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Research Article

ESTIMATION OF VILOXAZINE BY USING RP- HPLC METHOD

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ABSTRACT

The RP-HPLC technology was used to produce a straightforward, precise, and easy-to-understand approach for the quantification of Viloxazine. The conditions used in chromatography are the stationary phase The Azilent measuring 150 mm x 4.6 mm x 5 meters The following parameters were maintained: mobile phase diluent: 0.01N KH2po4: acetonitrile in a 70:30 ratio; flow rate: 1.0 ml/min; detection wavelength: 222 nm; column temperature: 30oC; and so on. Conditions were fine-tuned to provide the best possible outcome. The findings of studying the system suitability characteristics by injecting the standard six times were much lower than the acceptability criterion. After conducting a linearity analysis from 25% to 150%, the R2 value was determined to be 0.999. The results showed that the repeatability was 0.6 and the intermediate precision was 0.4.2. The limits of detection (LOD) are 0.07µg/ml and the limits of quantification (LOQ) are 0.20µg/ml. With the aforementioned procedure, 99.86% of the advertised formulation was detected. In all cases, the purity threshold was more than the purity angle and within the permissible range, according to the Viloxazine degradation experiments. We did not conduct a full-length technique analysis; nonetheless, this approach has the potential to be used for regular Viloxazine analysis.

Keywords: HPLC Viloxazine, Method development. ICH Guidelines.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a chronic condition that affects millions of children and often continues into adulthood. ADHD includes a combination of persistent problems, such as difficulty sustaining attention, hyperactivity and impulsive behavior.

Children with ADHD may also struggle with low self-esteem, troubled relationships and poor performance in school. Symptoms sometimes lessen with age. However, some people never completely outgrow their ADHD symptoms. But they can learn strategies to be successful.

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While treatment won't cure ADHD, it can help a great deal with symptoms. Treatment typically involves medications and behavioral interventions. Early diagnosis and treatment can make a big difference in outcome.[1]
Viloxazine is a selective norepinephrine reuptake inhibitor.[3] For decades, an immediate-release formulation of viloxazine has been used in Europe as an antidepressant. It was first approved in the UK in 1974; however, the immediate-release formulation was discontinued due to business reasons unrelated to drug safety and efficacy. In the US, viloxazine was assigned an orphan drug designation in 1984 under the brand name CATATROL: while this product was intended to treat cataplexy and narcolepsy, the drug was never approved for these therapeutic indications. In April 2021, an extended-release formulation of viloxazine under the brand name QELBREE was approved by the FDA for the treatment of attention deficit hyperactivity disorder (ADHD).[2]

There are many antidepressants in this group and they have no common features, apart from the fact they are not tricyclic antidepressants. Many of them are no longer new; for example, maprotiline and viloxazine have been available for over 16 years.[4]
A review of animal and clinical data confirmed the impression that viloxazine has efficacy comparable to that of imipramine but with a different adverse reactions profile . There is a reduced frequency of anticholinergic and sedative effects and a tendency to lose rather than to gain weight. However, viloxazine causes some limiting adverse reactions of its own. These include nausea, vomiting, and gastrointestinal distress, which may be reduced by the use of an enteric-coated formulatio. Viloxazine has also been implicated in migraine, even in patients with no previous history.[5]
The exact mechanism of action of viloxazine remains uncertain; however, research suggests that it might function as a modulating agent of serotonin and norepinephrine.[6] In addition to inhibiting norepinephrine transport, viloxazine has demonstrated the ability to increase 5HT levels in the prefrontal cortex. Notably, the drug acts as an agonist at the 5HT2C receptor and an antagonist at the 5HT2B receptor.[7]
As viloxazine has been found to possess epileptogenic properties in certain patients, caution should be exercised when prescribing the drug to individuals with a history of seizures or neurological disorders. Numerous studies have highlighted the absence of adverse anticholinergic effects in viloxazine compared to other tricyclic antidepressants. The lack of adverse anticholinergic effects makes viloxazine a potential candidate for treating depression in older populations.[8] Notably, viloxazine does not currently have FDA approval for treating depression in the United States.
This activity focuses on the recently FDA-approved extended-release viloxazine formulation authorized for ADHD therapy in April 2021. [9]
Few side effects of this drug are, Drowsiness, tiredness, headache, decreased appetite, nausea, vomiting, dry mouth, or constipation may occur.[10]
Viloxazine has undergone two randomized controlled trials for nocturnal enuresis (bedwetting) in children, both of those times versus imipramine.[11,12] By 1990, it was seen as a less cardiotoxic alternative to imipramine, and to be especially effective in heavy sleepers.[13]
In narcolepsy, viloxazine has been shown to suppress auxiliary symptoms such as cataplexy and also abnormal sleep-onset REM[14] without significantly improving daytime somnolence.[15] In a cross-over trial (56 participants) viloxazine significantly reduced EDS and cataplexy.[16] Viloxazine has also been studied for the treatment of alcoholism, with some success.[17]
Generic Name Viloxazine, sold under the brand name **Qelbree** and formerly as **Vivalan**

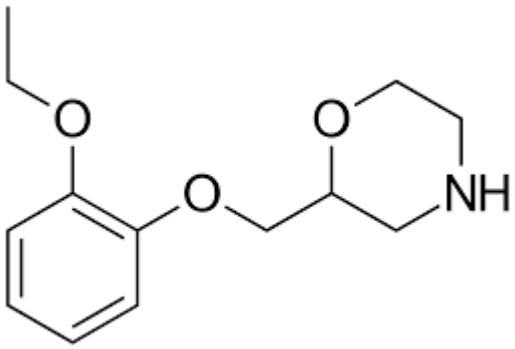

Figure 1: Structure of Viloxazine

A study of the literature says that there are different ways to measure these medicines at the same time, as well as ways to measure them separately or in combination with other medicines. Using RP-HPLC and UV-Spectrophotometry A review of the literature shows that there isn't a standard way to measure Viloxazine RP-HPLC simultaneously while showing stability in pharmacy dosage form. The main goal of this work is to come up with an RP-HPLC method that is quick, easy, and accurate for figuring out the amount and type of

Viloxazine medicines. As suggested by the ICH, a tried-and-true method was also used to guess how much Trilaciclib was present. [18-21]

MATERIALS AND REAGENTS

Spectrum Pharma Research Solutions in Hyderabad sent us pure Viloxazine, drugs. Viloxazine (Qelbree), a mixture drug, was bought at a nearby pharmacy. All of the materials and buffers used in this method came from Rankem in India. These included acetonitrile, phosphate buffer, methanol, potassium dihydrogen ortho phosphate buffer, ortho-phosphoric acid, distilled water, and phosphate buffer.

Instrumentation and Chromatographic Conditions: For the development and validation method, an automated sample injector was employed with a WATERS HPLC, model: 2695 SYSTEM with Photo diode array detector. For the separation, a Discovery 150 (C18 250 mm x 4.6 mm, 5µm) column was employed. Acetonitrile is employed as mobile phase B, while 0.1% ortho phosphoric acid is used as mobile phase A. (35:65 Ratio). The analysis was done in isocratic mode with an injection volume of 10 mL and a flow rate of 1 mL/min. The duration was six minutes. The measurements were made at 254 nm.

PREPARATION OF SOLUTIONS

Diluent: Based up on the solubility of the drugs, diluent was selected, Methanol and Water taken in the ratio of 50:50

Preparation of buffer:

0.1%OPA Buffer: 1ml of ortho phosphoric acid was diluted to 1000ml with HPLC grade water.

0.01N KH2PO4 Buffer: Accurately weighed 1.36gm of Potassium dihyrogen Ortho phosphate in a 1000ml of Volumetric flask add about 900ml of milli-Q water added and degas to sonicate and finally make up the volume with water (4.8-pH).

0.01N NA2HPO4 Buffer: Accurately weighed 1.41gm of Sodium Hydrogen Phosphate in a 1000ml of Volumetric flask add about 900ml of milli-Q water added and degas to sonicate and finally make up the volume with water (4.0-pH).

Preparation of Standard stock solutions: Accurately weighed 10mg of Viloxazine is transferred to 50ml volumetric flask. 3/4 th of diluents was added to the flask and sonicated for 10 minutes. Flask was made up with diluents and labeled as Standard stock solution. (200µg/ml of Viloxazine)

Preparation of Standard working solutions (100% solution): 1ml from each stock solution was pipetted out and taken into a 10ml volumetric flask and made up with diluent. (20µg/ml of Viloxazine).

Preparation of Sample stock solutions: 10 tablets were weighed and the average weight of each tablet was calculated, then the weight equivalent to 1 tablet was transferred into a 100ml volumetric flask, 50ml of diluents was added and sonicated for 25 min, further the volume was made up with diluent and filtered by HPLC filters (200µg/ml of Viloxazine)

Preparation of Sample working solutions (100% solution): 1ml of filtered sample stock solution was transferred to 10ml volumetric flask and made up with diluent. (20µg/ml of Viloxazine).

METHOD VALIDATION

To prove that the technique is suggested for routine analysis, the HPLC method's validation was done for the simultaneous estimation Viloxazine drug material in accordance with the ICH criteria.

Specificity: Checking of the interference in the optimized method. We should not find interfering peaks in blank and placebo at retention times of these drugs in this method. So this method was said to be specific.

Linearity: stock solutions of Viloxazine is taken in to 6 different volumetric flasks and diluted to 10ml with diluents. Linearity solutions are prepared such that 0.25, 0.5, 0.75, 1, 1.25, 1.5ml.

Accuracy: That is sometimes term of trueness. The Accuracy should be established across the specified range of the analytical procedure.

Preparation of Standard stock solutions: Accurately weighed 10mg of Viloxazine is transferred to 50ml volumetric flask. 3/4th of diluents was added to the flask and sonicated for 10 minutes. Flask was made up with diluents and labeled as Standard stock solution. (200µg/ml of Viloxazine)

Preparation of 50% Spiked Solution: 0.5ml of sample stock solution was taken into a 10ml volumetric flask, to that 1.0ml from each standard stock solution was pipetted out, and made up to the mark with diluent.

Preparation of 100% Spiked Solution: 1.0ml of sample stock solution was taken into a 10ml volumetric flask, to that 1.0ml from each standard stock solution was pipetted out, and made up to the mark with diluent.

Preparation of 150% Spiked Solution: 1.5ml of sample stock solution was taken into a 10ml volumetric flask, to that 1.0ml from each standard stock solution was pipetted out, and made up to the mark with diluent.

Acceptance Criteria:

The % Recovery for each level should be in between 98.0 to 102.

Robustness: Small deliberate changes in method like Flow rate, mobile phase ratio, and temperature are made but there were no recognized change in the result and are within range as per ICH Guide lines.

Robustness conditions like Flow minus (0.9ml/min), Flow plus (1.1ml/min), mobile phase minus, mobile phase plus, temperature minus (25°C) and temperature plus(35°C) was maintained and samples were injected in duplicate manner. System suitability parameters were not much affected and all the parameters were passed. %RSD was within the limit.

LOD sample Preparation: 0.25ml each from two standard stock solutions was pipetted out and transferred to two separate 10ml volumetric flasks and made up with diluents. From the above solutions 0.1ml of Viloxazine, solutions

Respectively were transferred to 10ml volumetric flasks and made up with the same diluents

LOQ sample Preparation: 0.25ml each from two standard stock solutions was pipetted out and transferred to two separate 10ml volumetric flask and made up with diluent. From the above solutions 0.3ml of Viloxazine, solutions respectively were transferred to 10ml volumetric flasks and made up with the same diluent.

System suitability parameters: The system suitability parameters were determined by preparing standard solutions of Viloxazine (20ppm) and the solutions were injected six times and the parameters like peak tailing, resolution and USP plate count were determined.

Degradation studies:

Oxidation:

To 1 ml of stock solution of Viloxazine 1 ml of 20% hydrogen peroxide (H2O2) was added separately. The solutions were kept for 30 min at 600c. For HPLC study, the resultant solution was diluted to obtain (20ppm) solution and 10 µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Acid Degradation Studies:

To 1 ml of s tock s solution Viloxazine 1ml of 2N Hydrochloric acid was added and refluxed for 30mins at 1c. The resultant solution was diluted to obtain (20ppm) solution and 10 µl solutions were injected into the system and the chromatograms were recorded to assess the stability of sample.

Alkali Degradation Studies:

To 1 ml of stock solution Trilaciclib 1 ml of 2 N sodium hydroxide was added and refluxed for 30mins at 60 OC. The resultant solution was diluted to obtain (60ppm) solution and 10 µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Dry Heat Degradation Studies:

The standard drug solution was placed in oven at 1050c for 6 h to study dry heat degradation. For HPLC study, the resultant solution was diluted to (20ppm) solution and10µl were injected into the system and the chromatograms were recorded to assess the stability of the sample.

Photo Stability studies:

The photochemical stability of the drug was also studied by exposing the (200ppm) solution to UV Light by keeping the beaker in UV Chamber for 7days or 200 Watt hours/m2 in photo stability chamber. For HPLC study, the resultant solution was diluted to obtain (20ppm) solutions and 10 µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Neutral Degradation Studies:

Stress testing under neutral conditions was studied by refluxing the drug in water for 6hrs at a temperature of 60ºc. For HPLC study, the resultant solution was diluted to (20ppm) solution and 10 µl were injected into the system and the chromatograms were recorded to assess the stability of the sample.

RESULTS AND DISCUSSIONS:

Table 1. System suitability table

S.No.	Viloxazine		
Injection	**RT (min)**	**USP Plate Count**	**Tailing**
1	2.229	4942	1.52
2	2.230	4920	1.53
3	2.232	5052	1.47
4	2.232	4985	1.44
5	2.233	5089	1.48
6	2.233	4708	1.48

Table 2. Specificity data

Sample name	Retention time(Mins)	Area

Viloxazine	2.248	893678

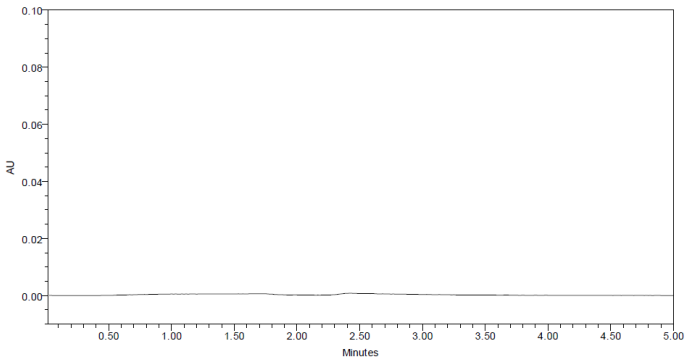

Figure 2. Blank Chromatogram

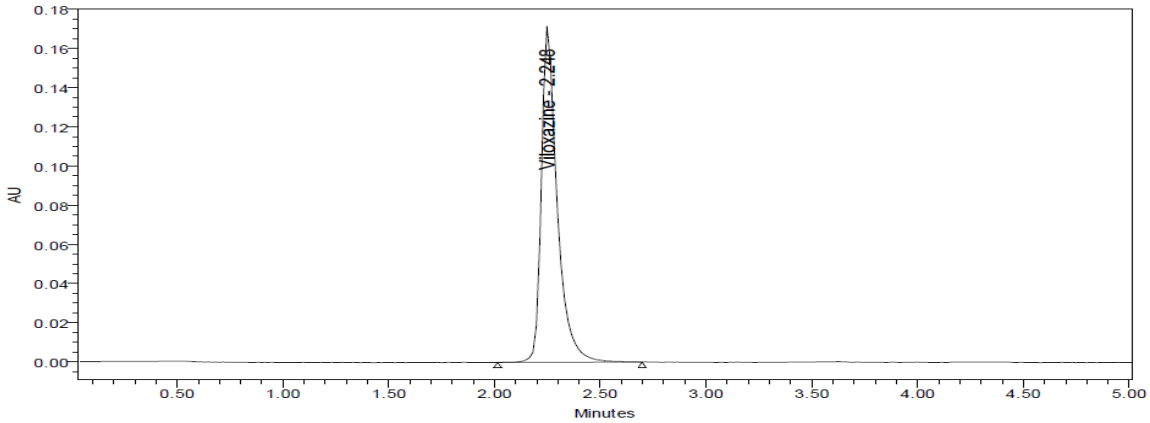

Figure 3. Specificity Chromatograms of Viloxazine

Linearity:

Table 3. Linearity table for Viloxazine:

Viloxazine		
Linearity Level (%)	**Concentration (ppm)**	**Area**
0	0	0
25	5	246037
50	10	458883
75	15	685586
100	20	913068
125	25	1137384
150	30	1355133

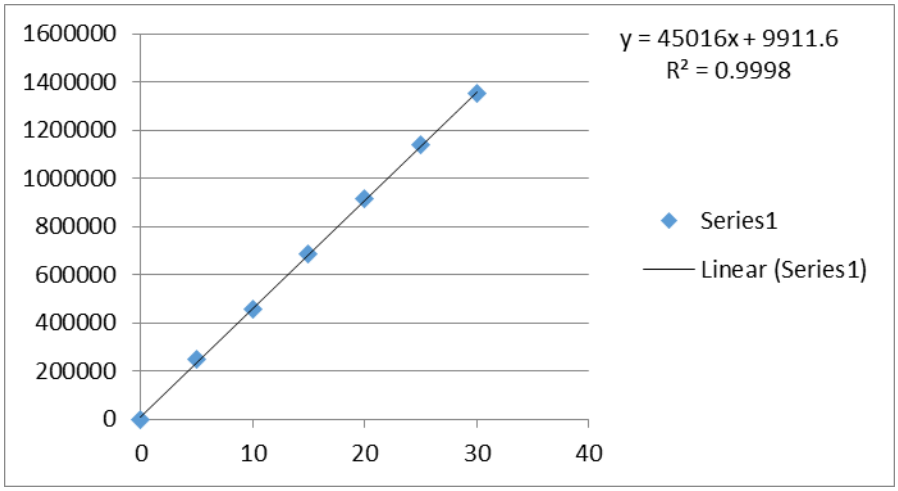

Figure 4. Viloxazine calibration Curve

Accuracy:

Table 4. Accuracy table of Viloxazine

% Level	Amount Spiked (µg/mL)	Amount recovered (µg/mL)	% Recovery	Mean %Recovery
50%	10	10.02	100.16	100.03%
	10	9.98	99.76	
	10	9.91	99.05	
100%	20	20.19	100.93	
	20	19.90	99.49	
	20	20.19	100.94	
150%	30	30.19	100.64	
	30	29.76	99.21	
	30	30.02	100.05	

System Precision: With regard to the working strength of Viloxazine six duplicate injections of the standard solution at 100% of the prescribed limit were analysed to determine the system accuracy. In Table 5, the results of the peak area are compiled.

Table 5. System precision

S. No	Area of Viloxazine
1.	846613
2.	845381
3.	848000
4.	840547
5.	854075
6.	842948
Mean	**846261**
S.D	**4660.6**
%RSD	**0.6**

The % RSD for the peak areas of Viloxazine obtained from six replicate injections of standard solution was within the limit of (<2%).

Method precision: Analyzing a sample of Viloxazine allowed researchers to gauge the method's accuracy (Six individual sample preparations). Table 6 provides a summary of the data.

Table 6. Method precision

S.no	Viloxazine
1	849958
2	844345
3	846554
4	844959
5	843933
6	845728
Avg	**845913**
Std dev	**2195.3**
%RSD	**0.3**

Results shows, the % RSD of Repeatability study was within the range for Viloxazine is (<2%)

Table 7. Robustness

S.No.	Condition	%RSD of Viloxazine.
1	Flow rate (-) 0.9ml/min	0.5
2	Flow rate (+) 1.1ml/min	0.5
3	Mobile phase (-) 60B:40A	1.0
4	Mobile phase (+) 70B:30A	1.2
5	Temperature (-) 25°C	0.3
6	Temperature (+) 35°C	0.7

Table 8. Forced degradation for Viloxazine

Stress condition	Solvent	Temp (^{0}C)	Exposed time
Acid	2N HCL	60^0c	30 mins
Base	2N NAOH	60^0c	30 mins
Oxidation	20% H_2O_2	60^0c	30 mins
Thermal	Diluent	105^0c	6 hours
Photolytic	Diluent	-	-
Hydrolytic	Water	60^0c	

DEGRADATION

Degradation Studies: Degradation studies were performed with the formulation and the degraded samples were injected. Assay of the injected samples was calculated and all the samples passed the limits of degradation

Table 9. Degradation results of Viloxazine

Type of degradation	Viloxazine	
	% RECOVERED	% DEGRADED
Acid	95.89	4.11
Base	95.48	4.52
Peroxide	96.27	3.73
Thermal	98.15	1.85
UV	97.98	2.02
Water	99.13	0.87

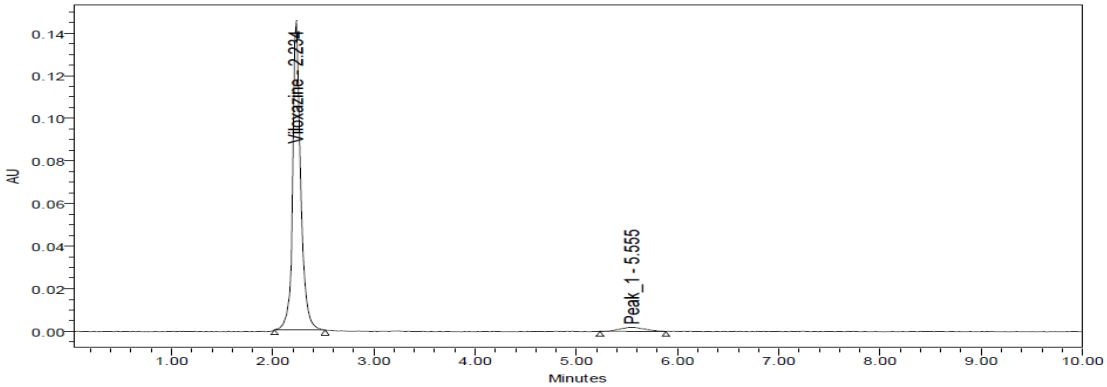

Figure 5. Acid chromatogram of Viloxazine

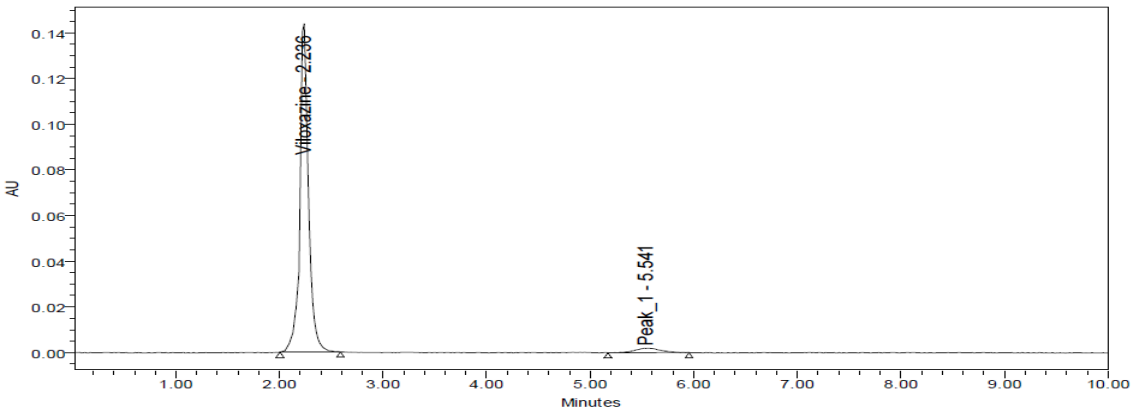

Figure 6. Base chromatogram of Viloxazine

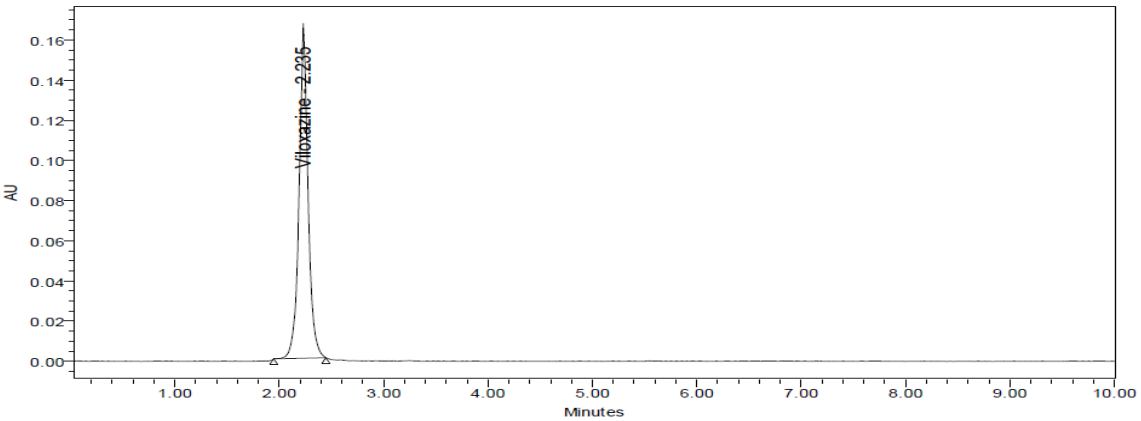

Figure 7. Peroxide chromatogram of Viloxazine

According to the results, samples were degraded when they were subjected to an acid, base, and oxidation interaction. Hydrolysis reaction, heat reaction, and light reaction all showed no deterioration. According to the stress research, none of the degradants co-eluted with the maxima of the active medication.

Assay: (Qelbree**)** bearing label claim, Viloxazine 100mg , assay was carried out by injecting sample into HPLC System.

Table 10. Assay data of Viloxazine

S.No.	Standard Area	Sample area	% Assay
1	846613	849958	100.34
2	845381	844345	99.67
3	848000	846554	99.93
4	840547	844959	99.75
5	854075	843933	99.63
6	842948	845728	99.84
Avg	**846261**	**845913**	**99.86**
Stdev	**4660.6**	**2195.3**	**0.2592**
% RSD	**0.6**	**0.3**	**0.3**

Table 11. Assay outcome for Viloxazine

Drug Name	Label claim dose	%Assay	Brand Name
Viloxazine	100mg	100.34	Qelbree

CONCLUSION

The proposed HPLC method was validated as per ICH guidelines and applied for the determination of Viloxazine in tablet dosage form. Chromatographic conditions used are stationary phase Ascentis C18 (150mm*4.6mm2.8m), Mobile phase 0.01N Kh2Po4: Methanol in the ratio of 55:45 and flow rate was maintained at 1.0ml/min, detection wave length was 253nm, column temperature was set to 30oC and diluent was mobile phase Conditions were finalized as optimized method. System suitability parameters were studied by injecting the standard six times and results were well under the acceptance criteria. Linearity study was carried out between 25% to150 % levels, R2 value was found to be as 0. 999.Precision was found to be 0.9 for repeatability and 0.7 for intermediate precision.LOD and LOQ are 0.14µg/ml and 0.41µg/ml respectively. By using above method assay of marketed formulation was carried out 100.31% was present. Degradation studies of Viloxazine were done, in all conditions purity threshold was more than purity angle and within the acceptable range. Full length method was not performed; if it is done this method can be used for routine analysis of Viloxazine.

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REFERENCES

1. https://www.mayoclinic.org/diseases-conditions/adhd/symptoms-causes/syc-20350889#:~:text=Attention%2Ddeficit%2Fhyperactivity%20disorder%20(ADHD)%20is%20a%20chronic,attention%2C%20hyperactivity%20and%20impulsive%20behavior
2. Findling RL, Candler SA, Nasser AF, Schwabe S, Yu C, Garcia-Olivares J, O'Neal W, Newcorn JH: Viloxazine in the Management of CNS Disorders: A Historical Overview and Current Status. CNS Drugs. 2021 Jun;35(6):643-653. doi: 10.1007/s40263-021-00825-w. Epub 2021 May 18.

3. FDA Approved Drug Products: QELBREE (viloxazine extended-release capsules), for oral use
4. Stephen Merson et al., Physical Treatments For Depression, Biological Aspects of Affective Disorders, 1991
5. In Meyler's Side Effects of Drugs (Sixteenth Edition), 2016
6. Findling RL, Candler SA, Nasser AF, Schwabe S, Yu C, Garcia-Olivares J, O'Neal W, Newcorn JH. Viloxazine in the Management of CNS Disorders: A Historical Overview and Current Status. CNS Drugs. 2021 Jun;35(6):643-653. [PMC free article] [PubMed]
7. Yu C, Garcia-Olivares J, Candler S, Schwabe S, Maletic V. New Insights into the Mechanism of Action of Viloxazine: Serotonin and Norepinephrine Modulating Properties. J Exp Pharmacol. 2020;12:285-300. [PMC free article] [PubMed]
8. Lippman W, Pugsley TA. Effects of viloxazine, an antidepressant agent, on biogenic amine uptake mechanisms and related activities. Can J Physiol Pharmacol. 1976 Aug;54(4):494-509. [PubMed]
9. Hafeez S, Saquib J, Qureshi NE. Viloxazine: A new miracle drug for attention deficit hyperactivity disorder (ADHD) or just another non-stimulant? Asian J Psychiatr. 2022 Jan;67:102948. [PubMed]
10. https://www.webmd.com/drugs/2/drug-181227/viloxazine-oral/details
11. Attenburrow AA, Stanley TV, Holland RP (January 1984). "Nocturnal enuresis: a study". The Practitioner. 228 (1387): 99–102. PMID 6364124.
12. Yurdakök M, Kinik E, Güvenç H, Bedük Y (1987). "Viloxazine versus imipramine in the treatment of enuresis". The Turkish Journal of Pediatrics. 29 (4): 227–230. PMID 3332732.
13. Libert MH (1990). "[The use of viloxazine in the treatment of primary enuresis]" [The use of viloxazine in the treatment of primary enuresis]. Acta Urologica Belgica (in French). 58 (1): 117–122. PMID 2371930
14. Guilleminault C, Mancuso J, Salva MA, Hayes B, Mitler M, Poirier G, Montplaisir J (1986). "Viloxazine hydrochloride in narcolepsy: a preliminary report". Sleep. 9 (1 Pt 2): 275–279. doi:10.1093/sleep/9.1.275. PMID 3704453.
15. Mitler MM, Hajdukovic R, Erman M, Koziol JA (January 1990). "Narcolepsy". Journal of Clinical Neurophysiology. 7 (1): 93–118. doi:10.1097/00004691-199001000-00008. PMC 2254143. PMID 1968069.
16. Vignatelli L, D'Alessandro R, Candelise L (January 2008). "Antidepressant drugs for narcolepsy". The Cochrane Database of Systematic Reviews. 2008 (1): CD003724
17. Altamura AC, Mauri MC, Girardi T, Panetta B (1990). "Alcoholism and depression: a placebo controlled study with viloxazine". International Journal of Clinical Pharmacology Research. 10 (5): 293–298. PMID 2079386
18. https://pubchem.ncbi.nlm.nih.gov/compound/Viloxazine
19. Ramchandran D et al.., STABILITY INDICATING AND COST EFFECTIVE ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF VILOXAZINE BY USING REVERSE PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAPHY, JCDR. 2021; 12(4): 1403-1412.
20. E. Manuela P. J. Garrido et al.., Voltammetric and DFT Studies on Viloxazine: Analytical Application to Pharmaceuticals and Biological Fluids Electroanalysis 20, 2008, No. 13, 1454 – 1462
21. Chungping Yu et al ew Insights into the Mechanism of Action of Viloxazine: Serotonin and Norepinephrine Modulating Properties, J Exp Pharmacol. 2020; 12: 285–300