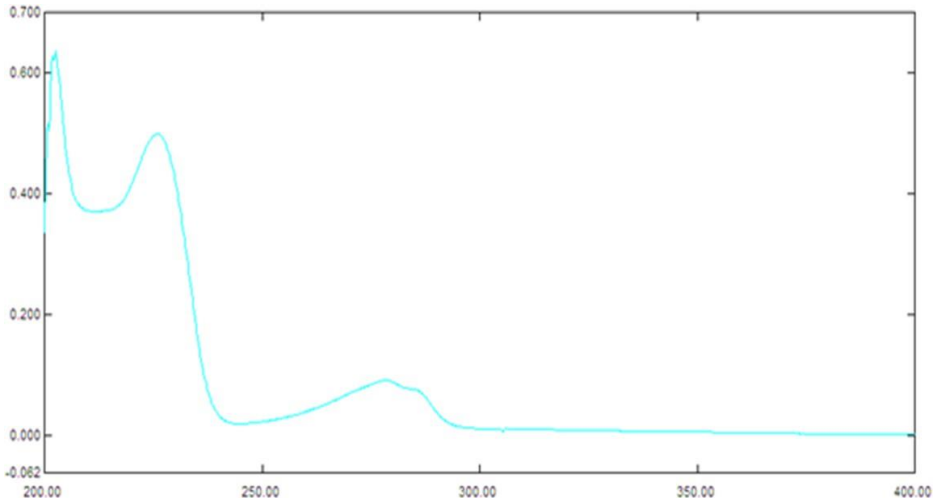

Fig 2: Spectrum of DS tablet

Table 1: Selection of wavelength at Absorption maxima

S.no	Type	Wavelength(nm)	Absorbance
1	Standard	227.40	0.472
2	Test	227.40	0.470

The absorption maximum of DS was found to be 227.40nm, in Ethanol.

Table 2: Method development

Parameters	Description
Solvent	Ethanol
Wavelength	227.40nm
Concentration volume	1µg/ml
Temperature	30°C

Table 3: Linearity

S.no.	Linearity Level	Concentration(µg/ml)	Absorbance
1.	10	0.1	0.051
2.	55	0.55	0.18
3.	100	1.00	0.352
4.	150	1.5	0.528
5.	200	2.00	0.68

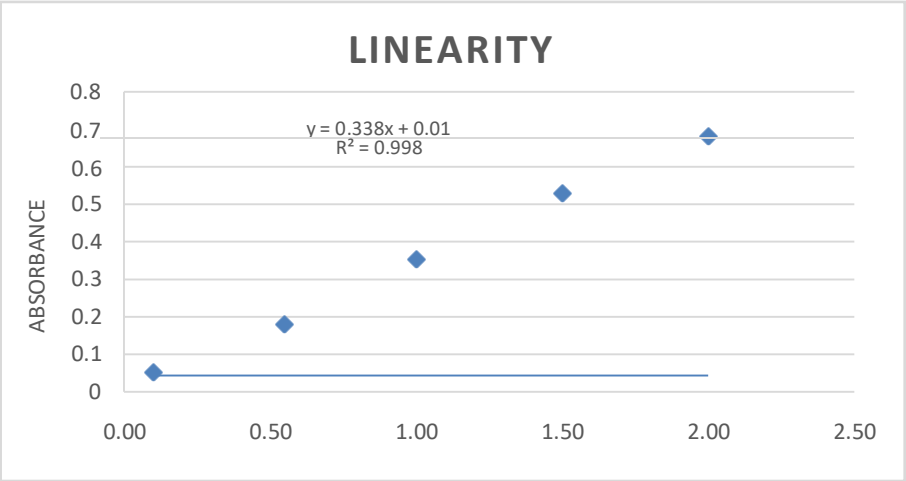

Fig 3: Linearity of DS by UV-Visible spectroscopic method

Specificity

Specificity of this proposed method does not shows any interference with solvent and excipients in API and Tablet dosage form, Following Figures shows the results

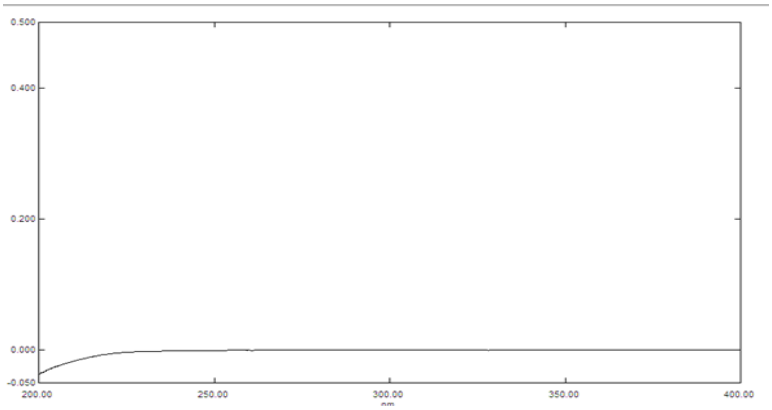

Fig 4: Blank spectrum by UV-Visible spectroscopic method.

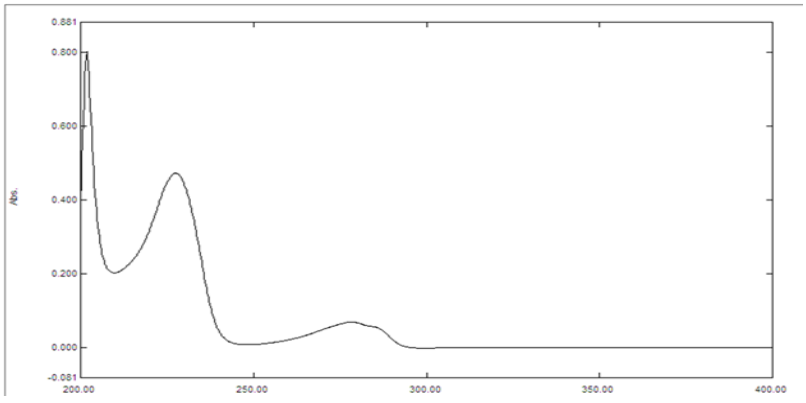

Fig 5: specificity spectrum of API by UV-Visible spectroscopicmethod.

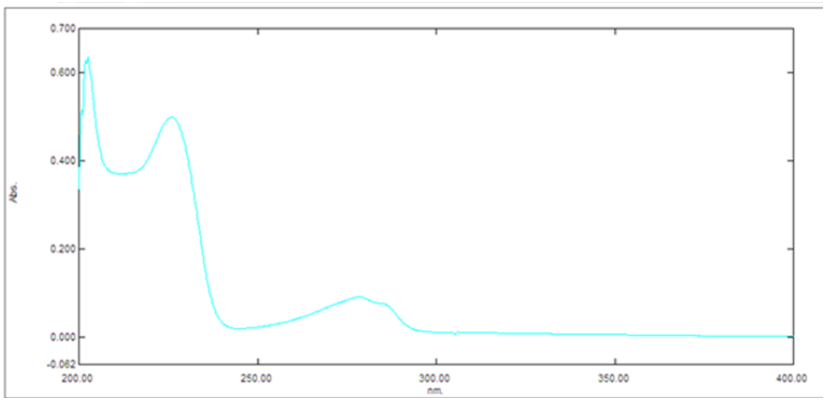

Fig 6: Specificity spectrum of Tablet by UV-Visible spectroscopic method.

Precision

According to ICH guidelines Inter day and Intraday was performed in 3 consecutive days & 3 times in a same day and %RSD in all the cases were found to beless than 2,

Table 4: Inter day Precision

S. No	Day 1		Day 2		Day 3	
	Absorbance	% Assay	Absorbance	% Assay	Absorbance	% Assay
1	0.469	99.36	0.469	99.36	0.468	99.15
2	0.468	99.15	0.471	99.79	0.471	99.79
3	0.471	99.79	0.47	99.58	0.468	99.15
4	0.470	99.58	0.468	99.15	0.471	99.79
5	0.469	99.36	0.47	99.58	0.469	99.36
6	0.471	99.79	0.469	99.36	0.47	99.58
Average	0.47	99.51	0.47	99.47	0.47	99.47
Std dev	0.001	0.26	0.001	0.22	0.001	0.29
% RSD	0.26	0.26	0.22	0.22	0.29	0.29

Table 5: Intraday Precision

S. No	9.30 AM		1.30 PM		5.30 PM	
	Absorbance	% Assay	Absorbance	% Assay	Absorbance	% Assay
1	0.468	99.15	0.466	98.73	0.469	99.36
2	0.470	99.58	0.471	99.79	0.466	98.73
3	0.469	99.36	0.469	99.36	0.47	99.58
4	0.471	99.79	0.47	99.58	0.466	98.73
5	0.468	99.15	0.465	98.52	0.469	99.36
6	0.466	98.73	0.467	98.94	0.469	99.36
Average	0.47	99.29	0.47	99.15	0.47	99.19
Std dev	0.002	0.37	0.002	0.50	0.002	0.36
% RSD	0.37	0.37	0.51	0.51	0.37	0.37

Accuracy

According to ICH guide lines, Accuracy was carried out by three differentconcentration levels & % Recovery was calculated. In this case it was found withinthe limits 98-102%. Table Shows the results of Accuracy.

Table 6: Accuracy

S. No	Accuracy Level	Wt. of Sample(mg)	Absorbance	Amount Added(µg/ml)	Amount Found (µg/ml)	% Recovery	Mean % Recovery
1	50%	19.749	0.233	49.72	49.36	99.29	98.87%
2		19.749	0.235	49.72	49.79	100.15	
3		19.749	0.231	49.72	48.94	98.44	
4		19.749	0.233	49.72	49.36	99.29	
5		19.749	0.23	49.72	48.73	98.02	

6		19.749	0.229	49.72	48.74	98.04	
7	100%	39.498	0.469	99.43	99.36	99.93	100.01%
8		39.498	0.471	99.43	99.79	100.36	
9		39.498	0.468	99.43	99.15	99.72	
10	150%	59.247	0.697	149.15	147.67	99.01	99.15%
11		59.247	0.698	149.15	147.88	99.15	
12		59.247	0.695	149.15	147.25	98.73	
13		59.247	0.699	149.15	148.09	99.29	
14		59.247	0.70	149.15	148.31	99.44	
15		59.247	0.699	149.15	148.09	99.29	

LOD & LOQ

LOD & LOQ was calculated from the slope and standard deviation of linearity graph, LOD & LOQ values must be Less than 3 & Less than 10respectively. In this case, it was found to be less than 3 & 10, Table No: 7.7 Shows the LOD & LOQ results.

Table 7: LOD & LOQ

Parameter	Result
Slope	0.3381
Std dev	0.0012
LOD	0.01(µg/ml)
LOQ	0.04(µg/ml)

Robustness

Robustness was carried out by two different parameters and % RSD should be less than 2. In this case it was found to be within the limits, Table shows the results of Robustness.

Table 8: Robustness

S. No	Parameter	Condition	Absorbance	% Assay
1	Wavelength	227.40nm	0.469	99.36
2		230.00nm	0.47	99.58
3		225.00nm	0.469	99.36

Degradation Studies

Degradation studies were carried out in 5 different Conditions. The % Degradation should not be more than 10%. In this study it was less than 10%. Table No: 7.9 shows the results of Degradation studies.

Table 9: Degradation Studies

S. No	Condition	Absorbance	% Assay	% Degradation
1	Acid (HCl)	0.425	90.04	9.96
2	Base (NaOH)	0.432	91.53	8.47
3	Hydrogen peroxide(H_2O_2)	0.429	90.89	9.11
4	UV	0.431	91.31	8.69
5	Heat	0.435	92.16	7.84

SUMMARY

Zero order, Visible, First order and Second order spectroscopic methods were developed and validated as per ICH guidelines. All the methods were found to besimple, sensitive, precise and accurate. These methods were tabulated with one another in table

Table 10: Summary of results

Parameter	UV-Spectroscopy	Visible – Spectroscopy	Firstorder	Secondorder
Wavelength	227.40nm	724nm	237.60nm	236.40nm
Concentration range(µg/ml)	0-2µg/ml	0.9-18µg/ml	160-240µg/ml	60-140µg/ml
Linearity	0.9982	0.9995	0.9986	0.9996
Assay	99.576	99.39	99.6	100
Inter-dayprecision	0.57	0.51	0.43	0.81
Intra-dayprecision	0.41	0.52	0.55	0.57
Accuracy	99.34%	98%	99.98%	99.39%
LOD(µg/ml)	0.01µg/ml	0.16µg/ml	2.91µg/ml	1.88µg/ml

LOQ(µg/ml)	0.04 µg/ml	0.53 µg/ml	9.70 µg/ml	6.26µg/ml

CONCLUSION

An attempt was made to develop and validate different UV-Spectrophotometric methods for the estimation of Desvenlafaxine succinate in bulk and pharmaceutical dosage form.The proposed Spectrophotometric methods were found to be simple, accurate, precise and rapid. By comparing the results of both UV & Visible spectroscopic methods. I found to be less accurate and precise than the first derivative zero crossing method.All the Spectrophotometric methods can be successfully utilized for the estimation of Desvenlafaxine succinate in the pharmaceutical dosage form without any prior separation of drug from the excipient matrix. So, these methods can be routinely used for the estimation of Desvenlafaxine succinate in bulk and its dosage forms.

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