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Research Article

NOVEL SPECTROPHOTOMETRIC METHODS FOR THE QUANTIFICATION OF DESVENLAFAXINE IN PURE AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

Objectives: Two simple, sensitive and economic spectrophotometric methods are developed for the determination of desvenlafaxine in pure and its pharmaceutical formulations.

Methods: The developed methods are based upon the reaction of oxidative coupling of desvenlafaxine with 3-methyl-2-benzthiazolinonehydrazone (MBTH) (Method A) and 2, 2' bipyridyl (Method B) in the presence of ferric chloride. The colored complex produced was measured at 663 nm, 522 nm for method A and B respectively against the reagent blank. The optimum experimental parameters for the color productions are selected.

Results: Beer's law is valid within a concentration range of 20-100 µg/ml and 5-25 µg/ml and for method A, B respectively. The percentage recoveries were found in the range of 99.47±0.1789 for method A and 100.08±0.144 for method B. The limit of detection and limit of quantification were found to be 0.825 µg/ml and 2.5 µg/ml respectively for method A and 0.1061 µg/ml and 0.321 µg/ml for method B respectively.

Conclusion: The developed methods are applied for the determination of desvenlafaxine in bulk and its pharmaceutical formulations without any interference from excipients.

Keywords*:* Spectrophotometric, Desvenlafaxine, Oxidative coupling, 3-methyl-2-benzthiazolinone hydrazone, 2, 2- bipyridyl, $FeCl_3$.

INTRODUCTION

Desvenlafaxine is chemically, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl) ethyl] phenol succinate hydrate (Fig. 1). It is an antidepressant of the serotonin-nor epinephrine reuptake inhibitor class. Desvenlafaxine is a synthetic form of the isolated major active metabolite of venlafaxine and is grouped as a serotonin nor epinephrine reuptake inhibitor [1]. Literature survey reveals some methods for quantitative analysis of desvenlafaxine. The methods adapted to the analysis of desvenlafaxine include high-performance liquid chromatography (LC) [2-5], spectrophotometric [6-12], LC-ultraviolet (UV) and LC-mass spectrometry [13]. The present study describes simple, rapid, accurate and reproducible methods for the estimation of desvenlafaxine in tablet formulation.

2, 2 bi-pyridyl and 3-methyl-2-benzthiazolinonehydrazone (MBTH) have been used as derivatizing reagent for the spectrophotometric determination of many pharmaceutical amines [14,15]. However, the reaction of MBTH reagent and 2, 2 bi-pyridyl with desvenlafaxine has not been investigated so far. The present study describes the evaluation of 2, 2-bipyridyl and MBTH as derivatizing reagents in the development of simple and fast spectrophotometric method for the determination of desvenlafaxine in its pharmaceutical dosage forms.

METHODS

Equipment

A shimadzu UV-visible spectrophotometer model 1800 with 1 cm matched quartz cell was used for the absorbance measurements. The systonics electronic balance was used for weighing the samples.

Reagents and solutions

All employed chemicals were of analytical grade and distilled water was used throughout the experiment. Desvenlafaxine pure sample was obtained as a gift sample from R L FINE Chemicals, Bengaluru, India.

MBTH 0.5% (w/v)

0.5 g of MBTH reagent was accurately weighed transferred into a 100 ml calibrated volumetric flask, dissolved in distilled water, and made up the volume to the mark to obtain a solution of 0.5% (w/v).

2, 2'bi-pyridyl 0.2% (W/V)

200 mg of 2,2' bi pyridyl reagent was accurately weighed transferred into 100 ml calibrated volumetric flask, dissolved in distilled water, made up the volume to the mark to obtain 0.2% (w/v).

Ferric chloride (1%)

It was prepared by dissolving 1 g of ferric chloride in 100 ml of distilled water.

Standard solutions

Desvenlafaxine stock solution (1000 µg/ml) was prepared by dissolving 100 mg of drug in 100 ml of methanol. Working solutions of the drug were prepared by dilution of the stock solution. The marketed tablets form of desvenlafaxine used in the determination was with a labeled strength of 50 mg.

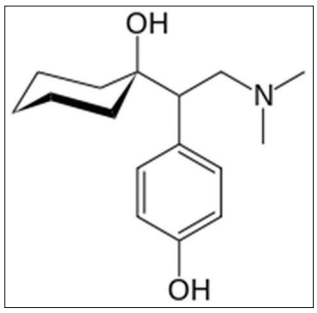

Fig. 1: Chemical structure of desvenlafaxine

Analytical method development

Method A

Standard solutions of desvenlafaxine in methanol, having final concentrations in the range of 20-100 µg/ml were transferred into a series of 10 ml volumetric flasks. To each 2 ml of MBTH, 2 ml of ferric chloride was added, and the volume was made up to mark with distilled water and allowed to stand for 20 minutes. The absorbance of each solution was measured at 663 nm against the reagent blank. The colored species was stable for 2 hrs and the amount of drug in the sample was computed from its calibration curve represented in Fig. 2. Overlain spectrum was represented in Fig. 3.

Method B

In method B, different aliquots of stock reference solution (1000 µg/ml) from 5 to 25 µg/ml were transferred into a series of 10 ml standard flasks. To each flask 0.5 ml of ferric chloride and 1.5 ml of 2,2' bi-pyridyl were added and kept in a water bath (60±1°C) for 15 minutes, then immediately cooled to room temperature (25±1°C) using a cold water. The absorbance of each solution was measured at 522 nm against the reagent blank. The amount of drug in the sample was computed from its calibration curve represented in Fig. 4 and overlain spectrum was represented in Fig. 5.

Quantification

The limits of the Beer's law, the molar absorptivity and the Sandell's sensitivity values were evaluated and are given in Table 1. Regression analyses of the Beer's law plots at their respective λmax values revealed a good correlation. Graphs of absorbance versus concentration showed zero intercepts and are described by the regression equation, y=bx+c (where y is the absorbance of a 1 cm layer, b is the slope, c is the intercept and x is the concentration of the drug in µg/ml) obtained by the least-squares method. The results are summarized in Table 1.

Procedure for analysis tablets

Twenty tablets were weighed accurately and ground into a fine powder. An amount of powder equivalent to 10 mg of desvenlafaxine was weighed and transferred in to a 100 ml volumetric flask, 50 ml of the distilled water was added and sonicated for 15 min, then the volume was made up to the mark with the same solvent, mixed well and filtered using a Whatman filter paper No. 41. The assay of the tablets was carried out according to the general procedure.

Table 1: Optical characteristics and validation data of desvenlafaxine

Parameters	Method A	Method B
λmax	663 nm	522 nm
Linearity (µg/ml)	20-100	5-25
Regression coefficient	0.967	0.9745
Wave length	663 nm	522 nm
LOD (µg/ml)	0.825	0.1061
LOQ (µg/ml)	2.5	0.321
Molar absorptivity (L/mol/cm)	1.0535×10^3	5.1095×10^3
Sandell' sensitivity (mg cm^{-2} per absorbance unit)	0.1470 A.U	0.02840 A.U

LOD: Limit of detection, LOQ: Limit of quantification

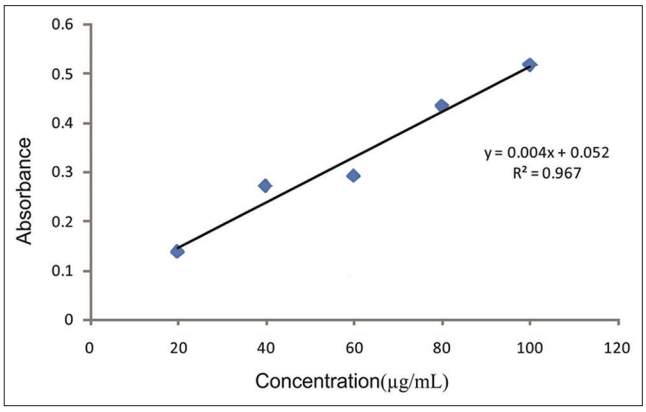

Fig. 2: Calibration curve of desvenlafaxine (method A)

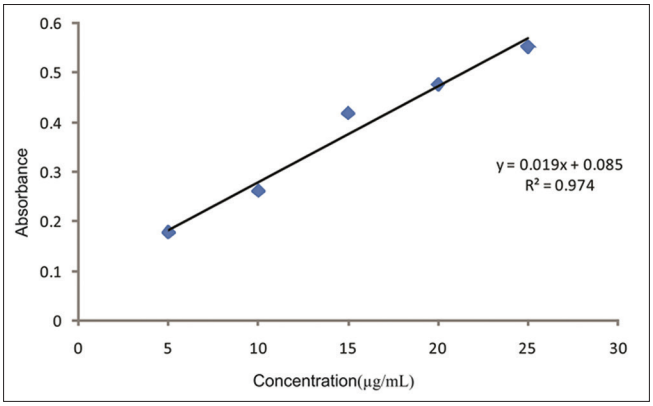

Fig. 4: Calibration curve of desvenlafaxine (method B)

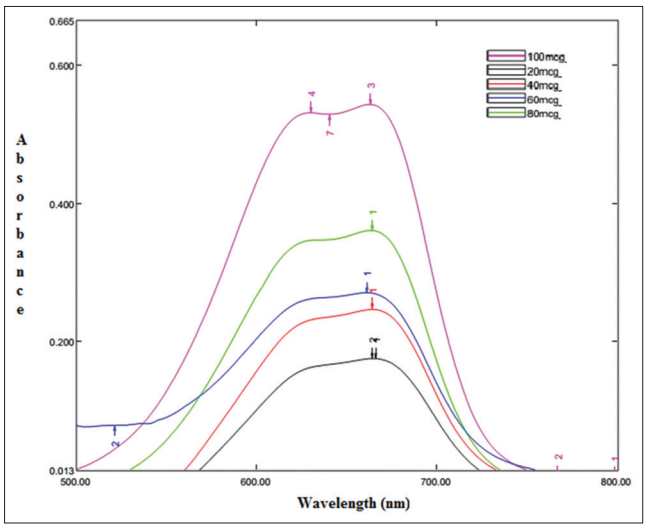

Fig. 3: Overlay linearity spectra of desvenlafaxine (method A)

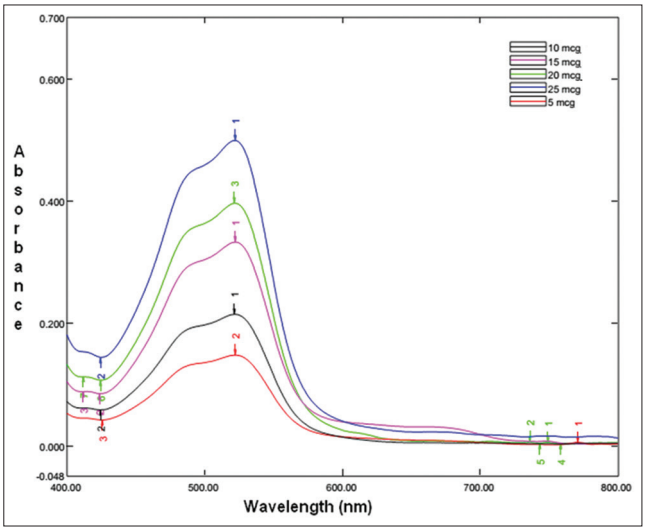

Fig. 5: Overlay linearity spectra of desvenlafaxine (method B)

Table 2: Recovery studies of desvenlafaxine for method A

S.No	Amount of drug taken (µg/ml)	Amount of drug added	Total amount of drug (µg/ml)	Total amount of drug found	% Recovery	% RSD
1.	40	20	60	59.5	99.1	0.279
				59.75	99.58	
				59.5	99.1	
				Mean±SD	99.26±0.277	
2.	40	40	80	79.5	99.37	0.179926
				79.5	99.37	
				79.75	99.68	
				Mean±SD	99.47±0.1789	
3.	40	60	100	99.5	99.5	0.144941
				99.5	99.5	
				99.75	99.75	
				Mean±SD	99.58±0.1443	

RSD: Relative standard deviation

Table 3: Recovery studies of desvenlafaxine for method B

S.No	Amount of drug taken (µg/ml)	Amount of drug added (µg/ml)	Total amount of drug (µg/ml)	Total amount of drug found	% Recovery	% RSD
1.	10	5	15	15	100.00	0.3289
				15.05	100.33	
				15.10	100.66	
				Mean±SD	100.33±0.33	
2.	10	10	20	20	100.00	0.1442
				20.05	100.25	
				20	100.00	
				Mean±SD	100.08±0.144	
3.	10	15	25	24.57	98.28	0.1408
				24.63	98.52	
				24.57	98.28	
				Mean±SD	98.36±0.1385	

RSD: Relative standard deviation

Table 4: Method precision data of desvenlafaxine for method A and B

Concentration (µg/ml)	Parameters	Intraday	Interday
Method A			
40	SD	0.000548	0.000548
	% RSD	0.203237	0.203237
Method B			
40	SD	0.000408	0.000548
	% RSD	0.156918	0.210258

RSD: Relative standard deviation

RESULT AND DISCUSSION

Analytical method validation

Recovery studies were performed by adding a known amount of standard drug (80%, 100% and 120%) to pre-analyzed sample and contents were reanalyzed by proposed method. The other validation parameter like precision (interday, intraday) were also studied (ICH Q2B). The results of validation studies for estimation of desvenlafaxine are presented in Tables 2-4.

The method developed for spectrophotometric determination of desvenlafaxine in tablet formulation was found to be simple and convenient for the routine analysis. Beer-lambert's law was obeyed in the concentration range of 20-100 µg/ml for method A and 5-25 µg/ml proves methods are sensitive. Coefficient of variation was found to be 0.967 for method A and 0.974 for method B. The percentage recoveries were found in the range of 99.47±0.1789 for method A and 100.08±0.144 for method B. The method was found to be precise with % relative standard deviation ± (0.203%) for the interday precision and ± (0.203%) for intraday for method A and ± (0.210%) for interday precision and ± (0.156%) for intraday precision. The limit of detection and limit of quantification were found to be 0.825 µg/ml and 2.5 µg/ml respectively for method A and 0.1061 µg/ml and 0.321 µg/ml for Method B respectively.

CONCLUSION

The reagents utilized in the proposed methods are cheap, readily available, and the procedures do not involve any critical reaction conditions or tedious sample preparation. Moreover, the methods are free from interference by common additives and excipients. The wide applicability of the new procedures for routine quality control was well established by the assay of des venlafaxine in pure form and in pharmaceutical preparations.

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