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A Validated RP-HPLC Method For The Estimation of Paroxetine Hydrochloride In Bulk and Tablet Dosage Form

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ABSTRACT

A simple, precise, rapid, and reproducible RP -HPLC method was developed and validated for the determination of Paroxetine in Pharmaceutical dosage form. Separation was achieved under optimized chromatographic condition on a PhenomenaxLunaC_{18} (ODS) column (150 X 4.6 mm i.d., particle size 5µ).The mobile phase consisted of Phosphate buffer at pH 6.0: Acetonitrile in the ratio 50: 50 v/v. An isocratic elution at a flow rate of 2 ml/ min at ambient temperature. The detection was carried out at 265 nm.using Shimadzu UV-Visible detector SpD-10AVP.The retention time of Paroxetine is found to be 3.5min and the calibration curve was linear in the concentration range of 20–100µg/ ml (r^2- 0.9999).The limit of detection and the limit of quantification were found to be 0.6327 µg/ml and 1.963 µg/ml respectively. The amount of Paroxetine present in the formulation (Allegro) was found to be 99.55. The method was validated statistically using the SD, %RSD and SE and the values are found to be within the limits and the recovery studies were performed and the percentage recoveries was found to be 99.53± 0.6327 %. So, the proposed method was found to be simple, specific, linear, and rugged. Hence it can be applied for routine analysis of Paroxetine in the Pharmaceutical formulations.

Key words: Paroxetine**;** RP-HPLC Method, Development; Validation; Tablet dosage form.

INTRODUCTION

In the present investigation Paroxetine Hydrochloride (PXT), this is an extended-spectrum, semi synthetic cephalosporin.the chemically paroxitine is PAXIL (paroxetine hydrochloride) is an orally administered psychotropic drug. It is the hydrochloride salt of a phenylpiperidine compound identified chemically as (-)-*trans*-4R-(4'-fluorophenyl)-3*S*-[(3',4'-methylene dioxyphenoxy) methyl] piperidine hydrochloride hemihydrate and has the empirical formula of $C_{19}H_{20}FNO_3$•HCl•1/2H_2O.[1-3] The molecular weight is 374.8 (329.4 as free base). The structural formula of paroxetine hydrochloride is :Fig.1.

Few UV[4] and HPLC[5-6], LC-MS/MS[7-8] one fluorimetric and one Electrochemical analysis methods assay procedures have been reported for the determination of PXT, even then, this part reports a sensitive and precise HPLC method for the determination of PXT in bulk samples and pharmaceutical formulations by using a spherisorb CNRP Column, mobile phase combination is buffer (pH 6.0): ACN (50:50).The method has been developed as per ICH guidelines[9-14].

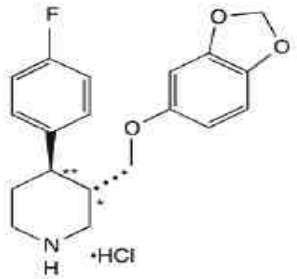

Fig.1.Chemical Structure of Paroxetine Hydrochloride.

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2.0. MATERIALS AND METHODS

2.1. Chemicals

Acetonitrile used was of HPLC grade from E. Merck, India. HPLC grade water was obtained using millipore water purification system. Working standard of Paroxetine Hydrochloride with potency of 99.67 % was obtained from Dr. Reddy's Laboratories, Hyderabad.Other chemicals were analytical grade of above 99% purity. All volumetric ware was pre-calibrated by the manufacturer (Borosil) and was of grade A. HPLC grade water was obtained using millipore water purification system. Commercial tablets containing Paroxetine (PAXIL-20mg) were procured from the local chemist shop.

2.2. Instrumentation

The validated method utilized on a HPLC was performed on a gradient High Pressure Liquid Chromatography (waters separation module) with variable wave length programmable Diode array Detector 2487, and spherisorb CNRP Column. The HPLC system was equipped with the software "Empower-2 series (Waters)".at ambient temperature. A rheodyne injector with 20 µl loop was used for injecting the sample. Shimadzu balance was used for weighing purpose in this method.

2.3. Chromatographic conditions

The analysis was carried out with UV detection at 265 nm using a 20 µl Injection volume.

Assay was performed using a C18 reversed-phase column eluted with phosphate buffer pH 6.0: Acetonitrile (50:50, v/v) at a flow rate of 2.0 ml/ min. Chromatography was carried out at ambient temperature. The solvents were mixed, filtered through a membrane filter of 0.45 micron pore and degassed in ultrasonic bath prior to use.

Preparation of standard drug solution:

Stock solutions (0.5mg/ml) of PXT (Paroxetine) was prepared by dissolving 50 mg of Paroxetine HCL in 100 ml volumetric flasks add about 70ml of diluent, sonicated for about 15 min. and then made up to volume with

diluent. About 5ml of working standard solutions of PXT is diluted to 25ml with diluent and mix well. Filter the solution through 0.45µm nylon filter. The stock contains of 100µg/ml.

Preparation of sample drug solution for pharmaceutical formulations:

Twenty tablets were weighed to get the average tablet weight and pulverized. The sample of the powdered tablets, Equivalent to 25 mg of active ingredient to a 25ml volumetric flask add about 70ml o f water stir on magnetic stirrer for about 15 min. then add 5ml of 0.05M HCL and 150ml of propanol and stir on a magnetic stirrer for about 15 mins, make up the volume with propanol and filter through 0.45µm nylon filter, Finally we get the concentration of 100µg/ml

3.0. METHOD VALIDATION1

3.1. Linearity

A series of standard curves were prepared over a concentration range of 20 -100µg/ml by diluting the standard stock solution of Paroxetine (1mg/ml) in mobile phase. The data from peak area versus drug concentration plots were treated by linear least square regression analysis and r^2 was found 0.9999. The standard curves were evaluated for intra-day and inter-day reproducibility. Each experiment was repeated in triplicate.

3.2. Precision

Precision was measured in accordance with ICH recommendations. The precision study was carried out by injecting sample preparation of 60 µg/ml concentration six times.

3.3. Accuracy

Recovery studies by the standard addition method were performed with a view to justify the accuracy of the proposed method. Previously analyzed samples Paroxetine (60 µg/ml) were spiked with known amount of standard so as to get three different levels (66.33, 88.33% and 100%) and the mixtures were analyzed by the proposed method. The experiment was performed in triplicate. Recovery (%), RSD (%) was calculated for each concentration.

RESULTS AND DISCUSSION

The appropriate wavelength in UV region was selected for the measurement of active ingredient in the proposed method. The method was validated by linear fit curve and all other parameters were calculated just like a visible spectrophotometric method and were discussed in the following pages.

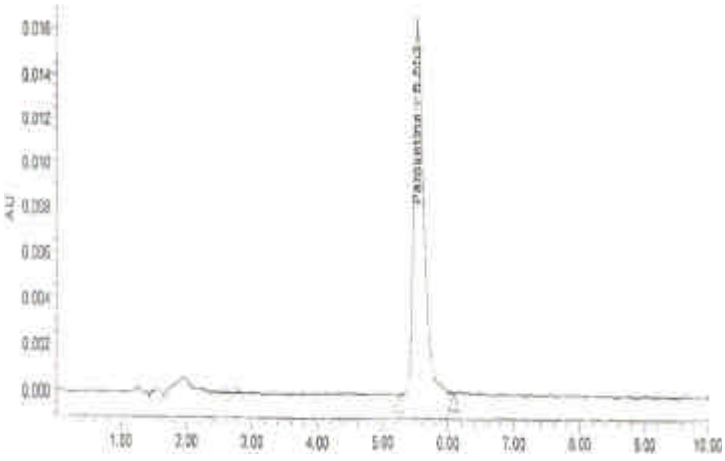

Fig. 2 Model Chromatogram for Paroxetine

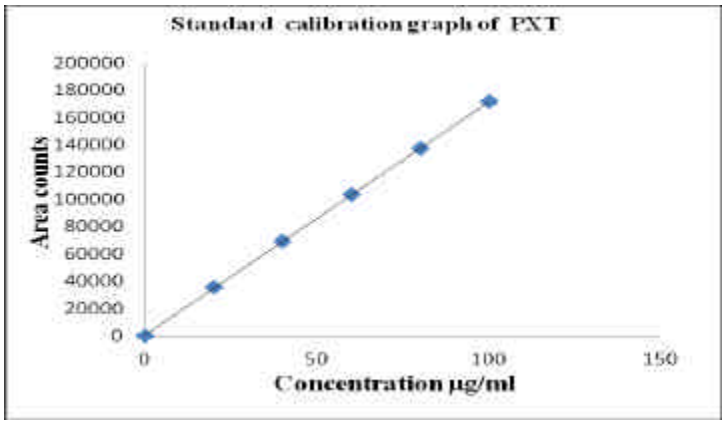

Fig.3 Linearity graph of Paroxetine Linearity

Table.1.Optical characteristic of Paroxetine

Linearity range (µg ml^{-1})	20-100
Regression equation (Y = a + bC)	
Slope (b)	1710
Intercept (a)	+637.7
Standard error of estimation (S_e)	1.85×10^{-2}
Correlation coefficient (r)	0.9999
Relative standard deviation (%)*	0.792
% Range of error (Confidence limits)*	
0.05 level	0.045
0.01 level	0.090
% Error in bulk samples**	0.062

* *Average of eight determinations*

***** Average of three determinations***

Table.2.System suitability parameters of Paroxetine

Parameter	PXT
Retention time (t) (min)	5.563
Theoretical plates (n)	1183
Plates per meter (N)	2643
Height equivalent to theoretical plate (HETP)(mts)	3.78×10^{-4}
Tailing factor (T)	1.37

Table.3.Intra-and inter-day precision for PXT assay in pharmaceutical dosage forms by the proposed method

Concentration of PXT (µg ml^{-1})	Observed concentration of PXT*(µg ml^{-1})			
	Intra-day		Inter-day	
	Mean	%CV	Mean	%CV
50	49.99	0.020	50.02	0.1269
70	70.07	0.065	70.03	0.0786
90	90.06	0.064	90.02	0.0705

**** Average of five determinations***

Table.4.Assay Results of PXT in Pharmaceutical Formulations

Pharmaceutical Formulation	Labeled amount(mg)	Amount found * ± S.D	% Recovery ±RSD
Tablet-1	20	19.96±0.02	99.8±0.1
Tablet-2	20	19.96±0.012	99.8±0.06
Tablet-3	20	19.97±0.015	99.85±0.075
Tablet-4	20	19.96±0.01	99.8±0.05

****Average ± standard deviation of eight determinations***

Table .5.Recovery Studies of PXT

Spike standard	Amount added 50 %	Amount found 50%	% recovery 50%
Sample-1	20	19.9	99.5
Sample-2	20	19.82	99.1
Sample-3	20	19.85	99.25
	100%	**100%**	**100%**
Sample-1	40	40.5	101.2
Sample-2	40	40.15	100.3
Sample-3	40	40.2	100.5
	150%	**150%**	**150%**
Sample-1	60	59.98	99.96
Sample-2	60	59.96	99.93
Sample-3	60	60.2	100.33

CONCLUSION

Though there are six HPLC, three LC-MS/MS, one GC/MS, one fluorimetric and six Spectrophotometric methods reported for the determination of PXT in the literature prior to the commencement of this work. Hence the HPLC method developed for its assay is valuable.The proposed method (HPLC) is simple, sensitive and reliable and can be used for the routine determination of PXT in bulk samples and pharmaceutical formulations depending upon the needs of the situation.

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