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Stability Indicating HPLC Method for Venlafaxine Hydrochloride Capsules

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A stability indicating HPLC method for the analysis of venlafaxine hydrochloride in its pharmaceutical dosage forms is developed employing Kromasil C_{18} column, mobile phase consisted of sodium acetate buffer-acetonitrile (65:35) with UV-detection at 226 nm. The method was validated as per ICH guidelines for specificity, linearity, precision and accuracy. Forced degradation studies were performed on the bulk sample using 0.5 N HCl, 0.1 N NaOH, 33 % H_2O_2 and heat (50 ºC).

Key Words: Venlafaxine hydrochloride, Solution stability, Forced degradation study, HPLC.

INTRODUCTION

Venlafaxine hydrochloride chemically is (R/S) [1-{(2-dimethylamino)-1-(4-methoxyphenyl)ethyl}cyclohexanol hydrochloride]. It is a second generation antidepressant and administered as racemic mixture. Venlafaxine hydrochloride is a serotonin and nor-adrenaline reuptake inhibitor (SNRI), but in contrast to other tricyclic amines (TCAs), it does not interact with cholinergic, adrenergic or histaminergic receptors[1,2]. Different methods have been reported in literature for monitoring plasma levels of venlafaxine hydrochloride. Most of the analytical methods carried out by HPLC to determine venlafaxine were aimed to quantifying it in biological fluids[3-21]. Therefore it is necessary to develop a simple, specific, rapid and sensitive analytical method for the quantification of venlafaxine hydrochloride. The present method is fast, accurate as compared to already existing methods. This work followed the validation as per the ICH guidelines to develop an analytical method with acceptable characteristics of suitability, reliability and feasibility.

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EXPERIMENTAL

Ranbaxy Research Lab., Gurgaon, supplied samples of venlafaxine hydrochloride. Venla (25 mg) capsules from Solus were used as formulation. All the reagents used were of HPLC grade and supplied by Ranbaxy Research Lab. High pure water was prepared by using Millipore Milli-Q plus purification system.

The HPLC system used for forced degradation studies, method development and method validation was waters with PDA detector set at 226 nm. Data acquisition and output signal was monitored and processed by using Empower Pro Software. The assay for venlafaxine hydrochloride was performed by using C_{18} Kromasil column (250 mm × 4.6 mm, particle size 5 µ).

Chromatographic conditions: The mobile phase consisted of 10 mM buffer of pH 5.5 and acetonitrile (65:35). Buffer of pH 5.5 was prepared by dissolving 1.64 g of sodium acetate in 1000 mL of water and pH was adjusted with acetic acid, filtered through 0.45 µm membrane filter, degassed with spurge and pumped to the column at a flow rate of 1 mL/min. The run time was set at 7 min and column temperature was ambient. The volume of injection loop was 20 µL. Before the injection of the drug solution, the column was equilibrated for at least 20 min with the mobile phase. The eluents were monitored at 226 nm. Mixture of water and acetonitrile in the ratio of 80:20 was used as diluent.

Sample preparation and analysis: The stock solution of 1000 µg/mL was prepared by dissolving the appropriate amount of venlafaxine hydrochloride in diluent (water and acetonitrile: 80:20). Stock solution was further diluted with diluent to obtain a standard solution of 100 µg/mL for assay. Similarly test solutions were prepared for the analysis.

Generation of stress sample: For acid hydrolysis the drug solution in 0.5 N HCl was kept at room temperature for 72 h. For neutral hydrolysis, drug solution in water was kept at room temperature for 10 d. For alkali hydrolysis drug solution in 0.1 N NaOH was kept at room temperature for 72h. For stress study under oxidative conditions, the drug solution was kept in 33 % hydrogen peroxide at room temperature for 72 h; for thermal stress testing, the bulk drug was subjected to dry heat at 105 ºC for 72 h, while for photodegradation bulk drug was subjected to UV-254 nm for 10 d.

RESULTS AND DISCUSSION

No degradation was observed for venlafaxine hydrochloride bulk and formulation samples during stress conditions. Peak purity test results confirm venlafaxine hydrochloride was homogeneous in all the stress conditions tested. The mass balance of venlafaxine hydrochloride on stress sample was 100 % (% assay + % degradation). Typical retention time of venlafaxine hydrochloride was 3.1 min. System suitability parameter results are presented in

Table-1. Assay method precision study was evaluated by carrying out independent assay of venlafaxine hydrochloride test sample against qualified reference standard and % RSD of six consecutive assays was found within the acceptable limits (RSD < 2 %). The limit of detection represents the concentration of analyte that would yield a signal to noise ratio of 3 and limit of quantification represents the concentration of analyte that would yield a signal to noise ratio of 10. Linearity for venlafaxine hydrochloride was evaluated by regression analysis. The method exhibited linearity in concentrations ranging from 70 to 130 μg/mL with a high degree of statistical significance ($r^2 > 0.99$). Accuracy of the assay method was evaluated in triplicate at three concentration levels, 80, 100, 120 % in bulk drug sample. The % recovery was calculated from the slope and y-intercept of the calibration curve obtained during linearity study of assay method. The % recovery of venlafaxine hydrochloride in bulk drug samples found within the acceptable limits (> 97 %). The robustness was determined by injecting triplicate sample solution at different conditions with respect to control conditions. Robustness of method was checked by varying the instrumental conditions such as flow rate (± 10 %), organic content in mobile phase ratio (± 2 %) and wavelength of detection (± 5 nm). The results are shown in Table-2.

TABLE-1
SYSTEM SUITABILITY OF VENLAFAXINE HYDROCHLORIDE

	USP Plate count	USP Tailing
System precision	8732	0.99
Method precision	8877	1.00
Accuracy	8875	0.98
Linearity	8888	1.03
Specificity	9014	1.05
Rugeddness	8778	0.99
Stability in solution	8734	1.02

TABLE-2
ROBUSTNESS OF VENLAFAXINE HYDROCHLORIDE (ASSAY)

S. No.	Set-1	Set-2	Set-3	Set-4	Set-5	Set-6	Set-7	Set-8	Set-9	Set-10	Set-11
1	24.87	24.91	25.43	25.25	25.26	24.94	25.26	24.99	25.22	24.9	25.42
2	24.88	25.46	25.42	25.33	25.30	24.94	24.41	24.94	25.31	24.93	25.09
3	24.89	25.30	25.27	25.30	25.00	25.29	24.94	25.27	24.91	24.95	25.04
Mean	24.88	25.22	25.37	25.29	25.19	25.06	24.87	25.07	25.15	24.93	25.18
SD	0.01	0.28	0.09	0.04	0.16	0.20	0.43	0.18	0.21	0.03	0.21
RSD%	0.04	1.12	0.35	0.15	0.64	0.80	1.70	0.70	0.83	0.10	0.79

Set-1: Control Sample, Set-2: Sample λ_{max} 220 nm, Set-3: Sample λ_{max} 230 nm, Set-4: Flow rate 1.35 mL/min, Set-5: Flow rate 1.65 mL/min, Set-6: Mobile phase ratio 60:40, Set-7: Mobile phase ratio 70:30, Set-8: Sample temperature 30 ºC, Set-9: Sample temperature 40 ºC, Set-10: Buffer pH 5.48, Set-11: Buffer pH 5.52.

REFERENCES

1. H.J. Kuss, in ed.: H. Engelhard, Practice of High Performance Liquid Chromatography, Springer Berlin, Vol. 94, p. 7 (1986).
2. K.D. Tripathi, Essentials of Medical Pharmacology, Jaypee Publishers, Vol. 419, p. 4 (1999).
3. L. Labat, M. Deveaux, P. Dallet and J.P. Dubost, *J. Chromatogr. B*, **773**, 17 (2002).
4. N.J. Langford, M.M. Ruprah and R.E. Ferner, *J. Clin. Pharm. Ther.*, **465**, 7 (2002).
5. M. Matoga, F. Pehoureq, K. Titier, F. Dumaro and C. Jarry, *J. Chromatogr.*, **213**, (2001).
6. M. Reis, J. Lundmark and F. Bjork, *Ther. Drug Monit.*, **545**, 24 (2002).
7. G. Tournel, N. Houdret, V. Hedouin, M. Deveau, D. Gosset and M. Lhermitte, *J. Chromatogr. B*, **761**, 143 (2001).
8. A.H. Veefkind, P.M.J. Hoffmans and E. Hoenecamp, *Ther. Drug Monit.*, **202**, 22 (2000).
9. R. Waschgler, M.R. Hubmann, A. Conca, W. Moll and P. Konig, *Int. J. Clin. Pharm. Ther.*, **545**, 40 (2002).
10. D.R. Hicks, D. Wolanimik, Russel, N. Cavanaugh and N.M.A. Krami, *Ther. Drug Monit.*, **100**, 16 (1994).
11. R.L. Vu, D. Helmeste, L. Albers and C. Reist, *J. Chromatogr. B*, **195**, 703 (1997).
12. R. Waschgler, W. Moll, P. Konig and A. Conca, *Int. J. Clin. Pharmcol. Ther.*, **724**, 42 (2004).
13. R. Mandrioli, L. Mercolini, R. Cesta, S. Fanali, M. Amore and M.A. Raggi, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, **856**, 88 (2007).
14. E.B. Asafu-Adjaye, P.J. Faustino, M.A. Tawakkul L.W. Anderson, L.X. Yu, H. Kwon and D.A. Volpe, *J. Pharm. Biomed. Anal.*, **43**, 1854 (2007).
15. Z. Wei, X. Bing-Ren and W. Cai-Yun, *Biomed. Chromatogr.*, **21**, 266 (2007).
16. W. Liu, H.L. Cai and H.D. Li, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, **850**, 405 (2007).
17. W. Liu, F. Wang and H.D. Li, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, **850**, 183 (2007).
18. P.D. Tzanavaras, A. Verdoukas and D.G. Themelis, *Anal. Sci.*, **21**, 1515 (2005).
19. H. Juan, Z. Zhiling and L. Huande, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, **820**, 33 (2005).
21. S.N. Makhija and P.R. Vavia, *J. Pharm. Biomed. Anal.*, **28**, 1055 (2002).

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