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Original Article

Development and Validation of RP-HPLC Method for Estimation of Quetiapine Fumarate in Pharmaceutical Formulations

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ABSTRACT

Objective: A simple, rapid, accurate and precise RP-HPLC method was developed for the determination of Quetiapinefumarate in pure and tablet dosage forms. **Materials and Method:** Separation of the drug was achieved on aisocratic Shimadzu prominence HPLC instrument on a Waters Xterra C_{18} column (250x4.6 mm, 5µ). **Results:** The method showed a linear response for concentration in the range of 50–150 µg/mL using buffer (9.2 ± 0.05) and acetonitrile in the ratio of 51:49 v/v with detection at 254 nm with a flow rate of 1.0 mL/min and retention time was 6.588 min. **Conclusion:** The method was statistically validated for linearity, accuracy, precision and selectivity. Quantitative and recovery studies of the dosage form were also carried out and analyzed, the %RSD from recovery studies was found to be less than 1.

Key words: Quetiapinefumarate, Isocratic, C_{18}, HPLC, Tablets.

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INTRODUCTION

Quetiapine fumarate (Figure 1) is dibenzothiazepine atypical antipsychotic. It is used in the treatment of schizophrenia and of bipolar disorder. Chemically it is 2-[2-(4-Dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl) ethoxy]ethanol fumarate (2:1) salt. It is reported to have affinity for serotonin (5-HT_2), histamine (H_1), and adrenergic (α_1 and α_2) receptors as well as dopamine D_1 and D_2 receptors.[1, 2] A few analytical methods have been reported for the determination of Quetiapine fumarate in pure drug, pharmaceutical dosage forms and biological samples using spectrophotometry[3,4], liquid chromatography[5-19], high performance thin layer chromatography[20, 21], gas chromatography[22], electrophoresis[23, 24] and polarography.[25]

MATERIALS AND METHODS

Instrumentation

The author had attempted to develop a liquid chromatographic method for quantitative estimation of Quetiapine fumarate using an isocratic Shimadzu prominence HPLC instrument on a Waters Xterra C_{18} column (250 mm × 4.6 mm, 5µ). The instrument is equipped with a LC 20AT pump and variable wavelength programmable UV-Visible detector, SPD-20A. A 20µL Hamilton syringe was used for injecting the samples. Data was analysed by using spinchrome software. Elico SL 159 UV-Visible spectrophotometer was used for spectral studies. Degassing of the mobile phase was done by using a Loba ultrasonic bath sonicator. A Shimadzu balance was used for weighing the materials.

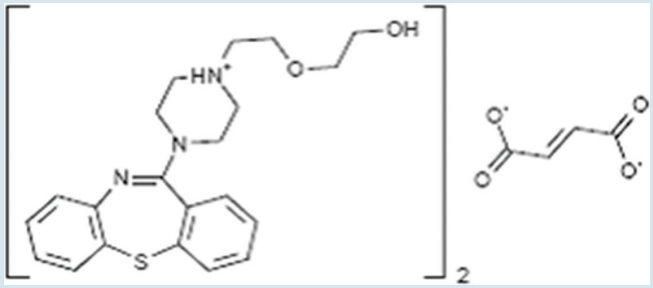

Figure 1: Chemical structure of Quetiapinefumarate.

Chemicals and Solvents

The reference sample of Quetiapine fumarate (API) was obtained from Ranbaxy laboratories limited, Gurgaon. The branded formulation of Quetiapine fumarate tablets (Socalm tablets containing 200 mg of Quetiapine fumarate) were procured from the local market. Acetonitrile, Water and ammonia solution used were of HPLC grade and ammonium formate AR grade were purchased from Merck Specialities Private Limited, Mumbai, India.

Preparation of mobile phase and diluents

The mobile phase was prepared by mixing 510 mL of the buffer and 490 mL of acetonitrile and this solution was degassed in an ultrasonic water bath for 5 minutes and filtered through 0.45 µm filter under vacuum. The same mobile phase was used as diluent.

Preparation of standard solution

About 50 mg of Quetiapine fumarate standard was weighed and transferred into a 50 mL volumetric flask containing 20 mL of mobile phase. The solution was sonicated for 15 min and then volume was made up with a further quantity of the mobile phase to get a concentration of 1 mg/mL solution. 10.0 mL of this solution was further diluted to 100 mL with mobile phase to get a concentration of 100µg/mL.

Preparation of sample solution

Twenty tablets were weighed and finely powdered. An accurately weighed portion of this powder equivalent to 50 mg of Quetiapine fumarate was transferred to a 50 mL volumetric flask containing 20mL of the mobile phase. The contents of the flask were sonicated for about 15 min for complete solubility of the drug and volume made up with further quantity of mobile phase. Then this mixture was filtered through whatman No.41filter paper. 10.0 mL of this filtrate was further diluted to 100 mL with mobile phase.

Procedure

A mixture of ammonium formate buffer (pH 9.2) and acetonitrile in the ratio of 51:49 v/v was found to be the most suitable mobile phase for ideal separation of Quetiapine fumarate. The solvent mixture was filtered through whatman No.41filter paper and sonicated before use. It was

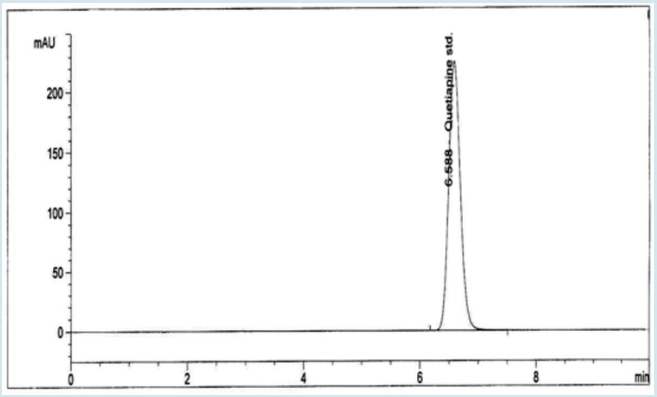

Figure 2: Typical chromatogram of Quetiapinefumarate.

pumped through the column at a flow rate of 1.0 mL/min. The column was maintained at ambient temperature. The column was equilibrated by pumping the mobile phase through the column for at least 30 min prior to the injection of the drug solution. Inject 20 µL of the standard, sample solutions into the chromatographic system and measure the area for the Quetiapine fumarate peak. The detection of the drug was monitored at 254nm. The run time was set at 10 min. Under these optimized chromatographic conditions the retention time obtained for the drug was 6.588 min. A typical chromatogram showing the separation of the drug (Figure 2).

Calibration Plot

About 50 mg of Quetiapine fumarate was weighed accurately, transferred into a 50 mL volumetric flask and dissolved in 20 mL of a 51:49 v/v mixture of ammonium formate buffer pH 9.2 and acetonitrile. The solution was sonicated for 15 min and the volume made up to the mark with a further quantity of the diluents. From this, a working standard solution of the drug (1000 µg/mL) was prepared by diluting 10mL of the above stock solution into a 100 mL volumetric flask and dilute up to the mark with diluent. Further dilutions ranging from 50-150 µg/mL were prepared from the stock solution in 10 mL volumetric flasks using the above diluent. 20 µL of each dilution was injected six times into the column at a flow rate of 1.0 mL/min and the corresponding chromatograms were recorded. From these chromatograms, the average area under the peak of each dilution was computed. The calibration graph constructed by plotting concentration of the drug against peak area was found to be linear in the concentration range of 50-150 µg/mL of the drug. The relevant data are furnished in Table 1. The regression equation of this curve was computed. This regression equation was later used to estimate the amount of Quetiapine fumarate in tablet dosage forms.

Validation of the proposed method

The specificity, linearity, precision, accuracy, limit of detection, limit of quantification, robustness and system suitability parameters were studied

Table 1: Calibration data

Concentration (µg/mL)	Peak area
50	887.63501
80	1405.99030
90	1600.21838
100	1777.25116
110	1952.27930
120	2130.48829
150	2638.04126

Table 2: System precision

Injection number	Peak area of Quetiapine fumarate
1	1763.01123
2	1763.80933
3	1763.83484
4	1764.95569
5	1764.32336
6	1764.86292
Mean	1764.132895
%RSD	0.04

Table 3: Method precision

Injection number	% Assay of Quetiapine fumarate
1	99.69
2	99.07
3	99.33
4	99.84
5	100.95
6	101.21
Mean	100.02
%RSD	0.87

Table 4: Intermediate precision

Injection number	% Assay of Quetiapine fumarate
1	100.12
2	99.73
3	99.99
4	99.70
5	99.51
6	99.84
Mean	99.81
%RSD	0.22

Table 5: Recovery studies

%Concentration (at specification Level)	Mean peak area	Amount of Quetiapine fumarate added (µg)	Amount of Quetiapine fumarate m found (µg)	%Recovery	Mean %Recovery
50%	1720	50	49.8	98.8	
100%	3440	100	100.1	99.9	99.3
150%	5160	150	148.4	99.3	

Table 6: System suitability parameters

Parameter	Result
Linearity (µg/mL)	50-150
Correlation coefficient	0.999
Theoretical plates (N)	10922
Tailing factor	1.21
LOD (µg/mL)	0.07
LOQ (µg/mL)	0.19

Table 7: Results of Assay

Formulation	Label claim (mg)	Amount found (mg)	% Amount found
Tablet	50	49.9	99.69

systematically to validate the proposed HPLC method as per the ICH guidelines.[26] Solution containing 100 µg/mL solution of Quetiapine fumarate was subjected to the proposed HPLC analysis to check system precision, method precision and intermediate precision of the method and the results are furnished in Table 2 to Table 4. The accuracy of the HPLC method was assessed by analyzing solutions of Quetiapine fumarate at 50, 100 and 150% concentration levels by the proposed method. The results are furnished in Table 5. The system suitability parameters are given in Table 6.

Estimation of Quetiapine fumarate in tablet dosage forms

Commercial formulation of tablets was chosen for testing the suitability of the proposed method to estimate Quetiapine fumarate in tablet formulations. Twenty tablets were weighed and powdered. An accurately weighed portion of this powder equivalent to 50 mg of Quetiapine fumarate was transferred into a 50 mL volumetric flask and dissolved in 20 mL of mobile phase. The contents of the flask were sonicated continuously for 15 min to ensure complete solubility of the drug. The volume was made up with the diluent and the solution was filtered through whatman No.41filter paper. This solution containing 100 µg/mL of Quetiapine fumarate was injected into the column six times. The average peak area of the drug was computed from the chromatograms and the amount of the drug present in the tablet dosage form was calculated by using the regression equation obtained for the pure drug. The relevant results are furnished in Table 7.

RESULTS AND DISCUSSION

In the proposed method, the retention time of Quetiapine fumarate was found to be 6.588 min. Quantification was linear in the concentration range of 50-150 µg/mL. The regression equation of the linearity plot of concentration of Quetiapine fumarate over its peak area was found to be $Y = 17.65X + 4.066$ (r^2=0.999), where X is the concentration of Quetiapine fumarate (µg/mL) and Y is the corresponding peak area. The number of theoretical plates calculated was 10922, which indicates efficient performance of the column. The limit of detection and limit of quantification were found to be 0.07 µg/mL and 0.19 µg/mL respectively, which indicate the sensitivity of the method. The use of mixture of ammonium formate buffer pH 9.2 and acetonitrile in ratio of 51:49, v/v resulted in peak with good shape and resolution. The high percentage of recovery indicates that the proposed method is highly accurate. No interfering peaks were found in the chromatogram of the formulation within the run time indicating that excipients used in tablet formulations did not interfere with the estimation of the drug Quetiapine fumarate by the proposed HPLC method.

CONCLUSION

The proposed HPLC method is rapid, sensitive, precise and accurate for the determination of Quetiapine fumarate and can be reliably adopted for routine quality control analysis of Quetiapine fumarate in its tablet dosage forms.

ABBREVIATION USED

RP-HPLC: Reversed Phase High Performance Liquid Chromatography; **%RSD:** % Relative Standard Deviation; **API:** Active Pharmaceutical Ingredient; **ICH:** International Conference on Hormonisation.

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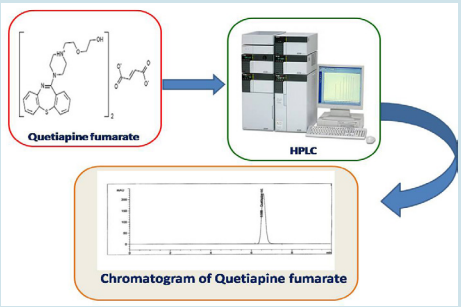
PICTORIAL ABSTRACT



SUMMARY

- A simple, rapid, accurate and precise RP-HPLC method was developed for the determination of Quetiapinefumarate in pure and tablet dosage forms.
- The method was statistically validated for linearity, accuracy, precision and selectivity.
- The proposed HPLC method is rapid, sensitive, precise and accurate for the determination of Quetiapinefumarate and can be reliably adopted for routine quality control analysis of Quetiapinefumarate in its tablet dosage forms.

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Dr. P. Nagaraju: Obtained his Ph. D. degree in 2010 from Acharya Nagarjuna University, Guntur. Currently he is working as Professor in Hindu College of Pharmacy, Guntur, Andhra Pradesh. His research mainly focuses on Method development and validation by using High Performance Liquid Chromatography.