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Review Article

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METHOD DEVELOPMENT AND VALIDATION FOR ESTIMATION OF VORTIOXETINEHYDROBROMIDE THROUGH HPLC METHOD

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ABSTRACT

Adults with major depressive disorder (MDD) are treated with the antidepressant vortioxetine. The mechanism of action (MOA) of vortioxetine is believed to be associated with the suppression of serotonin (5-HT) reuptake. It also possesses other properties, such as agonism of the 5-HT1A and 5-HT3 receptors, but it is uncertain if these have an antidepressant effect. There is no analytical work has been available regarding for estimation of Vortioxetine hydrobromide in Pharmacopoeia. The developed HPLC method for estimation of Vortioxetine hydrobromide makes use of a stationary phase of BDS (150mm x 4.6mm x 5µm), with a mobile phase composition of Acetonitrile: KH2PO4 (60:40). The flow rate was set at 1.0ml/min, and the detection wavelength was 260 nm. Column temperature was maintained at 30°C, with the mobile phase also serving as the diluent. These conditions were determined to be the optimized method. System suitability was assessed through six standard injections, with all results falling comfortably within the acceptance criteria. A linearity study conducted across the range of 25% to 150% levels yielded an R^2 value of 0.999. Precision metrics indicated a repeatability of 0.2 and intermediate precision of 0.6. The limits of detection (LOD) and quantification (LOQ) were established at 0.02µg/ml and 0.06µg/ml, respectively. Utilizing this method, the assay of a marketed formulation showed a 99.90% presence of the active ingredient. Recovery studies were carried out for both the developed method by addition of known amount of standard drug solution of **Vortioxetine hydrobromide** to pre-analyzed sample solution at three different concentration levels. The suggested techniques were used to analyze the final answers. The recovery studies were satisfactory which shows no interference from the excipients. Thus these developed methods can be used for the routine analysis of **Vortioxetine hydrobromide** from its dosage form.

INTRODUCTION[1-6]

Adult patients with depression are prescribed the medication vortioxetine hydrobromide. Itis a member of the class of serotonin modulators and stimulants (SMS) antidepressants. This drug lessens melancholy and feelings of worthlessness in depressed individuals while also enhancing mood and vigor. Its **IUPAC name is** 1-[2-(2,4-dimethylphenyl)sulfanylphenyl] piperazine; hydrobromide, Molecular formula is $C_{18}H_{23}BrN_2S$ with molecular weight is 379.4 g/mol. It is soluble in water.

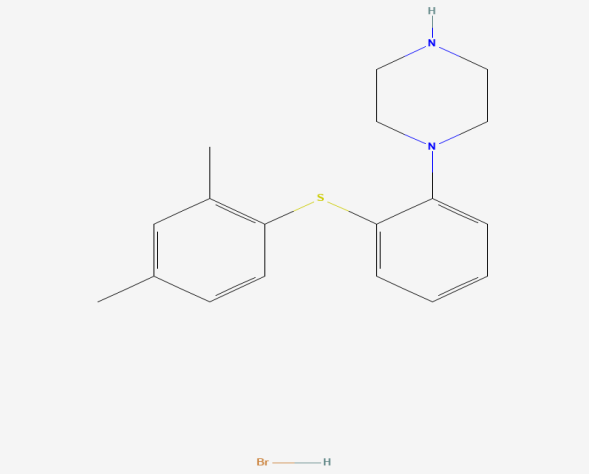

Figure 1: structure of Vortioxetine Hydrobromide.

Vortioxetine is orally administered once daily at 5- to 20-mg doses. Vortioxetine's pharmacokinetics are dose-dependent and linear, with a mean terminal half-life of roughly 66 hours and steady-state plasma concentrations typically reached two weeks after dosage.

From the literature review, it was observed that till today less methods have been reported for the estimation of Vortioxetine Hydrobromide in tablet dosage form by UV and HPLC. So, the Aim of present work is, to develop and validate a more simple, economic, accurate and precise HPLC method for estimation of Vortioxetine Hydrobromide in marketed formulation.

The drug was identified with determination of melting point through open capillary method by utilizing Thiel's tube. Melting point was found in the range of 232-235□ C.The solubility investigation of drug Vortioxetine Hydrobromide was detected by utilizing various solvents, for example, water, methanol, ethanol.

The RP- HPLC method for estimating Vortioxetine Hydrobromide was developed by considering the drug's solubility and Pka value, which guided the selection of conditions used in the method's development. Optimized chromatographic conditions were set by different trials.

The developed HPLC method for estimation of **Vortioxetine hydrobromide** makes use of a stationary phase of BDS (150mm x 4.6mm x 5µm), with a mobile phase composition of Acetonitrile: KH2PO4 (60:40). The flow rate was set at 1.0ml/min, and the detection wavelength was 260 nm. Column temperature was maintained at 30°C, with the mobile phase also serving as the diluent. These conditions were determined to be the optimized method.

Preparation of Standard stock solutions: 10mg of Vortioxetine Hydrobromide was accurately weighed and transferred to a 50ml volumetric flask. Three-quarters of the required volume of diluent was added before the mixture was sonicated for 10 minutes. The flask was then filled to volume with diluent and labeled as the Standard Stock Solution, resulting in a concentration of 200µg/ml of Vortioxetine Hydrobromide.

Preparation of Standard working solutions (100% solution): 1ml of the Vortioxetine Hydrobromide stock solution was pipetted into a 10ml volumetric flask and diluted to volume with diluent, achieving a concentration of 20µg/ml of Vortioxetine Hydrobromide.

Preparation of Sample stock solutions: Five tablets were weighed to calculate the average weight per tablet. The weight equivalent to one tablet was then transferred into a 100ml volumetric flask, to which 50ml of diluent was added. The solution was sonicated for 25 minutes, then filled to volume with diluent and filtered through HPLC filters, producing a concentration of 1000µg/ml of Vortioxetine Hydrobromide.

Preparation of Sample working solutions (100% solution):0.2ml of the filtered sample stock solution was transferred into a 10ml volumetric flask and diluted to volume with diluent, resulting in a concentration of 20µg/ml of Vortioxetine Hydrobromide.

Preparation of Buffer

Mix 600ml of Milli-Q water with 400ml of methanol, then degas and sonicate the solutionfor 10 minutes.

SYSTEM SUITABILITY

System suitability parameters were assessed by creating standard solutions of Vortioxetine Hydrobromide at a concentration of 20ppm. These solutions were injected six times to evaluate parameters such as peak tailing, resolution, and USP plate count and were found to be within the acceptable range.

Linearity

Different dilutions of 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, 25µg/ml, 30µg/ml were prepared from stock solution and calibration curve was plotted between conc. vs peak area.

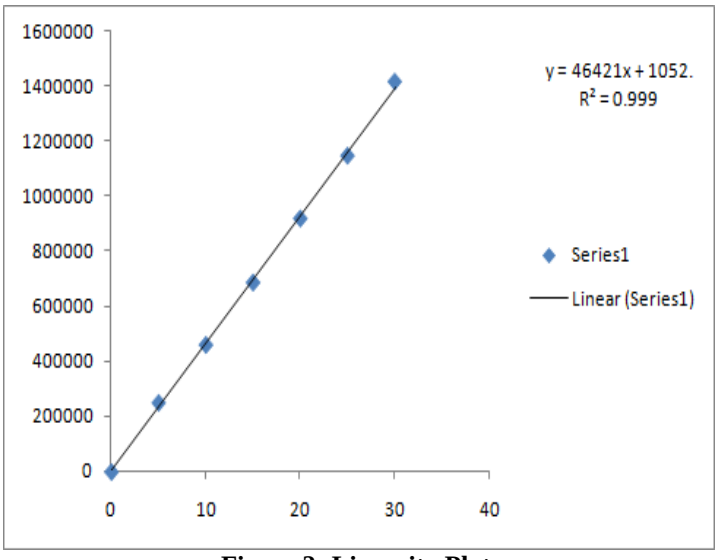

Figure 2: Linearity Plot.

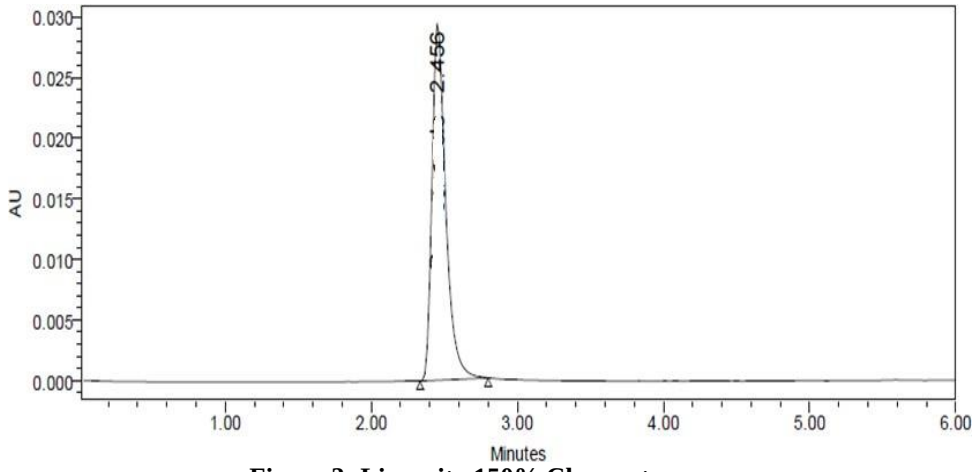

Figure 3: Linearity 150% Chromatogram.

ACCURACY

Three concentrations—50%, 100%, and 150%—were injected in triplicate, and the percentagerecovery was determined to be 100.40.

Table 1: Accuracy data.

% Level	Amount Spiked (µg/mL)	Amount recovered(µg/mL)	% Recovery	Mean %Recovery
50%	10	9.95	99.51	100.40%
	10	10.10	100.97	
	10	10.11	101.08	
100%	20	19.86	99.31	
	20	20.19	100.93	
	20	20.13	100.66	
150%	30	29.77	99.24	
	30	30.28	100.92	
	30	30.28	100.94	

LOD

Detection limit of the Vortioxetine Hydrobromide was found to be 0.02µg/ml.

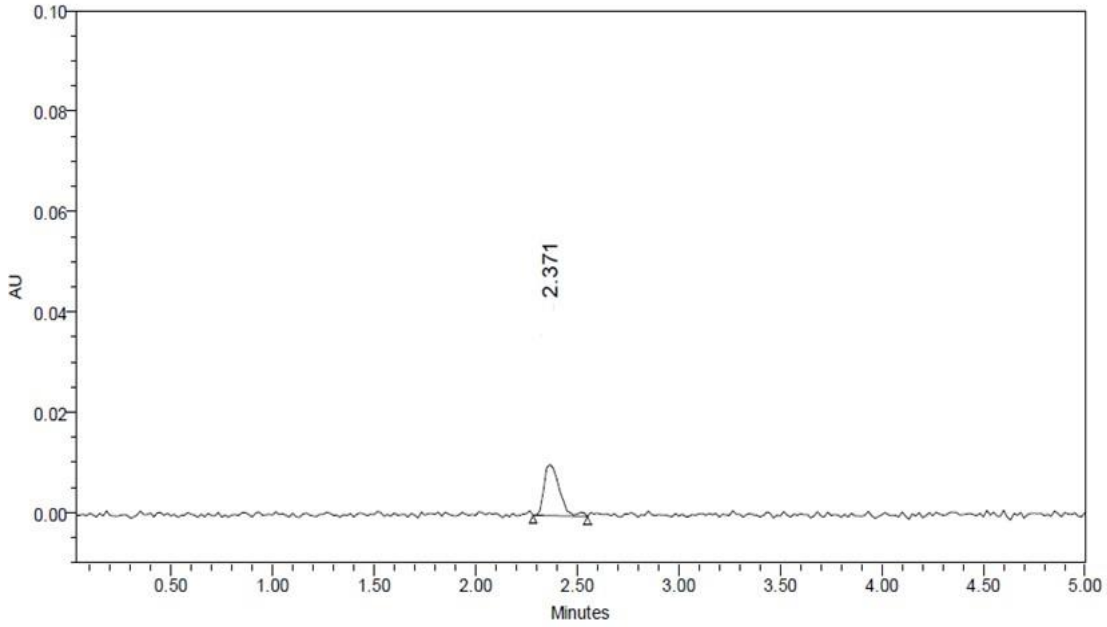

Figure 4: LOD Chromatogram of Vortioxetine Hydrobromide.

LOQ

Quantification limit of the Vortioxetine Hydrobromide was found to be 0.06µg/ml.

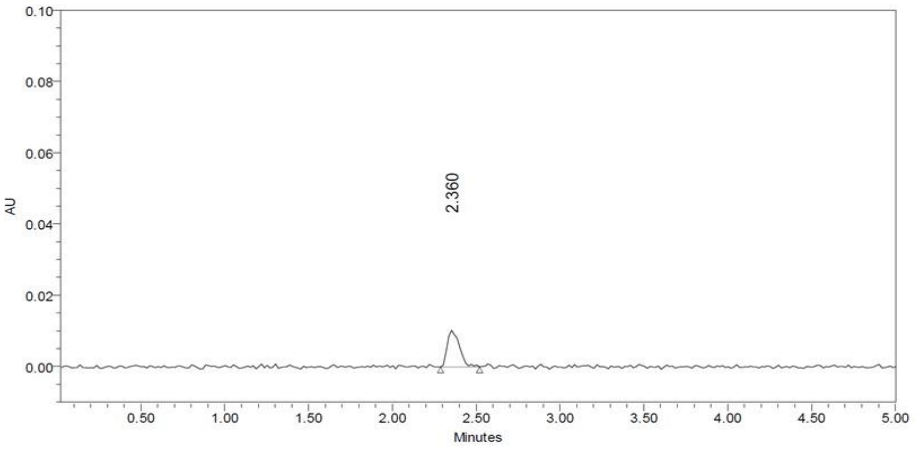

Figure 5: LOQ Chromatogram of Vortioxetine Hydrobromide.

ROBUSTNESS

Minor deliberate adjustments were made to the method, including decreasing and increasing the flow rate, reducing and augmenting the mobile phase composition, and lowering and raising the temperature. The percent relative standard deviation (%RSD) for these varied conditions was then calculated.

Table 2: Robustness Data.

Parameter	%RSD
Flow Minus	0.4
Flow Plus	0.5
Mobile phase Minus	0.3
Mobile phase Plus	0.6
Temperature minus	0.3
Temperature plus	0.4

ASSAY OF MARKETED FORMULATION

Standard solution and sample solution were injected separately into the system and chromatograms were recorded and drug present in sample was calculated using before mentionedformula.

Table 3: Assay of Formulation.

Sample No.	%Assay
1	99.63
2	99.79
3.	100.15
4.	99.84
5.	100.08
6.	99.88
AVG	99.90
STDEV	0.19
%RSD	0.19

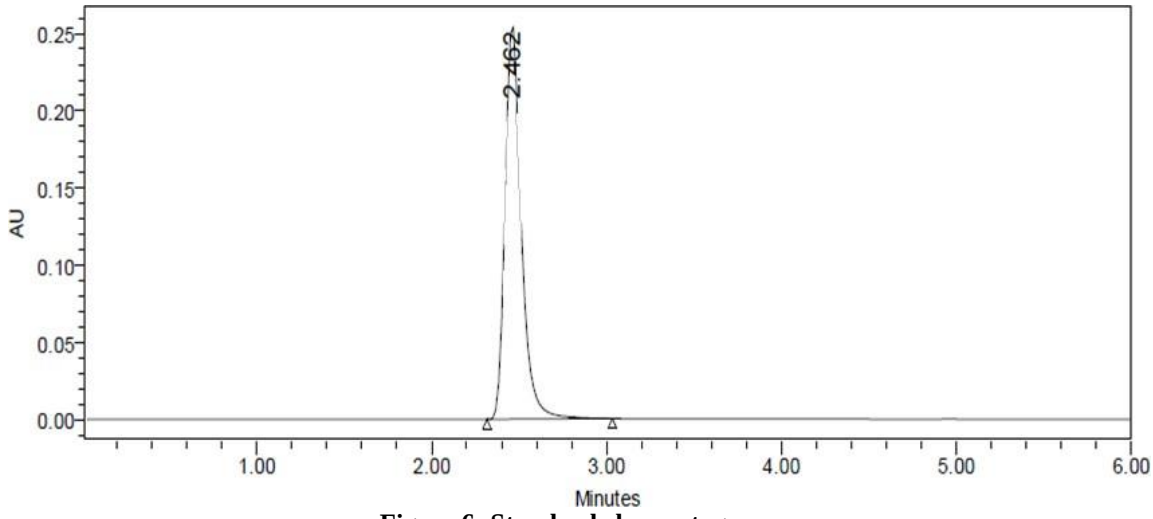

Figure 6: Standard chromatogram.

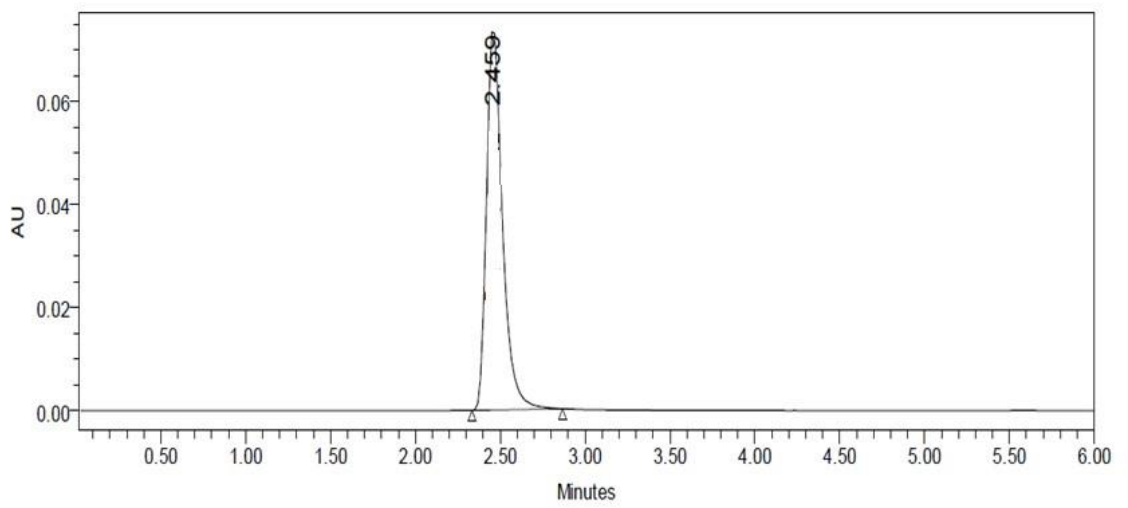

Figure 7: Sample chromatogram.

SUMMARY AND CONCLUSION

Analytical method development and validation are ongoing processes integral to research and development activities. Method development typically involves defining method specifications and selecting appropriate instrumentation. Method validation is the process of demonstrating that an analytical method is appropriate for its intended purpose, a critical step for ensuring analytical reliability. Validation ensures the reliability, consistency, and quality of analytical data, with parameters evaluated including accuracy, linearity, limits of detection and quantification, ruggedness, and robustness.

Vortioxetine is an antidepressant used to treat major depressive disorder (MDD) in adults. Vortioxetine is thought to work by increasing levels of serotonin in the brain, serotonin is a neurotransmitter. Vortioxetine's mechanism of action (MOA) is thought to be related to the inhibition of the reuptake of serotonin (5-HT), it has other activities, including 5-HT3 receptor antagonism and 5-HT1A receptor agonism, but it is unclear whether these have an antidepressant effect.

There is no analytical work related to the estimation of vortioxetine hydrobromide in pharmacopoeias. A new research effort was made to develop and validate an assay method using UV spectrophotometer and RP-HPLC.

The developed HPLC method for estimation of **Vortioxetine hydrobromide** makes use of a stationary phase of BDS (150mm x 4.6mm x 5µm), with a mobile phase composition of Acetonitrile: KH2PO4 (60:40). The flow rate was set at 1.0ml/min, and the detection wavelength was 260 nm. Column temperature was maintained at 30°C, with the mobile phase also serving as the diluent. These conditions were determined to be the optimized method.

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Recovery studies were carried out for both the developed method by addition of known amount of standard drug solution of **Vortioxetine hydrobromide** to pre-analyzed sample solution at three different concentration levels. The resulting solutions were analyzed by proposed methods. The recovery studies were satisfactory which shows no interference from the excipients. Thus these developed methods can be used for the routine analysis of**Vortioxetine hydrobromide** from its dosage form.

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