Est. 1984

ORIENTAL JOURNAL OF CHEMISTRY
An International Open Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2023, Vol. 39, No.(4):
Pg. 1040-1045

Analytical Method Development and Validation of Quetiapine Fumarate in API and Dosage form by Using RP–HPLC

SIVA SANKER REDDY LINGAREDDYGARI[1]*, NAGESWARA RAO RAVIKRINDHI[2], MADANA GOPAL NOOKALA[3], SHAIK MUNEER[4] and PRASAD NAKKA[5]

[1,2,3,4,5]Department of Pharmaceutical Analysis, Santhiram College of Pharmacy, Panyam, Nandyal, Andrapradesh, 518501, India.
*Corresponding author E-mail: shiva_s_rl@yahoo.co.in

http://dx.doi.org/10.13005/ojc/390430

(Received: May 27, 2023; Accepted: July 30, 2023)

ABSTRACT

RP-HPLC method developed is a simple, precise and functional technique for the calculation of amount of Quetiapine fumarate from marketed tablets and bulk form. The RP-HPLC analysis was carried out on Hyper chrome ODS-BP 5µm column (4.6mm×200mm) using a mobile phase 0.1% Orthophoshoric acid and Acetonitrile (80:20v/v) with pH 5.5. Quetiapine fumarate quantified by using UV detector at 210nm. The retention time of the Quetiapine fumarate was found to be 2.6 minute. The linearity of the drug concentration ranges from 20-400µg/mL. The detection and quantification limits were intended at 3.70µg/mL and 12.35µg/mL. The precision, accuracy, specificity, robustness and degradation studies were validated.

Keywords: RP-HPLC, Quetiapine fumarate, Acetonitrile, 0.1% Orthophoshoric acid, Validation.

INTRODCUTION

Quetiapine Fumarate is an Anti-psychotic agent and Anti depressive agent. It is designated chemically as a 2-[2-(4-Dibenzo [b, f][1,4] thiazepin-11-yl-1-piperazinyl) ethoxy] ethanol. The drug's solubility is in methanol, Ethanol, Water and higher soluble under acidic condition with pKa value-15.12 and 7.02 strongly basic PKa, half-life 6 h protein binding-83%, route of administration is oral, metabolism in liver and excretion by kidneys. The entire work was planned according to the ICH guidelines[1]. HPLC methods were reported in various journals-assay method[2], stability indicating method[3], isocratic method[4], and other RP-HPLC methods were taken into consideration for this study[5-12]. Many UV methods also exist for the estimation of Quetiapine, which one is referred in this context[13].

Methodology

Preparation of standard solution for system suitability

Accurately weighed 10 mg of Quetiapine, transferred into volumetric flask of 10 mL capacity and required quantity of mobile phase (0.1% OPA: ACN 80:20v/v) used to make up to the mark. The solution sonicated to be affirmative that the drug was dissolved. This solution was marked as the

stock solution. Further, pipetted out 2 mL from the stock solution into a volumetric flask of 10 mL capacity and addition of mobile phase till the mark, cyclomixer was used to make sure that the drug dissolved completely, filtered through the 0.45 µm Polytetrafluoroethylene membrane filters. The final concentration was 200 µg/mL.

In system suitability, 6 optimized concentrations were prepared, injected and noted the peak responses. Finally noted the areas, retention time, and theoretical plates of the all injections and compared with the limits.

Preparation of blank solution or Mobile phase

The preparation of mobile phase mainly consisted of two steps-firstly, 0.1 mL of orthophosphoric acid was taken by using 1 mL of calibrated pipette and dissolved in 100 mL of HPLC water and secondly, the mobile phase was prepared by using 0.1% Orthophosphoric acid and Acetonitrile in the ratio of 80:20v/v into calibrated volumetric flask, the pH was adjusted to 5.5 by using dilute sodium hydroxide solution.

Preparation of standard solution

The preparation of standard solution also discussed on system suitability parameter. Six optimized concentrations were prepared, injected and noted the peak responses.

Sample solution preparation

Weighed 10 Quetiapine tablets and then calculated the average weight of each tablet. Accurately, weighed tablet powder obtained from the crushed tablets, equivalent to 10 mg (20.8 mg) was emptied into volumetric flask (10 mL) and made up to the mark with the aid of mobile phase. Mixed well and then sonicated for dissolution and filtered it through 0.45 µm filter. Six optimized concentrations were prepared, injected and noted the peak responses.

Preparation of linearity concentrations

From the stock solution pipetted out 0.2 mL (20 µg/mL), 1.1 mL (110 µg/mL), 2 mL (200 µg/mL), 3 mL (300 µg/mL), 4mL (400 µg/mL) were transferred into 10 mL of different volumetric flasks and mobile phase added up to the mark of volumetric flask. These concentrations were filtered through 0.45 µL filter. Into the chromatographic instrument, injected each concentration and then measured the peak area. A graph was plotted with peak areas on X-axis and concentration on Y-axis. The correlation coefficient was calculated.

Intra–day precision

From the stock solution 6 optimized concentrations (200 µg/mL) were prepared and these optimized concentrations were injected the solutions for six times and measured the areas for all injections. From these replicate injections measured the %RSD and it was found to be within the specified limit %RSD<2%. These replicates were injected within a day, like morning, afternoon and evening.

Inter–day precision

For the evaluation of the inter–day precision were injected on three different days Every day 6 optimize concentrations were freshly prepared and the %RSD was compared less than 2.

Preparation of 50%, 100%, 150% solutions for accuracy

From the sample solution pipetted out 1 mL (50%) 100 µg/mL, 2 mL (100%) 200 µg/mL, 3 mL (150%) 300 µg/mL into different 10 mL of volumetric flask and addition of mobile phase up to the mark was carried out. Thoroughly shaken using cyclomixer, passed through the 0.45 micron filter.

Preparation of LOD solution (3.70 µg/mL)

The 100% concentration of sample solution preparation was already discussed in the subtitle accuracy parameter. From the 100 µg/mL solution pipetted out 0.037 mL into volumetric flask (10 mL) and then diluted(with mobile phase) as usual to the required mark. Shaken vigorously to dissolve, then made to pass through the 0.45 micron filter, injected and checked the detection limit.

Preparation of LOQ solution (12.35 µg/mL)

From the 100 µg/mL of sample solution, pipetted out 1.23 mL transfered into 10 mL of volumetric flask and mitigated with the mobile phase to required mark. Mixed well then allowed to pass through the 0.45 micron filter, injected and checked the quantitation limit.

Robustness

Robustness was conducted on different flow rates, different wave lengths and different ratio composition of mobile phase. The optimized

concentration of sample (200 µg/mL) was prepared and analyzed by using the varied flow rates, like 0.6 mL/min, 0.8 mL/min and 1 mL/min, different wavelengths 208nm, 210nm and 212nm and different mobile phase composition. The flow rate varied±2 to normal flow rate and also wavelengths±2, mobile phase composition ratios were ±10. When compared with normal conditions. In robustness %assay calculated between the ranges of 98-102%.

RESULTS AND DISCUSSION:

Establishment of wave length

A solution of Quetiapine (200 µg/mL) was used to know the λmax. 0.1% OPA: ACN 80:20v/v was used as diluents. The λmax was at 210nm and was used in the entire project work.

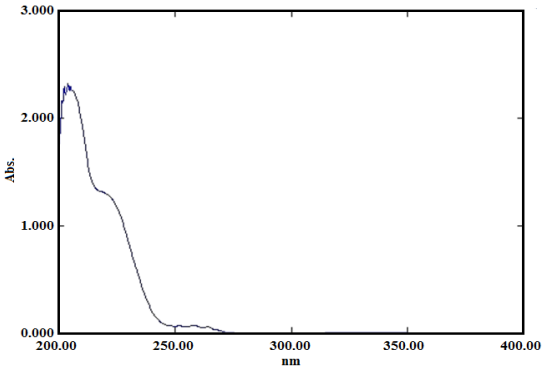

Fig. 1. UV-Spectrum

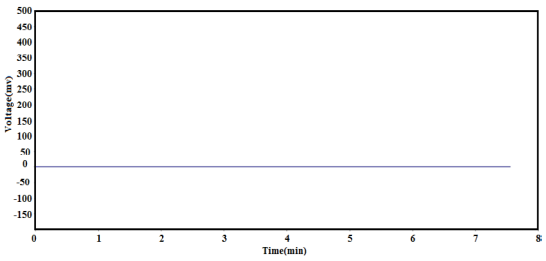

Fig. 2. Blank chromatogram

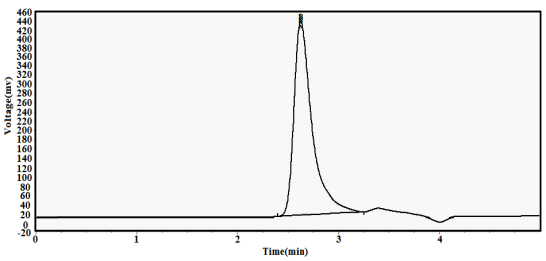

Fig. 3. Optimised chromatogram

Analytical Method Validation

Table 1: System suitability

S. No	Standard area	Theoretical plates	Tailing factor
1	5786394	3700	1.71
2	5750574	3787	1.73
3	5792625	3767	1.74
4	5703694	3752	1.72
5	5698380	3765	1.74
6	5680105	3764	1.71
Average	5735329	3756	1.73
Standard deviation	48086	29.59	0.01
%RSD	0.838	0.788	0.799

Table 2: Linearity

S. No	Concentration(µg/mL)	Area of the peak
1	20	1055037
2	110	3395819
3	200	5684881
4	300	8488555
5	400	11090213

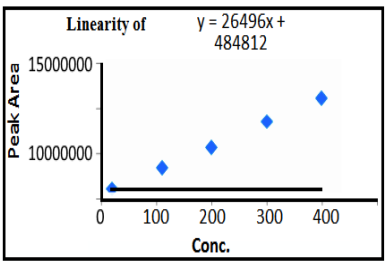

Fig. 4. Linearity of Quetiapine

Table 3: Inter–day precision

S. No	Sample weight	Sample peak area	%Assay
1	20.8 mg	5671040	98.88
2	20.8 mg	5743372	100.14
3	20.8 mg	5681301	99.06
4	20.8 mg	5693297	99.27
5	20.8 mg	5722491	99.78
6	20.8 mg	5678031	99.00
Average	5698255	99.35	
Standard deviation	28582	0.50	
%RSD	0.502	0.50	

Table 4: Intra–day precision

S. No	Sample weight	Sample peak area	%Assay
1	20.8 mg	5771040	100.62
2	20.8 mg	5693372	99.27
3	20.8 mg	5681301	99.06
4	20.8 mg	5683297	99.09
5	20.8 mg	5682491	99.08
6	20.8 mg	5678031	99.00
Average	5698255	99.35	
Standard deviation	36028	0.63	
% RSD	0.632	0.63	

Table 5: Accuracy

S.No	Spiked level(%)	Sample weight(mg)	Sample area	µg/mL added	µg/mL found	%Recovery	%Mean recovery
1	50	10.4	2871543	99.18	100.14	100.97	99.33
2	50		2873096	99.18	101.19	101.02	
3	50		2876831	99.18	100.32	101.15	
4	100	20.8	5667890	198.35	197.65	99.64	100.47
5	100		5787744	198.35	201.83	101.75	
6	100		5688744	198.35	198.38	100.01	
7	150	31.2	8529045	297.53	297.42	99.96	
8	150		8599960	297.53	299.89	100.79	99.79
9	150		8548159	297.53	298.09	100.19	

Table 6: Robustness

S. No	Flow rate (mL/min)	Peak area	%Assay
1	0.6	5696523	99.32
2	0.8	5699834	99.38
3	1	5708485	99.53
	Wave length(nm)		
1	208	5698030	99.35
2	210	5688031	99.18
3	212	5700030	99.38

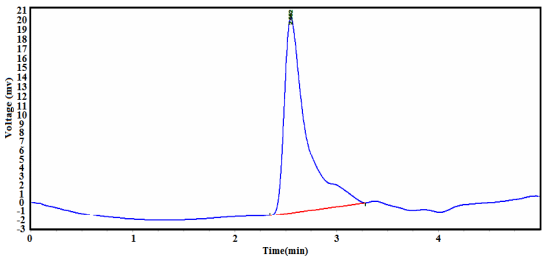

Fig. 5. LOD Chromatogram

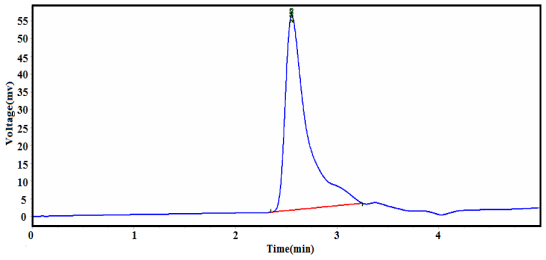

Fig. 6. LOD Chromatogram

Table 7: Degradation studies or Stability studies (Dosage form)

S. No	Component added to degrade the sample	Weight of the sample	Sample area	%Assay	% of Degradation
1	Acid	20.8mg	4707340	82.08	17.92
2	Base		4975858	86.76	13.24
3	Hydrogen Peroxide		4304962	75.06	24.94
4	Heat		4715977	82.23	17.77
5	UV light		4863820	84.80	15.20

SUMMARY

Precise, specific, more rapid, subtle, financial and reproducible, isocratic reverse phase HPLC method developed and validated for quantitative determination of Quetiapine in pharmaceutical dosage form and in API. The HPLC method was validated for linearity, accuracy, specificity, precision, range, LOD and LOQ, Rugged and Robustness as per ICH guidelines. Stability studies were also performed to determination the stability time period of test and standard solutions.

In HPLC developed method less and simple mobile phase composition with 0.1% OPA: ACN in the ratio of 80:20v/v and pH adjusted to 5.5 with retention time 2.6. All replicates were analyzed and detected at 210nm with UV-detector. The method was found to be linearity concentration range from 20 µg/mL to 400 µg/

mL. The correlation coefficient was found to be 0.999. The accuracy of method was performed at 50%, 100%, 150% to analyte concentration and %recovery was found to be 99.33%, 100.47%, 99.79% respectively. The range of the method was performed at lower and higher concentration from accuracy studies and obtained results represents the developed HPLC method was precise and accurate. System suitability parameters were performed when deliberate experimental changes like mobile phase flow rate, buffer pH, mobile phase composition to the selected method and obtained results were well accepted with accepted criteria. The results LOD and LOQ were found to be 3.70 µg/mL and 12.35 µg/mLrespectively. In degradation studies the method was able to detect the drug and was within the prescribed limits, without any inference of degradants.

CONCLUSION

Thus the proposed analytical method was simple, selective, rapid, precise, accurate, and financially feasible. The established analytical RP-HPLC technique was robust, rugged, and well-organized and represents specific procedure for quantitative determination of Quetiapine in bulk as well as in pharmaceutical dosage form. RP-HPLC method was successfully applicable for regular analysis of Quetiapine in quality control laboratories by following ICH guidelines. The developed method has advantage of short analysis time; cheaper solvents as well as less toxic solvents were used as mobile phase. The method also has wide concentration range to quantify.

ACKNOWLEDGMENT

The authors are thankful to Principal and management of Santhiram college of Pharmacy for the utilization of facilities. This work is not sponsored by any government or non government bodies/ institutions and is self financed.

Conflict of interest

The authors have no conflict of interest.

REFERENCES

1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline, Validation of Analytical Procedures: Text and Methodology Q2 (R1), Complementary Guideline on Methodology, London., **2005**.
2. Nikita, G.; Archana, D.; Dubey P.K. Development and validation of assay method for determination of quetiapine fumarate by RP-HPLC from bulk and pharmaceutical dosage form. *Int. J. Pharmaceutical Sciences & Medicine.,* **2022**, *7*(10), 65-96.
3. Talele, S. G; Derle, D. V. Stability-indicating high-performance liquid chromatography (HPLC) method development and validation for the determination of quetiapine fumarate in bulk and dosage form by HPLC. *Int. J. Green. Pharmacy*., **2018** (Suppl), *12*(1), S188-S193.
4. Rajendraprasad, N.; Basavaiah, K.; Anil Kumar, U. R. Isocratic ultra-performance liquid chromatographic assay of quetiapine fumarate in pharmaceuticals. *Tha.i J. Pharm Sciences*., **2017**, *41*(1), 6-11.
5. Chandra, R.; Ashwani, S.; Deepak. K. Augustin, K.B. "Development and validation a RP-HPLC method: Application for the quantitative determination of quetiapine fumarate from marketed bulk tablets", *J. Chem. Pharm. Res*., **2016**, *8*(1), 142-146.
6. Nagaraju, P. Development and validation of RP-HPLC method for estimation of Quetiapine fumarate in Pharmaceutical formulations. *Pharm Methods*., **2015**, *6*(2), 105-108.
7. Kiran B. V.; Sreenivas R. B.; Somshankar D. Validation of Quetiapine Fumarate in Pharmaceutical Dosage by Reverse-Phase HPLC with Internal Standard Method. *J. Chemistry*. **2013**, *2013*, 1-9.
8. Paulo, C. R.; Iury, F. R. P.; Markman, B. E. O.; Perazzo, F.F. Development and Validation of RP-HPLC Method for the determination of related compounds in Quetiapine hemifumarate raw material and tablets. *J. Applied. Pharm. Science*., **2013**, *3* (08), 6-15.

9. Pramod, L. I.; Sampada, D. D.; Sachin, V. G.; Laxmileena, D. P.; Deepali, D. J.; Yogita, A. K. Development of analytical method for determination of quetiapine fumarate in bulk & tablet dosage form. *Der. Pharm. Chemica*., **2013**, *5*(5), 26-30.
10. Pragati, T.; Sivasubramanian, L. Stability indicating RP-HPLC method for the estimation of quetiapine fumarate in bulk and tablet dosage form. *Int J Pharm Pharm Sci*., **2013**, *5*, (Suppl 4), 269-272.
11. Rakshit, K.T, Mukesh C. P. Development and validation of a stability indicating RP-UPLC method for determination of quetiapine in pharmaceutical dosage form. *Sci. Pharm*., **2011**, *79*(1), 97–111.
12. Korrapolu, S.; Bollineni, S.; Nalluri, B.N. Stability indicating RP-HPLC-PDA method for the estimation of quetiapine fumarate in bulk and pharmaceutical dosage forms. *J Chem Pharm Res*., **2012**, *4*(8), 3877-3884.
13. Bagade, S. B.; Narkhede, S.P;. Nikam, D. S.; Sachde. C. K. Development and validation of UV-Spectrophotometric method for determination of Quetiapine fumarate in two different dose tablets, *International Journal of ChemTech Research*., **2009**, *1*(4), 898-904.