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A VALIDATED RP-HPLC METHOD FOR THE ESTIMATION OF QUETIPINE FUMARATE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

A new sensitive, specific, linear, precise and accurate RP-HPLC method was developed and validated for estimation of Quetiapine fumarate in Bulk and Tablet dosage form. An isocratic, reversed phase HPLC method was developed. Shimadzu shim pack C18(150mm x 4.5µm, x 5µ) column. Shimadzu Prominence-I LC-2030C plus equipped with Auto sampler as the instrument model. Mobile phase consists of mixture of Acetonitrile: 0.1% Ortho phosphoric acid in Millipore water v/v: Methanol in the ratio (60:30:10 v/v) at a flow rate of 0.8mL /min with injection volume of 20µL. UV detection was performed at 252nm. The Linearity was established for Quetiapine fumarate in the range of 2-12µg/ml with correlation coefficient of 0.997. LOD and LOQ were found to be 1.053µg/ml and 1.161µg/ml respectively. Retention time of Quetiapine fumarate were found to be 3.4mins. % Recovery was found to be 98.99-100.5 and %RSD was found with in ± 2. The method has been validated according to ICH guidelines for linearity, precision, accuracy, robustness, ruggedness, LOD and LOQ. The developed validated method was successfully applied for reliable quantification of Quetiapine fumarate in bulk and pharmaceutical dosage form.

KEYWORDS

Quetiapine fumarate, RP- HPLC, Validation and Pharmaceutical formulations.

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INTRODUCTION

Quetiapine fumarate is a second-generation atypical antipsychotic medication used to treat certain mental /mood disorders (such as schizophrenia, bipolar disorder, sudden epoisodes of mania or depression associated with bipolar disorder)[1].

Quetiapine fumarate is chemically known as 2-(2-(4-Dibenzo[b, f] [1, 4] thiazepine-11-yl-1-piperazinyl) ethoxy) ethanol with a molecular formula of $C_{21}H_{25}N_3O_2S$ and a molecular weight of

383.51g/mol. Quetiapine fumarate drug substance is White to off-white Crystalline powder and it is Soluble in methanol, ethanol and 0.1NHCL

Literature survey revealed that there were few analytical methods have been reported for the determination of the Quetiapine fumarate in pure drug and pharmaceutical dosage form by using UV-Spectrophotometric[2-7], RP-HPLC[8-16] and HPTLC[17-20] so far.

The aim of the present work is to develop and validate a novel, rapid, precise and specific Area under curve UV spectrophotometric method for estimation of Quetiapine fumarate in bulk and tablet dosage form.

MATERIAL AND METHODS

Material and reagents

The Quetiapine fumarate was obtained as a gift sample from the pharmaceutical industry and Qutan 50mg tablet obtained from Pharmacy store. Acetonitrile, Orthophosphoric acid and Methanol were obtained Bharathi College of pharmacy, Bharathinagara, KM Doddi, Maddur Taluk, Mandya District, India. All chemicals used are of HPLC grade. Distilled water was used throughout the experiment.

Instrumentation

Chromatographic separation was performed on a Shimadzu Prominence-i LC-2030 plus equipped with Auto sampler comprising a variable wavelength programmable UV detector. Shimadzu shim pack C18 (150mm x 4.5µm x 5µ) column is used.

Preparation of solutions Mobile phase preparation

The mobile phase was prepared by mixing acetonitrile, 10mM phospahte buffer (pH 6.5) and methanol (60:30:10v/v/v).

Preparation of buffer

800ml of distilled water was taken in a suitable container. To that 20.214gm of sodium phosphate dibasic heptahydrate and 3.394gm of sodium phosphate monobasic monohydrate was added to the solution. pH of the solution was adjusted by adding Triethyl amine and final desired volume of 1litre solution was prepared by adding distilled water and filtered.

Preparation of sample Solution

The formulation tablets of Quetiapine fumarate (Qutan 50mg) were crushed to give finely powdered material. Qutan 10 tablets, marketed formulation of Quetiapine fumarate containing 50mg of the drug was calculated for the % assay of the Quetiapine fumarate in the formulation. A concentrated solution of 2-12µg/mL was obtained using a powder made up of 10mg. The filtered solution was employed in the HPLC apparatus to perform the percentage assay of Quetiapine fumarate.

Preparation of Standard solution

A standard stock solution of Quetiapine fumarate (1000µg/ml) was prepared individually by dissolving accurately weighed, 10mg of drug in 10ml volumetric flask in some quantity of mobile phase and final dilution up to the mark with the mobile phase. From this stock solution, 1ml aliquot was transferred and diluted up to the mark with diluents in 10ml volumetric flask to obtain a final concentration of 100µg/ml.

System suitability requirements from stock and standard solutions

Tailing factor: NMT 2.0

Theoretical Plates: NLT 2000

RESULTS AND DISCUSSION

Validation of the proposed method

The proposed method was validated as per ICH guidelines[21-23]. The parameters studied for validation were specificity, linearity, precision, accuracy, robustness, system suitability, limit of detection, limit of quantification, and solution stability.

Specificity

From the chromatograms of blank, standard (Prepared from Formulation). It was found that there is no interference due to excipients in the tablet formulation and also found good correlation between the retention time. The specificity results are shown in Table No.2.

Linearity

The linearity of the response of the drug was verified at six concentration levels, ranging from 2-12µg/ml of Quetiapine fumarate in each linearity level were prepared. 20µl of each concentration was injected into the HPLC system. The response was read at

252nm and the corresponding chromatograms were recorded. From these chromatograms, the mean peak areas were presented in Table No.3.

Precision

Precision of the method was performed as intraday precision, Inter day precision. To study the intraday precision, six replicate standard solutions (20µg/ml) of Quetiapine fumarate were injected. % RSD was calculated and it was found to be 0.516 and interday precision done same as intraday, six replicate standard solutions (20µg/ml) of Quetiapine fumarate were injected. %RSD was calculated and it was found to be 0.797 which are well within the acceptable criteria of not more than 2.0. Results of system precision studies are shown in Table No.4.

Accuracy

Accuracy of the method was studied by recovery experiments. The recovery experiments were performed by adding known amounts of the drugs in the placebo. The recovery was performed at three levels, 50, 100 and 150% of the label claim of the tablet (50mg of quetiapine fumarate). The average recoveries of three levels of Quetiapine fumarate were found to be 98.99-100.5%. The results are shown in the Table No.5.

Limit of detection and Limit of quantification

The limit of detection is an analytical method is the smallest amount of analyte in a sample which can be reliable detected by the analytical method.

The limit of quantitation is an individual analytical procedure is the smallest amount of the analyte in sample which can be quantitatively determined. LOD and LOQ were calculated using formula LOD = 3.3(SD)/S and LOQ = 10(SD)/S. Results were shown in Table No.6.

Ruggedness

The ruggedness of test method was demonstrated by carrying out precision study in six preparations of sample on a single batch sample by different analysts, the results of the precision study are tabulated as below Table No.7. The % RSD values are less than 2.

Robustness

Robustness is the measure of the capacity of the analytical method to remain unaffected by small but deliberate variation in the procedure. The robustness of the method was evaluated by analysing the system suitability standard and evaluating system suitability parameter data after varying individually, the HPLC pump flow rate, variation in volume of acetonitrile, detection wavelength (±2nm) shown in Table No.8.

Acceptance criteria

System suitability should pass as per test method at variable conditions.

Chromatographic conditions

Table No.1: HPLC method development parameters

S.No	HPLC method development parameters	
1	Column	C18, 150nm * 4.5µm *5µ
2	Flow rate	0.8ml /min
3	Wavelength	252nm
4	Column temperature	25˚C
5	Injection volume	20µL
6	Run time	10minutes
7	Diluents	Mobile phase
8	Elution	Isocratic

Table No.2: Specificity of Quetiapine fumarate

S.No	Name of the solution	Retention time in min
1	Blank	0
2	Quetiapine fumarate (Standard)	3.4

Table No.3: Linearity of Quetiapine fumarate

S.No	Concentration (µg/ml)	Peak area* (mv)
1	2	18353
2	4	34539
3	6	48858
4	8	68823
5	10	87115
6	12	108685

*Average of six determinations

Table No.4: Results of precision of Quetiapine fumarate

S.No	Intraday Names	Studies Peak area	Interday Names	Studies Peak area
1	Injection-1	54986	Injection-1	54056
2	Injection-2	54806	Injection-2	53858
3	Injection-3	54980	Injection-3	54252
4	Injection-4	54888	Injection-4	52867
5	Injection-5	54855	Injection-5	53765
6	Injection-6	54869	Injection-6	53214
7	AVG	54897.33	AVG	53668.66
8	STDEV	65.47179	STDEV	480.4205
9	%RSD	0.516	%RSD	0.797

Table No.5: Results of recovery of Quetiapine fumarate

S.No	Level of addition/ %	Amount added (µg/ml)	Amount found	%Recovery ±Standard deviation*	%RSD
1	50	2	2.01	100.5±0.408	0.405
			2.0		
			2.02		
2	100	6	5.96	99.38±0.207	0.208
			5.95		
			5.98		
3	150	12	11.89	98.99±0.177	0.179
			11.85		
			11.90		

*Average of three determinations

Table No.6: System suitability parameters

S.No	Parameters	Quetiapine fumarate
1	Linearity	2-12µg/ml
2	Regression equation	8890.4x-1003.5
3	Correlation coefficient	$R^2 = 0.997$
4	Retention time	3.4min
5	Run time	10min
6	Limit of detection (LOD)	1.053µg/ml
7	Limit of quantification (LOQ)	1.1617µg/ml
8	Tailing factor	1.110
9	Theoretical Plate	2153

Table No.7: Results of ruggedness of Quetiapine fumarate

By changing the analysts

S.No	Analysts	Analyst 1	Analyst 2
1	Mean peak area	445806.5	449306.5
2	±Standard deviation*	567.8067	491.4392
3	%RSD	0.127	0.109

*Average of three determinations

By changing the instrument

S.No	Instrument	Instrument 1	Instrument 2
1	Mean peak area	647773.5	640048.5
2	±Standard deviation*	163.3417	71.41778
3	%RSD	0.0252	0.0111

*Average of three determinations

Table No.8: Robustness results for Quetiapine fumarate

S.No	By change in flow rate		
1		**0.6mL/min**	**1mL/min**
	%RSD should not be more than 2.0%	0.11	0.3
	Theoretical plates should be not less than 2000	2345	2135
	Tailing factor should be not more than 2.0.	1.065	1.065
2	*By variation in volume of Acetonitrile*		
		50ml	**70ml**
	%RSD should not be more than 2.0%	0.46	0.78
	Theoretical plates should be not less than 2000.	2153	2155
	Tailing factor should be not more than 2.0.	1.10	1.11
3	**By variation in wavelength**		
	Wavelength	**Tailing Factor**	**%RSD**
	Decreased (-2nm)	1.10	0.18
	Decreased (+2nm)	1.12	

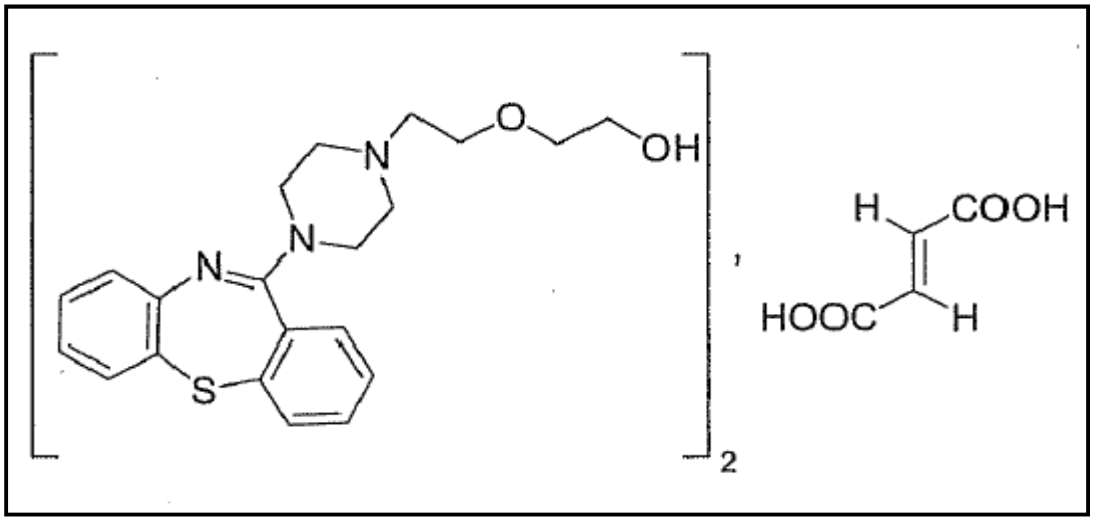

Figure No.1: Chemical structure of Quetiapine fumarate

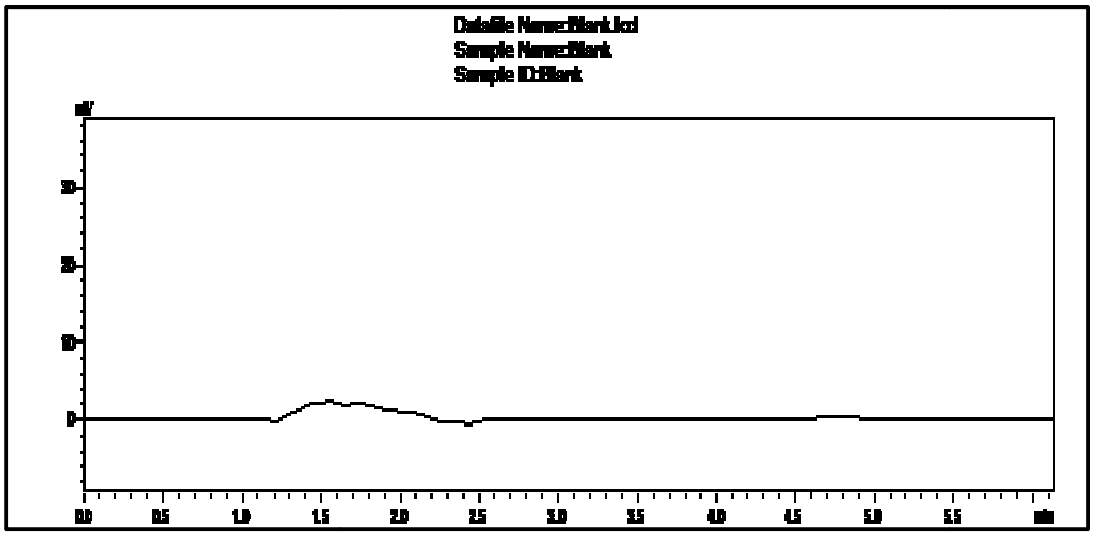

Figure No.2: Chromatogram of blank solution of Quetiapine fumarate

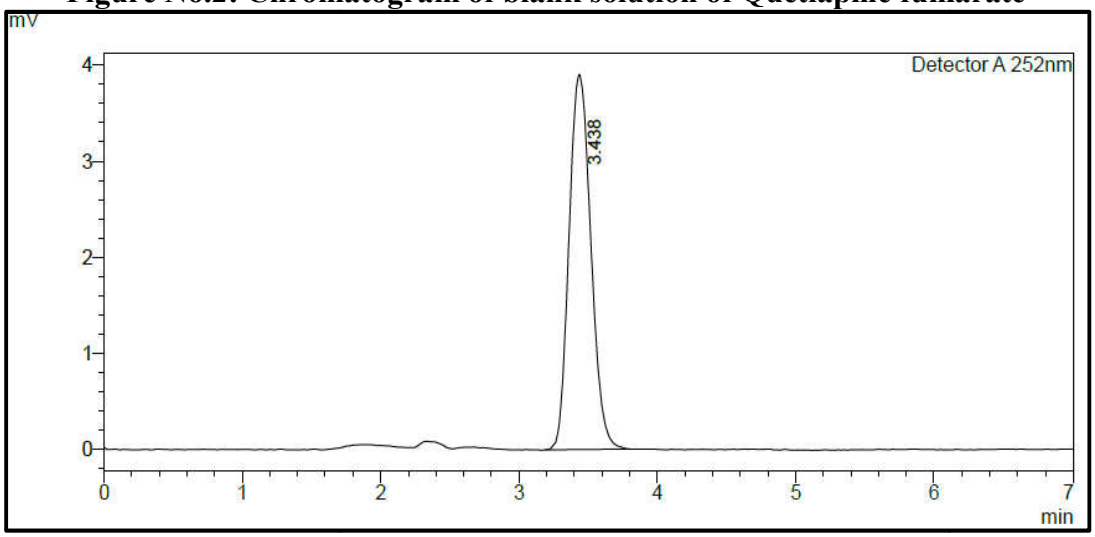

Figure No.3: Chromatogram of standard solution of Quetiapine fumarate

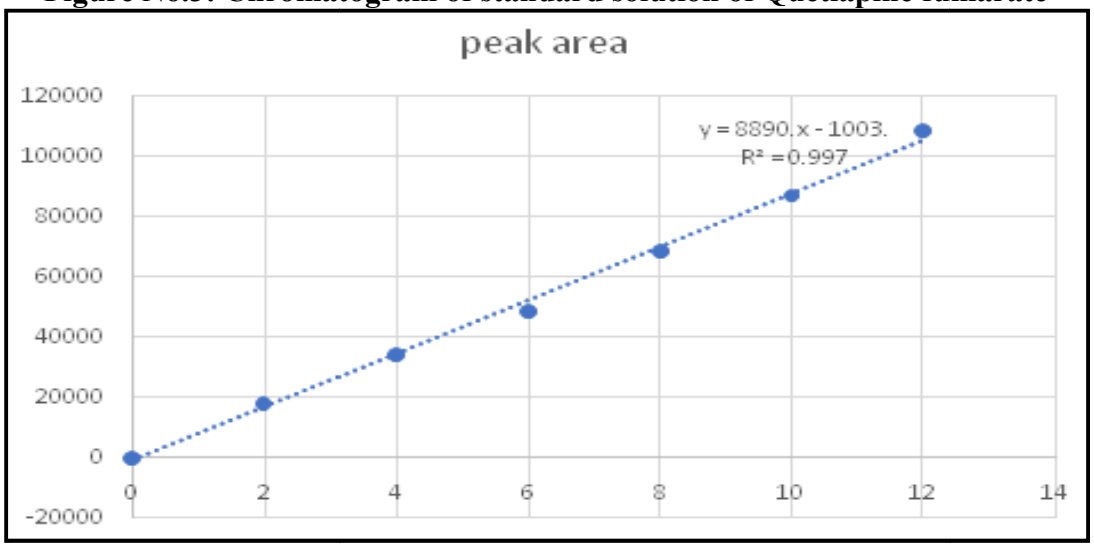

Figure No.4: Linearity of Quetiapine fumarate

CONCLUSION

The present analytical method was validated as per ICH guidelines and met the acceptance criteria. It was concluded that the developed analytical method was simple, accurate, economical and sensitive, and can be used for routine analysis of Quetiapine fumaratein bulk drug and pharmaceutical dosage forms.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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