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Development of analytical method for determination of quetiapine fumarate in bulk & tablet dosage form

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ABSTRACT

A new, simple, specific, sensitive, rapid, accurate and precise RP-HPLC method was developed for the estimation of quetiapine fumarate in bulk and pharmaceutical formulations. Quetiapine fumarate was chromatographed on Microsorb-MV 100-5 C-18 (250 x 4.6mm, 5 µm) column using UV detector. The mobile phase consisting acetonitrile and phosphate buffer (pH 3) in the ratio of 50:50 (v/v) at a flow rate of 1.0 ml/min with detection at 292 nm. The method was validated according to the ICH guidelines with respect to specificity, linearity, accuracy, precision and robustness.

Keywords: RP-HPLC, Quetiapine fumarate, Validation, Tablets.

INTRODUCTION

Quetiapine fumarate is an atypical antipsychotic agent indicated for the treatment of schizophrenia and for the treatment of acute manic episodes associated with bipolar disorder [1] . It is a selective monoaminergic antagonist. However, this effect is mediated through antagonism of dopamine type 2 (D_2) and serotonin type 2 ($5HT_2$) receptors. Quetiapine is a dibenzothiazepine derivative and is chemically 2, (2-[2-(4-Dibenzo [*b,f*] [1,4]thiazepin-11-yl-1-piperazinyl) ethoxy]ethanol) fumarate.

Quetiapine fumarate is not official in any pharmacopoeia [2] . Literature survey reveals that few LC-MS [3] , GC [4] , HPTLC [5] , HPLC [6-8] , spectrophotometric [10-11] , methods have been reported for the estimation of quetiapine. In the present study the authors report a simple, rapid, sensitive, accurate and precise HPLC method for the estimation of quetiapine in bulk and tablet dosage forms.

Figure 1. Chemical structure of quetiapine fumarate

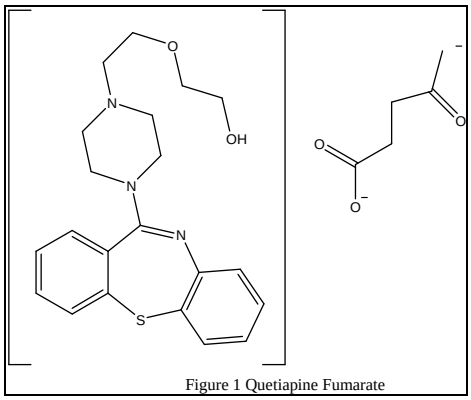

Figure 1 Quetiapine Fumarate

MATERIALS AND METHODS

Instrumentation

The HPLC system (Cyberlab LC 100) consisting of binary gradient pump, Microsorb-MV 100-5 C- 18 column (250 x 4.6mm, 5 µm), UV detector was employed for analysis. Chromatographic data was acquired using WS-100 Workstation software.

Reagents

Active pharmaceutical ingredient (API) working standards of Quetiapine fumarate, was obtained as gift sample from Lupin Limited, Pune, India. HPLC grade acetonitrile, methanol and orthophosphoric acid were obtained from Merck, Mumbai, India Limited. HPLC grade water was obtained from MOLYCHEM, Thane, India. The commercially available Quetiapine fumarate tablets (QUTAN-100, Intas Pharmaceuticals) were purchased from local market.

Chromatographic conditions

Microsorb MV 100-5 C-18 column (250mm×4.6 mm, 5µm) was used as a stationary phase. The isocratic mobile phase consisting of a mixture of phosphate buffer (pH 3.0 adjusted with ortho-phosphoric acid) and acetonitrile in the ratio of 50:50 (v/v) was used throughout the analysis. The flow rate of the mobile phase was 1.0 ml/min. Detector signal was monitored at a wavelength of 292 nm. Prior to the injection of the drug solution, the column was equilibrated for at least 30 min. The column temperature was kept ambient and injection volume was 20µl.

Solution preparation

Standard stock solution

Quetiapine fumarate (QTF) standard stock solution was prepared by transferring 10 mg of QTF working standard into a 100 ml volumetric flask, approximately 25 ml of diluent was added and sonicated for 20 min The volume was made up to 100 ml with diluent. This solution was filtered through a 0.45µm pore size Nylon 66 membrane filter. The subsequent dilutions were prepared by diluting stock solution with the mobile phase.

Sample solution

Weighed accurately twenty tablets, labeled as containing 100 mg with excipients, transferred to a clean and dry mortar and ground into a fine powder. A quantity equivalent to 10 mg of quetiapine was weighed accurately and transferred to 100 ml volumetric flask containing 25 ml of diluent. The contents were sonicated for 20 min and made up to the mark with the diluent. This solution was filtered through a 0.45µm pore size Nylon 66 membrane filter. The subsequent dilutions were prepared by diluting stock solution with the mobile phase.

Validation procedure

The specificity of the method was determined by injecting the sample solution containing excipients without drug having concentration same as that of the sample.

The linearity curve was obtained in the concentration range of 5-30 µg/ml. The linearity was evaluated by linear regression analysis.

The accuracy of the method was carried out by adding known amount of each drug corresponding to three concentration levels 80%, 100% and 120% of the label claim along with the excipients in triplicate.

The precision of the assay was determined in terms of intra-day and inter-day precision. The intra-day and inter-day variation in the peak area of drug solution was calculated in terms of percentage relative standard deviation (% RSD).

Robustness was performed by deliberately changing the chromatographic conditions. The flow rate of the mobile phase was changed from 1.0 ml/min to 0.8 ml/min. The organic strength was varied by ±5%, while pH was varied by ±0.5 units. Standard solution was injected six times in replicate for each change.

RESULTS AND DISCUSSION

Optimization of chromatographic conditions

The optimization of mobile phase was performed based on resolution, asymmetric factor and peak area obtained for Quetiapine fumarate. The mobile phase combination of phosphate buffer (pH 3.0 adjusted with o-phosphoric acid) and acetonitrile (60:40, 70:30 and 80:20 (v/v)) were tried. Acetonitrile: phosphate Buffer (50:50) pH 3.0 (adjusted with Orthophosphoric acid) at a flow rate of 1.0 ml/min found to be satisfactory and gave symmetric and well resolved peaks for QTF. The chromatogram was recorded at 292 nm as spectrum of QTF showed maximum response at this wavelength. The retention time for Quetiapine fumarate was found to be 5.42 min. the chromatogram of QTF in tablet is shown in figure no.2

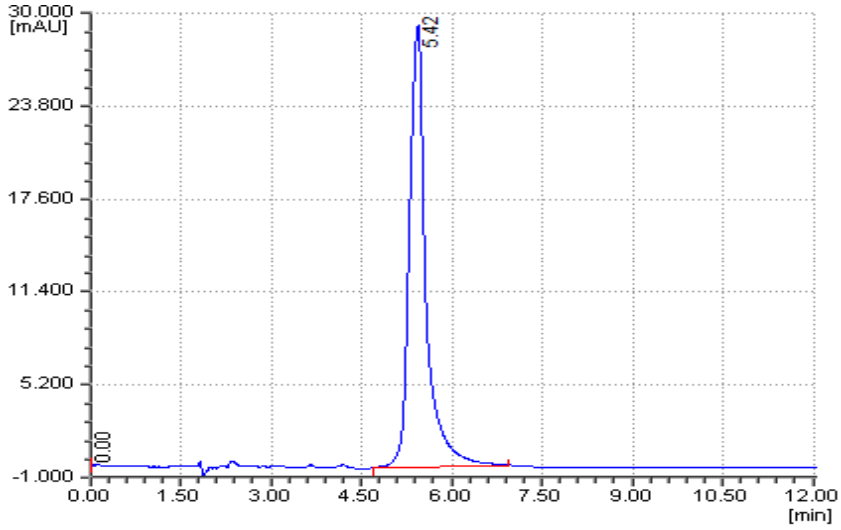

Figure-2: Chromatogram of Quetiapine fumarate in tablet

Method validation

The method was validated according to the ICH guidelines with respect to specificity, linearity, accuracy, precision, and robustness. System suitability was established by injecting standard solution and results are shown in Table 1.

Table 1: System suitability parameters

Component (n = 6)	Area Peak	Tailing Factor	Theoretical plates[a]	Capacity factor[a]	USP resolution[a]
QTF	61364.3	1.05	4655	3.7	4.03

Specificity
The chromatograms were checked for the appearance of any extra peaks. No chromatographic interference from the tablet excipients was found. Peak purity was verified by confirming homogeneous spectral data for Quetiapine fumarate.

Linearity
QTF showed linearity in the range of 5-30 µg/ml. The coefficient of variation in the peak area of the drug for 6 replicate injections was found to be less than 1%. Linear regression equations and correlation coefficient (R^2) are: Y = 2951 x + 2049 & R^2 = 0.999

Accuracy
The accuracy was expressed as the percentage of analytes recovered by the assay method. It was confirmed from results that the method is highly accurate. Results are shown in Table 2.

Table 2 : Accuracy data (analyte recovery)

Theoretical (% of target level)	Amount added (mg)	Amount recovered (mg)	Recovery (%)
80	18	17.9	99.44
100	20	19.87	99.35
120	22	22.17	100.78

n = 3 determination

Precision
The relative standard deviations for inter-day precision were found to be 0.543 % & R.S.D. for intra-day was 0.646 % this indicates that the method was sufficiently precise.

Robustness
In all deliberately varied conditions, the RSD of peak areas of Quetiapine fumarate was found to be well within the acceptable limit of 2%. The tailing factor for the peaks was found to be < 2.

CONCLUSION

The proposed method of HPLC is specific, accurate and precise for the determination of Quetiapine fumarate in bulk & pharmaceutical dosage form. The described method is suitable for routine analysis and quality control of pharmaceutical preparations containing this drug.

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