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ESTIMATION OF VORTIOXEINE IN BULK AND PHARMACEUTICAL FORMULATIONS BY UV SPECTROPHOTOMETRY

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ABSTRACT

A rapid, simple, selective and precise UV Spectrophotometric method has been developed for the determination of Vortioxeine in bulk form and solid dosage formulation. The spectrophotometric detection was carried out at an absorption maximum of 207 nm using acetonitrile as solvent. The method was validated for specificity, linearity, accuracy, precision, robustness and ruggedness. The detector response for the Vortioxeine was linear over the selected concentration range 2 to 18 µg/ml with a correlation coefficient of 0.9995. The accuracy was between 99.84& 100.18 %. The precision (R.S.D.) among six sample preparations was 0.75 %. The LOD and LOQ are 0.02 and 0.07 µg/ml, respectively. The recovery of Vortioxeine was about 100.4 %. The results demonstrated that the excipients in the commercial tablets did not interfere with the method and can be conveniently employed for routine quality control analysis of Vortioxeine Hydrochloride in bulk drug and marketed formulations.

KEYWORDS: Vortioxeine, UV Spectrophotometric method, Solid dosage formulation**,** Acetonitrile**.**

INTRODUCTION

Vortioxetine [1,2] is a novel antidepressant drug it may effectively treat for depression and cognitive dysfunction in adults with MDD. It increases serotonin concentrations in the brain by inhibiting its reuptake in the synapse, and by modulating (activating certain receptors while blocking, or antagonizing, others) certain serotonin receptors. This puts it in the class of atypical antidepressants known as serotonin modulators and stimulators. It is chemically 4-{2-[(2,4-dimethylphenyl)sulfanyl]piperazine-1-ium vortioxetine and its Molecular Formula and Molecular Weight $C_{18}H_{22}N_2S$ and 298.45 gm/mole.

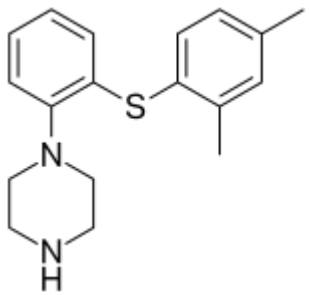

Fig. 1 Chemical structure of Vortioxetine.

Literature survey revealed that there HPLC[3,4] methods reported for estimation of Vortioxetine and its related impurities. Only few spectrophotometric methods[5] reported for estimation of Vortioxetine in bulk and pharmaceutical formulation. As spectrophotometric methods are economical and routinely used in various laboratories, so there is a need to develop a spectrophotometric methods. Here an attempt has made to develop a simple and rapid UV spectrophotometric method for estimation of Vortioxetine in bulk and pharmaceutical formulation.

MATERIALS AND METHODS

Instrumentation

An ELICO UV/Visible spectrophotometer model SL 210 with 10 mm matched quartz cells was used for all spectral measurements. An electronic analytical weighing balance (1 mg sensitivity, APEX) used for weighing purpose.

Chemicals and Reagents

All reagents and chemicals used were of Analytical Grade. Gift sample of Vortioxetine was supplied pharma industry. Marketed formulation Brintellix (AstraZeneca Pvt. Ltd. Bangalore) was procured from local market. The tablet dosage forms containing obtained was 10 mg of Vortioxetine for oral administration.

Preparation of standard stock solution

Accurately weighed 10 mg of Vortioxetine was transferred into 100 ml volumetric flask and the content was dissolved in acetonitrile and volume was made up to the mark with acetonitrile to get a stock solution containing 100 µg/ml.

Preparation of working standard solution

From the standard stock solution 1 ml was transferred to 10 ml volumetric flask and diluting to 10 ml with acetonitrile to get a concentration of 10 µg/ml. Working standard solution of Vortioxeine was scanned between 200-400 nm. The wavelength maximum exhibited for Vortioxeine was at 207 nm (Fig.2).

Fig: 2. Absorption spectrum of Vortioxeine Hydrochloride.

Procedure for Calibration Curve

Appropriate volume of aliquot (0.2-1.8 ml) from standard stock solution was transferred to volumetric flask of 10 ml capacity. The volume was adjusted to the mark with acetonitrile to give solutions concentrations in the range of 2-18 µg/ml. The absorbance measurements of these solutions were carried out against acetonitrile as blank at 207 nm. Calibration curve was constructed by plotting absorbance versus concentrations. Linear regression equation was obtained from this calibration curve.

Estimation of Vortioxeine in Tablet formulation

Accurately 20 Tablets of Vortioxeine were weighed and triturated to fine powder. Tablet powder equivalent to 100 mg of Vortioxeine was weighed and dissolved in 10 ml of Acetonitrile with shaking, sonicated for 3 min and final volume was made up to 100 ml with Acetonitrile. This was then filtered through whatmann's filter paper No.41 to get concentration of 1 mg/ml solution. This was then diluted to make the working concentration of 100 µg/ml with the Acetonitrile. From the above solution 10 µg/ml was taken and the same procedure described under bulk samples was followed. The contents of Vortioxeine in pharmaceutical preparation was calculated by means of calibration curve.

RESULTS AND DISCUSSION

Method Validation[6]

The developed method was validated in terms of Linearity, precision, accuracy, Limit of detection (LOD) and Limit of Quantitation (LOQ), robustness and ruggedness.

Linearity

Nine points calibration curve were obtained in a concentration range from 2-18 µg/ml for Vortioxeine. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y=0.0541x+0.0283 with correlation coefficient 0.9963 (Table 1 and 2, Fig. 2).

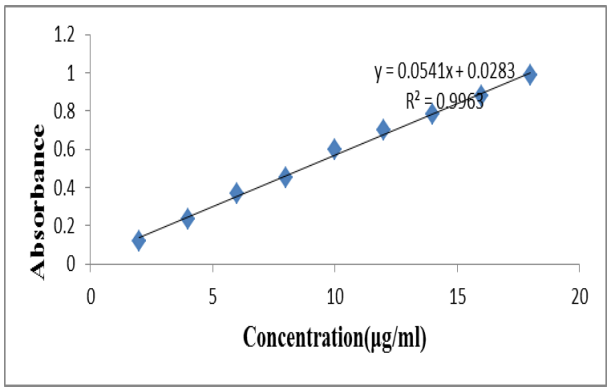

Fig: 3.Calbiration curve for Vortioxeine.

Table 1: Linearity Data for Vortioxeine.

S.No	Concentration (µg/ml)	Absorbance
1.	2	0.1202
2.	4	0.2322
3.	6	0.3671
4.	8	0.4533
5.	10	0.6011
6.	12	0.6998
7	14	0.7825
8	16	0.8798
9	18	0.9882

Table 2: Optical Characteristics of Vortioxeine

S.No	Parameters	Method
1.	λmax (nm)	207
2.	Beers law limit (µg/ml)	2-18
3.	Sandell's sensitivity(µg/cm^2/0.001 A.U)	0.0166
4.	Molar absorptivity(L mol^{-1} cm^{-1})	1.79 x 10^4
5.	Correlation coefficient (r)	0.9963
6.	Regression equation(Y=mX+c)	Y=0.054X + 0.0283
7.	Slope(m)	0.054
8.	Intercept(c)	0.0283
9.	LOD (µg/ml)	0.0243
10.	LOQ (µg/ml)	0.0738
11.	Standard error of mean of Regression line	0.00494

Precision

Precision was checked in terms of repeatability, inter and intraday precision. It was expressed in percentage RSD.

Repeatability

The repeatability was evaluated by assaying six times of sample solution prepared for assay determination. Percentage RSD was calculated (Table 3).

Table 3: Repeatability.

Concentration(µg/ml)	Absorbance
10	0.6850
10	0.6852
10	0.6950
10	0.6894
10	0.6906
10	0.6852
Mean	0.6884
Standard Deviation	0.00368
% RSD	0.754

Interday and Intraday precision

The intraday and interday precision study of Vortioxeine was carried out by estimating different concentrations of three times on the same day (intraday precision) and on three different days (interday precision) and the results were reported in terms of Percentage RSD. (Table 4).

Table 4: Interday & Intraday Precision.

S.No	Concentration (µg/ml)	Interday		Intraday	
		SD	%RSD	SD	%RSD
1	8	0.0057	1.07	0.0013	1.72
2	10	0.0025	1.63	0.0015	0.98
3	12	0.0032	1.17	0.0026	1.03

Accuracy

Accuracy was assessed by determination of the recovery of the method by addition of standard drug to the known amount of marketed formulation at three different concentration levels 80, 100 and 120 % taking into consideration percentage purity of added bulk drug samples. Each concentration was analyzed three times and average recoveries were measured (Table 5).

Table 5: Accuracy Studies.

Name of Drug	Spiked Level	Conc. Added (µg/ml)	Conc. Recovered (µg/ml)	%Recovery ± SD*
Vortioxeine	80%	8	8.01	100.18%±0.0256
	100%	10	9.98	99.84%±0.0582
	120%	12	11.89	99.95%±0.0421

*Average of three determinations

Robustness

The robustness of a method is its capacity to remain unaffected by small changes in conditions. To determine the robustness of the method, the experimental conditions were deliberately altered and assay was evaluated. The effect of detection wavelength was studied at ±2 nm. For changes of conditions, the sample was assayed in triplicates. When the effect of altering

one set of conditions was tested, the other conditions were held constant at the optimum values. Assay for all deliberate changes of conditions should be within 98.0–102.0 % for the proposed method (Table 6).

Table 6: Robustness Studies.

Formulation	Amount of drug taken from tablet(mg)	At 205 nm	At 209 nm
		(n=3)%Assay±%RSD	(n=3)% Assay±%RSD
Brintellix Tablets	10	99.73±0.313	99.91±0.224

Ruggedness

Ruggedness of the proposed method is determined by analysis of aliquots from homogeneous slot by two analysts using same operational and environmental conditions (Table 7).

Table 7: Ruggedness Studies.

Formulation	Amount of drug taken from tablet(mg)	Analyst 1	Analyst 2
		(n=3)%Assay±%RSD	(n=3)%Assay±%RSD
Brintellix Tablets	10	99.83±0.243	99.86±0.324

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The LOD and LOQ were calculated according to below equation given by

LOD= 3.3 σ/s

LOQ=10 σ/s

Where σ is the standard deviation of y intercepts of regression lines and s is the slope of the calibration curve (Table 2).

Application of method to formulation

The proposed was applied to pharmaceutical formulation of Vortioxeine (Table 8).

Table 8: Assay.

Formulation	Labeled Amount(mg)	Amount* Obtained(mg)	%Purity ± SD
Brintellix Tablets	10	9.86	99.86%± 0.685

*****Average of three determinations

CONCLUSION

The proposed UV method for Vortioxeine was found to be precise, sensitive, specific and accurate. The method has wider linear dynamic range with good accuracy and precision. The methods show no interference from the common excipients and additives. The percent recovery obtained indicates non interference from the common excipients used in the formulation. The statistical parameters and recovery data reveal the good accuracy and precision of the proposed methods. The reproducibility, repeatability and accuracy of these methods were found to be good, which is evidenced by low standard deviation. As such the method is suitable for routine analysis of Vortioxeine in bulk and pharmaceutical dosage forms and it is free from various interferences . Therefore, it is concluded that the proposed methods are simple, sensitive and rapid for the determination of Vortioxeine in commercial dosage forms**.**

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