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RESEARCH ARTICLE

Method Development and Validation of Visible Spectroscopic Method for the Estimation of Paroxetine Hydrochloride in Pure and Tablet Dosage Form

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Abstract: The present research work discusses the development of visible spectroscopic method for the estimation of paroxetine hydrochloride. The optimum conditions for the analysis of the drug were established. The maximum wavelength (λ_{max}) was found to be 538 nm. The validation was performed as per ICH guidelines for linearity, accuracy, precision, LOD and LOQ. The method shows high sensitivity with linearity in the range of 200-600 µg/mL and shows a linear relationship between the absorbance and concentration with coefficient of correlation 0.999. The regression of curve was Y = 0.001x+0.007. The precision of method was found to be good. The percentage recovery was found to be 105.02±0.0832. The optimized method showed good reproducibility and recovery with RSD <2%. The proposed method will be suitable for analysis of paroxetine hydrochloride in bulk as well as pharmaceutical formulations in quality control purpose. It is thus concluded that the proposed method is new, simple, cost effective, safe, accurate, precise and environmental friendly.

Keywords: Paroxetine hydrochloride, Visible spectroscopic method, Sensitive, Validation, ICH guidelines

Introduction

Paroxetine; (3S, 4R)-3-[(1,3-benzodioxol-5-vloxy)methyl]-4-(4-flurophenyl)piperidine (PRX, Figure 1) 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 post traumatic 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], high-performance liquid chromatography[9–14], gas chromatography[15–17] and capillary electrophoresis[18]. These methods offered the required sensitivity and selectivity for the analysis of PRX in biological fluids; however, their sophisticated instrumentation and high analysis cost limited their routine use in quality control laboratories for analysis of PRX in its pharmaceutical tablets.

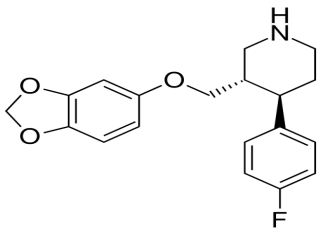

Figure 1. Structure of paroxetine hydrochloride

Experimental

A Lab India model 3000+ double beam UV-Visible spectrophotometer with two matched cuvette cells of one cm light path were used for the measurement of absorbance.

Preparation of standard stock solution

Accurately weighed 100 mg of paroxetine hydrochloride was transferred into 100 volumetric, methanol was added to dissolve and volume was made up to 100 mL with water to get a concentration of 1000 µg/mL.

Determination of λ_{max}

From the stock solutions, 6 mL of paroxetine hydrochloride was transferred to 10 mL volumetric flask, 1 mL of sulphanilic acid - Sodium nitrite solution was added and the volume was adjusted to the mark with distilled water to obtain strength of 600 µg/mL. The solution was scanned in the UV- Visible range 200-800 nm (Figure 2).

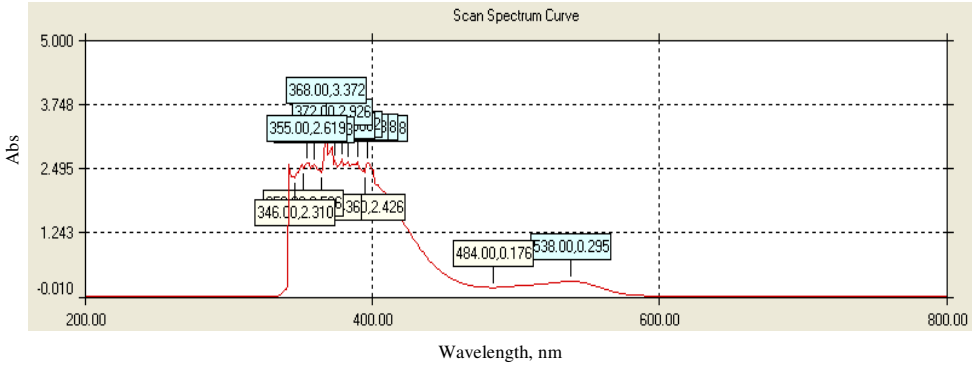

Figure 2. Spectrum of paroxetine hydrochloride

Preparation of sulphanilic acid- sodium nitrite reagent

0.1 g of Sulfanilic acid is added with 4 mL of HCl and water in a beaker. 0.1 g of sodium nitriteis added with 4 mL of water. These two solutions are mixed and maintained at 0-5 ^{o}C.

Construction of calibration curve

Calibration curve was plotted against concentration and absorbance, regression equation was computed. The results are tabulated in the Table 1 and Figure 3.

Table 1. Calibration of proposed method

S.No.	Conc. mcg/mL	Absorbance at 538 nm
1	200	0.260
2	300	0.394
3	400	0.523
4	500	0.634
5	600	0.787

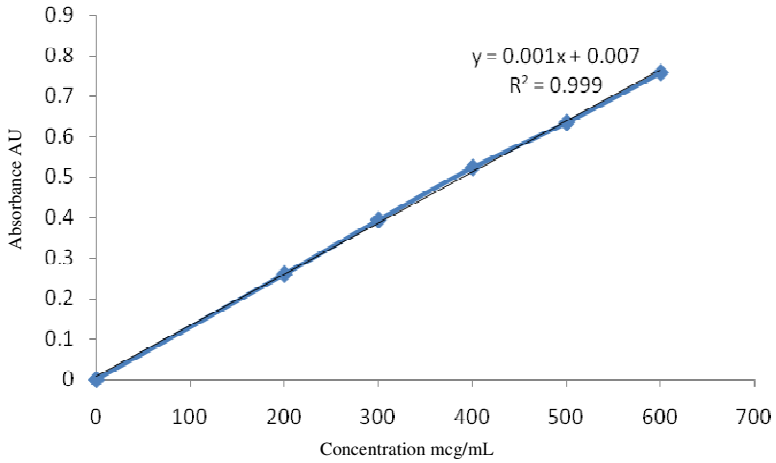

Figure 3. Calibration curve of paroxetine hydrochloride at 538 nm

Preparation of sample solution

10 Tablets were weighed, average weight was determined. Tablets were powdered and the quantity of powder equivalent to 200 mg of paroxetine HCl, 50 mL of methanol was added to dissolve. Excipients were filtered and to this solution 2 mL of sulfanilic acid reagent - sodium nitrite solution was added and the absorbance was measured.

Method validation

The proposed method was validated as per the ICH Q2 (R1) guidelines for linearity, accuracy, precision, LOD and LOQ.

Accuracy

Accuracy was carried out at 80%, 100% and 120% of target concentration. From the amount found, percentage recovery was calculated.

Precision

Precision of the method was studied by carrying out intraday, interday analysis and expressed as percentage relative standard deviation. For this purpose 200 (LQC), 400 (MQC) and 600 µg/mL (HQC) solutions were prepared and the absorbances of the solutions were measured for six times within the same day and in different days at 538 nm against blank.

Limit of detection (LOD) and Limit of quantification (LOQ)

LOD and LOQ of the drug were calculated using the following equations according to International Conference on Harmonization (ICH) guidelines

$$LOD = 3.3x\sigma/S \text{ and } LOQ = 10x\sigma/S$$

Where σ = the standard deviation of the response; S = the slope of the regression equation.

Results and Discussion

The proposed method for determination of paroxetine hydrochloride in marketed formulation (tablet) showed Sandell's sensitivity of 0.7692 μg/cm^2/0.001 absorbance units. Linear regression of absorbance on concentration gave the equation y = 0.001x + 0.007 with a regression co-efficient (r^2) of 0.999 and the linearity range was 200-600 μg/mL. The higher percentage recovery value indicates that there is no interference of the excipients present in the formulation (Table 2). Assay of paroxetine hydrochloride formulation was found to be 92% 0.33 is shown in Table 3. The accuracy studies and the percentage recovery was found to be 103.25± 0.091 to 106.64±0.090 (Table 4). Precision and accuracy were studied and % RSD value for all key parameters was less than 2% (Table 5). Thus the method is useful for the determination of paroxetine hydrochloride in bulk and pharmaceutical formulations.

Table 2. Optimum conditions, Optical characteristics and statistical data of the regression equation in visible spectroscopic method

Parameter	Colorimetric method
$\lambda_{max,}$ nm	538
Beer's law limits, mcg/mL	200-600
Sandell's sensitivity (mcg / cm^2-0.001 absorbance units)	0.7692
Regression equation (Y*)	y= 0.001x+ 0.007
Slope (b)	0.001
Intercept (a)	0.007
Correlation coefficient(r^2)	0.999
% RSD**	< 2%
Limit of detection, mcg/mL	85
Limit of quantitation, mcg/mL	268

**y=bx+a where x is the concentration of paroxetine hydrochloride in mcg/mL and Y is the absorbance at the respective max. **Average of six determinations*

Table 3. Assay of paroxetine hydrochloride formulation

S.No	Formulation	Label claim (mg/tab)	Amount found, mg (n=3) Mean ± SD	Assay	%RSD
1	Paxidep CR	25 mg	23±0.054	92%	0.33

Table 4. Determination of accuracy results for paroxetine hydrochloride

Name	Amount of sample mcg/mL	% of Spiked sample	Amount of drug added mcg/mL	Amount Recovered	% Recovery ±SD
Paxidep CR	1.6	80	2	383.93	106.64±0.090
Paxidep CR	2	100	2	413.00	103.25± 0.091
Paxidep CR	2.4	120	2	462.71	105.16±0.1

Table 5. Determination of precision results for paroxetine hydrochloride

Conc. mcg/mL	Inter-day Absorbance Mean ± SD*	% RSD	Intra-day Absorbance Mean ± SD*	% RSD
LQC, 200 mcg/mL	0.263±0.0025	0.951	0.266±0.0026	0.977
MQC, 400 mcg/mL	0.525±0.002	0.381	0.515±0.0032	0.621
HQC, 600 mcg/mL	0.784±0.0025	0.318	0.785±0.004	0.510

**Average of six determinations*

Conclusion

A simple, sensitive, accurate and precise visible spectroscopic method has been developed for quantitative determination of paroxetine hydrochloride in bulk and pharmaceutical dosage form (tablet). The solution was scanned between 400 to 800 nm and 538 nm was selected as maximum wavelength for absorption. Beer's law was obeyed in the concentration range of 200-600 µg/mL. % Recovery was found to be 103.25%-106.64% and the method was successfully applied to the pharmaceutical dosage form containing the paroxetine hydrochloride drug without any interference of the excipients. The method was fast and economical and it was also selective and sensitive for the desirable range. Results of the analysis were validated as per ICH guidelines and by recovery studies.

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