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DETERMINATION OF VILAZODONE IN PHARMACEUTICAL FORMULATIONS BY HPLC METHOD

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ABSTRACT

Vilazodoneisan anti-depressant drug. A simple, precise and rapid RP-HPLC method was developed for the estimation of Vilazodonein pharmaceutical dosage forms. The method was carried out on a C8(4.6x150 mm,3.5micron,make:Xterra)column using a mixture of Methanol: 10mM potassium dihydrogen phosphate (20:80 pH 3.5 adjusted with acetic acid). Retention time of Vilazodone was found to be 2.5 min+or-0.5 min.The detection was carried out at 257 nm .The linearity was found to be 2 to 12 µg/ml with correlation coefficient of 0.9996. The intra-day and inter-day precision (% RSD) were in the range of 0.29 to1.16 and 0.45 to 1.19, respectively. The percentage recovery was found to be 99.52±1.51 to 100.59±1.16. The result of analysis of marketed formulation was found to be 100.32±0.96 to100.95±0.69. The proposed method was successfully applied for the estimation of Vilazodonein pharmaceutical dosage forms.

Keywords: Vilazodone, RP- HPLC, Tablets, Validation.

INTRODUCTION

Vilazodone (VIL) is a novel antidepressant agent, approved by the US Food and Drug Administration (US FDA) for the treatment of major depressive disorder[1-2] . Chemically it is 5-[4-[4-(5-cyano-1H-indole-3-yl) butyl]-1-piperazinyl]-2 benzofurancarboxamide Hydrochloride (figure 1), with molecular formula of C26H27N5O2.HCl and it has the molecular weight of 477.99[3-4]. Vilazodone belongs to the benzofurans. Vilazodone's antidepressant effects are thought to be due to enhancement of serotonergic activity in the central nervous system (CNS) through selective inhibition of serotonin reuptake[5]. Literature review revealed that only pharmacological and clinical studies [6-8] have been reported for the determination of Vilazodone and a pharmacokinetic study which used LC-MS method for the determination of vilazodone[9]. HPLC has become a widely used tool for the routine determination and separation of drugs either alone in pure form or in admixture with other drugs or degradation products and in pharmaceutical formulations.[10-12]Existing literature reveals that there are only few methods for the assay of vilazodone in bulk and dosage forms[13-14].

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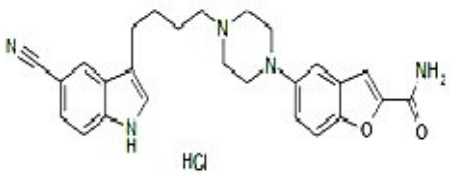
There is no official method for the estimation of vilazodone in the pharmacopoeia`s, it was necessary to develop a new sensitive method for the estimation of the parameters used for the developed method Hence an attempt has been made to develop new simple, reliable, and reproducible, isocratic RP-HPLC methods to estimate the vilazodone in bulk and pharmaceutical formulation with good precision, accuracy, linearity and reproducibility respectively.The proposed method was validated as per ICH guidelines [15].

Figure 1: Structure of Vilazodone



EXPERIMENTATION:

Equipment:

Chromatographic separation was performed on Waters HPLC system consist of model 486 having tunable absorbance detector and Rheodyne injector with 20µl loop volume. Empower software was applied for data collecting and processing.

Reagents and chemicals:

Methanol and water of HPLC grade were procured from Rankem lab ltd. Vilazo done was received as gift samples from Hetero Labs Ltd., Hyderabad, India,

respectively. VIIBRYD® (vilazodoneHCl) tablets purchased from localmarket

HPLC conditions.

A XterraC8 (4.6x150 mm, 3.5micron, column was used as the stationary phase. A mixture of Methanol: 10mM potassium dihydrogen phosphate (20:80 pH 3.5 adjusted with acetic acid) was used as a mobile phase .It was filtered through 0.45µ membrane filter and degassed. The mobile phase was pumped at 1.0 ml/min. The eluents were monitored at 257nm.The injection volumes of samples and standard were 20µl.

Standard solutions:

A stock solution containing 1000µg/ml of VIL was prepared by dissolving VIL in mobile phase. A working standard solution containing 2-12µg/ml of VIL was prepared from the above stock solution. All the stock solutions were covered with aluminum foil to prevent photolytic degradation until the time of analysis.

ASSAY OF TABLET FORMULATION:

Twenty tablets were weighed; each containing 10mg of VIL was weighed and finely powdered. A quantity of powder equivalent to 10mg of VIL was weighed and transferred to a 10ml standard flask. The drug was initially dissolved in methanol and sonicated for 15 minutes. The volume was made up to 10 ml with mobile phase. The solution was filtered using 0.2µm membrane filter. The 0.6ml of this solution diluted to 6 ml using mobile phase to get final concentration of 6µg/ml of VIL. Then 20µl of this solution was injected in to the column and chromatogram was recorded and shown in Fig.2 Concentrations of VIL in the tablet formulation were calculated by comparing area of the sample with that of standard. The percentage assay of individual drug was calculated and presented in Table1.

Fig 2: Sample Chromatogram of Vilazodone

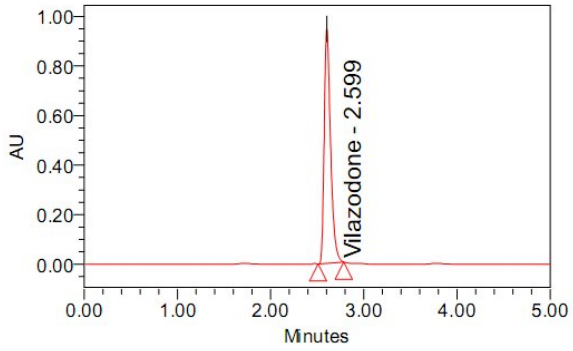


Table1: Table for Assay

Tablet formulation	Drug	Amount present (mg/tab)	Amount found* (mg/tab)	% label claim*
T1 T2	VIL VIL	10 20	9.861 20.032	99.30% 100.66%

T1 and T2 are two different brands of tablet formulations. VIL denotes Vilazo done respectively.*each value is average of six determinations.

VALIDATION OF THE METHOD:

System suitability studies

The system suitability test was carried out on freshly prepared stock solution of Vilazodoneto check various parameters such as column efficiency, tailing factor and number of theoretical and presented in Table 2. The values obtained were demonstrated the suitability of the system for the analysis of the drug. System suitability parameter may fall within ± 3% standard deviation range during routine performance of the method.

Table 2: System Suitability Studies

S. No	Parameters	Vilazodone
1	Retention time	2.578
2	USP Tailing factor	0.893
3	Theoretical plate /meter No	8618.30
4	Calibration Range (µg/ml)	2-12
5	Area	2457.63
6	LOD (µg/ml)	0.015
7	LOQ (µg/ml)	0.2.97

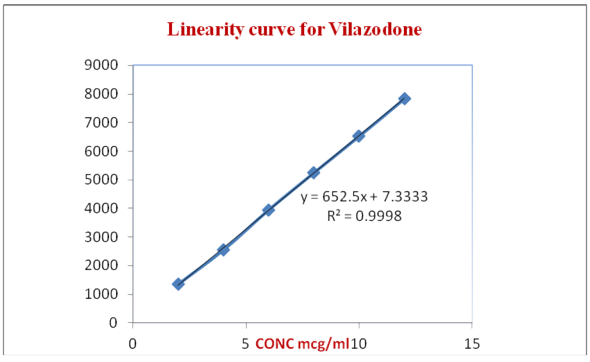
Linearity and Range

Linearity was studied by preparing standard solution at five different concentration levels. The linearity range was found to be 2-12µg/ml. 20µl of each solution was injected into chromatograph. Peak areas were recorded for all the chromatogram. Calibration curve was constructed by plotting peak areas (Y axis) against the amount of drug in µg/ml(X axis). Peak area of linearity range and the parameters were calculated and presented in Table 3 respectively. The linearity curve of Vilazodonewas shown in Figure no.3.

Table 3: Analytical performance parameters of linearity curve

S. No	parameters	Vilazodone
1	Linear dynamic range(µg/ml)	2-12
2	Correlation coefficient (r)	0.9998
3	Slope (m)	652.5
4	Intercept (c)	
5	Curve fitting	99.98

Figure 3: Linearity curve of Vilazodone



Accuracy

The accuracy of the method was determined by recovery experiments. Placebo was spiked with known quantities of standard drugs at levels of 80 to 120% of label claim. The recovery studies were carried out 3 times and the percentage recovery and standard deviation of the percentage recovery were calculated and presented in Table 4. The mean recovery is well within the acceptance limit, hence the method is accurate.

Table 4: Recovery studies of Vilazodone

Labeled	Amount mg/tab Found*	%Label Claim (n=6)	Recovery Studies (n=3)			
			Amount added (mg)	Amount recovered (mg)	%Recovery	% RSD
Vilazodone 10mg	10.923	100.25±0.2971	8	8.31±0.066	80.66	0.2858
			10	10.62±0.110	99.24	0.3845
			12	12.07±0.0518	118.14	0.1667

*Average of six or three determinations, Mean ± Standard Deviation

Precision

a) System precision

The system precision of the method was established by six replicate injections of the standard solution containing Vilazo done. The percentage RSD were calculated and presented in Table 5. From the data obtained, the developed RP-HPLC method was found to be precise.

b) Method precision

The method precision of the method was established by carrying out the analysis of Vilazodone(n=6) using the proposed method. The low value of the relative standard deviation showed that the method was precise. The results obtained were presented in Table 5.

Table 5: Precision studies of Vilazodonein dosage forms

Precision	%Assay*	%RSD of Assay(n=6)
System Precision	100.41±0.1034	0.7810
Method Precision	100.12±0.1100	0.2100

*Average of six determinations, mean ± SEM

Specificity

Specificity of the method was determined by injecting the diluted placebo. There was no interference of placebo with the principle peak, hence the developed analytical method was specific for Vilazodonein tablet dosage form.

Standard and sample solution stability

Standard and sample solution stability was evaluated at room temperature and refrigerator temperature for 24h. The relative standard deviation was found below 2.0%. It showed that both standard and sample solution were up to 24h at room temperature and refrigerator temperature.

Ruggedness and Robustness

The ruggedness of the method was determined by carrying out the experiment on different instruments like Shimadzu HPLC (LC2010 A4T), Water Alliance HPLC 2695 by different operators using different columns of similar type like Kromosil C_8 column and Xterra C8 column. Robustness of the method was determined by making slight change in the chromatographic condition. It was observed that there were no marked changes in the chromatograms, which demonstrated that the RP-HPLC method developed is rugged and robust. The results of ruggedness were presented in Table 6. The results of robustness were presented in Table 7.

Table 6: Method Ruggedness of Vilazodone in Dosage Forms

%Assay* (n=6)	%RSD of Assay(n=6)
Day -1 , Analyst-1, Instrument-1&Column-1	
100.51± 0.144	0.4224
Day -2 , Analyst-2, Instrument-2&Column-2	
100.10 ± 0.242	0.5216

*Average of six determinations, mean ± Standard Deviation

Table 7: Method Robustness of Vilazodone in Dosage Forms

Condition	Change	%RSD
Temperature	**Normal**	0.2140
	-5ºC	0.2106
	+5ºC	0.4709
pH	**Normal**	0.4761
	-0.2unit	0.9541
	+0.2unit	0.4971
Flow Rate	**Normal**	0.8430
	-10%	0.7812
	+10%	0.5107
Mobile phase ratio	**Normal**	0.2528
	-2%	0.5814
	+2%	0.7627
Detection wavelength	**Normal**	0.3980
	-0.2unit	0.4015
	+0.2unit	0.9200

CONCLUSION

The proposed RP-HPLC method for the estimation of vilazodone in tablet dosage forms is accurate, precise, linear, rugged, robust, simple and rapid. Hence the present RP-HPLC method is suitable for the

quality control of the raw material, formulation and dissolution studies.

The method validation shows satisfactory data for all the method validation parameter tested.

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