

DEVELOPMENT OF ANALYTICAL METHOD FOR QUETIAPINE FUMARATE BY UV SPECTROPHOTOMETRY

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ABSTRACT

A Simple, sensitive, specific, Spectrophotometric method has been developed for the detection of quetiapine fumarate in pure form and in Pharmaceutical formulations. The optimum condition for the analysis of the drug was established. Quetiapine Fumarate exhibiting absorption at 242nm and obeyed beers law in the concentration range 5 to 25µg/ml. The lower limit of detection was found to be 3.5×10^{-2} and the limit of quantification to be 11.6×10^{-2} . The regression equation was $y = 0.037x + 0.007$. The precision of the method was found to be 100.14 mg at 242 nm against the label claim of 100 mg. The sample solution was stable up to 24 hours. The assay results were found to be in good agreement with label claim. The proposed method was simple sensitive, precise, quick and useful for routine quality control.

KEYWORDS: Spectrophotometry; Quetiapine Fumarate; Determination.

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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, like clozapine (the archetypal atypical antipsychotic), interacts with a broad range of neurotransmitter receptors and has a higher affinity for serotonin (5-HT_{2A}) receptors relative to dopamine (D₂) 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.¹⁻⁴

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.⁵⁻⁹ Several large, placebo- and active-controlled, multicenter trials have shown quetiapine to be effective against both positive (e.g., hallucinations, delusions) and negative symptoms (e.g., emotional withdrawal, apathy) and to have benefits in reducing hostility, aggression and affective symptoms.¹⁰⁻¹³ 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, e.g., elderly patients with psychotic symptoms and other neurological disorders such as Parkinson's and Alzheimer's disease.¹³

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.

MATERIAL AND METHOD**Instrumentation**

A double-beam spectrophotometer shimadzu was used for the detection of absorbance, Mettler Toledo as Weighing balance and Misonix sonicator, borosil glass apparatus were used for experimental purpose.

Chemicals and Reagents

Quetiapine Fumarate working standard was supplied by M/S IPCA pharmaceutical Pvt. Ltd., Ratlam (M.P.). All other chemicals used in the analysis were AR grade.

PROCEDURE**Preparation of stock solution**

100mg of mg pure drug was weighed and transferred to a 100ml volumetric flask, 50ml Phosphate Buffer pH 6.8 was added to the above flask, dissolved and sonicated for 15 min the volume was made up with the Phosphate Buffer pH 6.8.

Preparation of sample solution

The average weight of the tablets was determined by weighing 10 tablets and these were powdered. Tablet powder equivalent to 100 mg of quetiapine fumarate was weighed and transferred to a 100ml volumetric flask. About 20ml of phosphate buffer pH 6.8 was added and sonicated for 15min for complete dissolution of drugs the volume was made up with phosphate buffer pH 6.8 and filtered through filter paper. Six replicates of analysis were carried out with sample weighed individually. The average weight of tablet was found to be 419.829 mg.

METHOD VALIDATION

Validation of the analytical method¹⁴ for the determination of Quetiapine Fumarate in Pure form and in pharmaceutical formulation was carried out as per ICH guidelines.

Linearity

The method was validated according to ICH Q2B guidelines¹⁵ for validation of analytical procedures^{14,16-17} in order to determine the linearity, sensitivity, precision and of the analyse for quetiapine fumarate, five point calibration curves were generated with the appropriate volumes of the working standard solutions for UV methods. The linearity was evaluated by the least-square regression method using unweighted data.

Precision

Precision is the degree of repeatability of an analytical method under normal operational conditions. The precision and were determined with standard quality control samples (in addition to calibration standards) prepared in triplicate at different concentration levels covering the entire linearity range. The precision of the

assay was determined by repeatability (intra-day) and intermediate precision (inter-day) and reported as RSD % for a statistically significant number of replicate measurements. The intermediate precision was studied by comparing the assays on three different days and the results are documented as the standard deviation and RSD %. Accuracy^{15-16,18-19} is the percent of analyses recovered by assay from a known added amount. Data from nine determinations over three concentration levels covering the specified range were obtained.

Limit of Detection and Limit of Quantification

The limit of detection (LOD)¹⁶⁻¹⁷ is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from back-ground levels. In this study, LOD and LOQ were determined based on the standard deviation of the response and the slope of the corresponding curve using the following equations:

$$\text{LOD} = 3.3 \frac{s}{m}$$

$$\text{LOQ} = 10 \frac{s}{m}$$

Where s, the noise of estimate, is the standard deviation of the absorbance of the sample and m is the slope of the related calibrations graphs.

The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision and variability.

Stability

The stability^{15,17,19-24} of quetiapine fumarate in phosphate buffer pH 6.8 solution was studied by the UV method. Sample solutions were prepared in triplicate and stored at 5°C and 27°C for 30, 60, 90, 120min and 24 hours. The stability of these solutions was studied by performing the experiment.

RESULTS AND DISCUSSION

Linearity studies were carried out in the concentration range of 5-25 µg/ml and the sample solution is obtained from the stock solution. The readings are obtained by measuring the absorbance at 242nm presented in **table 1** and the curve was shown in **fig.1**.

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 phosphate buffer pH 6.8 and analyzed with the relevant calibration curves to determine the intra and inter day variability. The intra and inter day precision were determined as the RSD %. The precision, of the results are given in **table 2**, which demonstrate a good precision and the consolidated recovery data was presented in table 3.

The proposed methods can be successfully applied for quetiapine fumarate assay in tablet dosage forms without any interference. The assay showed the drug content of this product to be in accordance with the labelled claim 100mg. The values of LOD and LOQ are given in **table 3**.

The stability²⁵⁻²⁶ of quetiapine fumarate in phosphate buffer pH 6.8 solution was studied by the UV method. Sample solutions were prepared in triplicate and stored at 5 and 27°C for 24hrs. The stability of these solutions was studied by performing the experiment. The stability of quetiapine fumarate in phosphate buffer pH 6.8 solution was evaluated to verify whether any spontaneous degradation occurs, when the samples were prepared. The stability profile for 24 hrs was studied. The results were expressed as a percentage of the drug remaining. The obtained data showed that the sample solutions were stable up to 24hrs.

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 5-25µg/ml at 242nm and it shows regression more than 0.999. The precision of the method was found to be 100.02%. It could be precisely detected and quantified at 3.5×10^{-2} and 11.6×10^{-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.

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Table 1: Linearity profile of Quetiapine Fumarate

S. No	Concentration (µg/ml)	Absorbance at 242 nm
1	0	0.000
2	5	0.183
3	10	0.365
4	15	0.545
5	20	0.744
6	25	0.950
Correlation coefficient = 0.999		
Absorbance = 0.037 × concentration - 0.007		
Values in parenthesis indicates standard deviation (n = 3)		

Table 2 Precision data for Quetiapine Fumarate in formulation

S. No.	Weight (mg)	Absorbance (A°)	Amount (mg)
1	419.82	0.379	99.89
2	420.13	0.386	100.23
3	419.84	0.376	99.94
4	419.98	0.384	100.11
5	420.27	0.387	100.45
6	419.80	0.382	99.85
Average			100.078
SD			0.231

Table 3: Validation parameter of Quetiapine Fumarate

S. No.	Parameters	Quetiapine Fumarate
1	Measured Wavelength (λ _{max})	242
2	Linearity Range (µg/ml)	5-25
3	Slope	0.037
4	Intercept	0.007
5	Percentage Recovery	99.92
6	Correlation Coefficient (r)	0.999
7	Limit of Detection (LOD), (µg/ml)	0.0237
8	Limit of Quantification (LOQ), (µg/ml)	0.123

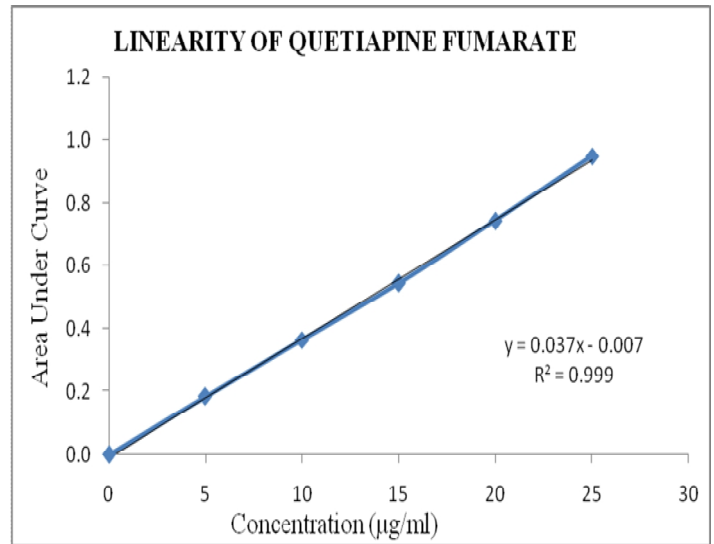


Figure 1: Linearity curve of Quetiapine Fumarate

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