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The Estimation of Taineptine in tablet dosage forms by RP-HPLC

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Abstract

A simple, precise, rapid and accurate reverse phase HPLC method was developed for the estimation of Taineptine in tablet dosage form. An Inertsil ODS-3V analytical column (250 x 4.6 mm, 5 µm partical size) with mobile phase consisting of mixture of buffer 0.1% *ortho*-phosphoric acid in water and acetonitrile in the gradient program was used. The flow rate was 1.0 mL/min and the effluents were monitored at 220 nm. The retention time was 8.6 min. The detector response was linear in the concentration of 1-12 mcg/mL. The respective linear regression equation being y=1025.6x-1028.4. The limit of detection and limit of quantification was 0.005mcg /mL and 0.015mcg/mL respectively. The percentage assay of Taineptine was 99.6 %. The method was validated by determining its accuracy, precision and linearity. The results of the study showed that the proposed RP-HPLC method is simple, rapid, precise and accurate, which is useful for the routine determination of Taineptine in bulk drug and in its pharmaceutical tablet dosage form.

Keywords: Taineptine, RP-HPLC and Tablets

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1. Introduction

Tianeptine [1] is a selective serotonin reuptake enhancer (SSRE) drug used for treating Major depressive episodes (mild, moderate, or severe). Unlike conventional tricyclic antidepressants, tianeptine enhances the reuptake of serotonin instead of inhibiting it, opposite to the action of SSRIs. Moreover, it enhances the extracellular concentration of dopamine in the nucleus accumbens. Tianeptine exerts its antidepressant action by increasing the presynaptic re-uptake of serotonin. Chemically[2], Taineptine is: (*RS*)-7-(3-chloro-6-methyl-6,11-dihydrodibenzo [*c*,*f*] [1,2] thiazepin-11-ylamino)heptanoic acid *S*,*S*-dioxide. The empirical formula is $C_{21}H_{25}ClN2O_4S$, with a molecular weight of 436.953 g/mol. Taineptine is soluble in water methanol and in DMSO. The drug exists as two isomers, of which the leavo isomer seems to be the therapeutically active form and shows serotonergic activity by enhancing the presynaptic reuptake of serotonin. In the literature, several analytical techniques like HPLC[3-7], PIF methods including Flow Injection analysis, Spectrofluorometric Voltametric [10], GC, and UV spectrophotometric

methods have been reported for its determination in biological fluids and formulations. The main purpose of the present study was to establish a relatively simple, sensitive and validated liquid chromatographic methods for the determination of tianeptin in pure form and in pharmaceutical dosage forms. The availability of an HPLC method with high sensitivity and selectivity will be very useful for the determination of Taineptine in pharmaceutical formulations. The method was validated by determining its accuracy, precision and linearity as per ICH guidelines.

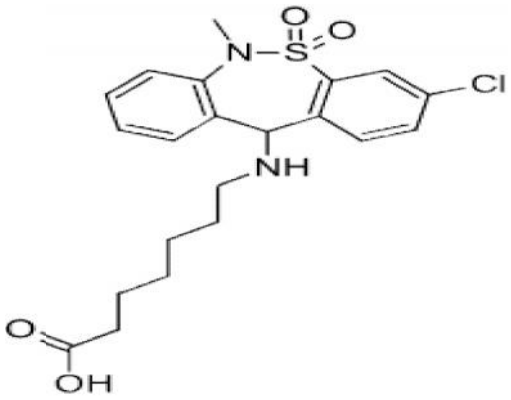

Figure 1. Structure of Taineptine

2. Experimental

Materials and Methods:

Taineptine was obtained as a gift sample from M/s. Vishnu Chemicals Ltd, Hyderabad. Acetonitrile, *ortho*-phosphoric acid and water used were of HPLC grade (Qualigens). Commercially available Taineptine Tablets 125mg (Stablon® 125 mg, Serdia Pharmaceuticals, India) were procured from local market.

Instrument:

Quantitative HPLC was performed on liquid chromatography, Waters Alliance system with equipped with Diode Array Detector and automatic injector with injection volume 20 µl. The HPLC data was analyzed with Empower-2 Software.

HPLC Conditions:

The contents of the mobile phase were mixture of buffer 0.1% *ortho*-phosphoric acid in water and acetonitrile in the gradient program was used (shown in table-IV). They were filtered before use through a 0.45 µm membrane filter, and pumped from the respective solvent reservoirs to the column at a flow rate of 1.0 mL/min. The run time was set at 25.0 min and the column temperature was ambient. Prior to the injection of the drug solution, the column was equilibrated for at least 25 min with the mobile phase flowing through the system. The eluents were monitored at 220 nm.

Preparation of Standard Stock solution:

A standard stock solution of the drug was prepared by dissolving 10 mg of Taineptine in 100 mL volumetric flask and dissolved in diluent (Acetonitrile and Water:50:50), sonicated for about 15 min and then made up to 100 mL with diluent get 100 mcg/mL standard stock solution.

***Working Standard solution*:**

1.0 mL of the above stock solution was taken with micropipette in 10 mL volumetric flask and thereafter made up to 10 mL with diluent (Acetonitrile and Water: 50:50) to get a concentration of 10mcg/mL.

Preparation of Sample solution:

Twenty tablets (Stablon® 125 mg, Serdia Pharmaceuticals, India) were weighed, and then powdered. A sample of the powdered tablets, equivalent to 10mg of the active ingredient, was mixed with 30 mL of diluent in 100 mL volumetric flask. The mixture was allowed to stand for 15 min with intermittent sonication to ensure complete solubility of the drug, and then filtered through a 0.45 µm membrane filter, followed by adding diluent up to 100 mL to obtain a stock solution of 100mcg/mL. 1 mL of the above solution was taken and further diluted with diluent up to 10 mL to get working sample solution of 10 mcg/mL.

Linearity:

Aliquots of standard Taineptine stock solution were taken in different 10 mL volumetric flasks and diluted up to the mark with the diluent such that the final concentrations of Taineptine are in the range of 1-12 µg/mL. Each of these drug solutions (20 µL) was injected three times into the column, and the peak areas and retention times were recorded. Evaluation was performed with Diode Array detector at 220 nm and a Calibration graph was obtained by plotting peak area versus concentration of Taineptine (Fig 3).

The plot of peak area of each sample against respective concentration of Taineptine was found to be linear in the range of 1–12 mcg/mL with correlation coefficient of 0.9999. Linear regression least square fit data obtained from the measurements are given in table I. The respective linear regression equation being y=1025.6x-1028.4. The regression characteristics, such as slope, intercept, and %RSD were calculated for this method and given in table I.

Assay:

20 µL of sample solution was injected into the injector of liquid chromatography. The retention time was found to be 8.6 minutes. The amount of drug present per parentaral was calculated by comparing the peak area of the sample solution with that of the standard solution. The data are presented in table II.

Recovery Studies:

Accuracy was determined by recovery studies of Taineptine, known amount of standard was added to the preanalysed sample and subjected to the proposed HPLC analysis. Results of recovery study are shown in table II. The study was done at three different concentration levels.

3. Results and Discussion

The system suitability tests were carried out on freshly prepared standard stock solution of Taineptine. The parameters studied to evaluate the suitability of the system are given in table III**.**

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection (LOD) and limit of quantification (LOQ) for Taineptine were found to be 0.005 mcg/mL and 0.015 mcg/mL respectively. The signal to noise ratio is 3 for LOD and 10 for LOQ. From the typical chromatogram of Taineptine as shown in fig 2, it was found that the retention time was 8.6 min. A mixture of buffer 0.1% ortho-phosphoric acid in water and acetonitrile in the gradient program was used (shown in table-IV) was found to be most suitable to obtain a peak well defined and free from tailing. In the present developed HPLC method, the standard and sample preparation required less time and no tedious extraction were involved. A good linear relationship (r^2=0.9999) was observed between the concentration range of 1-12 mcg/mL. Low values of standard deviation are indicative of the high precision of the method. The assay of Taineptine tablets was found to be 99.6 %. From the recovery studies it was found that about 99.2% of Taineptine was recovered which indicates high accuracy of the method. The absence of additional peaks in the chromatogram indicates non-interference of the common excipients used in the tablets. This demonstrates that the developed HPLC method is simple, linear, accurate, sensitive and reproducible. Thus, the developed method can be easily used for the routine quality control of parental dosage forms of Taineptine within a short analysis time.

Table I. Linear Regression Data for Calibration curves

Drug	Taineptine
Concentration range (mcg/mL)	1-12
Slope (m)	1025.6
Intercept (b)	-1028.4
Correlation coefficient	0.9999
% RSD	0.24

Table II. Results of HPLC Assay and Recovery studies

Sample	Amount claim (mg/Tablet)	% found by the proposed method	% Recovery*
1.	125	99.7	99.1
2.	125	99.6	99.1
3.	125	99.5	99.4

*Average of three different concentration levels.

Table III. Validation Summary

Validation Parameter	Results
System Suitability	
Theoretical Plates (N)	14868
Tailing factor	0.98
Retention time in minutes	8.6
% Area	99.64
LOD (mcg/mL)	0.005
LOQ (mcg/mL)	0.015

Table IV. Gradient Program in HPLC method

Time in mins	Buffer	Acetonotrile
0.01	70	30
4	70	30
10	20	80
20	20	80
21	70	30
25	70	30

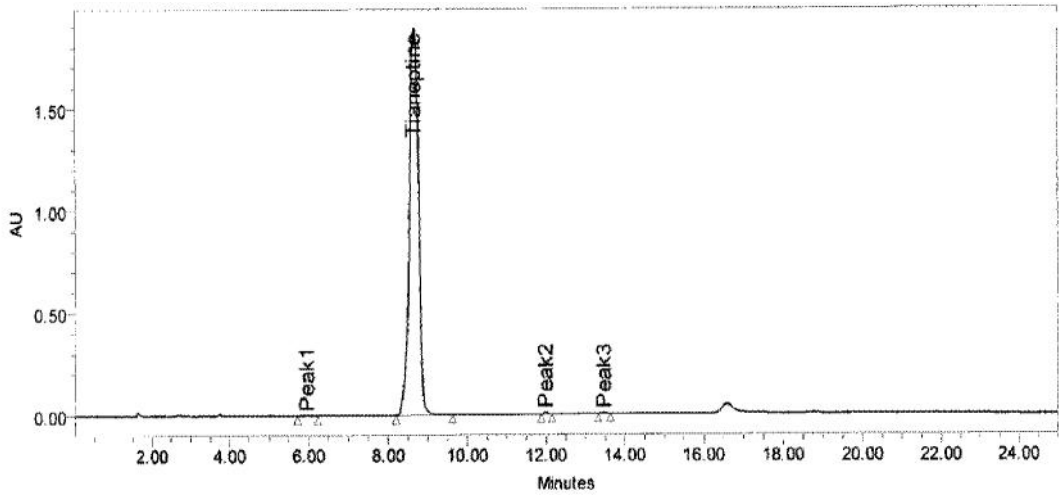

Figure 2. Typical Chromatogram of Taineptine by HPLC

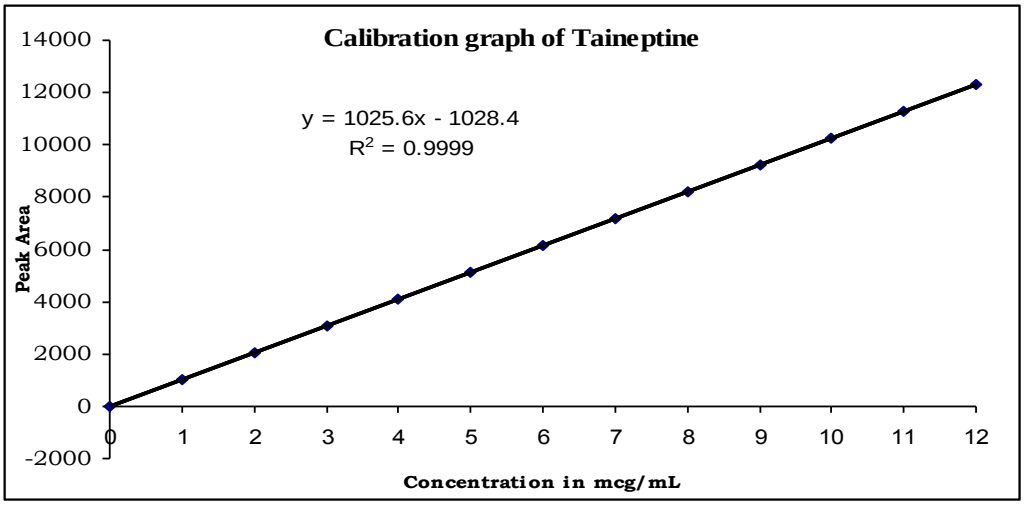

Figure 3. Calibration curve of the Taineptine by RP-HPLC

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5. References

1. O' neil M.J., Smith A., Heckelman P.E, Obenchain JR., Gallipeau JAR, D'Arecca MA., "Merck Index" 13 th ed., Merck Co., Inc., **2001**, 1679.
2. "European Pharmacopeia", vol. 2, 5th ed. Strasbourg, Council of Europe, **2005**, pp. 2575-2576.
3. Ulu S.T. Determination of tianeptine in tablets by HPLC with fluorescence detection. Journal of AOAC International, **2007**, 90(3): 720-724.
4. Nicot G, Lachatre G, Gonnet C, Mallon J, Mocaer E. Ion pair extraction and HPLC determination of tianeptine and its metabolites in human plasma, urine and tissues. J. Chromatogr, **1986**, 381(1): 115-126.

5. Ulu S.T. Determination of tianeptine in human plasma using HPLC with fluorescence detection. Journal of Chromatography B, **2006**, 834(1-2): 62-67.
6. Khedr A. High performance liquid chromatographic stability indicating assay method of tianeptine sodium with simultaneous fluorescence and UV detection. J Chromatogr Sci. **2007**, 45(6): 305-310.
7. Gaulier JM, Marquet P, Lacassie E, Desroches R, Lachatre G. RP-HPLC method with UV detection for determination of tianeptine in biological fluids. J. Chromatogr. B, **2000**, 748: 407-414.
8. Bulaceanu-Mac-Nair M, Aaron JJ, Prognon P, Mahuuzier G. Photochemically induced fluorimetric detection of tianeptine and some of its metabolites. Application to pharmaceutical preparation. Analyst, **1998**, 123: 2267-2270.
9. Dikici E, Deo SK, Daunert S. Spectrofluorometric determination of tianeptine in biological fluids. Anal. Chem. Acta, **2003**, 500: 237-245.
10. Gazy AA, Mahgoub H, Khamis EF, Youssef RM, El-Sayed MA. Differential pulse, square wave and adsorption stripping Voltammetric quantification of tianeptine in tablets. J. Pharm. Biomed. Anal., **2006**, 41(4): 1157-1163.
11. Nicot G, Lachatre G, Gonnet C, Valette JP, Merle L, Nouaille Y, Bromet N.GC method for determination of tianeptine in biological fluids. J. Chromatogr. Biomed. Appl., **1984**, 31: 279-290.
12. Badjatya JK, Bodla RB, Prashant Soni, Mradula Sachan, Sumita Shukla. A method for spectrophotometric determination of tianeptine in bulk and capsule dosage form. Asian Journal of Pharmacy and Medical Science, **2012**, 2(5): 83-85.