

# THIRD ORDER DERIVATIVE SPECTROPHOTOMETRIC ESTIMATION OF VENLAFAXINE HYDROCHLORIDE IN BULK AND PHARMACEUTICAL FORMULATIONS

Vimal D. Shirvi\*, G. Vijaya Kumar, K. P. Channabasavaraj

Department of Pharmaceutical Analysis, Bharathi College of Pharmacy,  
Bharathinagara, Maddur, Karnataka-571422, India.

\*Corres.author: vimalshirvi@gmail.com

**ABSTRACT:** A simple, sensitive and accurate third order derivative spectrophotometric method has been developed for the estimation of Venlafaxine hydrochloride in raw material and pharmaceutical dosage form. In this method Venlafaxine hydrochloride showed zero crossing at 274 nm, with a sharp peak at 285 nm when  $n=1$ . Beer's law was obeyed in the concentration range of 40-120  $\mu\text{g/ml}$ . The limit of detection and limit of quantitation were found to be 1.82  $\mu\text{g/ml}$  and 5.49  $\mu\text{g/ml}$ , respectively. The method was successfully applied to the determination of Venlafaxine hydrochloride in tablets. Results were validated statistically as per ICH guidelines. It was found that the excipients present in the commercial formulation did not interfere with the method.

**Keywords:** Derivative spectrophotometric, Venlafaxine hydrochloride, Method validation

## 1. INTRODUCTION

Venlafaxine hydrochloride is a structurally novel antidepressant for oral administration. It is designated 1-[(1RS)-2-(dimethylamino)-1-(4-methoxyphenyl)ethyl] cyclohexanol hydrochloride [1-2]. It is referred to as serotonin and noradrenalin reuptake inhibitor (SNRT), because it inhibits uptake of both these amine but, in contrast to older Tricyclic antidepressants (TCAs), does not interact with cholinergic, adrenergic or histaminergic receptors or have sedative property [3-5]. For antidepressant action, initially 75 mg a day is administered and dose is gradually increased up to 225 mg a day, not to exceed 375 mg a day in severe cases [6-8].

A survey of literature has revealed, several analytical methods for the determination of Venlafaxine hydrochloride in pharmaceutical preparation including several spectrophotometric methods [9-14], reversed-phase high-performance liquid chromatographic (RP-HPLC) method using internal standard [15], and stability indicating LC method have been reported [16-17].

In the present study, a simple, precise and accurate third order spectrophotometric method for the estimation of Venlafaxine hydrochloride in pure form and in solid dosage form was developed. The results of the analysis were validated by statistical method and recoveries studies.

## 2. EXPERIMENTAL

### 2.1 Instruments and reagents

Pure sample of Venlafaxine hydrochloride was obtained from Torrent pharmaceuticals Ltd. (Ahmedabad, India). Analytical grade methanol was used as solvent for dilution. A Shimadzu UV-1800 UV/VIS spectrophotometer was used with 1 cm matched quartz cell. Tablet formulation [VENTAB XL (Brand I), Intas pharmaceuticals Ltd., Ahmedabad and VEXOR (Brand II), Cadila pharmaceuticals Ltd., Ahmedabad] were procured from a local pharmacy with labeled amount 37.5 mg per tablet.

### 2.2 Preparation of working standard drug solution

The standard Venlafaxine hydrochloride (100 mg) was

weighed accurately and transferred to volumetric flask (100 ml). It was dissolved properly and diluted up to the mark with methanol to obtain final concentration of 1000 µg/ml and the resulting solution was used as working standard solution.

### 2.3 Analysis of marketed formulations

For the estimation of Venlafaxine hydrochloride in tablets formulations by this method, 20 tablets of brand were weighed and triturate to fine powder. Tablet powder equivalent to 100 mg of Venlafaxine hydrochloride was weighed and transfer into 100 ml volumetric flask than dissolved with methanol and further diluted with methanol. It was kept for ultrasonication for 30 min; this was filtered through Whatman filter paper No. 41 and then final dilution was made with methanol to get the final stock solution of 1000 µg/ml. From this stock solution, various dilutions of the tablet solution were prepared and analyzed.

### 2.4 Third order derivative spectroscopic method

Derivative spectrophotometry is an analytical technique of great utility for extracting both qualitative and quantitative information from spectra composed of unresolved bands, and for eliminating the effect of baseline shifts and baseline tilts. It consists of calculating and plotting one of the mathematical derivatives of a spectral curve. Derivative spectrophotometry is now a reasonably prized standard feature of modern micro-computerized UV spectrophotometry.

The third order derivative spectra, showed zero crossing at 274nm, with a sharp peak at 285 nm when n=1 (Figure 1). The absorbance difference at n=1 (dA/dλ) is calculated by the inbuilt software of the instrument which was directly proportional to the concentration of the standard solution. The standard drug solution was diluted so as to get the final

concentration in the range of 40-120 µg/ml and scanned in the third order derivative spectra. The calibration curve of dA/dλ against concentration of the drug showed linearity. Similarly absorbance of sample solution was measured and amount of Venlafaxine hydrochloride was determined from standard calibration curve.

## 3. RESULT AND DISCUSSION

The method was validated according to International Conference on Harmonization guidelines for validation of analytical procedures [18-20].

The third order derivative spectra, showed zero crossing at 274nm, with a sharp peak at 285 nm when n=1. Regression analysis using the method of least squares was made for the slope, intercept and correlation coefficient values and given in Table 1. The range was found to be 40-120 µg/ml.

Limit of detection and limit of quantitation were determined by using the formula based on the standard deviation of response and the slope. The limit of detection and limit of quantification were calculated by using the equation  $LOD = 3.3 \times \sigma / S$  and  $LOQ = 10 \times \sigma / S$ , where  $\sigma$  is the standard deviation of intercept, S is the slope and it is mentioned in Table 1.

To study the accuracy of the proposed methods, and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method. This study was performed by addition of know amounts of Venlafaxine hydrochloride to preanalyzed solutions of commercial tablets. The mean recoveries were found to be 99.25-100.48 %.

The results of analysis of marketed formulation are shown in Table 3. The values obtained are within the limit.

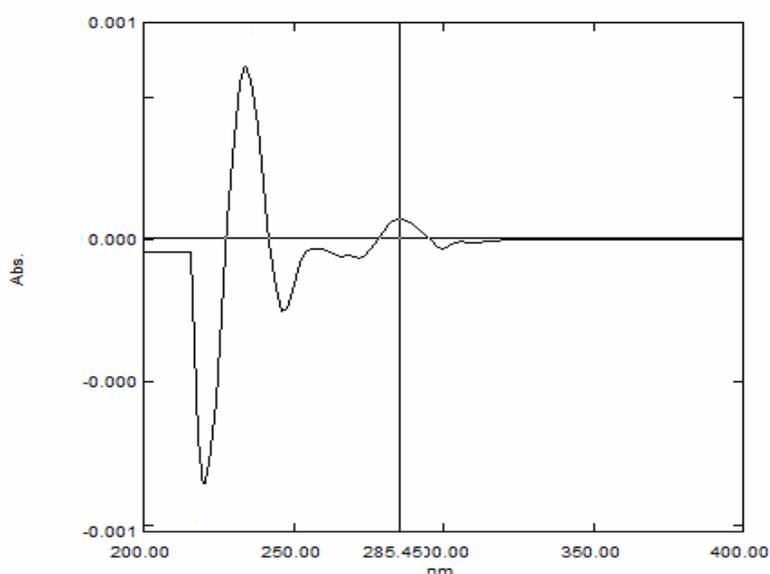


Figure 1: Third order derivative spectrum of Venlafaxine hydrochloride with n=1

**Table 1: Calibration Parameters**

S.No	Parameter	Results
1	Absorption Maxima (nm)	285
2	Beer's Law limits( $\mu\text{g/ml}$ )	40-120
3	Regression equation (y)* Slope (b) Intercept (a)	0.000005 0.000004
4	Correlation coefficient	0.9985
5	Limit of detection ( $\mu\text{g / ml}$ )	1.82
6	Limit of quantification ( $\mu\text{g / ml}$ )	5.49

\* $y = a + bx$ ; when x is the concentration in  $\mu\text{g/ml}$  and y is absorbance unit.

**Table 2: Recovery study Data**

Sample	Label claim (mg)	Amount added (%)	Amount recovered ( $\mu\text{g/ml}$ )	Recovery $\pm$ SD (%)	% RSD
BRAND I	37.5	0	37.22	99.25 $\pm$ 0.55	0.554
	37.5	80	37.41	99.76 $\pm$ 0.29	0.290
	37.5	100	37.37	99.65 $\pm$ 0.42	0.421
	37.5	120	37.54	100.10 $\pm$ 0.33	0.329
BRAND II	37.5	0	37.31	99.49 $\pm$ 0.38	0.381
	37.5	80	37.68	100.48 $\pm$ 0.22	0.218
	37.5	100	37.49	99.97 $\pm$ 0.73	0.730
	37.5	120	37.29	99.44 $\pm$ 0.47	0.472

**Table 3: Analysis of tablets formulation**

Tablet	Label claimed (mg)	Amount found (mg)	%Recovery $\pm$ SD
BRAND I	37.5	37.4 $\pm$ 0.22	99.73 $\pm$ 0.37
BRAND II	37.5	37.2 $\pm$ 0.35	99.20 $\pm$ 0.76

#### 4. CONCLUSION

The developed method was found to be simple,, sensitive, accurate and reproducible and can be used for routine quality control analysis of Venlafaxine hydrochloride in bulk and in pharmaceutical formulations.

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