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Research Article

ESTIMATION OF QUETAPINE DRUG PRESENT IN FORMULATION BY VALIDATED RP-HPLC METHOD

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Abstract:

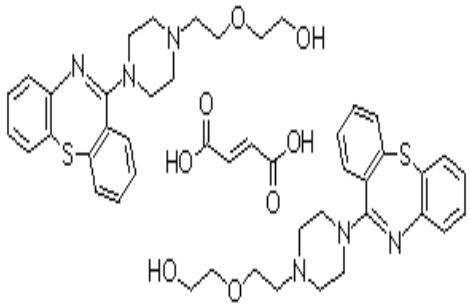
A simple, accurate, sensitive and précised reverse phase liquid chromatographic method was developed for quantitative estimation Quetapine Fumarate drug present in commercial dosage forms. Mobile phase was found to be a suitable extraction solvent for tablets and for the preparation of sample solutions. The samples were chromatographed on Symmetry C18 (4.6 x 150mm, 5 µm, Make: XTerra) and UV detected at 291 nm. The elution was achieved isocratic ally with a mobile phase of 0.05M phosphate buffer pH 3.0(60%) and Acetonitrile (40%).the method was validated for Linearity, precision, accuracy, limit of detection and quantification. The recovery for tablets was 98.7% with retention time of 3.26 and linearity was found to be 0.999 correlation value.

Key words: HPLC, Method Development, Validation Quetapine.

Introduction:

Quetapine Fumarate is chemically 2-[2-(4-dibenzo [b, f] [1, 4] thiazepin-11-yl-1-piperazinyl) ethoxy] hemifumarate, $(2(C_{21}H_{25}N_3O_2S)\cdot C_4H_4O_4)$ an molecular weight of 883.09 [1].Quetapine is an oral antipsychotic (atypical) drug used for treating schizophrenia and bipolar disorder. Quetapine is a potent Serotonin and Dopamine receptor antagonist used to treat major depressive disorders. by to blocking of the dopamine type 2 (D2) and serotonin type 2 (5-HT2) receptors[2,3,4,5,6].Earlier LC-MS, HPLC estimation of drug in plasma studies are available in the Literature[7,8,9,10].

Recently HPLC, UV and HPTLC methods for estimation of Quetapine drug in bulk and formulation were published [11, 12, and 13]. Current developed HPLC method was simple and rapid. Validated for Accuracy, Linearity, Precision, Limit of Detection and Quantification [14]



Quetapine Fumarate 1

Chromatographic Parameters

Equipment	: High performance liquid chromatography equipped with Auto Sampler and DAD or UV detector.
Column	: Symmetry C18 (4.6 x 150mm, 5 µm, Make: XTerra) or equivalent
Flow rate	: 0.8 mL per min
Wavelength	: 291 nm
Injection volume	: 20 µl
Column oven	: Ambient
Run time	: 5 min

Preparation of Phosphate buffer: Weigh 7.0 grams of Potassium dihydrogen Phosphate into a 1000ml beaker, dissolve and diluted to 1000 ml with HPLC water. Adjusted the pH to 3.0 with ortho Phosphoric acid.

Preparation of mobile phase:

Mix a mixture of above buffer 600mL (60%) and 400 mL of Acetonitrile HPLC (40%) and degas in ultrasonic water bath for 5 minutes. Filter through 0.45 µ filter under vacuum filtration.

Preparation of the Quetapine Fumarate Standard & Sample Solution

Standard Solution Preparation: Accurately weigh and transfer 10mg of Quetapine Fumarate Working standard into a 10mL volumetric flask add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution).

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

Sample Solution Preparation:

Weigh 5 Quetapine Fumarate Tablets and calculate the average weight. Accurately weigh and transfer the sample equivalent to 10 mg of Quetapine Fumarate into a 10 mL volumetric flask. Add about 7 mL of diluent and sonicate to dissolve it completely and make volume up to the mark with diluent. Mix well and filter through 0.45µm filter.

Further pipette 0.6ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

Calculation:

$$\text{Assay \%} = \frac{AT}{AS} \times \frac{WS}{DS} \times \frac{DT}{WT} \times \frac{P}{100} \times \frac{\text{Avg. Wt}}{\text{Label Claim}} \times 100$$

Where:

AT = Peak Area of Quetapine Fumarate obtained with test preparation

AS = Peak Area of Quetapine Fumarate obtained with standard preparation

WS = Weight of working standard taken in mg

WT = Weight of sample taken in mg

DS = Dilution of Standard solution

DT = Dilution of sample solution

P = Percentage purity of working standard

Results and discussion:

System Suitability:

Tailing factor for the peak due to Quetapine Fumarate in Standard solution should not be more Than 1.5.

Theoretical plates for the Quetapine Fumarate peak in Standard solution should not less than 2000.

Precision:

Accurately weigh and transfer 10 mg of Quetapine Fumarate Working standard into a 10 mL volumetric flask add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter

The standard solution was injected for five times and measured the area for all five injections in HPLC. The %RSD for the area of five replicate injections was found to be within the specified limits.

Intermediate Precision/Ruggedness:

To evaluate the intermediate precision (also known as Ruggedness) of the method, Precision was performed on different day by using different make column of same Dimensions accurately weigh and transfer 10 mg of Quetapine Fumarate Working standard into a 10mL Volumetric flasks add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution). Further pipette 0.6 ml. The above stock solution into a 10ml volumetric flask and dilute up the mark with diluent. Mix Well and filter through 0.45µm filter. The standard solution was injected for five times and measured the area for all five injections in HPLC. The %RSD for the area of five replicate injections was found to be within the specified limits.

Accuracy: Preparation of stock solution:

Accurately weigh and transfer 10mg of Quetapine Fumarate Working standard into a 10mL volumetric flask add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

Preparation Sample solutions:

For preparation of 50% solution (With respect to target Assay concentration):

Accurately weigh and transfer 4.9mg of Quetapine Fumarate API sample into a 10 mL volumetric flask add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

For preparation of 100% solution (With respect to target Assay concentration):

Accurately weigh and transfer 10mg of Quetapine Fumarate API sample into a 10 mL volumetric flask add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

For preparation of 150% solution (With respect to target Assay concentration):

Accurately weigh and transfer 14.8mg of Quetapine Fumarate API sample into a 10 mL volumetric flask add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

Inject the standard solution, Accuracy -50%, Accuracy -100% and Accuracy -150% solutions.

Calculate the Amount found and Amount added for Quetapine Fumarate and calculate the individual recovery and mean recovery values.

Linearity:

Preparation of stock solution:

Accurately weigh and transfer 10mg of Quetapine Fumarate Working standard into a 10mL volumetric flask add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Preparation of Level – I (20 µg/ml):

0.2ml of stock solution has taken in 10 ml of volumetric flask dilute up to the mark with diluent.

Preparation of Level – II (40 µg/ml):

0.4ml of stock solution taken in 10 ml of volumetric flask dilute up to the mark with diluent.

Preparation of Level – III (60 µg/ml):

0.6ml of stock solution taken in 10 ml of volumetric flask dilute up to the mark with diluent.

Preparation of Level – IV (80µg/ml):

0.8ml of stock solution taken in 10 ml of volumetric flask dilute up to the mark with diluent.

Preparation of Level – V (100µg/ml):

1ml of stock solution taken in 10 ml of volumetric flask dilute up to the mark with diluent.

Inject each level into the chromatographic system and measure the peak area.Plot a graph of peak area versus concentration (on X-axis concentration and on Y-axis Peak area) and calculate the correlation coefficient.

Limit of Detection:

Preparation of 60µg/ml solution:

Accurately weigh and transfer 10mg of Quetapine Fumarate Working standard into a 10 mL

Volumetric flasks add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

Preparation of 0.124% solution At Specification level (0.074µg/ml solution):

Pipette 1mL of 10µg/ml solution into a 10 ml of volumetric flask and dilute up to the mark with diluent.Pipette 0.124mL of 10µg/ml solution into a 10 ml of volumetric flask and dilute up to the mark with diluent.

Limit of Quantification:

Preparation of 60µg/ml solution:

Accurately weigh and transfer 10mg of Quetapine Fumarate Working standard into a 10 mL

Volumetric flasks add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.6 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Mix well and filter through 0.45µm filter.

Preparation of 0.124% solution At Specification level (0.074µg/ml solution):

Pipette 1mL of 10µg/ml solution into a 10 ml of volumetric flask and dilute up to the mark with diluent.Pipette 0.124mL of 10µg/ml solution into a 10 ml of volumetric flask and dilute up to the mark with diluent.

Robustness:

As part of the Robustness, deliberate change in the Flow rate, Mobile Phase composition,

Temperature Variation was made to evaluate the impact on the method.

A. the flow rate was varied at 0.7 to 0.9ml/min. Standard solution 60 µg/ml was prepared and analysed using the varied flow rates along with method flow rate.
B. The Organic composition in the Mobile phase was varied from 35% to 45%.Standard solution 60 µg/ml was prepared and analysed using the varied Mobile phase composition along with the actual mobile phase composition in the method.

C. **Table:**

Precision

Injection	**Area**
Injection-1	1091661
Injection-2	1067002
Injection-3	1055772
Injection-4	1038372
Injection-5	1068256
Average	1064213
Standard Deviation	19471.29
%RSD	1.82

Intermediate precision

Injection	**Area**
Injection-1	1224468
Injection-2	1226996
Injection-3	1221453
Injection-4	1221135
Injection-5	1222433
Average	1223297
Standard Deviation	2443.0
%RSD	0.20

Accuracy

%Concentration (at specification Level)	**Area**	**Amount Added (mg)**	**Amount Found (mg)**	**% Recovery**	**Mean Recovery**
50%	614050	4.9	4.81	98.3%	98.7%
100%	1256512	10	9.86	98.6%	
150%	1873581	14.8	14.7	99.3%	

Linearity:

S.No	**Linearity Level**	**Concentration**	**Area**
1	I	20µg/ml	408926
2	II	40µg/ml	782082
3	III	60µg/ml	1250954
4	IV	80µg/ml	1638675
5	V	100µg/ml	1998003
Correlation Coefficient			0.999

Limit of Detection:

Component	Working conc. (mg/ml)	Signal To Noise Ratio
Quetapine	0.074µg/ml	2.84

Limit of Quantification:

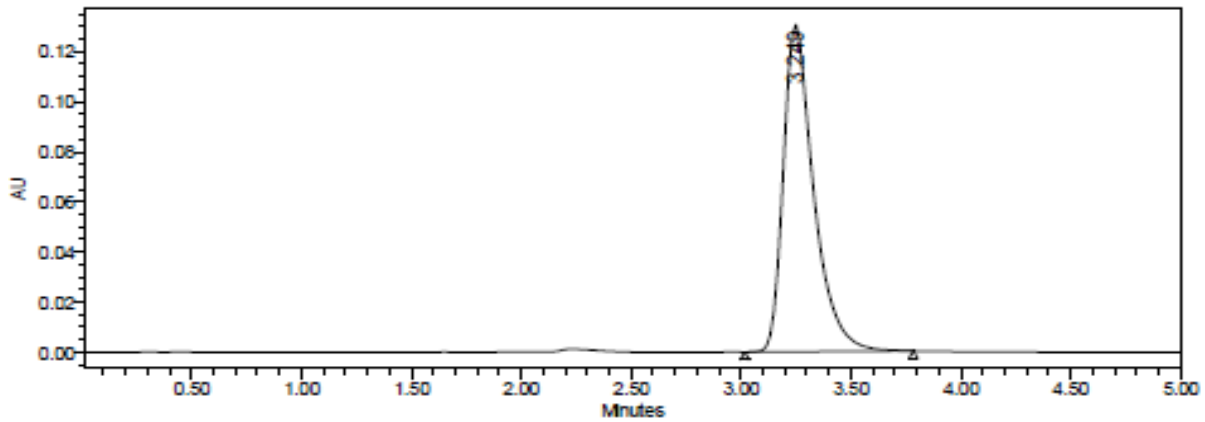
Component	Working conc. (mg/ml)	Signal To Noise Ratio
Quetapine	0.24µg/ml	9.84

Robustness:

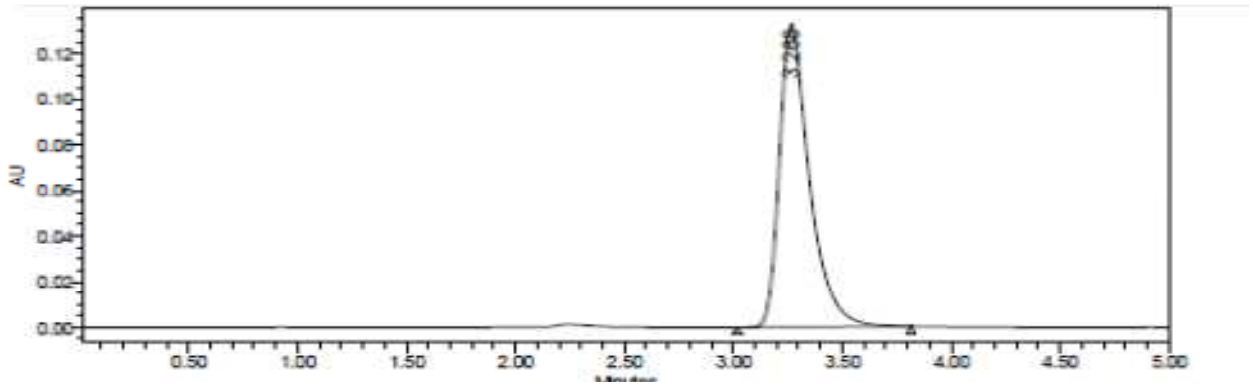
S.No	Flow Rate (ml/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1	0.7	2792	1.5
2	0. 8	2841	1.5
3	0.9	2647	1.4

Chromatograms:

Sample



Standard



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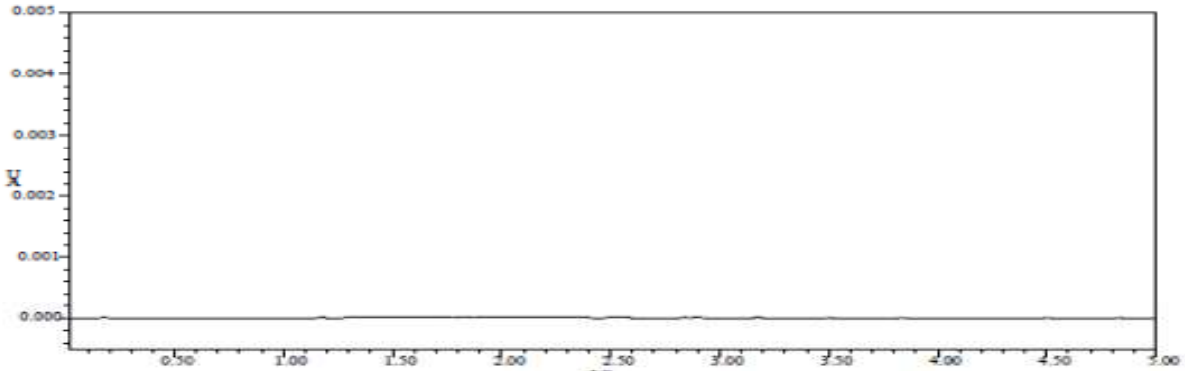

Conclusion:

The proposed method is simple, specific, accurate and precise and hence can be used in routine for estimation of Quetapine in tablet dosage. Statistical analysis of the results has been carried out revealing high accuracy and good precision. The percentages RSD for all parameters was found to be less than two, which indicates the validity of the method and assay results obtained by this method are in fair agreement. The developed method can be used for routine quantitative estimation of Quetapine in tablet dosage form.

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