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Research Article

RP-HPLC METHOD FOR ESTIMATION OF QUETIAPINE HEMI FUMARATE IN TABLET DOSAGE FORM

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ABSTRACT
A simple, sensitive, rapid, robust and reproducible method for the determination of Quetiapine Hemi Fumarate (QHF) in bulk and Pharmaceutical Formulation (Tablets) was developed using Reverse Phase High Performance Liquid Chromatographic method (RP-HPLC). The RP-HPLC analysis was performed isocratically on XTERRA C_{18} (4.6 X 150 mm), analytical column using a mobile phase consisting of Acetonitrile and methanol in the ratio of 60 : 40 v / v, with a flow rate of 1 ml / min. The analyte was monitored with UV detector at 290 nm. The developed method Quetiapine hemi fumarate elutes at a run time of 10 minutes. The proposed method is having linearity in the concentration range from 20 to 100 µg / mL of Quetiapine hemi fumarate. The present method was validated with respect to system suitability, linearity, precision, limit of detection (LOD) and limit of quantification (LOQ), accuracy (recovery), and robustness as per ICH Guidelines. The proposed method can be readily utilized for bulk drug and pharmaceutical formulations.
Keywords: Quetiapine Hemi Fumarate (QHF), RP-HPLC.

INTRODUCTION

Chemically, Quetiapine hemi fumarate is 2-[2-(4-{2-thia-9-zatricyclo [9.4.0.0^{3,8}] pentadeca-1(11),3(8),4,6,9,12,14-heptaen-10-yl}piperazin-1-yl)ethoxy]ethan-1-ol. The antipsychotic effect of Quetiapine is thought by some to be mediated through antagonist activity at dopamine and serotonin receptors[3]. It is not official in any of the pharmacopoeias. It is listed in The Merck Index and Martindale[1,2]. Literature survey reveals that there are few methods like separation and identification of QHF metabolite by using RP- HPLC and HPLC-EIMS in human plasma[4]. Hence the objective of the work has been made to develop new RP-HPLC methods for pharmaceutical formations with good accuracy, simplicity, precision and economy[5].

MATERIALS AND METHODS

Instrumentation

A gradient HPLC (Merck Hitachi) with L-7100 double reciprocating pump, L-7400 UV detector and Rp-C_{18} column (5 mcm particle size) was used and the system equipped with Winchrome software.

Chromatographic Conditions

The mobile phase consisting of Acetonitrile: methanol was filtered before use through 0.4 mc membrane filter and was pumped by the dual plunger reciprocating pump (L-7100 Lachrome, Hitachi) at a flow rate of 1 ml / min in the ratio of 60:40. The separation was carried out on a C_{18} column (5 mc, 250(L) x 4.6 i.d., Kromasil). The column temperature was maintained at room temperature. The sample was injected through a Rheodyne injector and was analyzed by variable length detector set at 290 nm. The data was acquired, stored and analyzed using Winchrome software.

Preparation of Stock Solutions

About 10 mg of QHF was accurately weighed and transferred to 100 mL volumetric flasks respectively and was dissolved in Acetonitrile+Methanol (60:40).

Procedure

The standard stock solution of each drug was suitably diluted with mobile phase to obtain standard solution of different solution was injected six times into the column at a flow rate of 1 ml / min. The linearity was obtained in the concentration range of 20-100 µg / mL for QHF.

Analysis of the Marketed Formulation (Assay of Tablet)

To estimation of QHF in tablet formulation, twenty tablet i.e. T_1 were weighed. The tablet content was weighed and triturated to fine powder. Tablet powder equivalent to 25 mg of QHF was weighed and transferred to a 100 ml volumetric flask and dissolved in 50 ml of mobile phase. It was kept for ultrasonication for 45 minutes; finally the volume was made up to the mark with mobile phase; this was then filtered through Whitman filter paper no.41 and 0.2 µ membrane filter get tablet stock solution of the concentration of 100 µg / ml. The tablet solutions were further diluted with mobile phase to obtain sample solution within the Beer Lambert's concentration range for the drug solution. A sample solution of concentration 20 µg / ml of QHF was prepared from the stock solution and injected into the sample injector of HPLC six times (n = 6) under the chromatographic condition as was described above. Area of each peak was measured at 290 nm. The amount of each drug present in the sample was determined using the peak area of QHF present in the pure drug. Figure 1 represents the chromatogram of QHF in tablet formulation. The results were statistically evaluated Table 1 and 2.

Validation of HPLC Method

The Proposed method was validated as per ICH guidelines [6-8].

RESULTS

Precision

Intra-day and Inter day precision was determined by repeating assay three times on the same day for intra-day and on different day for inter day precision (Table 5).

Table 1: Analysis of the Tablet formulation (T_1)

Amount present (µg / ml)	Amount found (µg / ml)	Label claim present (µg / Tab.)	Label claim found (µg / Tab)	% Label claim
50	50.003	50	50.001	100.006
	50.066	50	50.033	100.132
	50.360	50	50.180	100.72
	50.998	50	50.999	101.996
	50.907	50	50.953	101.814
	50.839	50	50.919	101.678

Tablet T_1: Quetiapine

Table 2: Statistical Validation of Tablet Analysis

Tablet	% Mean	S.D.*	% R.S.D.*	S.E.*
T_1	101.057	0.8848	0.8755	0.3612

*n = 6, Tablet T_1

Table 3: Recovery Studies

Tablet Sample	Level of recovery (%)	Amount present (mg / tab)	Amount of Std. added (mg)	Total amount recovered (mg)	% Recovery
T_1	80	50	8	57.898	99.824
		50	8	58.000	100
		50	8	57.905	99.836
	100	50	10	59.834	99.723
		50	10	59.998	99.99
		50	10	59.614	99.35
	120	50	12	61.674	99.474
		50	12	61.531	99.243
		50	12	61.776	99.638

*n = 3 at each level of recovery

Table 4: Statistical Validation of Recovery Study

S. No.	Tablet Sample	Type of Recovery (%)	(%) Mean*	S.D.*	C.O.V.*	S.E.*
1	T_1	80	99.88	0.09833	0.004912	0.05677
2		100	99.68	0.3215	0.005359	0.1856
3		120	99.45	0.1984	0.1586	0.1146

*n= at each level of recovery

Table 5: Validation and System Suitability Studies

Parameter	Quetiapine hemi fumarate
Linearity Range (µg / ml)	20-100
Correlation coefficient	0.999
Limit of detection (µg / ml)	0.000473×10^{-05}
Limit of quantization (µg / ml)	0.00014×10^{-03}
Retention of time (min.)	1.926
Robustness	Robust
Precision(% R.S.D)	
Inter –day (n = 3)	0.3154
Intra- day (n = 3)	0.5257
Tailing factor	0.65
Theoretical Plates	801
Mean % Recovery	99.04

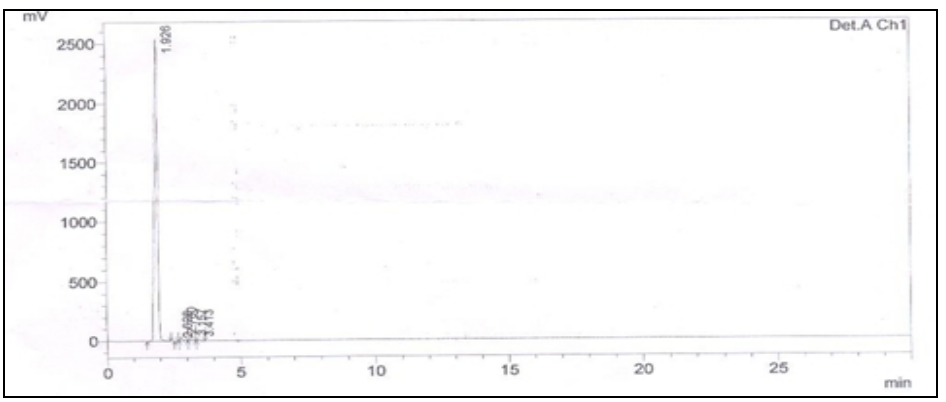

Figure 1: HPLC Chromatogram of Standard Quetiapine Hemi Fumarate

Table 6: Robustness Evaluation of the RP-HPLC method (n = 3*)

Factor	Level	Chromatographic changes t_R	t
Flow Rate (ml / min)			
0.80	-1	1.922	0.66
1.00	0	1.926	0.65
1.20	1	1.936	0.63
Mean ± S.D. (n = 3)		1.928 ± 0.0072	0.64 ± 0.0152
% of Acetonitrile in the mobile phase (v/v)			
58:42	-1	1.929	0.56
60:40	0	1.926	0.65
64:36	1	1.931	0.73
Mean ± S.D. (n = 3)		1.71 ± 0.3686	0.64 ± 0.085
Temperature (^{0}c)			
23	-1	1.926	0.62
25	0	1.926	0.65
27	1	1.926	0.60
Mean ± S.D. (n = 3)		1.962 ± 1.327	0.62 ± 0.025
PH			
1.3	-1	1.931	0.64
1.9	0	1.926	0.65
2.1	1	1.934	0.67
Mean ± S.D. (n = 3)		1.930 ± 0.004	0.065 ± 0.015

Where t_R= Retention time and t=Tailing factor.

Accuracy

To check the accuracy of the proposed method, recovery studies were carried out at 80, 100,120 % of the test concentration as per ICH guidelines. The result of the recovery studies and its statistical validation data was given in Table 6 indicates high accuracy of the proposed method.

LOD and LOQ

The LOD and LOQ were separately determined based on the standard deviation of response of the calibration curve. The residual standard deviation of the regression lines and slope of the calibration curves were used to calculate the LOD and LOQ (Table 5).

Robustness

To evaluate the robustness of the developed method, deliberate variations were made in the method parameters such as the flow rate, pH of the mobile phase, ratio of mobile phase and the column temperature (Table 6).

Specificity

The specificity of the HPLC method was ascertained by analyzing standard drug and sample solutions. The retention time of QHF was confirmed by comparing the retention time with that of the standard.

DISCUSSION

The goal of this study was to develop a rapid and sensitive HPLC method for the analysis of QHF in bulk drug samples and its formulation using the most commonly employed RP-C_{18} with UV detection. The mobile phase consisted of Acetonitrile and methanol in the ratio of 60:40. The run time was set at 10 minutes and the retention time for QHF was 1.926 minutes (Figure 1). The peak area of the drug was reproducible as indicated by RSD values less than 2 %. When the calibration curve for concentration of QHF and its respective peak area was plotted, a good linear relationship was observed between the concentration and their respective peak areas in the range of 20-100 mcg / mL QHF. The results of formulation analysis, recovery studies and its statistical validation data given in Table 1 and Table 3 indicate high degree of precision and accuracy of the proposed method. The results of the validation and system suitability studies are given in Table 5. Hence it can be concluded that the developed RP-HPLC method can be employed successfully for the estimation of QHF in both bulk and single component formulation.

CONCLUSION

The developed method was found to be accurate, precise, robust, linear and specific over the given concentration range studied. The method can also be used for routine Q.C analysis of QHF in bulk and tablet dosage form.

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