Development and Validation of a UV-Visible Spectrophotometric Technique for the Quantification of Quetiapine Fumarate in Bulk and Formulated Products.

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Abstract

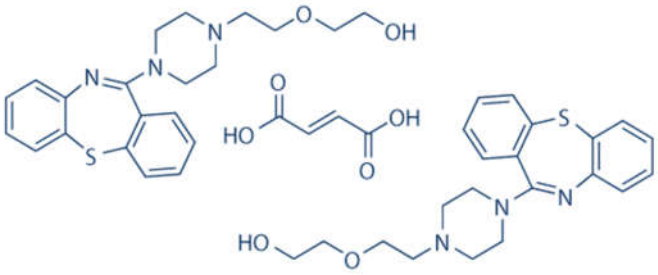
A rapid, precise, and cost-effective UV spectrophotometric technique has been established utilizing methanol as a solvent for the quantification of Quetiapine Fumarate in both bulk substances and pharmaceutical formulations. This method operates at a designated wavelength of 264.8 nm and demonstrates linearity within a concentration range of 10 to 50 µg/ml, achieving a high correlation coefficient ($R^2 = 0.9986$). The technique was effectively employed to assess the Quetiapine Fumarate content in various commercially available products, yielding results that align with the stated label specifications. Comprehensive statistical validation and recovery studies were conducted to evaluate the method's linearity,precision, repeatability, and reproducibility. The results suggest that this method is suitable for the routine analysis of Quetiapine Fumarate in both bulk and commercial formulations.

Introduction

Quetiapine Fumarate,is characterized as a white crystalline powder that exhibits insolubility in water. It possesses a molecular weight of 883.10 g/mol, a melting point range of 174 to 186 °C, and a log P value of 2.93. As a derivative of dibenzothiazepine, quetiapine is classified as an atypical antipsychotic, demonstrating a higher in vitro binding affinity for serotonin 5-HT2 receptors compared to dopamine D2 receptors. This medication is effective in alleviating both the positive and negative symptoms associated with schizophrenia, and it has been shown to produce extrapyramidal symptoms at a rate comparable to that of a placebo across its entire dosage spectrum.[1]

The pharmacological action of Quetiapine Fumarate primarily involves antagonism at various neurotransmitter receptors within the central nervous system. Its therapeutic efficacy is largely due to its interactions with: Dopamine D2 Receptors, where it exhibits a moderate binding affinity that aids in mitigating psychotic symptoms and enhancing mood stabilization; and Serotonin 5-HT2A Receptors [2], which it antagonizes, thereby contributing to its beneficial effects in mood disorders while minimizing the likelihood of extrapyramidal side effects in comparison to conventional antipsychotics.

Quetiapine is indicated for the management of schizophrenia symptoms, including hallucinations, delusions, and disorganized thought processes. It is also effective in addressing both manic and depressive episodes in bipolar disorder[3] Furthermore, quetiapine may serve as a maintenance therapy to avert the recurrence of mood episodes. In certain instances, it is utilized as an adjunctive treatment for major depressive disorder, particularly when monotherapy with other antidepressants proves to be inadequate.[4]



Structure of Quetiapine Fumarate

Numerous HPLC assay techniques have been documented for the quantification of Quetiapine Fumarate.[5] A comprehensive review of the literature indicates that various analytical approaches, including high-performance thin-layer chromatography (HPTLC) and high-performance liquid chromatography (HPLC), have been utilized for the estimation of Quetiapine Fumarate.[6]Additionally, recent studies have introduced several UV spectrophotometric methods for the determination of Quetiapine Fumarate, employing methanol as the solvent.

In this investigation, a straightforward, efficient, and cost-effective UV spectrophotometric method was established using methanol for the quantification of Quetiapine Fumarate in both raw materials and commercially available dosage forms. The method underwent optimization and validation in accordance with the International Conference on Harmonization (ICH) guidelines, showcasing remarkable specificity, linearity, precision, and accuracy in the quantification of Quetiapine Fumarate.

Materials and methods

Apparatus

A double beam UV–visible spectrophotometer (Systronics 2201) was employed for all absorbance measurements, utilizing matched quartz cells along with volumetric flasks, pipettes, and a sonicator.

Materials

All chemicals and reagents utilized in this study were of analytical or HPLC grade. Quetiapine Fumarate was acquired from Balaji Drug Dealers: API & Pharmaceutical Polymers located in Surat, India, and the marketed formulation of Quetiapine Fumarate served as the reference standard.

Preparation of a working standard drug solution

The process commenced with the accurate measurement of 10 mg of Quetiapine Fumarate standard, which was subsequently placed into a 10 mL volumetric flask. The compound was fully dissolved, and the resulting solution was diluted to the calibration line with Methanol, resulting in a final concentration of 1000 µg/ml (Stock-1). Subsequently, Stock-1 was diluted further with methanol to produce a 100 µg/ml (Stock-2) solution.

Determination of the wavelength of maximum absorbance (λmax)

The Stock-2 sample was analyzed in full output mode at a moderate scanning speed across the entire range of the UV-VIS Spectrophotometer, spanning from 200 to 400 nm, with a co-solvent

system employed as the blank. After obtaining the spectrum, the maximum wavelength (λmax) was identified. This process was repeated three times.

Development of Calibration Curve

The calibration curve was developed by utilizing Stock-2 to create five separate calibration standards with concentrations of 10, 20, 30, 40, and 50 µg/mL. The absorbance for each standard was recorded at a wavelength of 264.8 nm, employing a fixed wavelength measurement approach. Calibration curves, illustrating the correlation between concentration and absorbance, were generated using Microsoft Excel. This procedure was repeated several times to ensure the accuracy and consistency of the results.

Method Validation

The ultraviolet (UV) technique developed for the quantification of Quetiapine Fumarate was subjected to validation across several parameters, such as linearity, range, precision, robustness, ruggedness, accuracy, limit of quantification (LOQ), and limit of detection (LOD). This validation process employed established calibration standards, which are outlined in the following sections.

Linearity and range

The linearity of the proposed ultraviolet (UV) method was assessed through the use of five separate calibration standards. The analysis of these standards facilitated the construction of calibration curves, illustrating the correlation between absorbance and concentration. These curves were further evaluated using linear least squares regression. The R^2 value emerged as a significant parameter in validating the linearity of the proposed method. The acceptable linearity range was established based on the difference between the upper and lower concentration thresholds of the proposed UV method.

Accuracy

Accuracy can be quantified as the proportion of analyte recovery achieved from the examination of a predetermined amount of analyte introduced into the sample. Additionally, it can be characterized as the difference between the average measured value and the accepted true value, along with the corresponding confidence intervals.

Intra-day precision and Inter-day precision

The reliability of the assay method was assessed in terms of repeatability through the execution of five independent assays within the Quetiapine Fumarate testing framework. The percentage relative standard deviation (%RSD) of the measurements was determined for intra-day evaluations. To establish the intermediate precision of the method, the same procedure was implemented over a span of three consecutive days.

Stability study

Samples intended for the repeatability study were maintained at room temperature for a period of 24 hours and were then analyzed the following day to evaluate their short-term stability.

Robustness

The assessment of robustness must be taken into account during the development stage and is contingent upon the specific procedure, which involves intentional alterations to method parameters. If the measurements are vulnerable to fluctuations in analytical conditions, it is essential to either maintain sufficient control over these conditions or to incorporate a cautionary note within the procedure. In this study, the absorption maxima were modified by 1 nm in both directions, and the analysis was performed using a standard solution of 30 µg/ml.

Limit of Quantification (LOQ)

In UV method development LOQ was determined by utilizing the following equation.

LOQ = 10xSD/S

Where, S= slope

SD= Standard deviation of Y-intercepts

Estimation of Quetiapine Fumarate content in marketed formulation

A pre-validated UV-Vis analytical method was effectively employed to determine the concentration of quetiapine fumarate in a marketed formulation. In this study, SEROQUELTablets were procured from a local pharmacy in Solapur, and the active ingredients were extracted from the tablets. Appropriate dilutions were prepared using a pre-optimized solvent system. The extracted samples were then analyzed using the established UV method, and the results were reported as the average percentage of the assay.

Results and Discussion

Method development and optimization

The identification of the wavelength corresponding to maximum absorbance is crucial for performing quantitative UV analysis. Solutions with absorbance values below 1 are generally considered suitable for determining the wavelength of maximum absorbance. Adhering to this principle, the maximum wavelength for a Quetiapine Fumarate solution at a concentration of 100 µg/mL was ascertained using the full scan mode of a UV-Visible spectrophotometer (see Figure 2). The full scan was executed with UV software, which aided in pinpointing λmax. The peak absorbance wavelength for Quetiapine Fumarate was found to be 264.8 nm.

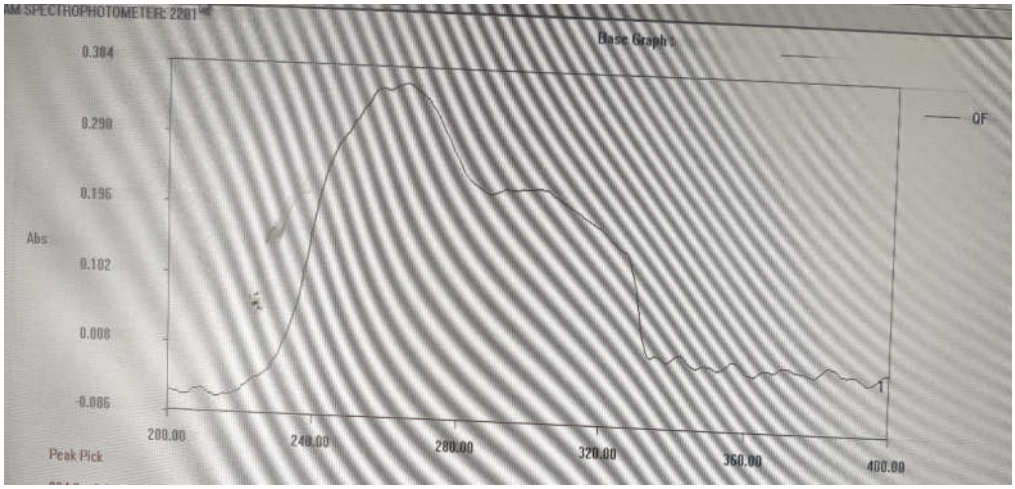


Fig. 2: UV-visible spectra of Quetiapine Fumarate

Preparation of calibration curve

To accurately quantify unknown samples using a UV-Visible spectrophotometer or a comparable analytical device, it is essential to establish a dependable calibration curve, accompanied by an equation that articulates the correlation between concentration and the observed response. This approach is esteemed for its reliability and consistency in comparison to graphical methods. In the precise quantitative analysis of Quetiapine Fumarate, a calibration curve was generated utilizing five calibration standards. The absorbance of these standards was recorded at a wavelength of 264.8 nm, employing the fixed wavelength mode of the UV-Visible spectrophotometer. The calibration curve was developed on three distinct occasions, with the resulting data summarized in Table 1.

Table no.1

Standard	**Concentration (µg/ml)**	**Absorbance**
QTF STD-1	10	0.327
QTF STD-2	20	0.384
QTF STD-3	30	0.459
QTF STD-4	40	0.528
QTF STD-5	50	0.594

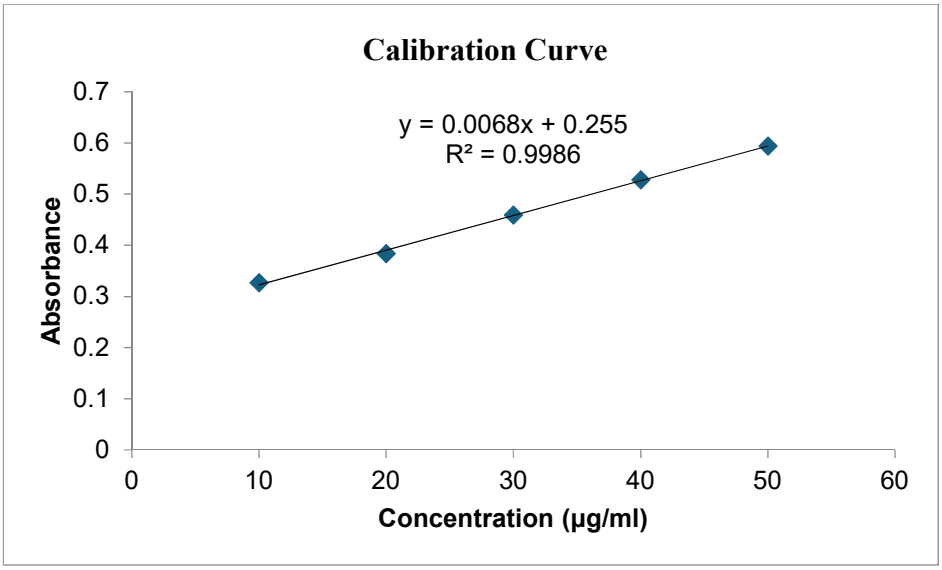


Fig 3: Calibration curve for Quetiapine Fumarate

Accuracy

Accuracy serves as an essential parameter that indicates the degree to which the experimental value aligns with the actual concentration of a substance within a specific matrix. It is imperative to assess accuracy throughout the full calibration range of the analytical technique to ensure the dependability of results at every measurement interval. In the ultraviolet (UV) method employed for the analysis of Quetiapine Fumarate, accuracy was evaluated via recovery studies. The percentage recovery of Quetiapine Fumarate was determined by introducing the analyte at concentrations of 80%, 100%, and 120%.

Table 2: Accuracy data of UV method for Quetiapine Fumarate.

Recovery Level (%)	Concentration of Sample(µg/ml)	Amount added (µg/ml)	% Recovery
80	10	8	98.5
100	30	30	98.8
120	50	60	99.3

Precision

Precision serves as a critical metric that reflects the extent of variability in measurements, thereby illustrating the dependability of results generated by a particular analytical technique. An effective analytical method should yield results that are consistently reproducible. Attaining precision within an analytical process is vital for guaranteeing accurate results. To assess the reproducibility and reliability of the UV method, both intra- and inter-day precision were evaluated at a concentration of 10µg/ml. The findings remained within acceptable thresholds, demonstrating a relative standard deviation (RSD) of under 1%.

Table 3: Intra-day precision data of UV method for Quetiapine Fumarate

Sr. No	Concentration	Absorbance
1	10(µg/ml)	0.328
2		0.327
3		0.329
4		0.326
5		0.325
	Mean	0.3276
	SD	0.001581
	%RSD	0.48

Inter-day precision data of UV method for Quetiapine Fumarate

Sr. no	Concentration	Absorbance (1st day)	Absorbance (2nd day)
1	10(µg/ml)	0.328	0.327
2		0.325	0.326
3		0.327	0.329
4		0.329	0.328
5		0.327	0.326
	Mean	0.3272	0.3267
	SD	0.001483	0.001304
	%RSD	0.4532	0.3991

Robustness

Robustness in an analytical method refers to its ability to yield reliable results consistently, even when minor, intentional modifications are made to its parameters. This attribute is essential, as unforeseen variations, such as alterations in solvent composition or pH, can arise during standard use and potentially affect the method's effectiveness. A robust method is designed to ensure that such fluctuations do not significantly impair its performance. For example, a robust method would demonstrate minimal variation in the absorption of a Quetiapine Fumarate solution in Methanol when evaluated across different wavelengths (±2nm).

Table 5: Robustness data of UV method for Quetiapine Fumarate

Sr. no	Absorbance at 264.8nm	Absorbance at 268nm
1	0.326	0.340
2	0.327	0.338
3	0.328	0.343
SD	0.001528	0.002082
%RSD	0.34	0.46

Limit of Quantitation (LOQ) and Limit of Detection (LOD)

The Limit of Quantification (LOQ) is defined as the minimum concentration that can be reliably measured with both accuracy and precision. Typically, it serves as the main calibration standard. In the proposed ultraviolet (UV) method, the Limit of Detection (LOD) and Limit of Quantification (LOQ) were determined to be 0.561 and 1.47µg/ml, respectively, as presented in Table 7. The comparatively low LOQ suggests that this method is highly effective for analyzing samples with minimal concentrations of Quetiapine Fumarate.

Table 7: LOD & LOQ data for UV method for Quetiapine Fumarate

LOD	0.561µg/mL
LOQ	1.47µg/mL

Estimation of Quetiapine Fumarate

The developed ultraviolet (UV) method was successfully employed to quantify the Quetiapine Fumarate concentration in SEROQUEL Tablet 50 mg. The mean percentage assay of Quetiapine Fumarate in the tablet was found to be 96.4%.

Conclusion

An effective and validated UV-Visible spectrophotometric method for the quantification of Quetiapine Fumarate has been developed. This technique demonstrated both robustness and reliability, making it suitable for the estimation of Quetiapine Fumarate.

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