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ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR QUETIAPINE FUMARATE BY UV SPECTROPHOTOMETRY

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ABSTRACT

A simple, sensitive, specific spectrophotometric method has been developed for the determination of Quetiapine fumarate in pure form and in pharmaceutical formulations. Quetiapine fumarate exhibited maximum absorption at 278nm and obeyed Beer's law in the concentration range of 10-80µg/ml. LOD was found to be 10.3 X $10^{-2}$and LOQ was found to be 18.9 X 10^{-2}. The regression equation was found to be y = 0.1892x + 0.0037. The sample solution was stable for 24hrs. The assay procedures showed good agreement with label claim. The proposed method was found to be simple, precise, specific and quick for routine quality control.

Keywords – Quetiapine fumarate, Determination, Spectrophotometry, UV

1. INTRODUCTION

Quetiapine fumarate is the most recently introduced atypical antipsychotic and is indicated for the management of the manifestations of psychotic disorders and schizophrenia. Quetiapine interacts with a broad range of neurotransmitter receptors and has a higher affinity for serotonin receptors relative to dopamine receptors in the brain. Further, quetiapine's pharmacological effects appear selective for the mesolimbic and mesocortical dopamine systems, which are believed to be the areas of the brain responsible for the therapeutic effects of antipsychotics.

In contrast to most standard antipsychotics and some atypical antipsychotics, quetiapine's effects on the nigrostriatal dopamine system, which is responsible for the extrapyramidal (or motor) side effects, are minimal. Quetiapine also has minimal activity on dopamine receptors in the tubero infundibular dopamine system, thereby avoiding the problem of hyperprolactinemia, common with the standard antipsychotics and some atypical antipsychotics. Because of these properties, quetiapine is an effective antipsychotic agent with a relatively benign side effect profile.

Patients on long-term treatment report high compliance, good satisfaction, increased ability to function and improvements consistent with a better quality of life. Because of quetiapine's excellent tolerability profile, its use is particularly appropriate in patients especially sensitive to adverse effects.

However, no literature was found on quantitation of quetiapine fumarate in tablets. The aim of the present work is to find out a simple, specific, sensitive, spectrophotometer method developed for the detection of Quetiapine Fumarate in pure form and in pharmaceutical formulation.

2. MATERIAL AND METHODS

2.1 Instrumentation

A double–beam spectrophotometer of Systronics was used for the detection of absorbance, Shimadzu was used as electronic balance and borosil glass apparatus were used for experimental purpose.

2.2 Chemicals and Reagents

Quetiapine Fumarate working standard was supplied by SUN Pharmaceuticals Pvt. Ltd. All the other chemicals used in the analysis were of AR grade.

2.3 Procedure

2.3.1 Preparation of Standard solution

10mg of Quetiapine fumarate standard was accurately weighed and transferred into a 10ml volumetric flask. Then 1ml of 0.1M sulphuric acid was added and the volume was made upto the mark with distilled water. From the stock solution 0.5ml was pipetted out into a 10ml volumetric flask and the volume was made up to the mark with distilled water.

2.3.2 Preparation of Sample solution

20 tablets were randomly selected and weighed. Then the average weight was calculated and the sample equivalent to 10mg was weighed and transferred into a 10ml volumetric flask. 1ml of 0.1M sulphuric acid was added and the volume was made up to the mark with distilled water. The solution was then shaken well to dissolve the contents and then filtered. 0.5ml of the filtrate was diluted to 10ml with distilled water.

2.4 Method Validation

Validation of the analytical method for the determination of Quetiapine Fumarate in pure form and in pharmaceutical formulation was carried out as per ICH guidelines.

2.4.1 Linearity

Linearity of an analytical method is its ability to elicit test results that are directly proportional to the concentration of analyte in samples within a given range. The linearity of the analytical method was determined by mathematical treatment of test results obtained by analysis of samples with analyte concentrations across the claimed range. Absorbance values were plotted graphically as a function of analyte concentration. Percentage curve fitting was also calculated.

2.4.2 Specificity

The specificity of an analytical method is its ability to measure accurately and specifically the analyte in the presence of compounds that may be expected to be present in the sample matrix. The specificity of the analytical method was determined by analysing the placebo solution under the same experimental conditions as the assay.

2.4.3 Precision

Precision of an analytical method is the degree of agreement among individual test results when the procedure is applied repeatedly to multiple sampling of a homogenous sample. Precision of analytical method is usually expressed as the standard deviation and relative standard deviation. The relative standard deviation should be within 2.0%

2.4.4 System Precision

System precision was determined by preparing the standard solution for six times and measuring the absorbance of each of the prepared solutions. The standard deviation and relative standard deviation were calculated.

2.4.5 Method Precision

The method precision was determined by preparing the sample of single batch of Quetiapine fumarate tablets for six times and the absorbances of the six solutions were measured.

2.4.6 Ruggedness

The ruggedness of an analytical method is degree of reproducibility of test results obtained by the analysis of the same samples under a variety of normal test conditions, such as different laboratories, different analysts, different instruments, different lots of reagents, different elapsed assay times, different assay temperatures, different days, etc. Ruggedness is normally expressed as a lack of influence on test results of operational and environmental variables of the analytical method.

The standard stock solution and sample stock solution were prepared by different analysts on different days and the absorbances of the resulting solutions were measured. The value should be between 92-102%.

2.4.7 Accuracy

The accuracy of an analytical method is the closeness of test results obtained by that method to the true value. Accuracy may often the expressed as percent recovery by the assay of known added amounts of analyte.

The accuracy of the analytical method is determined by applying the method to analyzed samples, to which known amounts of analyte have been added. The accuracy is calculated from the test results as the percentage of analyte recovered by the assay. Percentage recovery should be within 98-102%.

2.4.8 Solution Stability

To establish the stability of analytical solutions by measuring the absorbance of the standard and sample solutions at periodic intervals upto 24hrs. The absorbances of the blank, standard and sample preparation were measured. The %RSD of absorbance of both standard and sample solutions at periodic intervals should not be more than 2.0%.

2.4.9 Limit of Detection

It is the lowest amount of analyte in a sample that can be detected but not necessarily quantified as an exact value under the stated, experimental conditions. Several approaches for determining the detection limit are possible, depending on whether the procedure is non-instrumental or instrumental. A specific calibration curve was studied using samples containing an analyte in the range of detection limit. The residual standard deviation of a regression line or the standard deviation of y-intercepts of regression lines may be used as the standard deviation.

2.4.10 Limit of Quantitation

It is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. Several approaches for determining the quantitation limit are possible, depending on whether the procedure is a non-instrumental or instrumental. A specific calibration curve was studied using samples containing the analyte in the range of quantitation limit. The residual standard deviation of a regression line or the standard deviation of y-intercepts of regression lines may be used as the standard deviation.

3. RESULTS AND DISCUSSION

Linearity studies were carried out in the concentration range of 10-80 µg/ml and the sample solution is obtained from the stock solution. The readings obtained by measuring the absorbance at 278nm are presented in table 1 and the curve was shown in fig.1.

Table 1: Linearity data

Sl.No	Concentration (µg/ml)	Concentration(%)	Absorbance
1	10	20	0.814
2	20	40	0.378
3	30	60	0.569
4	40	80	0.766
5	50	100	0.961
6	60	120	1.151
7	70	140	1.342
8	80	160	1.488

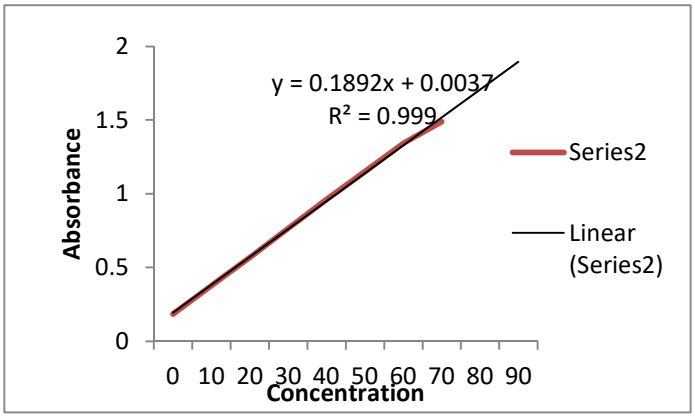

Fig. 1 : Calibration curve

Performing replicate analyses of the standard solutions was used to assess the precision and reproducibility of the proposed methods. The selected concentration within the calibration range was prepared in 0.1M sulphuric acid. The precision of the results are given in table 2, which demonstrate a good precision.

Table 2 (a) : Results of System precision

Sl.No.	Absorbance
1	0.937
2	0.946
3	0.931
4	0.937
5	0.935
6	0.929
MEAN	0.936
S.D	0.005947
% RSD	0.6353

Table -2 (b) : Results of method precision

Sl.No	Absorbance	Amount Present in Tablet (mg)	Percentage label claim
1	0.948	25.3	101.2
2	0.942	25.1	100.4
3	0.931	24.8	99.2
4	0.924	24.6	98.4
5	0.955	25.5	102
6	0.930	24.8	99.2
MEAN		25.01	100.06
STANDARD DEVIATION		0.3430	1.3721
%RSD		1.3714	1.3712

Specificity of the method was found out through non-interference of placebo in identical conditions of assay. This confirms the specificity of the developed method and the result are given in table 3.

Table 3: Specificity for Quetiapine fumarate

Sl.No	Sample	Absorbance obtained
1	Placebo	0
2	Standard	0.964
3	Standard + Placebo	0.977

Detection limit was done by calibration curve method. The results of LOD and LOQ were given in table 4 and 5.

Table 4: Limit of detection

Sl.No.	Absorbance
1	0.937
2	0.946
3	0.931
4	0.937
5	0.935
6	0.929
MEAN	0.936
S.D	0.005947
% RSD	0.6353

Table 5: Limit of Quantitation

Sl.No.	Absorbance
1	0.937
2	0.946
3	0.931
4	0.937
5	0.935
6	0.929
MEAN	0.936
S.D	0.005947
% RSD	0.6353

Stability of the method was determined by assays of the drug formulation up to 24hrs. There was almost no appreciable change in absorbance up to 24hrs. The results are given in table 6.

Table-6 : Stability data

Sl.No	Time Intervals	Absorbance Of blank	Absorbance Of placebo	Absorbance Of Standard	Absorbance Of Sample
1	0	0	0	0.962	0.978
2	30min	0	0	0.962	0.978
3	1hr	0	0	0.962	0.978
4	1hr 30min	0	0	0.962	0.979
5	2hr	0	0	0.960	0.979
6	2hr 30min	0	0	0.959	0.979
7	3hr	0	0	0.960	0.979
8	3hr 30min	0	0	0.960	0.975
9	4hr	0	0	0.957	0.976
10	4hr 30min	0	0	0.958	0.976
11	5hr	0	0	0.958	0.976
12	5hr 30min	0	0	0.956	0.975
13	6hr	0	0	0.956	0.973
14	6hr 30min	0	0	0.956	0.975
15	7hr	0	0	0.957	0.975
16	7hr 30min	0	0	0.957	0.975
17	24hr	0	0	0.953	0.973
MEAN				0.958	0.976
STANDARD DEVIATION				0.0026	0.0020
% RSD				0.2713	0.2049

Accuracy of the method was determined through recovery studies of the drug and the results are given in table 7.

Table 7: Recovery study of Quetiapine fumarate

S.No	SAMPLE - ID	Amount added (mg)	Absorbance observed	Amount found (mg)	% Recovery
1.	80%	8	0.740	7.89	98.6
		8	0.742	7.91	98.8
		8	0.738	7.86	98.2
2.	100%	10	0.947	10.09	100.9
		10	0.943	10.05	100.5
		10	0.948	10.10	101.00
3.	120%	12	1.110	11.83	98.58
		12	1.117	11.90	99.16
		12	1.115	11.88	99.00

Ruggedness was determined by performing the same assay on different days and the assay being carried out by different analyst. The results are given in table 8.

Analyst 1

Table 8: Ruggedness of Quetiapine fumarate

S.No	Date of Analysis	Standard Absorbance	Sample absorbance	Assay Value in (mg)	% Label Claim w/w
1	2/9/2011	0.939	0.928	24.7	98.8
2	2/9/2011	0.942	0.935	24.8	99.2
3	5/9/2011	0.939	0.930	24.7	98.8
	MEAN				98.9333
	STANDARD DEVIATION				0.2309
	% RELATIVE STANDARD DEVIATION				0.2333

Analyst 2

Table 8: Ruggedness of Quetiapine fumarate

S.No	Date of analysis	Standard absorbance	Sample absorbance	Assay Value in (mg)	% Label Claim w/w
1	2/9/2011	0.949	0.956	25.1	100.4
2	2/9/2011	0.945	0.936	24.7	98.8
3	5/9/2011	0.951	0.946	24.8	99.2
	MEAN				99.4666
	STANDARD DEVIATION				0.8326
	% RELATIVE STANDARD DEVIATION				0.8370

4. CONCLUSION

The developed spectrophotometric method was simple, sensitive, and specific, for the determination of quetiapine fumarate in pure and pharmaceutical formulations. The linearity of quetiapine fumarate, which obeys beer's law, was 10-80µg/ml at 278nm and it shows regression more than 0.999. It could be precisely detected and quantified at 10.3×10^{-2} and 18.9×10^{-2} respectively. The sample solution was stable up to 24 hrs. The proposed method will be suitable for the analysis of quetiapine fumarate in pure and tablet dosage form.

REFERENCES

1. B.B Hiraman, V. Sandip, Lohiya R.T, Umerkar M.J, Spectrophotometric determination of an atypical antipsychotic compound in pharmaceutical formulation, Int.J. ChemTech Res, 2009,1(4),1153-1161
2. B.K Sharma, Ultraviolet and visible spectroscopy, Manjula Sharma, 25th ed, Instrumental methods of chemical analysis, Meerut, Krishna Prakashan Media,2006,S77-80
3. 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, Int.J. ChemTech.Res ,2009;1(2),898-904.

4. Davis PC, Wong J, Gefvert O, Analysis and pharmacokinetics of quetiapine and two metabolites in human plasma using RP-HPLC with ultraviolet and electrochemical detection, J Pharm Biomed Analysis,1999;20(1-2),271-82
5. Donald L Pavia,Gary M Lampman,George Kriz, James R Vyvyan, Ultraviolet Spectroscopy,4th ed, Spectroscopy, Newdelhi, Cengage learning,2010,369-372
6. Douglas A Skoog, F James Holler, Timothy A Niemann, An introduction to ultraviolet/visible molecular absorption spectrometry,5th ed, Principles of instrumental analysis, Thomas Brooks/Cale,2003,302
7. Gurdeep R Chatwal, Sham K.Anand, Instrumental methods of chemical analysis.2008,5thed,2.107-2.117-2.124
8. Hobart H Willard, Lynne Merritt, John A Dean, Frank A Settle, Ultraviolet and visible spectrometry-Instrumentation,7th ed, Instrumental methods of analysis,Delhi, CBS publishers and distributors,1987,118-119,140-142
9. ICH topic q2a, "Validation of analytical procedures" 6th NOV,1999
10. K.B.Vinay, H.O.Revanasiddappa, P.J. Ramesh, N.Rajendraprasad, Titrimetric And Sensitive Spectrophotometric Methods for the assay of Quetiapine fumarate in pharmaceutical formulations, Chemical Industry And Chemical Engineering Quarterly,2011;17(1), 99-106.
11. Nagaraju Rajendraprasad, Kanakapura Basavaiah, Kanakapura Basavaiah Vinay, Extractive spectrophotometric determination of quetiapine fumarate in pharmaceuticals and human urine using calmagite as an ion-pair reagent, CI & CEQ,2011; 17(3),259-267
12. Nagaraju Rajendraprasad, Kanakapura Basavaiah, Kanakapura.B.Vinay, Sensitive and selective extraction-free spectrophotometric determination of Quetiapine fumarate in pharmaceuticals using two sulphonthalein dyes, Journal of Pre-Clinical and Clinical Research,2010;4(1),024-03.
13. Sahu Deepak, Rana A.C, Development of analytical method for Quetiapine fumarate by UV spectrophotometry, IJRAP; 2011,2(2), 588-591.
14. Susamma Cicy Eapen, V G Prasanth, Sheeja Velayudhan Kutty, T S Jyothi, Development and validation of UV-spectrophotometric method for determination of Quetiapine fumarate in pure and pharmaceutical formulation,IJPT, 2011;3(4),3535-3542
15. Vincenzo Pucci, Roberto Mandrioli, Anna Ferranti, Sandra Furianetto, Maria Augusta Raggi, Quality control of commercial tablets containing the novel antipsychotic quetiapine, Journal of pharmaceutical and biomedical analysis,2003,32(4-5),1037-1044
16. W.B.Li, Y.Z.Xue, Y.M.Zhai, J.Zhang, G.X.Guo, C.Y.Wang, Z.J.Cai, Determination of Quetiapine fumarate in serum by HPLC with ultraviolet detection, Yaowu Fenxi Zazhi,2003,23(4),247-251.