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A Simple Rapid and Sensitive Method Development for Quantification of Quetiapine Fumarate in Bulk and Dosage Forms Using RP-HPLC

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ABSTRACT

A simple, rapid and sensitive RP-HPLC method was developed by trial and error and validated for the estimation of Quetiapine Fumarate in tablet dosage form. Chromatography was carried out by using pre-packed Luna C18, 5µ (250 x 4.6) mm phenomex column as a stationary phase with the mobile phase containing a mixture of 0.1% Formic acid (pH 4 Adjusting with Triethylamine) and Acetonitrile in the ratio of 50:50v/v. The flow rate is 1 ml/min. The effluent was monitored at 290nm and the retention time of drug is 3.5 mins. The calibration curve was plotted with a range of 1-6µg/ml for Quetiapine fumarate and the correlation was found to be 0.999.The assay was validated in terms of linearity, precision, accuracy, and specificity, limit of quantification and limit of detection. The accuracy range was found between 99.7%-100.5% and % RSD values for all parameters are less than 2 as per the ICH guidelines. The developed method can be used for routine determination of Quetiapine fumarate in pharmaceutical dosage forms.

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INTRODUCTION

Quetiapine fumarate is an oral antipsychotic drug belongs to Chemical Class, the benzodiazepine derivative. It is used in treating schizophrenia and bipolar disorder is known as manic-depression. The trade name of Quetiapine fumarate is SEROQUEL. IUPAC name 2,[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]ethanol)fumarate Quetiapine blocks 5-HT_{1A} and 5-HT_2, D_2, alpha-1, alpha-2 and H_1 receptors in brain, but D_2 blocking activity is low in brain[1].

A few Spectrophotometric2 and Chromatographic methods like HPLC3, HTPLC4 methods were reported for estimation of Quetiapine fumarate in pharmaceutical dosage forms. The present study describes a new quantitative method development by using RP-HPLC. The purpose of developing and validating an analytical method is to be a simple, rapid, sensitive, precise, and accurate. The present method was optimized with low retention time and less runtime which reduce the consumption of mobile phase which in turn makes the method economical and rapid.

MATERIALS AND METHODS

Reagents and chemicals: HPLC grade Acetonitrile, 0.1% formic acid, HPLC grade water were obtained from SD fine chem. Limited and SRL limited. Quetiapine fumarate was a gift sample from Aurobindo Pharma Limited, Hyderabad. The Quetiapine tablets were procured from the local medical shop.

Instrumentation

The Shimadzu 20AD HPLC instrument with UV detector and an injector with a 20 mL loop was used to inject the sample. The separation was carried with C18 column (250 ×4.6mm). The analyte was scanned with Elico UV- spectrophotometer at 290nm. Other equipment like Analytical balance (Contech) pH meter (Elico), and Micropipettes (p' fact A) were used during the study

Chromatographic conditions

The HPLC was operated at isocratic elution mode with the mobile phase 0.1% formic acid: Acetonitrile (50:50v/v) at pH 4 which was filtered through the 0.45µ membrane filter and degassed before use. Then pumped from the solvent reservoir. The flow rate of elution was 0.1ml/min. The detection was monitored at 290 nm. The volume of injection is 20µL. The

Column was equilibrated for at least 30 minutes with mobile phase. The HPLC system was kept at ambient temperature throughout the experiment.

Preparation of 0.1% Formic Acid (pH 4)

Accurately measured 0.1 ml of formic acid in 100 ml water, mix and adjusted to the pH 4 with the mixture of orthophosphoric acid and triethylamine. Filtered through 0.45µ membrane

Preparation of Mobile Phase

Mix 50ml of pH (4) 0.1% formic acid and 50 ml volume of Acetonitrile, sonicated for 15 minutes, and filtered through 0.2µ membrane filters.

Preparation of Stock Solution

100 mg of Quetiapine fumarate was accurately weighed and taken into 100 ml volumetric flask containing 50 ml of mobile phase and sonicate it for 2 minutes and later the solution was made up to the mark by using mobile phase.

Preparation of Sample Solution

Accurately weighed 20 tablets and calculated the average weight. Powdered the tablets and transferred the powder equivalent to 100mg of Quetiapine fumarate into the 100ml volumetric flask. To this flask added 50ml of diluent, sonicated to dissolve it completely, and made up to the mark with diluent.

Trails:

Trail-1

Diluent **:** Mobile phase

Column **:** phenomenex (250X4.60mm) 5 micron

Mobile phase **:** (pH-4.5) Orthophosphoric acid: Methanol (30:70)

Injection volume **:** 20ul

Flow rate **:** 1.0ml/min

Detection wavelength: 291nm

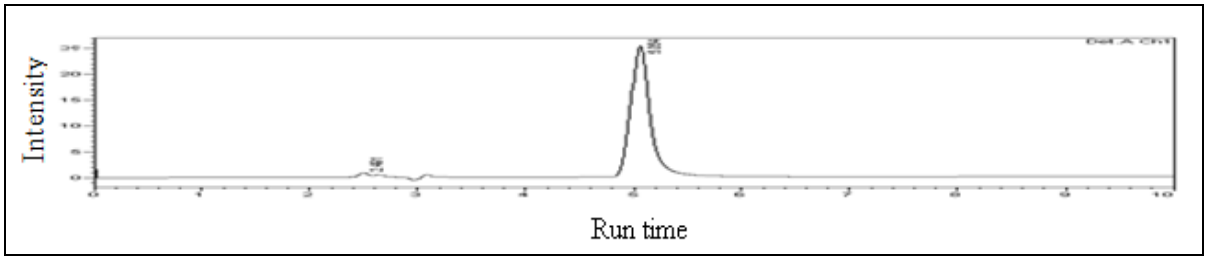

Figure: 1 Chromatogram of trail-1

Table: 1 Results of trial -1

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	5.0min	4057.348	1.2	10.6

Trail-2

Diluent: Mobile phase

Column: Phenomenex (250X4.60mm) 5micron

Mobile phase: (pH4.5) Orthophosphoric acid: Methanol (10:90)

Injection Volume: 20µL

Flow rate: 1.0ml/min

Detection wavelength: 291nm

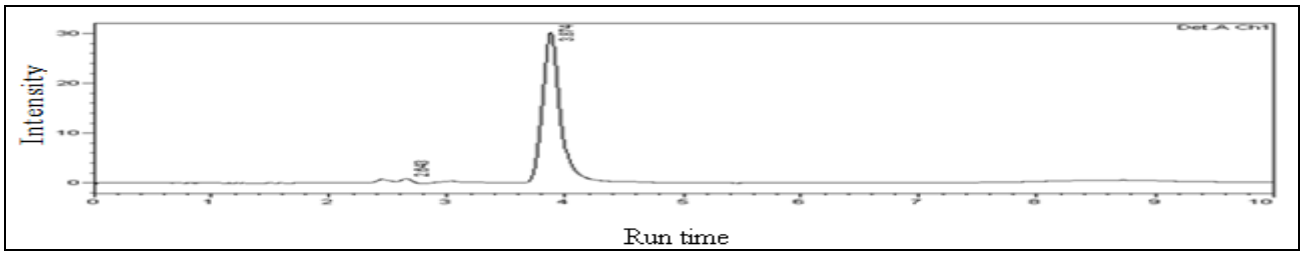

Figure: 2 Chromatogram of trail-2

Table: 2 Results of trial -2

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	3.8 min	3301.260	1.26	5.59

Trail-3

Diluent **:** Mobile phase

Column **:** Phenomenex (250 x 4.60mm) 5micron

Mobile phase **: (**pH 3) orthophosphoric acid: Acetonitrile (50:50)

Injection Volume **:** 20 µL

Flow rate **:** 1.0 ml/ min

Detection wavelength **:** 290nm

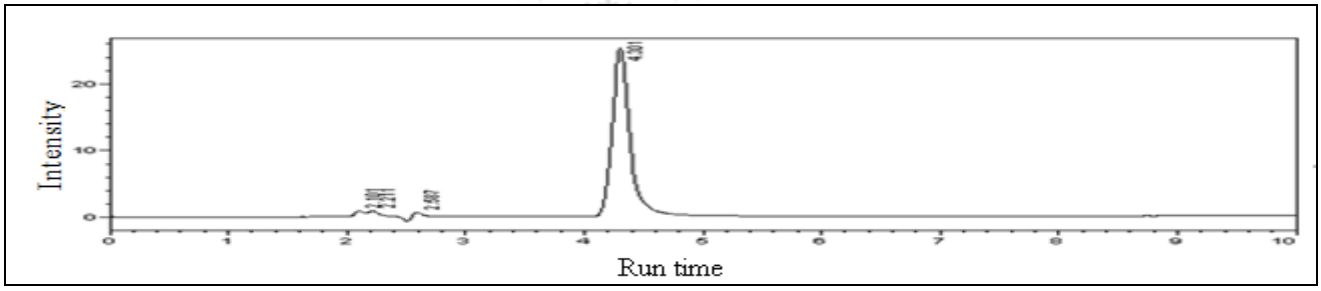

Figure: 3 Chromatogram of trail-3

Table: 3 Results of trial -3

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	4.3 min	1790.697	1.2	12.9

Trail-4

Diluent: Mobile phase

Column: Phenomenex (250 x 4.60mm) 5micron

Mobile phase: **(**pH 3) orthophosphoric acid: Acetonitrile (70:30)

Injection Volume: 20 µL

Flow rate: 1.0 ml/ min

Detection wavelength: 290nm

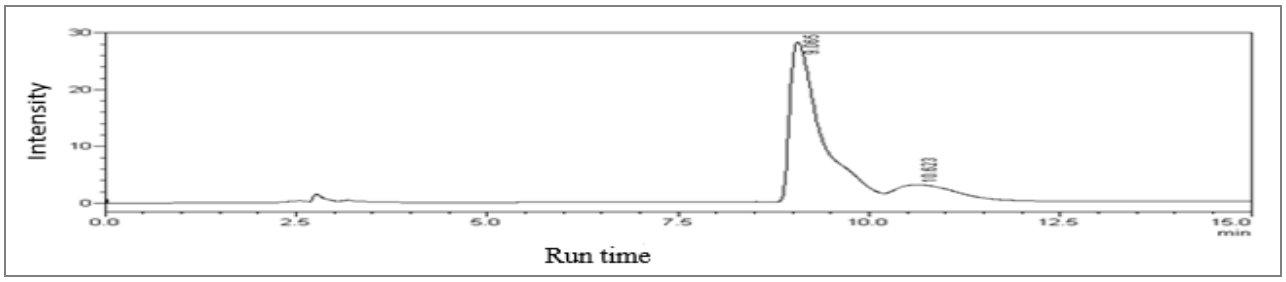

Figure: 4 Chromatogram of trail-4

Table: 4 Results of trial -4

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	9.065 min	2754.026	2.8	12.04

Trail-5

Diluent: Mobile phase

Column: Phenomenex (250X4.60mm) 5 micron

Mobile phase : (pH4) Formic Acid: Acetonitrile (80.20)

Injection Volume: 20µL

Flow rate: 1.0ml/min

Detection wavelength: 292 nm

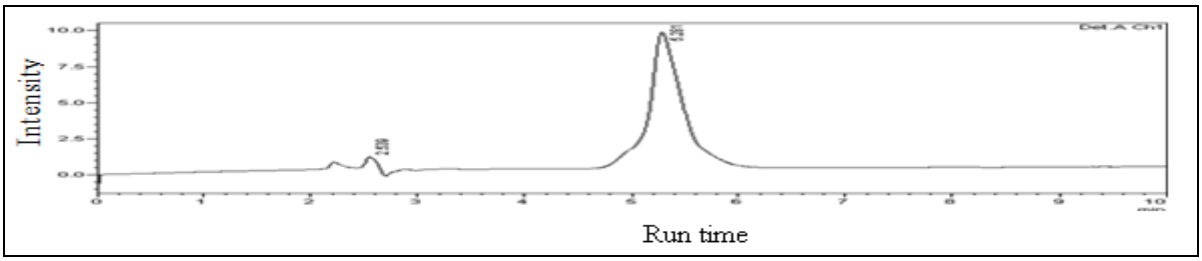

Figure: 5 Chromatogram of trail-5

Table: 5 Results of trial -5

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	5.2 minutes	1741.558	1.156	7.887

Trail: 6

Diluent: Mobile phase

Column: Phenomenex (250X4.60mm)5 micron

Mobile phase: (pH4) Formic Acid: Acetonitrile (70.30)

Injection Volume: 20µL

Flow rate: 1.0ml/min

Detection wavelength: 292 nm

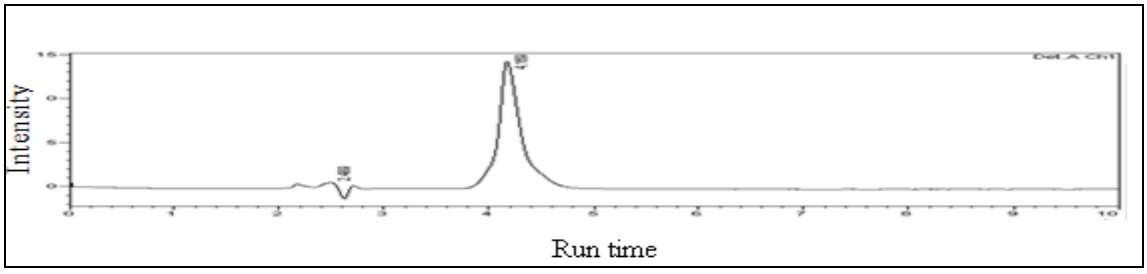

Figure: 6 Chromatogram of trail-6

Table: 6 Results of trial -6

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	4.1 minutes	2325.820	1.346	5.831

Trail: 7

Diluent: Mobile phase

Column: Phenomenex (250X4.60mm) 5 micron

Mobile phase: (pH4) Formic Acid: Acetonitrile (66:44)

Injection Volume: 20µL

Flow rate: 1.0ml/min

Detection wavelength: 292 nm

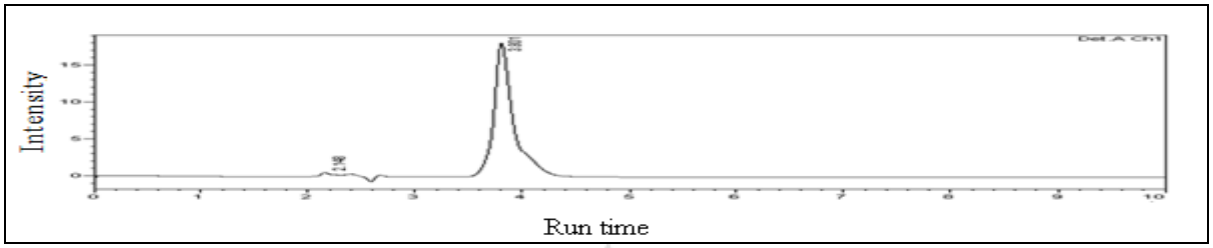

Figure: 7 Chromatogram of trail-7

Table: 7 Results of trial -7

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	3.8 minutes	2744.958	1.455	7.509

CONCLUSION:

Trial 1**:** Retention time is more and resolution is more it is not satisfactory.

Trial 2: solvent consumed is more so it is not satisfactory.

Trial 3**:** Resolution is there between mobile phase (blank) and drug peak but theoretical plates are less than 2000.

Trial 4: peak shape is asymmetrical, retention time is more and tailing factor is not within the limits

Trial 5**:** Drug peak is asymmetric and retention time as increased

Trial 6: By changing the mobile phase ratio retention time has been increased so further trial has been performed for better retention time

Trial 7: Drug peak is asymmetric so by changing the mobile phase ratio for the further better peak.

Optimized method:

Diluent: Mobile phase

Column: Phenomenex (250X4.60mm) 5 micron

Mobile phase: (pH4) formic Acid: Acetonitrile (50:50)

Injection Volume: 20µL

Flow rate: 1.0ml/min

Detection wavelength: 292 nm

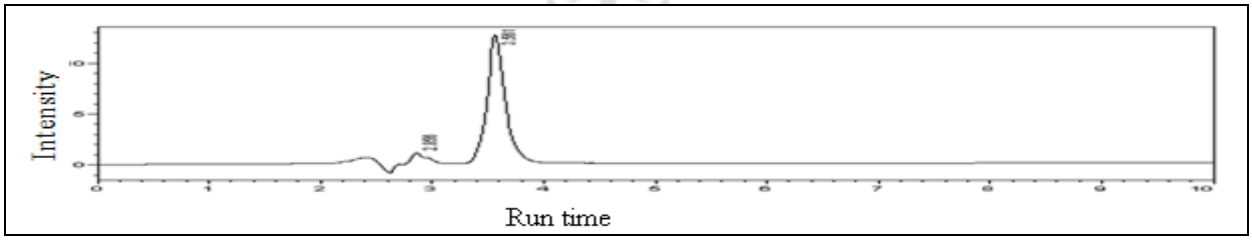

Figure no 8. Chromatogram of optimized method

Table: 8 optimized method

Name	R_T	Theoretical plate	Tailing factor	Resolution
Quetiapine fumarate	3.5 minutes	2515.209	1.212	3.021

Conclusion: compared to all trials. Trial 8 is satisfactory and so trail 8 is considered for the final method.

Method Development And Validation Parameters[5]

System Suitability

System suitability is defined as "the checking of a system, before or during analysis of unknowns, to ensure system performance." System suitability criteria may include such factors as plate count, tailing factor, retention, and resolution.

Specificity

Specificity is the ability to assess unequivocally the analyte in the presence of components, which may be expected to be present. Typically, these might include impurities, degradants, matrix, etc.

Accuracy

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted as either a conventional true value or an accepted reference value and the value found.

Precision

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at three levels repeatability, intermediate precision and reproducibility

Repeatability

Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed as intraassay precision.

Intermediate precision

Intermediate precision expresses within – laboratories variations: different days, different analyte, different equipment etc.

Reproducibility

Reproducibility expresses the precision between laboratories

Limit of Detection

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value

Limit of Quantification

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. The quantization limit is a parameter of quantitative assays for low levels of compounds in sample matrices and is used particularly for the determination of impurities and /or degradation products.

Linearity

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample

Range

The range of an analytical procedure is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy, and linearity

Robustness

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage

RESULTS AND DISCUSSIONS

Specificity: the specificity of the method was determined by checking the interference of the analyte and the proposed method were eluted by checking the peak purity of Quetiapine fumarate.

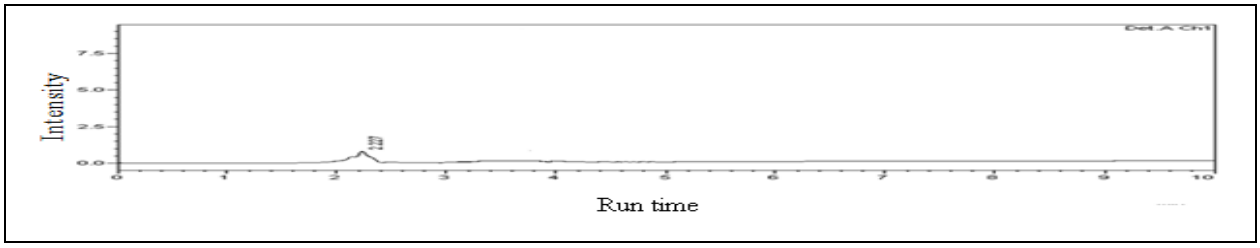

Figure 9: Chromatogram of blank

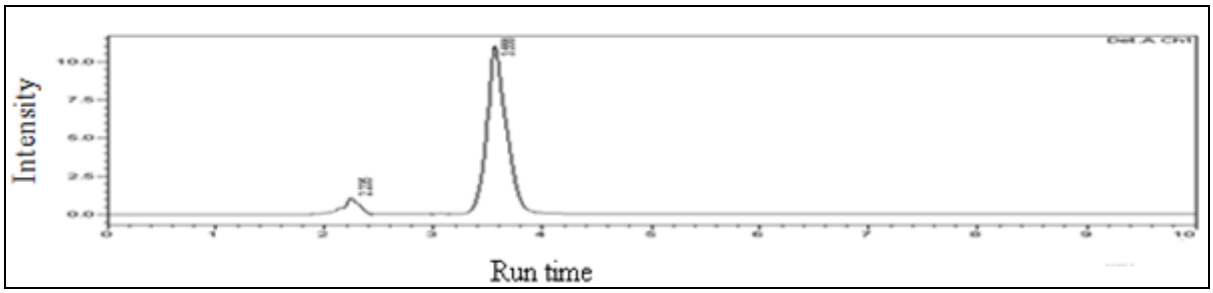

Figure 10: Chromatogram of standard

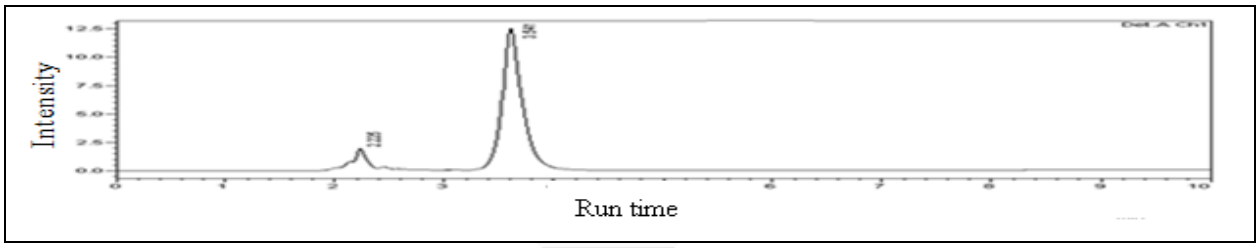

Figure 11: Chromatogram of sample

System suitability:

Six replicates of injections at the concentration of 4µg/ml were prepared separately and injected and all the parameters were calculated.

Table 9: Results of system suitability

Sr. No.	Rt	Area	Theoretical plate	Tailing factor	Resolution
1	3.556	126467	2008.610	1.239	4.749
2	3.552	126521	2025.817	1.222	4.881
3	3.556	126773	2003.346	1.264	4.745
4	3.537	126629	2020.304	1.242	4.923
5	3.568	126153	2005.796	1.231	4.914
6	3.578	126527	2006.868	1.241	5.102
MEAN	3.55	126511.6	2011.790167	1.239	4.885
SD	0.015	188.42			
%RSD	0.43%	0.1%			

Linearity: The linearity curve was obtained in the concentration range of 1-6µg/ml. the linearity was evaluated by linear regression analysis.

Table 10: Results of linearity

Concentration	Retention time	Peak area	Theoretical plate	Tailing factor
1µg/ml	3.574	33075	3048.092	1.393
2µg/ml	3.559	66719	2489.146	1.317
3µg/ml	3.554	99058	2114.666	1.26
4µg/ml	3.556	126773	2003.346	1.26
5µg/ml	3.529	157685	2006.111	1.22
6µg/ml	3.566	186670	2357.024	1.27

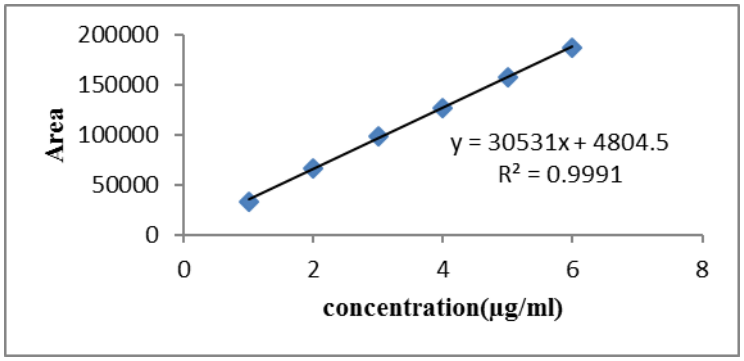

Figure 12: Linearity graph of Quetiapine fumarate

Accuracy: The accuracy of the method was carried out by adding known amount of each drug corresponding to three concentration levels 80%, 100%, 120%

Table 11: Results of Accuracy

SAMPLE ID	CONCENTRATION (µg/ml)		TOTAL CONC	AREA	% RECOVERY	AVG% RECOVERY	SD	%RSD
	Amount of pure drug	Amount of sample						
80 80 80	1.6 µg/ml 1.6 µg/ml 1.6 µg/ml	2 µg/ml 2 µg/ml 2 µg/ml	3.6µg/ml	113891 114090 114947	99.8% 99.8% 100.5%	100.3%	793.55	0.6%
100 100 100	2 µg/ml 2 µg/ml 2 µg/ml	2 µg/ml 2 µg/ml 2 µg/ml	4µg/ml	126459 126822 126910	99.7% 100.3% 100.1%	99.6%	338.08	0.2%
120 120 120	2.4 µg/ml 2.4 µg/ml 2.4 µg/ml	2 µg/ml 2 µg/ml 2 µg/ml	4.4µg/ml	139773 139374 138684	100.2% 99.9% 99.3%	99.8%	361.01	0.2%

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

Table 12: Results of Intraday precision

Sr. No.	RETNTION TIME	AREA	% ASSAY
1	3.556	127238	100.2%
2	3.562	127767	100.6%
3	3.557	127797	100.4%
4	3.539	127800	100.7%
5	3.564	127443	100.4%
6	3.558	127469	100.2%
MEAN	3.55	127585.6	-
SD	0.00011	215.3	-
%RSD	0.30%	0.1%	-

Table 13: Results of Interday precision

Sr. No.	RETENTION TIME	AREA	% ASSAY
1	3.551	127285	100.2%
2	3.541	127088	100.1%
3	3.586	127667	100.6%
4	3.537	127477	100.2%
5	3.555	127438	100.4%
6	3.550	127125	100.1%
MEAN	3.55	127346.6	-
SD	0.0158	203.2	-
%RSD	0.4%	0.1%	-

Robustness:

Table 14: Results of change in Flow rate

Sr. No.	1.1ml/min			0.9ml/min		
	Rt	AREA	% ASSAY	Rt	AREA	%ASSAY
1	3.432	126449	99.6%	3.662	126399	99.4%
2	3.478	126391	99.5%	3.658	126586	99.6%
3	3.489	126122	99.2%	3.642	126170	99.2%
MEAN	3.46	378962	-	3.654	379915	-
SD	0.0313	142.4	-	0.0086	170.1	-
%RSD	0.9%	0.1%	-	0.23%	0.1%	-

Table 15: Results of change in mobile phase

Sr. No.	Mobile phase 48:52			Mobile phase 52:48		
	Rt	AREA	% ASSAY	Rt	AREA	%ASSAY
1	3.630	125592	98.9%	3.401	126292	99.4%
2	3.649	126553	99.6%	3.401	126728	99.8%
3	3.613	126356	99.5%	3.483	126433	99.4%
MEAN	3.630	378501	-	3.42	379453	-
SD	0.0146	414.4	-	0.0395	181.6	-
%RSD	0.4%	0.3%	-	1.1%	0.1%	-

Table 16: Results of change in pH

Sr. No.	pH 3.8			pH 4.2		
	Rt	AREA	% ASSAY	Rt	AREA	%ASSAY
1	3.483	125955	99.2%	3.694	125687	98.9%
2	3.384	126210	99.4%	3.613	126442	99.6%
3	3.483	126945	100.1%	3.616	126816	99.9%
MEAN	3.45	379110	-	3.65	378945	-
SD	0.0466	419.7	-	0.033	469.5	-
%RSD	1.3%	0.3%	-	0.9%	0.3%	-

CONCLUSION

An RP-HPLC was successfully developed and validated for the estimation of Quetiapine fumarate in pharmaceutical dosage forms and validation parameters results have proved that the method is proved to be selective, precise, accurate, and linear as per the validation parameters.

The developed method was validated as per the International Conference on Harmonization ICH (Q2B) guidelines and was found to be applicable for routine quantitative analysis of Quetiapine fumarate by RP-HPLC in tablet dosage forms.

This method is more sensitive than previously reported methods, due to its wider linearity range.

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REFERENCES

1. Tripathi K. D Essentials of medicinal pharmacology 6th edition (2006)
2. Analytical method development of Quetiapine fumarate in bulk and its tablet formulation by simple UV spectrophotometry
3. Method development and validation of Quetiapine fumarate bulk and its tablet dosage form by using UV-spectrophotometry
4. Development and validation of Quetiapine fumarate in pure and pharmaceutical formulation by UV-Spectrophotometric method
5. Development and validation of RP-HPLC method: Application for the quantitative determination of Quetiapine fumarate from marketed bulk tablets
6. Development of analytical method for determination of Quetiapine fumarate in bulk &tablet dosage form
7. Development and validation of RP-HPLC method for estimation of Quetiapine fumarate in pharmaceutical formulations

8. Development and validation of RP-HPLC method for determination of Quetiapine fumarate from pharmaceutical preparation
9. A validated RP-HPLC method for the estimation of Quetiapine in bulk and pharmaceutical formulations
10. Development and validation of assay method for estimation of Quetiapine fumarate by RP-HPLC
11. Stability indicating RP-HPLC method for the estimation of Quetiapine fumarate in bulk as well as in pharmaceutical dosage form
12. Development and Validation of HPTLC Method for Estimation of Quetiapine in Bulk Drug and in Tablet Dosage Form
13. www.inchorg/filed min/public-web site/ICH products/guidelines/quality/Q2R1/step-4/Q2R1-guideline pdf.