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Research Article

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RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR THE ANALYISIS OF QUETIAPINE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A simple, selective, linear, precise and accurate RP-HPLC method was developed and validated for rapid assay of Quetiapine in tablet dosage form. Isocratic elution at a flow rate of 1ml min^{-1} was employed on a symmetry C18 column at ambient temperature. The mobile phase consisted of Methanol:Acetonitrile:OPA 35:35:30 (v/v/v). The UV detection wavelength was at 238nm.Linearity was observed in concentration range of 10-35ppm. The retention time for Quetiapine was 7.33 min. The method was validated as per the ICH guidelines. The proposed method can be successfully applied for the estimation of Quetiapine in pharmaceutical dosage forms.

Key words: Quetiapine, Determination, RP-HPLC, Validation.

INTRODUCTION

Quetiapine is an atypical antipsychotic approved for the treatment ofschizophrenia, and bipolar disorder. Quetiapine is used to treat either schizophrenia or bipolar disorder. Quetiapine is ineffective in reducing agitation among people with Alzheimer's, whose usage of the drug once constituted 29% of sales. Quetiapine worsens cognitive functioning in the elderly with dementia and thus is not recommended. It is sometimes used off-label, often as an augmentation agent, to treat conditions such as obsessive-compulsive disorder, post-traumatic stress disorder, autism, alcoholism, Borderline Personality Disorder, depression, Tourette syndrome, and has been used by physicians as a sedative for those with sleep disorders or anxiety disorders. The most common side-effect of quetiapine is somnolence. Other common side-effects include: sluggishness, fatigue, dry mouth, sore throat, dizziness, abdominal pain, constipation, upset stomach, orthostatic hypotension, inflammation or swelling of the sinuses or pharynx, increased appetite, and weight gain. It is marketed as one of the most sedating of all anti-psychotics, although those claims are contested. Beginning users may feel extremely tired and 'out of it' for the first few days, and sometimes longer. Quetiapine's newest indication, for bipolar depression, usually specifically calls for the entire dose to be taken before bedtime due to its sedative effects. The sedative effects may disappear after some time on the drug, or with a change of dosage, and with possibly different, non-sedative side-effects emerging.

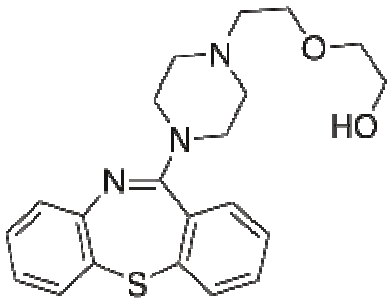

Figure1; Structure of Quetiapine

EXPERIMENTAL

Chemicals and reagents

All HPLC SOLVENTS used like Acetonitrile, Methanol, THF which are of HPLC grade were purchased from E.Merck,

Instrumentation and analytical conditions

The analysis of the drug was carried out on Shimadzu HPLC model (VP series) containing LC-10AT (VP series) pump, variable wave length programmable UV/visible detector SPD-10AVP and rheodyne injector (7725i) with 20µl fixed loop. Chromatographic analysis was performed using Inertsil ODS C-18 column with 250 x 4.6mm internal diameter and 5µm particle size. Shimadzu electronic balance (AX-200) was used for weighing. Isocratic elution with Methanol,Acetonitrile,,OPA 35:35:30 (v/v/v) was selected with a flow rate of 1.0 ml min^{-1}.The detection wavelength was set at 238 nm with a runtime of 10 min. The mobile phase was prepared freshly and it

was degassed by sonicating for 5 min before use. The column was equilibrated for at least 30min with the mobile phase flowing through the system. The column and the HPLC system were kept at ambient temperature.

Preparation of Stock, working standard solutions and Sample solutions

100mg of Quetiapine was weighed and transferred (working standard) into a 100ml volumetric flask. The diluent methanol was added and sonicated to dissolve it completely and made up to the mark with the same solvent. Further 1ml of the above stock solution was pipetted into a 10ml volumetric flask and diluted up to the mark with diluent. The contents were mixed well and filtered through Ultipor N_{66} Nylon 6, 6 membrane sample filter paper. The calibration curve was plotted with the concentrations of the 35 to 10 ppm working standard solutions. Calibration solutions were prepared and analyzed immediately after preparation.

The formulation tablets of Quetiapine were crushed to give finely powdered material. Powder equivalent to 10 mg of drug was taken in 10 ml of volumetric flask containing 5 ml of mobile phase and was shaken to dissolve the drug and then filtered through Ultipor N_{66} Nylon 6,6 membrane sample filter paper. Volume of the filtrate was adjusted to the mark with the same solvent to obtain concentration of 20 ppm.

Method Validation procedure

The objective of the method validation is to demonstrate that the method is suitable for its intended purpose as it is stated in ICH guidelines. The method was validated for linearity, precision, accuracy, specificity, and limit of detection, limit of quantification, robustness and system suitability.

Linearity

The developed method has been validated as per ICH guidelines (Zucman D, 2007). Working standard solutions of Quetiapine in the mass concentration range of 10 ppm to 35 ppm was injected into the chromatographic system. The chromatograms were developed and the peak area was determined for each concentration of the drug solution. Calibration curve of Quetiapine was obtained by plotting the peak area ratio versus the applied concentrations of Quetiapine. The linear correlation coefficient was found to be 0.999.

Table 1: Linearity of Quetiapine

S.NO	CONC	AREA
1	10	85273
2	15	120498
3	20	160393
4	25	195665
5	30	237254
6	35	271065

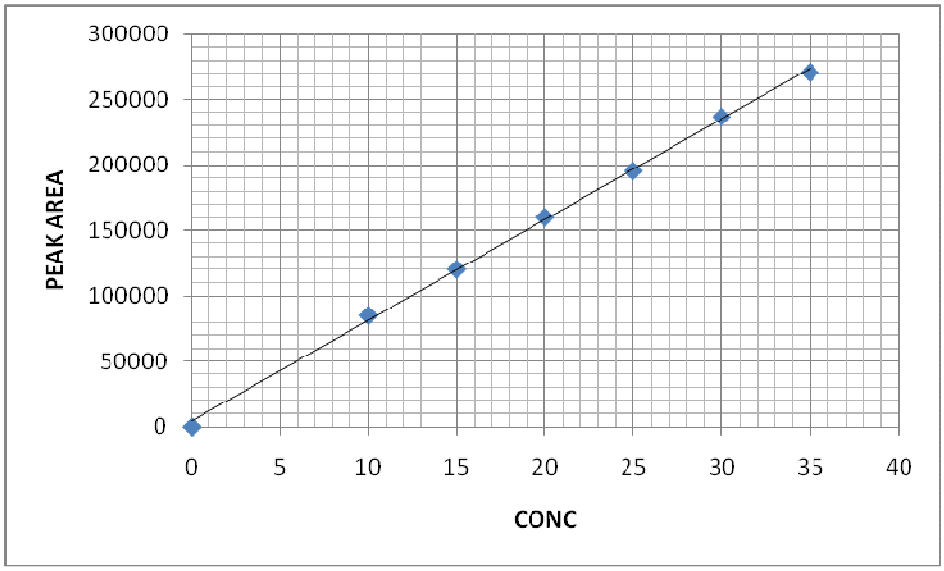

Figure 2: Calibration curve of Quetiapine

Table.2 Linear Regression Data for Calibration curve

Drug	Quetiapine
Concentration range	35-10ppm
Slope (m)	7718.374
Intercept (b)	8047.87
Correlation coefficient	0.999
% RSD	0.43

Precision

Repeatability of the method was checked by injecting replicate injections of 20 ppm of the solution for six times on the same day as intraday precision study of Quetiapine and the RSD was found to be 0.43

Table 3: Precision parameters of Quetiapine

INJECTION	CONCENTRATION	PEAK AREA (INTRA DAY)	PEAK AREA (INTERDAY)
1	20 ppm	160931	161764
2	20 ppm	160800	161240
3	20 ppm	161042	161448
4	20 ppm	159528	161984
5	20 ppm	159818	160049
6	20 ppm	160008	162067

Accuracy

The accuracy of the method was determined by calculating recovery of Quetiapine by the method of standard addition. Known amount of Quetiapine (10ppm, 20ppm and 30ppm) was added to a pre quantified sample solution and the amount of Quetiapine was estimated by measuring the peak area ratios and by fitting these values to the straight line equation of calibration curve. The recovery studies were carried out three times over the specified concentration range and amount of Quetiapine was estimated by measuring the peak area ratios by fitting these values to the straight line equation of calibration curve. From the above determination, percentage recovery and standard deviation of percentage recovery were calculated.

Figure 3: Typical chromatogram of Quetiapine Formulation

Specificity

The specificity of the method was determined by comparing test results obtained from analysis of sample solution containing excipients with that of test results those obtained from standard drug.

LOD and LOQ

Limit of detection (LOD) and limit of quantification (LOQ) were calculated as 0.02 ppm and 0.06 ppm respectively as per ICH guide-lines.

Robustness

To determine the robustness of the method, two parameters from the optimized chromatographic conditions were varied.

Ruggedness

Inter day variations were performed by using six replicate injections of standard and sample solutions of concentrations which were prepared and analyzed by different analyst on three different days over a period of one week. Ruggedness also expressed in terms of percentage relative standard deviation.

System Suitability Parameter:

System suitability tests were carried out on freshly prepared standard stock solutions of Quetiapine and it was calculated by determining the standard deviation of Quetiapine standards by injecting standards in six replicates at 6 minutes interval and the values were recorded.

Table 4: System suitability parameters of Quetiapine

Parameters	Values
λ max (nm)	238
Beer's law limit (µg/ml)	35 – 10ppm
Correlation coefficient	0.999
Retention time	7.33 min
Theoretical plates	64833

Tailing factor	1.84
Limit of detection	0.02 ppm
Limit of quantification	0.06 ppm

RESULT AND DISCUSSION

Optimization of the chromatographic conditions

The nature of the sample, its molecular weight and solubility decides the proper selection of the stationary phase. The drug Quetiapine being non-polar is preferably analyzed by reverse phase columns and accordingly C18 column was selected. So the elution of the compound from the column was influenced by polar mobile phase. The concentration of the methanol and Acetonitrile were optimized to give symmetric peak with short run time based on asymmetric factor and peak area obtained. Different mobile phases were tried but satisfactory separation, well resolved and good symmetrical peaks were obtained with the mobile phase Methanol,Acetonitrile,OPA 35:35:30 (V/V/v). The retention time of Quetiapine was found to be 7.33 min, which indicates a good base line. The RSD values for accuracy and precision studies obtained were less than 2% which revealed that developed method was accurate and precise. The system suitability and validation parameters are given in Table 4. The high percentage of recovery of Quetiapine was found to be 99.65 indicating that the proposed method is highly accurate. Proposed liquid chromatographic method was applied for the determination of Quetiapine in tablet formulation. The result for Quetiapine was comparable with a corresponding labelled amount (Table 5). The absence of additional peaks indicates no interference of the excipients used in the tablets.

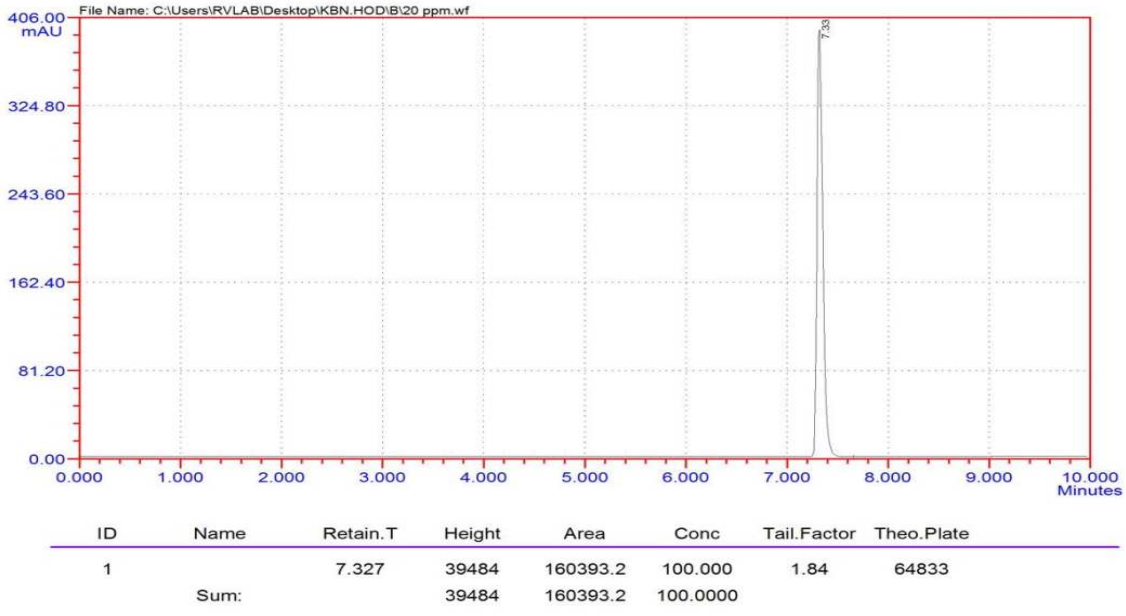

Figure 5: Typical chromatogram of Quetiapine

Table 5: Chromatographic conditions of Quetiapine

Formulation	Tablet dosage	Sample concentration	Amount of drug estimated	% of Quetiapine in Tablet
Q PIN	50mg	50 ppm	49.95 ppm	99.725

CONCLUSION

A validated RP-HPLC method has been developed for the determination of Quetiapine in tablet dosage form. The proposed method is simple, rapid, accurate, precise and specific. Its chromatographic run time of 6 min allows the analysis of a large number of samples in short period of time. Therefore, it is suitable for the routine analysis of Quetiapine in pharmaceutical dosage form.

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