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VALIDATED SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF PAROXETINE HCL BULK AND TABLET DOSAGE FORM USING FERRIC CHLORIDE

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The method allows rapid analysis of binary pharmaceutical formulation with accuracy. Analysis was validated by statistically and recovery studies which was found satisfactory. The method describes simultaneous determination of Paroxetine HCl dosage form. UV spectrophotometric method involves first derivative and Absorption Maxima spectroscopy using 323 nm & 351 nm as Method A and Method B respectively. For spectrophotometric method, Ferric Chloride was used as a solvent. Linearity was observed in concentration range of 10-120 μg/ml of Paroxetine HCl. Results of analysis were validated statistically and by recovery studies.

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1. Introduction

Paroxetine;(3S,4R)-3-[(1,3-benzodioxol-5-vloxy)methyl]-4-(4-flurophenyl) piperidine (PRX) is a new generation antidepressant drug. It exerts its antidepressant effect through a selective inhibition for the reuptake of the neurotransmitter serotonin by the presynaptic receptors. PRX is comparable to the tricyclic antidepressants in their clinical efficacy, however, PRX is safer and has greater acceptance by the patients [1]. It is also prescribed in the treatment of related disorders, such as obsessive-compulsive disorder, panic fits, social phobia, and posttraumatic stress [2]. PRX is devoid of sedative effect and remarkably safe in overdose. PRX takes 5.2 hours to reach the peak, with extended half-life (21 hours) that allowed the introduction of formulations for once-daily dosing [3]. These combined qualities made PRX the most widely prescribed antidepressants [4]. The methods reported for quantitative determination of PRX in tablets and/or biological fluids include voltammeter [5, 6], densitometry [7, 8], HPLC [9–14].

2. Material and methods

UV Visible spectrophotometer (Shimadzu Model 1601) was employed with spectral bandwidth of 1 nm and wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 1 cm matched quartz cells). All chemicals used in this study were analytical grade and used without further purification. FeCl3 6H2O (0.8%) and $1x10^{-3}$ M solution in ethanol standardized against standard KMnO4 after reduction [15].

Method

Accurately transfer volumes of standard drug solution in ethanol (1mg/ml) equivalent to 0.4-1mg Paroxetine HCl into a series of 10ml volumetric flask add 0.5ml of 0.8% FeCl3 and heated in a water bath at 77±3^{o}C for 35 minutes, cool and complete volume with ethanol. Measure the absorbance of an orange chelate of Paroxetine HCl with Fe (II) at 455nm against reagent blank. Stock solutions were prepared separately in 0.5 mg Ferric Chloride to obtain 100 µg/ml of all drugs. The five working mixed standard were prepared by dilution of stock solution in same solvent system in concentration range 5-35 µg/ml of Paroxetine. Paroxetine HCl initially scanned for determining sampling wavelength in range 200-400 nm. Sampling wavelengths were 245 nm for Paroxetine HCl. Calibration graphs were constructed from the absorbances at respective wavelength.

Method A: First Order Derivative Spectroscopic method

15 µg/mL solution of Paroxetine HCl was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. The absorption spectra thus obtained were derivatized from first to fourth order. First order derivative spectra were selected for analysis of drug. First order derivative spectra of drug showed a sharp peak at 323 nm, which was selected for its quantitation. The calibration curves for Paroxetine HCl was plotted in the concentration range of 5-40 µg/mL at wavelength 323 nm The concentration of the drug present in the mixture was determined against the calibration curve in quantitation mode.

Method B: Absorption Maxima Method

For the selection of analytical wavelength, 15 µg/mL solution of Paroxetine HCl was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. From the spectra of drug, λ max of Paroxetine HCl, 351 nm was selected for the analysis. The calibration curve was prepared in the concentration range of 5-40 µg/mL at 280 nm. By using the calibration curve, the concentration of the sample solution can be determined.

Application of the proposed procedure for the determination in tablets

The proposed method was applied in order to determine the Paroxetine HCl, in tablets formulation. The marketed tablet formulation of Paroxetine HCl was used for this. Twenty tablets were weighed and average weight was calculated, crushed to fine powder. The powder equivalent to 150 mg of Paroxetine HCl was transferred in 100 ml volumetric flask and dissolved in $FeCl_3$ by shaking. The volume was made up to mark to get final concentration of 1mg/ml. Frequent shaking given and volume was made up to 100ml mark with $FeCl_3$. The solution was then filtered through Whattman filter paper #41.This filtrate was diluted suitably with $FeCl_3$ to get the solution of 100µg/ml concentration. The working solution of drug (100µg/ml) was prepared from standard stock solution in $FeCl_3$. The absorbance of this solution was measured and amount of Paroxetine HCl was calculated from the calibration curve. The readings were taken in triplicate. In Method-A, the concentration of Paroxetine HCl was determined by measuring the absorbance of the sample at 323 nm in zero order spectrum modes. By using the calibration curve, the concentration of the sample solution can be determined. Method-B, the concentration of Paroxetine HCl was determined by measuring the absorbance of the sample at 351 nm, in first order derivative mode. The results of the tablet analysis were calculated against the calibration curve in quantitation mode. Results of tablet analysis are shown in Table- 1.

Table -1 Results of Analysis of Tablet Formulation

Method	Label claim	Amount of drug estimated	%Label claim ±SD	Recovery % ±SD
A	10	9.970	99.96 ± 0.321	99.96
B	10	9.991	99.98 ± 0.114	99.99

3. Validation of the developed methods

The developed methods for simultaneous estimation of Paroxetine HCl validated as per ICH guidelines.

Accuracy

To check the accuracy of the developed methods and to study the interference of formulation additives, analytical recovery experiments was carried out by standard addition method. From that total amount of drug found and percentage recovery was calculated. The results were reported in Table 2.

Table 2- Result of tablet dosage form containing Paroxetine HCl.

Parameters	Method-A	Method-B
Label claim (mg/Tab)	10	10
Found (mg/Tab)	9.87	9.92
Drug content[a]	98.81	99.93
±S.D	0.111	0.126
%COV	0.07	0.21
SE	0.32	0.11

Precision

To check the degree of repeatability of the methods, suitable statistical evaluation was carried out. Five samples of the tablet formulations were analyzed for the repeatability study. The standard deviation, coefficient of variance and standard error was calculated. The results were reported in Table 3.

Intermediate Precision (inter-day and intra-day precision)

The intra and inter-day precision was calculated by assay of the sample solution on the same day and on different days at different time intervals respectively. The results are presented in Table 3.

Stability

Long-term stability was studied in order to be sure that analytes present in samples do not degrade in the storage conditions before being analyzed. Hence, long-term stability was studied on matrix-based samples stored at −5 ◦C for 3 months. Short-term stability after 6 and 24 h at room temperature was studied to verify if analyses degrade over the course of analyses. Short-term stability can be evaluated by analyzing either working solutions or matrix-based samples added to working solutions and kept at room temperature before the extraction step.

Table 3.Intraday, Interdays, data of Tablet formulation.

Method	Drug	Intra day precision %COV (n =5)	Interday precision %COV		
			Day 1[a]	Day 2[a]	Day 3[a]
Method A	10	0.48	0.354	0.311	0.265
Method B	10	0.26	0.154	0.296	0.224

[a]Mean of five determinations, COV: Coefficient of variance,

4. Results and discussion

The development of spectrophotometer methods for the determination of drugs has increased considerable in recent years because of their importance in pharmaceutical analysis. The calibration curve for Paroxetine HCl was obtained by plotting the peak area versus concentration. U.V spectra of Paroxetine HCl in $FeCl_3$ have a sharp peak at 387 nm. When reacting with Fe (III) in ethanol an orange coloured chelate was formed and have high absorption band at 395 nm. The composition of the chelate of drug with metal ions using job's method, chelate of 5:2 ratio were obtained between drug and Fe (II). The stability constants were calculated [16]. Due to greater solubility in Fe (II), it was selected for further study. The values of standard deviation and coefficients of variation were satisfactorily low. The percentage recovery range of 98% to 102% was indicating the accuracy of method. It was found that the % RSD is less than 2, which indicates that the method is highly reproducible. The coefficient of variation (CV) on the basis of the absorbance for six triplicate measurements found to be between 0.09 and 0.80%. Paroxetine (10 mg) were analyzed and the results obtained.

Analytical validation parameters

Parameter	Result	
	Method A	Method B
Absorption maxima(nm)	323 nm	351 nm
Linearity Range (µg/ml)	10-120	10-120
Standard Regression Equation	Y = 0.009*x* +0.0325	Y = 0.006*x* +0.0324
Correlation Coefficient (r2)	0.9954	0.9993
Accuracy (% recovery ±SD)	98.56±0.238	98.56±0.238
LOD (µg/ml)	3.32	4.12
LOQ (µg/ml)	11.154	10.432
%Drug found in tablet formulation	99.76	99.82

5. Conclusions

The obtained and statistical parameters for determination of paroxetine in raw material and formulation that the proposed UV spectrophotometer method by is simple, accurate, fast and precise. The method showed acceptable linearity and accuracy. The proposed method is usefully Fe (II) highly sensitive; therefore it could be used easily for the routine analysis of pure drugs and their formulations. The proposed visible Spectrophotometric methods were found to be simple,

stability, sensitive, selective, accurate, precise and economical and can be used in the determination of Paroxetine HCl in bulk and pharmaceutical dosage forms in a routine manner.

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References

[1] W. Z. Potter, L. E. Hollister "Antidepressant agents," in Basic & Clinical Pharmacology. 9th ed.New York: McGraw Hill; 2004.
[2] Sweetman SC. Martindale: The Complete Drug Reference. 34th ed. London, (UK): Pharmaceutical Press , 2005.
[3] Tucker P, Zaninelli R , Yehuda R, Ruggiero L , Dillingham K ,Pitts CD,Journal of Clinical Psychiatry; **62**(11), 860 (2001).
[4] Iversen L, Glennon RA: Abraham D.J, editors. Burger'sMedicinal Chemistry and Drug Discovery. New York : John Wiley & Sons; 2003.
[5] Nouws HPA , Delerue Matos C , Barros AA , Rodrigues JA,Journal of Pharmaceutical and Biomedical Analysis; **42**(3), 341 (2006).
[6] Erk N, Biryol J ,Pharmazie; **58**(10), 699 (2003).
[7] Robert S , Genowefa M , Marcin K ,Journal of Planar Chromatography, **16**(1), 19 (2003)
[8] Venkatachalam A, Chatterjee VS,Analytica Chimica Acta; **598**(2), 312–17. 2007
[9] Zainaghi IA , Lanchote VL , Queiroz RHC,Pharmacological Research **48**(2), 217 (2003).
[10] Zhu Z , Neirinck L , Journal of Chromatography; **780**(2) 295 (2002).
[11] Massaroti P , Cassiano NM , Duarte LF ,Journal of Pharmacy and Pharmaceutical Sciences; **8**(2) 340 (2005).
[12] British Pharmacopoeia 2003, The Stationary Office, London,UK, 2003.
[13] United States Pharmacopeial Convention, The United States Pharmacopeia 31, The National Formulary 26, United States Pharmacopeia, Rockville, Md, USA, 2008.
[14] Eap CB , Bouchoux G , Amey M , Cochard N , Savary L ,Baumann P,Journal of Chromatographic Science; **36**(7), 365 (1998).
[15] Basset J, R.C Denney G.H Jeffery, J. Mendham (Eds), Vogels textbook of Quantitative Inorganic Analysis fourth ed., , **348-351**, 370 (1978).
[16] Inczedy J, Analytical applications of Complex Equilibria, College House, Westergate, U.K, first ed., 1976, 140.

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