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DEVELOPMENT AND VALIDATION OF SPECTROSCOPIC METHODS FOR THE ESTIMATION OF VILAZODONE IN BULK AND IN TABLET FORMULATION

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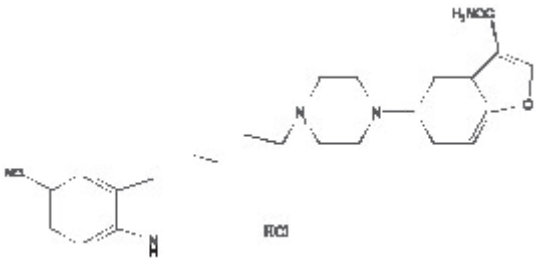
ABSTRACT
Two rapid, specific and economic methods have been developed using methanol as solvent for spectrophotometric determination of vilazodone HCl in bulk and in tablet formulation. Vilazodone HCl showed maximum absorption at 241nm (method A) and same spectrum was derivatised into first order derivative at Ä ë=2; amplitude of trough was recorded at 246nm (method B). In both methods vilazodone HCl follows linearity in concentration range 1-6µg/ml and exhibited good correlation coefficient (r^2=0.999) and excellent mean recovery (98.32%) and (99.53%). The methods were validated statistically and by recovery studies for linearity, precision, repeatability, and reproducibility. The obtained results proved that both the methods can be employed for routine analysis of vilazodone HCl in bulks as well as in the commercial tablet formulation.

Keywords: *Vilazodone HCl; UV spectroscopy; derivative spectroscopy; validation.*

INTRODUCTION

Vilazodone HCl (VLN, Fig. 1) is chemically 5-(4-[4-(5-cyano-1*H*-indol-3-yl)butyl] piperazin-1-yl) benzofuran-2-carboxamide hydrochloride[1]. It contains an indole-piperazine that utilizes its function as an SSRI and 5-HT_{1a} receptor partial agonist[2]. It belongs to the category of serotonergic antidepressant approved by FDA (Food and Drug Administration) for treatment of depressive disorder [3, 4]. It is a novel serotonin reuptake inhibitor and serotonin 1A receptor partial agonist[5] having strong affinity for D2 dopaminergic receptors[6]. It has actions at several 5-HT (serotonin) receptor subtypes [7,8]. Thus, at the moment, available literature only highlights therapeutic and pharmacological profile of drug but no published methods validated for its estimation in pharmaceutical formulations.

Fig. 1: *Chemical structure of Vilazodone HCl*



This encourages undertaking this work, so that quantitative estimation of VLN can be done and hence can be used for routine analysis of bulk and tablet formulation as well. Revolutionary efforts are undertaken for the first time to develop and validate rapid, simple, specific, sensitive, accurate and precise spectroscopic methods for the determination of VLN in bulk and in tablet dosage form. This preliminary successful approach also motivated us to extend the work developing HPLC method which might be undertaken in due course of time.

EXPERIMENTAL

Reagents and chemicals

Vilazodone HCl was supplied as a gift sample by Glenmark Pharmaceuticals Ltd., Mumbai (India). All chemicals and reagents used were of analytical grade. Methanol was selected as the solvent for sample preparation.

Instrument

A double beam UV-Visible spectrophotometer (UV-2450, Shimadzu, Japan; software UVProbe2.21) with specific measurements, using a pair of 10mm matched quartz cells. All weights were taken on electronic balance (Shimadzu AUX 120).

Preparation of Standard stock solutions

Accurately weighed 10 mg of VLN transferred to 100 ml volumetric flasks. It was dissolved in methanol and volume was made up to the mark with same solvent to obtain final strength 100 µg/ml.

Method-A UV Spectrophotometry[9]

From the stock solution dilution was made in order to get the concentration of 3µg/ml. The solution was

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scanned in the UV range of 200-400 nm; VLN showed absorbance maximum at 241nm (Fig. 2).

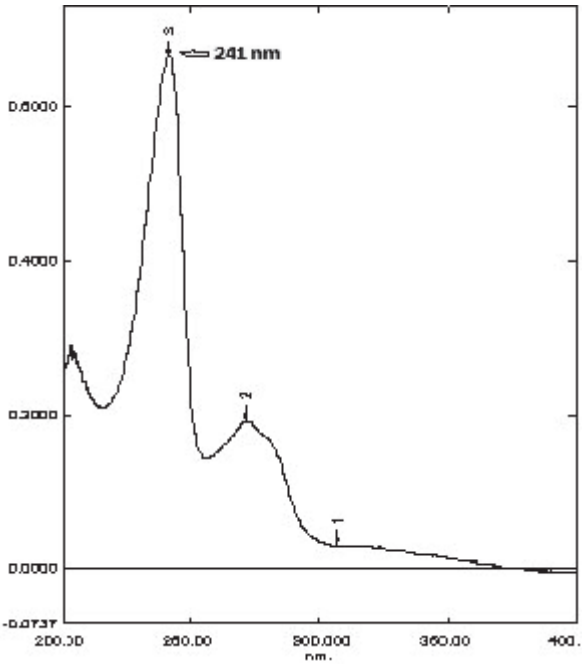

Fig. 2: *Simple UV spectrum of VLN in methanol showing λ max at 241 nm*

Method-B First Order Derivative Method[9]

The zero order derivative spectra of concentration 3µg/ml were derivatised into first order using UV probe software of the spectrophotometer; amplitude of the trough was recorded at 246nm (Fig. 3).

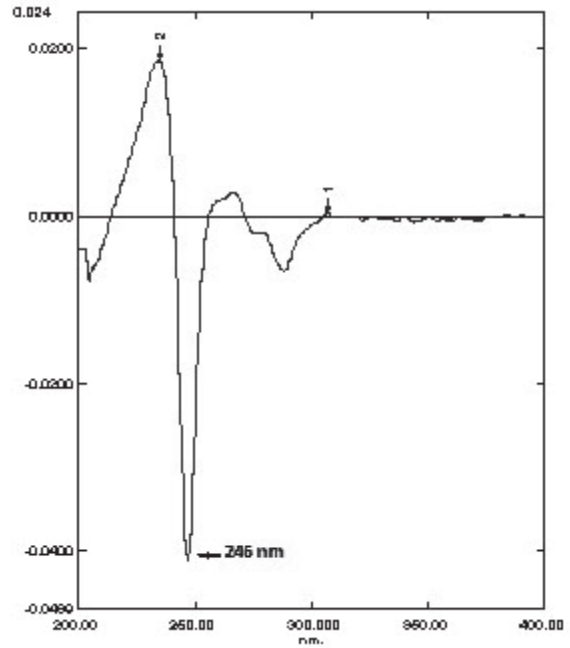

Fig. 3: *First order derivative spectrum of VLN in methanol showing amplitude at 246 nm*

Analysis of tablet formulation

Twenty tablets were accurately weighed, powdered and the quantity equivalent to 10 mg of VLN was transferred to a 100ml volumetric flask and volume made up to 50ml with methanol and sonicated for 20 min. The solution was filtered through Whatman filter paper no. 41 and the resultant solution was diluted with same solvent to get final concentration 5 µg/ml for both methods. The amount of drug present in sample solution was determined using the calibration curve of standard drug.

Validation of proposed method[9]

Linearity

Appropriate known volumes of aliquots from standard VLN stock solution were transferred to series of six 10 ml volumetric flasks. The volume was adjusted to the mark with methanol to get concentrations of 1-6µg/ml for both methods. Calibration curve was plotted for both methods as absorbance *vs* concentration (Fig. 4) and concentration *vs* amplitude (Fig. 5).

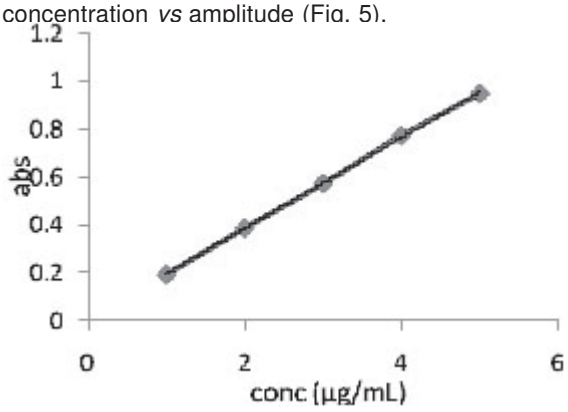

Fig. 4: *Calibration curve of UV- spectrophotometry method of Vilazodone HCl*

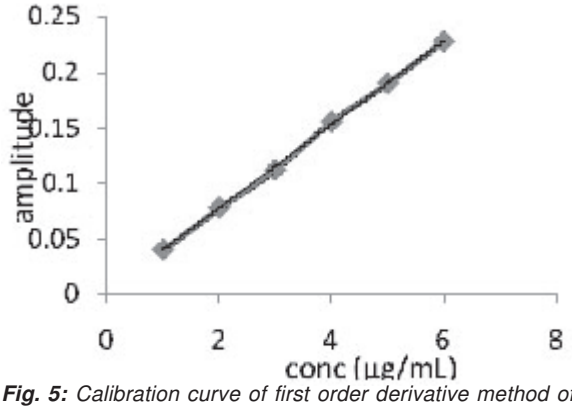

Fig. 5: *Calibration curve of first order derivative method of Vilazodone HCl*

Precision

Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing 2, 3 and 4 µg/ml of VLN

solutions for three times on the same day. Inter-day precision was determined by analyzing 2, 3 and 4µg/ml of VLN solutions daily for three consecutive days over a period of week.

Accuracy (Recovery studies)

To assess the accuracy of the proposed method, a known amount of standard stock solution was added at different levels i.e. 80, 100 and 120%, to the pre-analyzed sample solutions. The absorbance of solutions was recorded; results of recovery studies are reported in **Table 1**. High recovery and low standard deviation confirmed that proposed method is accurate for determination of VLN in pharmaceutical formulation.

Table 1: *Summary of validation parameters for proposed methods*

Parameters	Method A	Method B
Linearity(µg/ml)	1-6	1-6
Y=mx+C	Y = 0.1896x + 0.0063	Y=0.0378x+0.0016
Correlation coefficient	0.9996	0.9994
LOD (µg/ml)	0.112	0.150
LOQ (µg/ml)	0.341	0.454
% Recovery*	98.32	99.53
%RSD	0.95	0.57
Precision (%RSD)		
Intra- Day*	0.72-1.51	0.06-0.47
Inter- Day*	0.05-1.83	0.03-0.35
Repeatability#	1.07	0.18
Ruggedness (%RSD)#		
Analyst I	1.12	0.18
Analyst II	1.70	0.81

**n = 3 #n = 6*

Repeatability

Repeatability was determined by analyzing 3 µg/ml concentration of VLN solution for six times. The absorbance of solution was recorded and spectra were derivative.

Sensitivity

Sensitivity of the proposed method was estimated in terms of limit of detection (LOD) and limit of quantitation (LOQ). The LOD and LOQ were calculated by the use of equation, LOD = SD/S x 3.3 and LOQ = SD/S x 10, where SD is the residual standard deviation of the peak areas of the drug (n=6) and 'S' is the slope of the line. Sensitivity was performed between 2-3 µg/ml, for both spectroscopic methods.

Ruggedness

Ruggedness of the proposed method is determined by analysis of aliquots from homogenous slot by two different analysts using same operational and environmental conditions.

RESULTS AND DISCUSSION

VLN in methanol showed maximum absorbance at 241nm. The same spectrum was derivatized into first order derivative. In these methods VLN followed linearity in concentration range 1-6µg/ml. The developed methods were applied for pharmaceutical formulations. The %amount of VLN from tablet formulation by method A and method B was found to be 100.18 % (RSD 0.52) and 98.32% (RSD 0.45), respectively. The amount of VLN estimated by methods was found to be within acceptance criteria. The detailed results from validation of proposed methods are tabulated Table 1. Precision study at different time and day interval in both methods showed low standard deviation and % RSD less than 2 indicate that the proposed methods are precise for determination of VLN. High recovery and low standard deviation confirmed that proposed methods are accurate for determination in pharmaceutical formulation. Also these methods were rugged as low value of %RSD was obtained. Determination of LOD and LOQ indicates adequate sensitivity of the methods. Thus, both the methods are found to be simple, economical and can suitably apply for the routine analysis of vilazodone HCl in pharmaceutical tablet formulation.

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