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Development and Validation of UV Spectrophotometric Rp-Hplc Method For Simultaneous Estimation of Fluvoxamine in Tablet and Bulk

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ARTICLE DETAILS

Research Paper

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ABSTRACT

An Analytical Method for the Estimation of Fluvoxamine in Tablet dosage Form has been devised for RP-HPLC that is straightforward, specific, accurate, and exact. Quartz quartz quvets were utilized for sample analysis, and the Spectra Manager UV spectrophotometer was utilized to obtain the spectra scan. 230 nm was discovered to be the wavelength at which fluvoxamine may be detected by consuming an excess. Acetonitrile: 0.1% OPA in Water (80:20%V/V) was the mobile phase used in the Agilent Poroshell C18, 150 mm X 4.6 mm, 5 µm column to achieve separation using the RP-HPLC technique. The 1.19 ml/min flow rate that was recorded. Fluvoxamine retention time was reported to be 8 minutes. In each case, a good linear response was found between 2 and 30 µg/ml. Fluvoxamine recoveries were discovered to range at 99.34%. Fluvoxamine was found to have a LOD (limit of detection) of 0.394µg/ml and a LOQ (limit of quantitation) of 1.193µg/ml. The suggested technique was successfully applied to the estimation of fluvoxamine in tablet dosage form and validated in accordance with ICH requirements using various criteria such as linearity, precision, accuracy, LOD and LOQ, range of selectivity,

roubstness, and rouggedness.

Introduction

Chemically speaking, fluvoxamine maleate (FLV) is an antidepressant that works as a selective serotonin reuptake inhibitor (SSRI). It is also known as (E)-5-methoxy-1-[4-(trifluoromethyl) Phenyl] pentan-1-one O-2-aminoethyl oximemaleate.Additionally, it is prescribed to treat anxiety disorders like panic disorder and post-traumatic stress disorder (PTSD) as well as major depressive disorder (MDD). It is soluble in ethanol, methanol, and chloroform and has a molecular weight of 434.4. According to a review of the literature, RP-HPLC techniques are described for estimating fluvoxamine in plasma, either alone or in combination with other medications. Additionally, a few RP-HPLC techniques for the drug's tablet analysis have been published. The application of specific stability indication with degradation kinetics and the RP-HPLC method for drug estimate from its pharmaceutical dose form is reported in this publication.

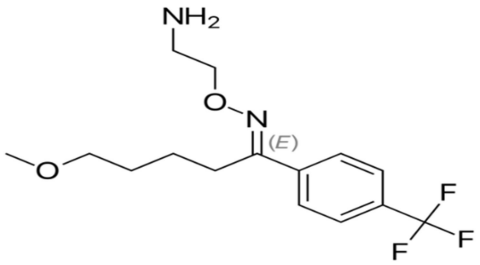

Fig.1: Structure of Fluvoxamine

According to the literature review, different analytical methods have been reported for fluvoxamine in UV spectrometry, HPLC, and RP-HPLC separately and collectively. The development and validation of the RP-HPLC method for the simultaneous quantification of fluvoxamine in tablet dosage form is demonstrated in this work.

MATERIALS AND METHOD

Materials: Fluvoxamine pure API, tablet of drug (Fluvoxine), Distilled water, Methanol, ortho phosphoric acid, Acetonitrile.

Instruments: Electronic balance, pH meter, Ultrasonicator, HPLC system, Uv-VIS spectrophotometer.

Preparation of Sample stock solutions : A precise weight of 10 mg of fluvoxamine was added to a 10 ml volumetric flask, agitated briskly for five minutes, and then the volume was adjusted with diluent. Pipette out 1 ml from 10 ml, dilute with diluent to make 10 ml, which is equivalent to 100 ug/ml of fluvoxamine.

20 pills that were weighed, moved to a mortar and pestle, and ground into a fine powder. Equally combine the items with the butter paper. The powder material equivalent to 50 mg of fluvoxamine was weighed and then placed to a 100 mL volumetric flask that had been cleaned and dried. added 70 milliliters of Metahnol and sonicated with sporadic shaking for ten minutes. Allow the solution to reach room temperature after ten minutes, then add methanol to bring the volume up to the desired level. 3-5 mL of the initial filtrate were discarded after filtering the mixture using an appropriate 0.45 µ syringe filter. 20 mcg of fluvoxamine were added to 25 ml of methanol-diluted 1.0 ml of filtered stock solution. The resulting solution was then injected, and the chromatograms and results were recorded.

Determination of Analytical wavelength: Diluent was used to dilute the standard stock solution of standard fluvoxamine, resulting in a final concentration of 100µg/ml. The UV-Visible Spectrophotometer was used to scan for each solution ,in the range of wavelength 400 nm to 200 nm. Absorption maxima observed at 230 nm.

Fluvoxamine has favorable resolution, plate count, tailing factor, and asymmetry; thus, this approach was refined and verified. According to ICH criteria, every system suitability metric was within the acceptable range.

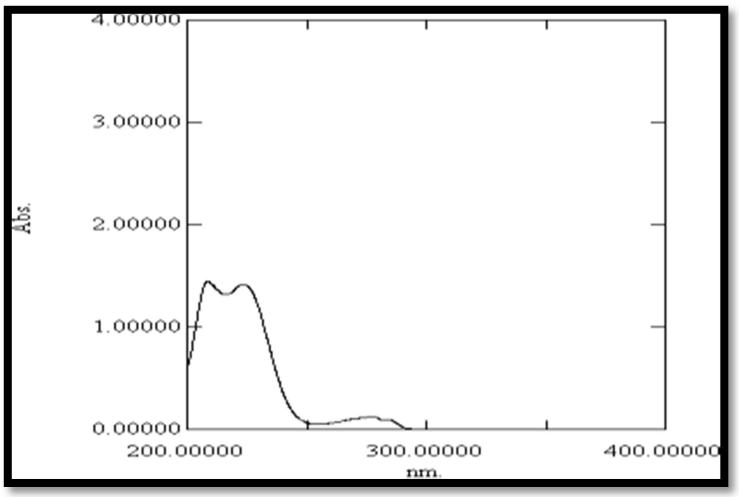

Fig:2 The Mximum Wavelength For Fluvoxamine @230 nm

Linearity: The process of linearity involved diluting the standard stock solution. Aliquots of0.5,0.75,1.0,1.25, and 1.50 ml from the stock solution were diluted to 10 ml with diluent so that the final concentration of fluvoxamine was between 50 and 150 µg/ml. For both medications, the correlation coefficient was 0.999.

FLUVOXAMINE			
Sr.No.	**Concentration (µg/mL)**	**Area**	**RT (min)**
1	50	1496153	2.663
2	75	2131656	2.660
3	100	2851193	2.660
4	125	3553563	2.695
5	150	4213282	2.665
Correlation coefficient (R2)		0.999	
Slope		27423.46	
Intercept		106763.4	

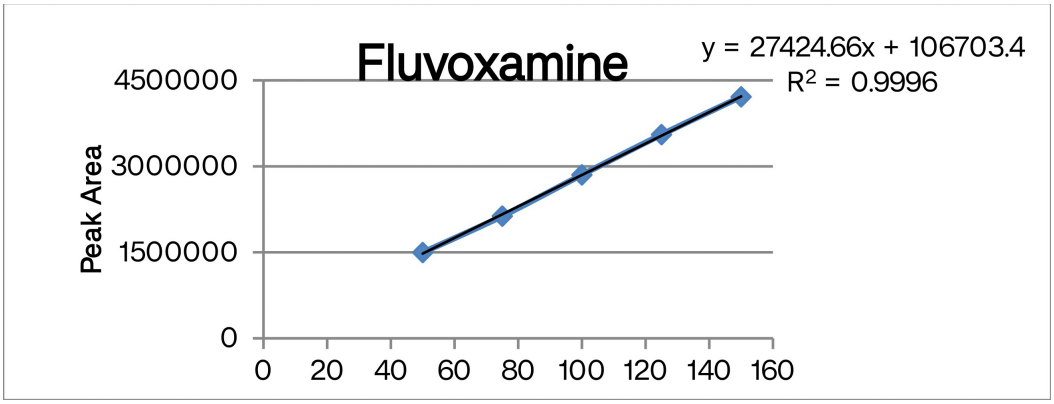

Fig 3.Calibration curve for Fluvoxamine

Precision: The degree of agreement between a set of measurements taken from several samples of the same sample is referred to as precision. After precisely weighing and transferring Fluvoxamine (10 mg) as working standard in a volumetric flask (10 ml), 7 ml of diluent was added, and the mixture was mixed

to make up the volume with the remaining diluent ml. The concentration used as a working standard is 1000µg/ml. 1.25 ml of the solution is taken diluted it up to 10 ml.

Exp	Sr. No.	Fluvoxamine	
		Concentration (ug/ml)	Area
Interday	1	125	3553211
	2	125	3552212
	3	125	3553263
Intraday	4	125	3553001
	5	125	3552001
	6	125	3553113
Mean		3552800.16	
S.D.		500.965	
%RSD		0.014	

Accuracy:

Sr. no.	Conc. level	Conc. (ug/ml)	Amount added (ug/ml)	Area	Amountfound (ug/ml)	% Recovery	Average % Recovery	% RSD
1	50%	50	25	2131356	23.82	98.42	98.44	0.020
		50	25	2132256	23.85	98.47		
		50	25	2131602	23.83	98.44		
2	100%	50	50	2850213	50.04	100.04	100.18	0.235
		50	50	2849129	50.00	100.00		
		50	50	2852530	50.12	100.12		
3	150%	50	75	3553002	75.66	100.52	100.50	0.938
		50	75	3552112	75.63	100.50		
		50	75	3552221	75.63	100.50		

Table No.7 Result and statistical data of Accuracy of Fluvoxamine

Overall Recovery: 99.44 %

%RSD for Overall Recovery: 0.779

Preparation of standard stock solution

After precisely weighing and transferring 10 mg of the Fluvoxamine working standard into a 10 ml volumetric flask, 7 ml of diluent was added, and the mixture was mixed to make up the volume with the remaining diluent ml. This was a stock solution containing 1000 µg of fluvoxamine per milliliter. solution in three duplicates that is 50%, 100%, and 150%. Every concentration that was added to the HPLC apparatus.

Preparation of Tablet stock solution

After carefully weighing and transferring a quantity of tablet powder equal to 10 mg of fluvoxamine into a 100 ml volumetric flask, 70 ml of diluent was added and sonicated to dissolve the tablet powder. The volume was then made up with diluent ml up to 100 ml and mixed. This was a stock solution containing 100 µg of fluvoxamine per milliliter. Blend thoroughly and pass through Whatman filter paper.

Procedure for Preparation of sample Solution:

Utilizing stock solutions equal to 50%, 100%, and 150%, each in triplicate, prepare the standard solution. Every concentration that was added to the HPLC apparatus.

LOD (Limit of detection): The calibration curve method is used to determine the LOD (limit of detection) and LOQ (limit of quantitation) of fluvoxamine. In the range of linearity, dilutions were made. The following formula was used to obtain the average area, which was plotted against concentrations.

- **LOD,LOQ: Limit of Detection (LOD) and Limit of Quantitation (LOQ):**
  - **LOD** = 3.3 XSD/slope

    = 3.3 X 500.965/27423.46

    = 0.060 mg/mL

  LOQ = 10 X SD/slope

= 10 X 500.965/27423.46

= 0.18 mg/mL

Robustness:

It indicates the method's dependability when used normally and measures its ability to withstand little but intentional variations in method parameters.

- **Change in Wavelength**

Sr No.	Conc. µg/ml	Area		
		As such 230nm	235nm	225nm
1	125	3553211	3552112	3551120
2	125	3552212	3551900	3552212
3	125	3553263	3552221	3551502
Mean		3552895.33	3552077.66	3551611.33
SD		483.656	133.21	452.45
%RSD		0.013	0.003	0.012

- **Change in Mobile Phase composition**

Sr No.	Conc. µg/ml	Area		
		As such 88+12	89+11	87+13
1	125	3553211	3551179	3533429
2	125	3552212	3553021	3533397
3	125	3553263	3551170	3534237
Mean		3552895.33	3551790	3533687.66
SD		483.656	870.44	388.66
%RSD		0.013	0.024	0.010

Determination:

Analyzing aliquots from homogenous lots using various physical characteristics, physical Parameters that may vary but remain within the Assay's defined parameters allows one to assess the robustness of an analytical approach. For instance, alterations in the physical properties of the mobile phase, such as its pH, ratio, and wavelength. Changes in wavelength (±5nm wavelength) Changes in ratio of mobile phase (± 01 of mobile phase)

CONCLUSION

Fluvoxamine-containing single-dose tablets, known as Fluvoxin 100mg, are marketed for the treatment of obsessive-compulsive disorder. For the following reasons, single component formulation is becoming more popular than single component formulation.
The reduction of treatment costs and the synergy of effects.

The analytical chemist's challenges are increased by the present study, which developed and validated an analytical approach for antidepressant drugs from their bulk preparation and pharmaceutical formulation. A technique that can distinguish between two or more components is needed for medication estimation from formulations with only one component. Techniques for single component analysis categorised into two groups: those not really separate the components and those that sporadically physically separate the components before processing. The goal of the current work was to create an accurate, precise, straightforward, and appropriate RP-HPLC method for drug measurement in single-component tablet formulation.

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Thus, the simultaneous estimation of fluvoxamine is reported using the RP-HPLC method in the dissertation. The estimate of fluvoxamine was performed using an Agilent Poroshell C18, 150 mm X 4.6

mm, 5 µm column with Methanol 88: buffer 12 pH 2.92 as the mobile phase @ 1.19 ml/min. Fluvoxamine was detected at a wavelength of 230 nm. Fluvoxamine was discovered to have an 8-minute retention time per milliliter. According to ICH requirements, the analysis's results for accuracy, precision, ruggedness, linearity, and range were validated. The research findings indicate that the RP-HPLC method, which has been developed, can be effectively employed to estimate the amount of fluvoxamine present in tablet formulations. The new RP-HPLC method is economical, quick, repeatable, sensitive, accurate, and specific.

In both of the developed methods, there is no influence from additives or matrix. These studies would be better illuminated by additional research on different medication formulations.

REFERENCES:

1) Vaishnav R., Anju G. Introduction to high performance liquid chromatography, International Journal of Pharmaceutical Erudition (Rajasthan)Inaia, 2007; 2249-3875.

2) Simpson C.F practical High Performance Liquid Chromatography, International Journal of Pharmaceutical Compounding.2004; Volume:8, Issue 3;223-225

3) Sethi P.D., estimation of Pharmaceutcal product,1st Edition, CBS publisher and distributors, New Delhi,2001,3-11,116-120.

4) LloyedR.Snyder. Joseph j. Kirkland, practical HPLC Method Development, 2nd edition, John Wiley &Sons,INC, 266-288.

5) Agrawal Y.P., Gautam S.P, Analytical Techniques Pelagia Research Library, Der Pharm Sin.,(2012) 337-342.

6) Rudy B., Recent Applications of Analytical Techniques in Quantitative estimation in Pharmaceuticals. A review WSEAS Transaction on biology and Biomedicine.2010; Vol-4, Issue 7:1109-1118.

7) Alain B., Countercurrent chromatography In Analytical Chemistry. Pune and Appiled Chemistry.2009; Vol-81, Issue2 : 355-387.

8) Guido F.P., Samuel M.Pro.,J.Brent F. Countercurrent seperation of Natural Products, Journal of Natural products. 2008;Vol-7, Issue 1: 1489-1508.

9) Duncan W.P Traditional Analytical Methods, Kirk-Othmer Encyclopedia of Chemical Technology. 2000; Vol-2, Issue-3: 1117-1123.

10) Gearien J., Bernard F., Grabowski D. Methods of Drug Analysis, Cole Singpure. 2010; Vol:8, Issue 2: 896-906.

11) Kitson .F.G., Larsen B.S., Mcewen C.N Gas Chromatography and Mass Spectroscopy-A Practical Guide. Acedemic Press, London.6th edition,1996; 522-536.

12) Scott P.W. Gas Chromatography, Library Science,UK.2003;245-250.

13) Kalsi P. Spectroscopy of organic compounds. 6th edition., New age Int. (P) Ltd. Publishers., New Delhi.2004.

14) Kennedy J.H Analytical Chemistry Principles, Harcourt Brace Jovanovic, London. 6th edition ,1984; 540-549.

15) Chatwal G.R and Anand S.K Instrumental Methods of chemical Analysis.5th edition., Himalaya Publishing House, New Delhi,2002.

16)RaviShankar S. Pharmaceutical Analysis. 3rd Edition., Rx Publication, Tirunelveli,2001.

17) Khanna P.K and Krishna B. Proc. Natl. Acad. Sci, 1997

18) Pernarowski M. Knevel A. and Christian J.J Pharm. Sci., 1960.

19) Willard H.H., Merritt L.L.,Dean J.A and Settle F.A. Instrumental Methods of Analysis. 7th edition ., CBS Publisher and Distributors, New Delhi, 2002.

20) Sharma B.M Instrumental Methods of Chemical Analysis. 26th edition., GOEL publishing house, New Delhi,2007.

21) Sethi P.D, Analysis of Drugs in Pharmaceutical Formulations. 3rd edition. CBS Publisher and Distributors, New Delhi, 1997.

22) Kasture A., Wadodkar S.,Mahadik S. and More H. Pharmaceutical Analysis. 10th edition Vol-2, NiraliPrakashan,Pune 2004.

23) West, Donald A., West Donald M., Fundamentals of Analytical chemistry,(1996), Philadelphia: Saunders College Pub. ISBN 0-03-005938-0

24) Nieman, 30. Timothy A., Douglas a., Holler F., James, Principles of instrumental analysis,(1998), Pacific Grove, CA:Brooks/.Cole. ISBN 0-03-002078

25) Jiawen Den, Evaluating fluvoxamine for the outpatient treatment of COVID-19: A systematic review and meta-analysis DOI:10.1002/rmv.2501

26) Vikas P. Sukhatme, Fluvoxamine: A Review of Its Mechanism of Action and Its Role in COVID-19, doi: 10.3389/fphar.2021.652688, Vol(12)

27). K.Kavitha, Analytical method development and validation for clomipramine and fluvoxamine by using RP-HPLC technique, et al / Journal of Pharmacreations Vol-9(2) 2022 [94-100]

28).DasariVasavi Devi, Development and validation of a reversed phase hplc method for simultaneous estimation of clomipramine and fluvoxamine, j. global trends pharm sci, 2023; 14(3): 658 – 669.

29). SEJAL PATEL, Simultaneous RP-HPLC and HPTLC Estimation of Fluoxetine Hydrochloride and Olanzapine in Tablet Dosage Forms, Indian Journal of Pharmaceutical Science, July - August 2009: 477-480.

30) EffatSouri, A Stability Indicating HPLC Method for the Determination of Fluvoxamine in Pharmaceutical Dosage Forms, Iranian Journal of Pharmaceutical Research (2015), 14 (4): 1059-1065

31) Atul T Hemke, Force degradation study and rp-hplc method development for estimation of fluvoxamine maleate in tablet, International Journal of Pharmacy and Pharmaceutical Sciences ISSN-0975-1491 Vol 7, Issue 6, 2015

32) Jeffery G.H Meendharm J., Denny C.R., Vogels Textbook of Quantitative Chemical Analysis, Adison Wesley Loongman Ltd. 2000; 292-305

33) The United State Pharmacopoeia (USP30-NF2), National Publishing Philadelphia Publishing, Asian Edition.2007 ; 2514-2517.

34) Krull I ,In Chromatography and Seperation Chemistry: Advance and Developments, Washington.1986;137.

35)A. Sailaja1, Somasubra Ghosh1, Thumma Praveen Kumar Reddy1, PN. Deepthi2 and David Banji1,A Review on Trouble Shooting In HPLC and its Solutions, International journal of Pharmaceuticals and chemical science.(2014)Vol. 3 ,Issue 3.

36)Ravisankar M. International Research Journal of Pharmacy. 2012;3(9):34-38

37)Kasture AV and Wadodkar SG. Textbook of P'ceutical Analysis, volume II, published by NiraliPrakashan, 49

38) http://www.Chemistry.nmsu.edu

39) William K.OrganicSpecroscopy.Palgrave,New York,2005.

40) International Conference on Hormonization (ICH),HormonizedTripatite Guidelines on validation of Analytical Procedure, Methodology, Q2(R2);1994.

41) Diode Aeery J.C., Miller, S.A., George, and B.G Willis, Science.1982;218-241.

42) Skood D., Holler J. and Nieman T. Principle of Instrumental Analysis. 5thEd.,Saunders College Publishing, New Delhi,1998.

43) Kamboj P.C Pharmaceutical Analysis, Vallabh publications, New Delhi, 1st edition, 2003;Vol:1 Issue 2 ;415

44) R.Ashwini,MM.Eswarduand P. SrinivasaBabu, A Review on Analytical Methods for Estimation of Fluvoxamine and Saxagliptin in bulk and in Pharmaceutical DosagrForm,IJPRC (2018), Vol:8,Issue3.

45) B.RamaRaoa,V.VenkataRaob, B. S. Venkateswarluc RP- HPLC Method for Simultaneous Estimation of Fluvoxamine and Saxagliptin in Bulk Samples,Journal of Pharmaceutical science and Research, (2019). Vol. 11(1),254-257