SENNOS

Journal of Drug Delivery and Biotherapeutics

Journal homepage: https://sennosbiotech.com/JDDB/1

Research Article

Analytical Method Development and Validation for Venlafaxine Hydrochloride: UV-Visible Spectrophotometric Estimation in Bulk and Pharmaceutical Dosage Forms

Alka Zade[a*], Payal Kabra

Department of Pharmaceutics, Mup's College of Pharmacy, Degaon. Risod, Maharashtra, India 425405

ARTICLEINFO

ABSTRACT

This abstract presents the development and validation of a UV-visible spectrophotometric method for the accurate estimation of Venlafaxine HCl, a commonly prescribed antidepressant, in bulk and pharmaceutical formulations. The method utilizes purified water as the solvent, with a maximum absorbance identified at 224.60 nm. It exhibited excellent linearity within a concentration range of 5-35 µg/ml, with a high correlation coefficient (R^2 = 0.999) and consistent mean recovery rates between 99.00% and 100.0%. The method's cost-effectiveness and simplicity make it an ideal candidate for routine quality control. Validation was performed following ICH guidelines, ensuring reliability across parameters such as linearity, repeatability, precision, accuracy, ruggedness, and determination of LOD & LOQ. Recovery studies further confirmed the method's applicability for the routine analysis of Venlafaxine HCl in both active pharmaceutical ingredients and commercial tablet formulations. In conclusion, this validated method provides a reliable, swift, and economical approach for the quality control of Venlafaxine HCl, making it a valuable addition to existing analytical techniques.

Keywords: Antidepressant; Venlafaxine HCL; Analytical Validation; Method development; ICH guidelines

Corresponding Author:

Alka Zade*
E-mail addresses: zadealka777@gmail.com

Received date: 05-Mar-2024 Revised date: 29-Mar-2024, Accepted date: 11-Apr-2024

Crossref DOI: https://doi.org/10.61920/jddb.v1i01.17

1. INTRODUCTION

The antidepressant Venlafaxine HCl is (Bicyclic antidepressant). It is known as SNRI (inhibitor of serotonin-norepinephrine reuptake), but it has also been referred to as SNDRI (Serotonin norepinephrine-dopamine reuptake inhibitor). It functions by blocking the reuptake of the transporter protein for the mood of the main neurotransmitter [1]. This leaves the neurotransmitter more involved in the synapse. The impaired neurotransmitters are serotonin and norepinephrine, although in large concentrations it often weakly stimulates dopamine reuptake, with new research suggesting that some dopamine is also transmitted through the norepinephrine transporter, as dopamine is inactivated in the frontal cortex through norepinephrine reuptake. Dopamine transporters are primarily used in the frontal cortex, so Venlafaxine HCl can improve dopamine neurotransmission in these areas of the brain [2]. Venlafaxine HCl has been shown to increase the pain threshold in mice, indirectly influencing opioid receptors as well as alpha 2-adrenergic receptors. The naloxone and opioid blocker reversed these pain benefits, thereby endorsing an opioid mechanism [3].

The literature survey on the estimation of venlafaxine also focuses on the estimation of venlafaxine for other HPLC and UV Spectrometric products. Venlafaxine HCl is a 2007 British Pharmacopoeia official. Via potentiometric titration, the assay of the drug according to BP is processed. It needs and performs simple, quick and cost-effective analytical methods for routine analysis. A UV spectroscopic approach for estimating venlafaxine biological fluids, such as serum plasma urine, was disclosed in a literature survey. The chromatographic process is time-consuming, expensive and highly trained. The UV spectrometric technique is simple and precise. It can be incredibly beneficial for routine bulk analysis, sample composition and dissolution. The main objective of this study was to establish a simple, precise and accurate and economical method for estimating Venlafaxine HCl in bulk pharmaceutical formulations with a better detection range [4].

2. UV- VISIBLE SPECTROPHOTOMETRIC METHOD

UV-visible spectroscopy examines a typical sample's wavelength. Broad use for test detection is beneficial for detailed estimates of UV-visible spectra with vast highlights [4]. The most important technique of the spectrophotometric method is to identify the substance factor on-premise of the material's transmitting or reflection properties as the wavelength power, adhering to the law of Beer-Lambert and a synthetic compound bearing a bunch of chromophores for light retention. When compared with other methods, it devotes less time and offers phenomenal precision in viable [5]. The writing description teaches the UV techniques and the guarantee of venlafaxine HCL is provided for by the RP-HPLC approach solely with various medications. The present review involves enhancement and acceptance of modern UV spectroscopy techniques for unadulterated assurance of venlafaxine HCL and economic conditions are indicated by its pharmaceutical plans. The investigation plan was approved by the criteria of ICH rules acceptance [6][7].

To develop a fair UV-visible spectrophotometric technique for the investigation of venlafaxine hydrochloride in-depth, distilled water was studied. The parameters used for the selection of the media were affectability of the procedure, ease of research preparation, dissolvability of the drug, solvent costs and suitability of the approach.

3. MATERIAL AND METHOD

3.1 Apparatus

A Shimadzu UV visible double beam spectrophotometer (UV mini-1900, Shimadzu Corporation, Kyoto, Japan) was used for all absorbance measurements with matched quartz cells.

3.2 Materials

All chemicals and reagents were of analytical or HPLC grade. Venlafaxine HCl was supplied from Mylan Laboratories Hydrabad as gift sample and distilled water, methanol should be used for the method utilization. Pharmaceutical grade excipients were obtained from lab of R.C Patel Institute of pharmaceutical education and Research, Shirpur Dhule.

3.3 Determination of Wavelength of Maximum Absorption

The bulk solution was prepared by using purified water as a solvent. By dissolving 10 mg of venlafaxine bulk drug into 100 ml, the normal stock solution of venlafaxine HCl was prepared. Then 1 ml of the sample was withdrawn from 100 ml of stock solution to assess the lambda max of the substance and diluted up to 10 ml of distilled water, so the concentration is 10 µg/ml. The sample concentration filled in the UV cuvette and the UV visible spectrometer tracks the lambda max in spectrum mode. 10 µg/ml of the sample was scanned in the 400-200nm UV visible spectrometer range. The lambda max was determined to be 224.60 nm of Venlafaxine HCl [8].

3.4 Assay Determination

In a 100 ml volumetric flask, a quantity of venlafaxine HCl equal to 100 mg of venlafaxine hydrochloride was taken and dissolved in 10 ml of water and mixed with water up to the level. For 5 minutes, the resulting solution was ultarasonicated. Using Whatman filter paper No.40, the solution was then filtered. Relevant dilutions of water are made from the filtrate. Preferred concentration (10µg/ml) to be obtained. This solution was then tested in UV and the outcome was calculated by the percentage amount found (Table 1) [9].

4. PARAMETERS

4.1 Linearity

The calibration curve was reported by the UV visible spectrometer photometric process. The linearity spectrum should be based on a 10 µg/ml concentration assay of lambda peak absorbance. The linearity spectrum was known to be 5µg/ml, 10 µg/ml, 15 µg/ml, 20µg/ml, 25 µg/ml, 30 µg/ml, 35 µg/ml, based on absorbance so the absorbance vs concentration calibration curve is plotted and it is necessary to record the graph.

4.2 Repeatability

The repeatability of the procedure was calculated by the preparation of six 15 µg/ml dilutions of the same mean concentration concentrations as those of the lambert beer range.

4.3 Accuracy

The accuracy of Venlafaxine HCl was calculated by the preparation of two stock solutions as a bulk drug and the dosage type being marketed. Dilutions of 80 %, 100 %, 120 % are prepared for precision determination, in which the quantity is maintained constant if 15 µg/ml is marketed. The quantity of pure drugs ranged from 12 µg/ml, 15 µg/ml, and 18 µg/ml to 80%, 100%, and 120%, respectively. The dilutions were prepared in triplicate and the percentage recovery indicated precision [12].

4.4 Precision

By preparing three middle levels of concentration dilution to become 10 µg/ml, 15 µg/ml, 20µg/ml,

respectively, the precision form of Venlafaxine HCl was shown. The methodology was revealed by Intraday and Inter day variance research. In the intraday analysis, the solution is prepared for three separate ranges and analysed three times a day, morning, midday, evening. In an inter-day analysis, three solution concentration ranges were prepared and analysed three times a day, i.e. day 1, day 2, day 3. The outcome was reported by Percentage RSD [13].

4.5 Ruggedness

It was calculated by the preparation of 6 medium concentration dilutions of 15µg/ml. The findings evaluated by two separate observers were observed, as well as on two different instruments and the respective absorption. The outcome was reported by Percent RSD [14].

4.6 Limit of detection (LOD)

The detection limit for venlafaxine HCl was determined by the preparation of dilutions ranging from 5-10 µg/ml at various concentrations. The detection limit of an individual analytical technique is the smallest quantity of analyte in a sample that can be detected as an exact value but not necessarily quantitated.

4.7 Limit of quantitation:

For a defined degree of precision and accuracy, the LOQ is the concentration that can be quantified accurately. Using a formula involving standard deviation response and calibration curve slope, the LOQ was calculated.

5. RESULTS AND DISCUSSION

Venlafaxine is a drug used as an antidepressant. The analysis of validity processed by the UV spectroscopic system. For the routine estimate of venlafaxine HCL in bulk drug and pharmaceutical dosage forms, the proposed method was found to be quick, sensitive, reliable, accurate, economical, and rapid. The validation parameter summary of the spectrometric method proposed is shown in Table 1.

Table 1: Summary of validation

Parameter	Results
Lambda max	224.60 nm
Linearity range	5-35µg/ml
Linearity indicated by the correlation coefficient	0.9955
Linear regression equation	y = 0.0253x + 0.2405
Repeatability indicated as % RSD	1.7081%
Accuracy indicated by % recovery	99-100 %
Precision indicated by %RSD	Intraday- 1.6392% Interday- 1.7612%
Ruggedness indicated by %RSD	1.8285%
LOD	0.308µg/ml
LOQ	3µg/ml
Assay %	98%

5

.1 Selection of wavelength

Scan the standard UV spectrophotometer solution in spectrum mode from 200 nm and 400 nm, using diluents as blanks. Venlafaxine HCL shows the 224 nm λmax seen in Figure 1.

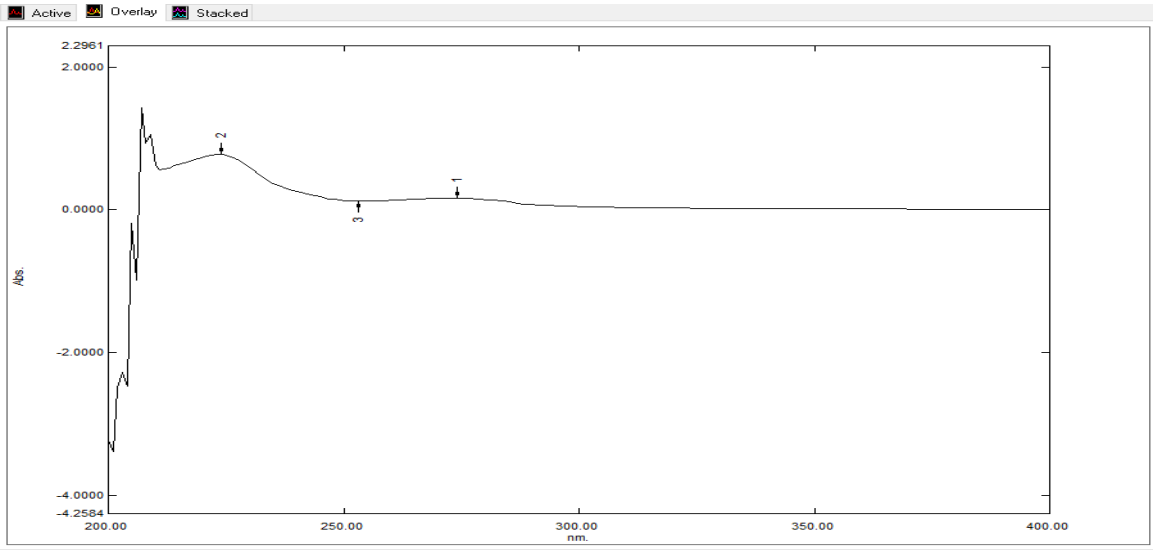

Fig.1: Lambda max of venlafaxine HCL

5

.2 Linearity and range

The obtained calibration curve was assessed by its coefficient of correlation. The absorption of 5-30 µg/ml samples was linear with a correlation coefficient (R2) of 0.9955, as shown in Figure 2 and Table 2.

Table 2: Preparation of Standard Calibration Curve

Conc.(µg/ml)	Absorbance
5	0.380
10	0.491
15	0.595
20	0.749
25	0.894
30	0.994

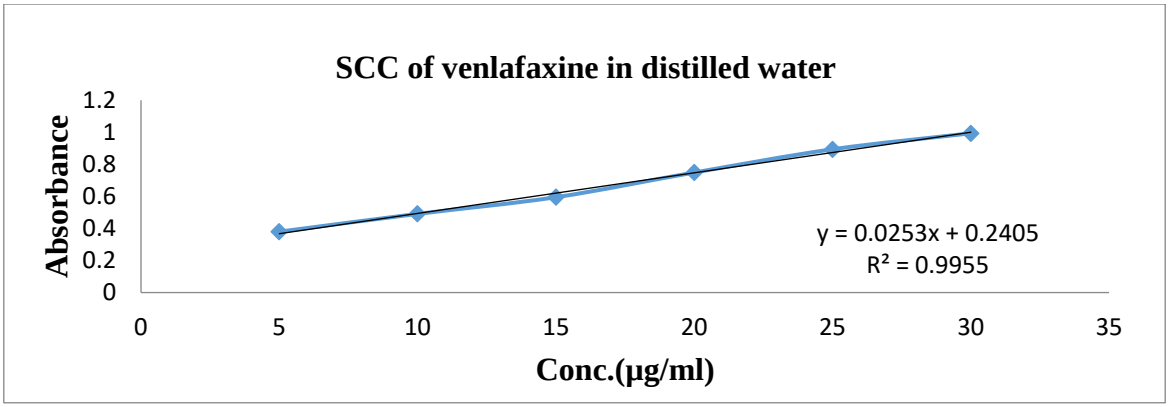

Fig.2: Calibration Curve of Venlafaxine HCl

5.3 Repeatability

Repeatability (% R.S.D.) at all concentration levels ranged from 1.70 % (Table 3). Repeatability results indicate precision over a limited interval of time and inter-assay accuracy under the same operating conditions.

Table 3: Repeatability of venlafaxine HCl

Sr. no	Conc.(µg/ml)	Absorbance	Amount	% Amount
1	15	0.525	12.25	81.66667
2	15	0.531	12.4	82.66667
3	15	0.535	12.5	83.33333
4	15	0.511	11.9	79.33333
5	15	0.523	12.2	81.33333
6	15	0.521	12.15	81
	Average	0.524333	12.23333	81.55556
	SD	0.008359	0.208966	1.393105
	%RSD	**1.594144**	**1.708167**	**1.708167**

5.4 Accuracy

The similarity of the test results to the true value is the accuracy of an analytical method. The application of the analytical procedure to recovery studies where a sufficient concentration of standard is spiked in pre-analysed sample solutions has been determined. The % recovery for the standard analysis and reference analysis method for all the three concentration levels 80%, 100%, 120% ranged from 99.6770 %, 91.0666%, 100.3958% with % RSD, 0.01608%, 0.01580%, 0.2214% respectively become showing that any small change in the drug concentration can be accurately determined with high accuracy. The results obtained from the standard method of addition and reference analysis have confirmed the accuracy of the proposed method (Table 4) (Figure 3).

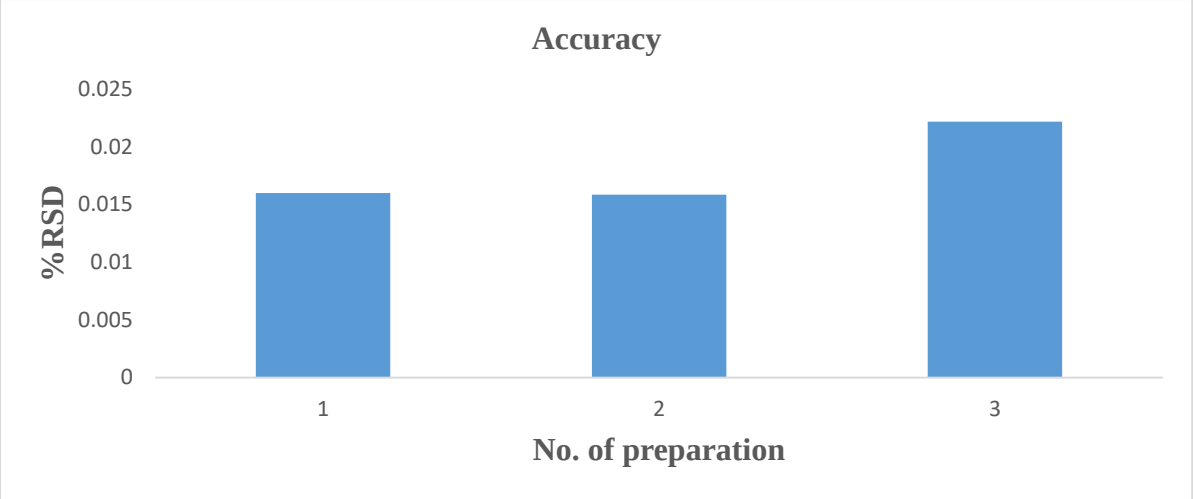

Fig.3: Accuracy Readings of Venlafaxine hydrochloride

Table 4: Accuracy Readings of Venlafaxine hydrochloride

Observation/ Results						
No. of preparation	**Conc. (µg/ml)**		**% Recovery**	**Statistical Results**		
	Formulation	Pure Drug		Mean	SD	%RSD
80%	15	8	97.9065	**99.6770**	1.6036	0.0160
80%	15	8	101.0313			
80%	15	8	100.0938			
100%	15	10	91.1500	**91.0666**	0.1443	0.01585
100%	15	10	90.9000			
100%	15	10	91.1500			
120%	15	12	102.9583	**100.3958**	2.2233	0.022174
120%	15	12	98.9791			
120%	15	12	99.2500			

5.6 Precision

The precision of the analytical method specifies, under recommended conditions, the degree of dispersion between a set of measurements obtained from multiple samples of the same homogeneous sample. Intraday precision refers to short use of the analytical technique within a laboratory using the same operator and the same equipment, while Interday precision involves the estimation of analysis differences when different analysts use a method inside a laboratory on different days. The developed method's intra-day and the inter-day

precision study confirmed adequate sample stability and method reliability where all the % RSDs were less than 2% (Table 5, 6) (Figure 4, 5).

Table 5: Precision (Intraday) readings of Venlafaxine hydrochloride

Conc.(µg/ml)	**Morning**			**Afternoon**			**Evening**		
10	Abs.	Amt.	% Amt.	Abs.	Amt.	% Amt.	Abs.	Amt.	% Amt.
	0.3930	8.94	89.4	0.3880	8.825	88.25	0.399	9.1	91.00
15	0.5760	13.53	90.2	0.571	13.4	89.3333	0.598	14.075	93.8333
20	0.7300	17.377	86.88	0.734	17.475	87.375	0.788	18.825	94.125
AVG		13.282	88.8291		13.2333	88.319		14	92.9861
SD		4.2241	1.7284		4.3274	0.9810		4.8629	1.7261
%RSD	1.9458			1.1107			1.8564		

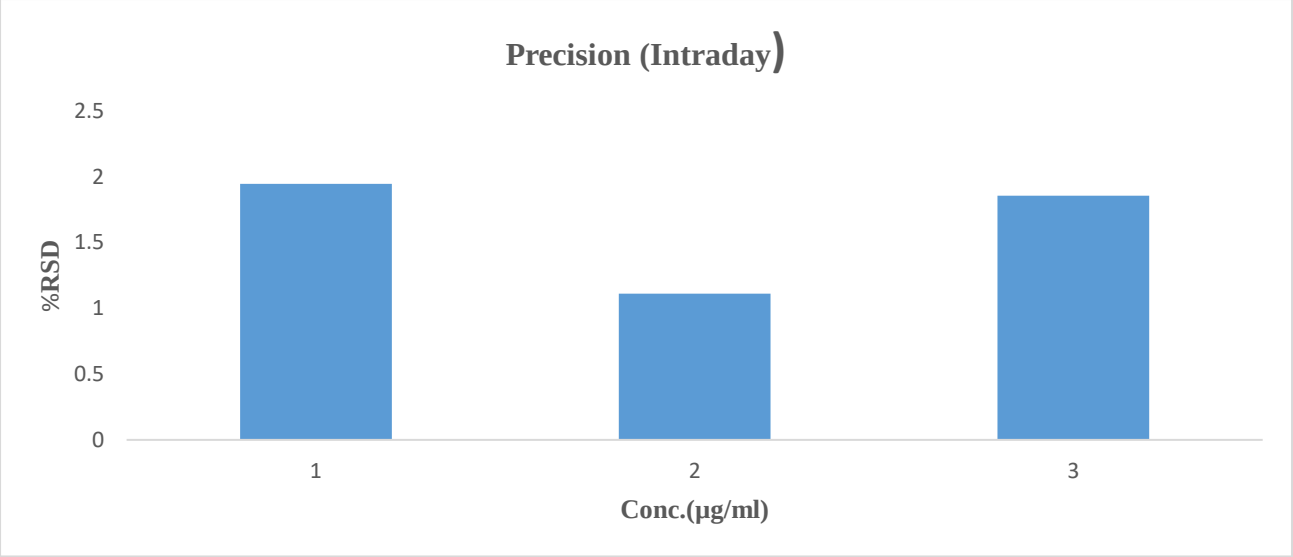

Fig. 4: Precision (Intraday) readings of Venlafaxine hydrochloride

Table 6: Precision (Interday) analyses of Venlafaxine hydrochloride

	Day 1			**Day 2**			**Day 3**		
Conc.(µg/ml)	Abs.	Amt.	% Amt.	Abs.	Amt.	% Amt.	Abs.	Amt.	% Amt.

10	0.3930	8.94	89.4	0.394	8.98	89.8	0.399	9.1	91.00
15	0.5760	13.53	90.2	0.555	12.99	86.6	0.555	12.99	86.6
20	0.7300	17.377	86.88	0.746	17.76	88.82	0.744	17.725	88.62
AVG		13.282	88.8291		13.245	88.4083		13.2716	88.7416
SD		4.2241	1.7284		4.3980	1.6402		4.3193	2.2023
%RSD	1.9458			1.8552			1.4817		

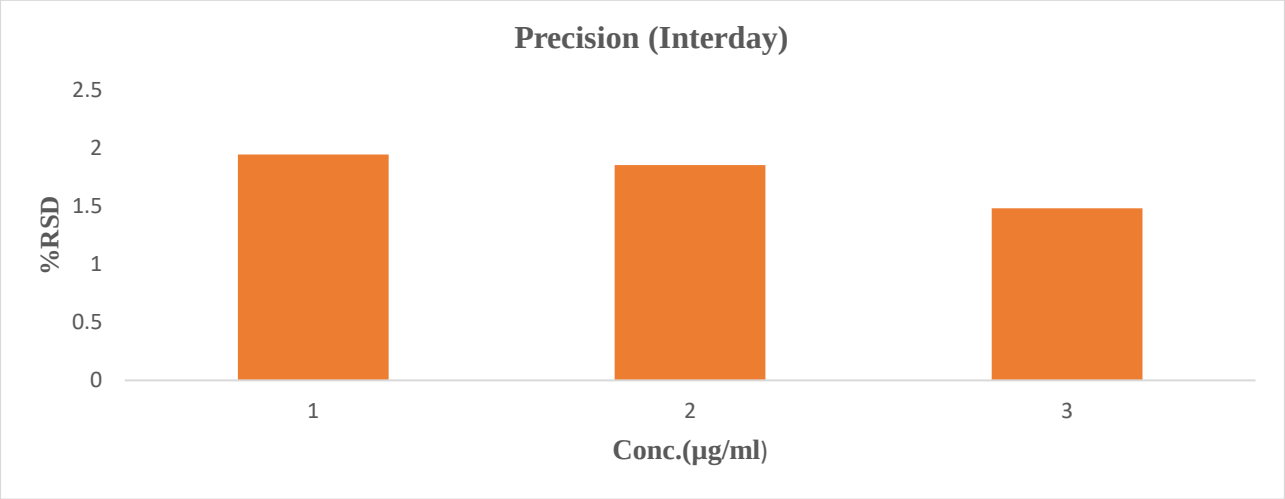

Fig.5: Precision (Interday) analyses of Venlafaxine hydrochloride

5.7 Ruggedness

The ruggedness of the analytical approach is the ability of a technique in unkindness of powerful environmental factors to resist the change in its results. Rugged analytical methods are chosen so because the effect of environmental factors is free from these methods. Two analysts 1 and 2, respectively, analysed venlafaxine solution 15 ug/ml to determine the superiority of the proposed UV process. Test analysis and data processing resulted in RSD values of 1.7081 and 1.9489 percentage values. The results revealed that the proposed UV approach was robust as it showed less than 2 %RSD values, as seen in Table 7.

Table 7: Results Showing Ruggedness of Method for Venlafaxine hydrochloride

	Analyst-1			**Analyst-2**		
Conc.(µg/ml)	**absorbance**	**amount**	**%amount**	**absorbance**	**amount**	**% amount**
15	0.525	12.25	81.66	0.510	11.87	79.16
15	0.531	12.40	82.66	0.531	12.40	82.66

15	0.535	12.50	83.33	0.532	12.42	82.83
15	0.511	11.90	79.33	0.511	11.90	79.33
15	0.523	12.20	81.33	0.521	12.15	81.00
15	0.521	12.15	81.00	0.524	12.22	81.50
AVG		15.23	81.55		12.16	81.08
SD		0.2089	1.390		0.2370	1.580
%RSD			**1.7081**			**1.9489**

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

LOQ represents the lowermost concentration that can be analysed with acceptable accuracy and precision. Generally, LOQ is the first calibration standard. LOD and LOQ of the proposed UV method were found to be 0.308 µg/ml and 3 µg/ml respectively.

6. CONCLUSION

The results and the statistical parameters validate the modest, rapid, specific, precise and accurate projected UV spectrophotometric method. Consequently, this method may even be used in bulk or dosage formulations for the determination of venlafaxine, without interference with normally used excipients and related substances.

ACKNOWLEDGEMENT

We wish to thank Mylan Laboratories Hydrabad for supplying the reference standard, Venlafaxine HCL and the Pharmaceutical Lab of MUPs college of pharmacy, Risod for forgives guidance and support for conducting a research study.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

AUTHORSHIP CONTRIBUTION STATEMENT

Alka Zade: Supervision, Validation, Methodology, Data Curation, Investigation, Writing – original draft, **Payal Kabra:** Conceptualization, Administration, Funding.

ABBREVIATIONS

Serotonin-norepinephrine reuptake inhibitor: SNRI

Serotonin norepinephrine-dopamine reuptake inhibitor: SNDRI

Reverse phase high pressure liquid chromatography: RP-HPLC

International conference on harmonization: ICH

Standard Calibration Curve

Limit of Quantitation: LOQ

Limit of Detection: LOD

REFERENCES

1. S.P. Rossby, D.H. Manier, S. Liang, I. Nalepa, F. Sulser, Pharmacological actions of the antidepressant venlafaxine beyond aminergic receptors, Int. J. Neuropsychopharmacol. 2 (1999) S1461145799001273. https://doi.org/10.1017/S1461145799001273.
2. J. Maj, Z. Rogóz, Pharmacological effects of

venlafaxine, a new antidepressant, given repeatedly, on the α1-adrenergic, dopamine and serotonin systems, J. Neural Transm. 106 (1999) 197–211. https://doi.org/10.1007/s007020050151.

3. S.M. Holliday, P. Benfield, Venlafaxine: A Review of its Pharmacology and Therapeutic Potential in Depression, Drugs. 49 (1995) 280–294. https://doi.org/10.2165/00003495-199549020-00010
4. K.N. Prashanth, K. Basavaiah, C.M. Xavier, Development and validation of UV-spectrophotometric methods for the determination of sumatriptan succinate in bulk and pharmaceutical dosage form and its degradation behavior under varied stress conditions, J. Assoc. Arab Univ. Basic Appl. Sci. 15 (2014) 43–52. https://doi.org/10.1016/j.jaubas.2013.03.004.
5. R. Nikzad-Langerodi, W. Zellinger, S. Saminger-Platz, B.A. Moser, Domain adaptation for regression under Beer–Lambert's law, Knowledge-Based Syst. 210 (2020) 106447. https://doi.org/10.1016/j.knosys.2020.106447
6. A. Rignall, ICHQ1A(R2) Stability Testing of New Drug Substance and Product and ICHQ1C Stability Testing of New Dosage Forms, in: ICH Qual. Guidel., John Wiley & Sons, Inc., 2017: pp. 3–44. https://doi.org/10.1002/9781118971147.ch1
7. P. Borman, D. Elder, Q2(R1) Validation of Analytical Procedures, in: ICH Qual. Guidel., John Wiley & Sons, Inc., 2017: pp. 127–166. https://doi.org/10.1002/9781118971147.ch5.
8. A.S.L. Mendez, M. Steppe, E.E.S. Schapoval, Validation of HPLC and UV spectrophotometric methods for the determination of meropenem in pharmaceutical dosage form, J. Pharm. Biomed. Anal. 33 (2003) 947–954. https://doi.org/10.1016/S0731-7085(03)00366-2.
9. R.B. Friedrich, A. Ravanello, L.C. Cichota, C.M.B. Rolim, R.C.R. Beck, Validation ofa simpleand rapid uv spectrophotometric method for dexamethasone assay in tablets, Quim. Nova. 32 (2009) 1052–1054. https://doi.org/10.1590/S0100-40422009000400038.
10. G. Murtaza, S.A. Khan, A. Shabbir, A. Mahmood, M.H.H. Bin Asad, K. Farzana, N.S. Malik, I. Hussain, Development of a UV-spectrophotometric method for the simultaneous determination of aspirin and paracetamol in tablets, Sci. Res. Essays. 6 (2011) 417–421. https://doi.org/10.5897/SRE10.925.
11. An Introduction to ICH Quality Guidelines, in: ICH Qual. Guidel., John Wiley & Sons, Inc., 2017: pp. 1–2. https://doi.org/10.1002/9781118971147.ch0.
12. P.V. Kadam, C.L. Bhingare, R.Y. Nikam, S.A. Pawar, Development and validation of UV Spectrophotometric method for the estimation of Curcumin in cream formulation, Pharm. Methods. 4 (2013) 43–45. https://doi.org/10.1016/j.phme.2013.08.002.
13. S. Sethuraman, K. Radhakrishnan, T.A. Solomon, Analytical Method Development and Validation of Caffeine in Tablet Dosage Form By Using UV-Spectroscopy, International Journal of Novel Trends in Pharmaceutical Sciences, Sponsored by ScienzTech, 2013. www.ijntps.org (accessed January 2, 2021).
14. S. Behera, UV-Visible Spectrophotometric Method Development and Validation of Assay of Paracetamol Tablet Formulation, (2012). https://doi.org/10.4172/2155-9872.1000151.