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# Analytical method development of Quetiapine Fumerate in bulk and its Tablet Formulation by simple UV Spectrophotometry

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**Abstract**

Quetiapine fumerate (QTF) (bis [2-(2-[4-(dibenzo [b, f][1,4]thiazepin-11-yl]ethoxy) ethanol]fumarate) is the most recent agent introduced on the drug market for the treatment of psychotic disorders. Spectrophotometric analytical methods for the quality control of Quetiapine Fumarate in two different commercial marketed tablet dosage form (BRAND A & BRAND B) of same strength 25 mg have been developed. The absorbance data was obtained by the measurements at selected wavelength of 290 nm by using Methanol: water in the ratio 50:50v/v as solvent. Beers Lambert's law obeyed at concentration range 15.99 - 24.09 µg/mL concentration range of Quetiapine for spectrophotometric methods at selected wavelength. Proposed method gave satisfactory results in terms of precision and repeatability for both the brands i.e. 100.41% and 99.77% respectively. Also accuracy values were very good for both brands i.e.100 % and 99.83 % resp. which is drawn out by recovery studies, were found satisfactory. The spectroscopic method have excellent linearity and range (r2 =/0.9997). The procedures do not require any separation step. These methods were successfully applied to any solid dosage form containing same drug and was found to be utter, swift, simple, fast, reliable, sensitive, specific and efficient for their estimation from pharmaceuticals.

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***Key words:***
Quetiapine fumerate, method development, validation, UV spectrophotometry, tablet dosage form.

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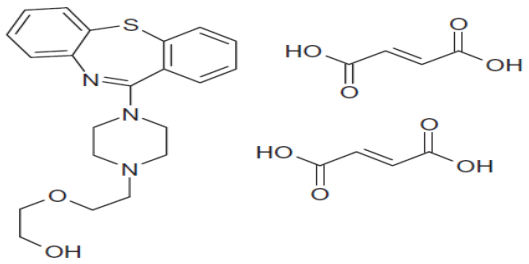
## INTRODUCTION

Quetiapine fumerate[1] is an atypical antipsychotic approved for the treatment of schizophrenia, acute episodes of bipolar disorder (manic, mixed or depressive), and a n augmenter for the maintenance

treatment of depression and bipolar disorder. Quetiapine[1,2] is a dopamine, serotonin, and adrenergic antagonist, and a potent antihistamine with clinically negligible anticholinergic properties. Quetiapine received its initial indication from the U.S. Food and Drug Administration for treatment of schizophrenia in 1997. In 2004, it received its second indication for the treatment of mania-associated bipolar disorder. In 2007 and 2008, studies were conducted on quetiapine's efficacy in treating generalized anxiety disorder and major depression. Quetiapine fumerate[3,4] (QTF) is 2- (2- (4-dibenzo[*b*,*f*] [1,4] thiazepine- 11-yl- 1-piperazinyl) ethoxy) ethanol. QTF Appears as white crystalline solid and Stored at room temperature. It is soluble in methanol, ethanol, Chloroform, 0.1 M HCl, phosphate buffer, sparingly soluble in water. Its structure is given below.



Qutiapine[6] binds strongly to serotonin receptors. Serial PET scans evaluating the $D_2$ receptor occupancy of quetiapine have demonstrated that quetiapine very rapidly disassociates from the $D_2$ receptor. Theoretically, this allows for normal physiological surges of dopamine to elicit normal effects in areas such as the nigrostriatal and tubero-infundibular pathways, thus minimizing the risk of side-effects such as pseudo-parkinsonism as well as elevations in prolactin. Some of the antagonized receptors (serotonin, norepinephrine) are actually auto receptors whose blockade tends to increase the release of neurotransmitters.

Several methods have been reported for the quantitative determination of quetiapine in bulk, and pharmaceutical and biological samples. These methods include UV-Visible spectrophotometric[10-15], HPLC methods[16-19] , HPTLC[20] , UPLC[21], complexometric method[22] and Hyphenated techniques such as LC-MS[23], HPLC-MS-MS method[24] and HPLC electro-spray mass spectrophotometry[25].

The aim of present study was to develop and validate [7,8,9] an accurate, specific and reproducible UV method for determination of quetiapine fumarate as in marketed tablet dosage formulation .

## MATERIALS AND METHODS

### Chemicals and Reagents

Pure sample of Quetiapine fumarate (QTF) was generous gift from Wockhardt Pharmaceuticals Ltd., Aurangabad. Tablets of same strength and different brands were procured from local pharmacy, Water, Methanol, Mortar pestle, Whattman filter paper no.1, all other reagents used were of analytical grade.

### Instrumentation

A double beam UV spectrophotometer TECHCOMP was used for the detection of absorbance, Denwer Semi micro as analytical weighing balance and PCI analytics sonicator of 1.5 litres, borosil glass apparatus were used for experimental purpose.

### UV Spectroscopic Method

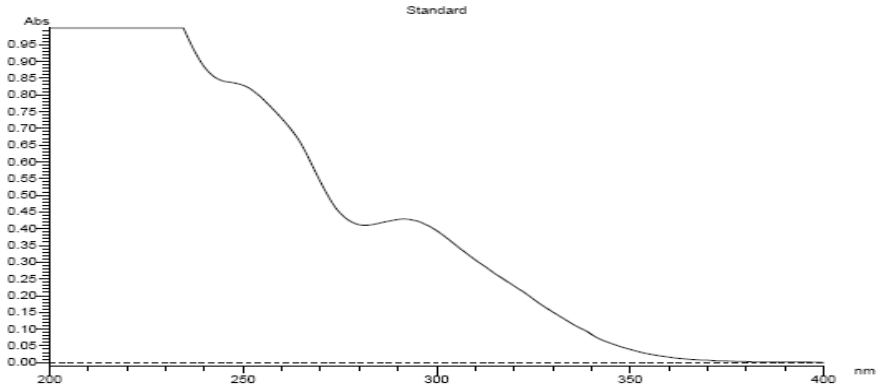
### Preparation of Stock Solutions

Standard solution of QTF was prepared by dissolving 29 mg of Quetiapine fumarate in 25 ml of methanol solution to get concentration of 1000 µg/ml.

### Determination of λ max

From the stock solutions, a working standard was prepared. The absorption spectrum for Quetiapine, was recorded using 20 µg/ml solution and the maximum absorption was found to be 290 nm (Fig.1).

**Fig 1:** Absorbtion Spectra of QTF bulk




**Preparation of Standard Solutions**

Different aliquots of stock solution were transferred into series of 25 ml volumetric flasks and the volume was made up to the mark with methanol : water in the ratio of 50:50v/v to obtain concentrations 15.99-24.09 µg/mL. Scanning range was finalized for study and solutions were scanned on spectrophotometer in the UV range of 200 - 400 nm and the Calibration curves were prepared for QTF. The plots of Beer's law limit are shown in Fig. 2.

**Fig. 2:** Linearity of QTF

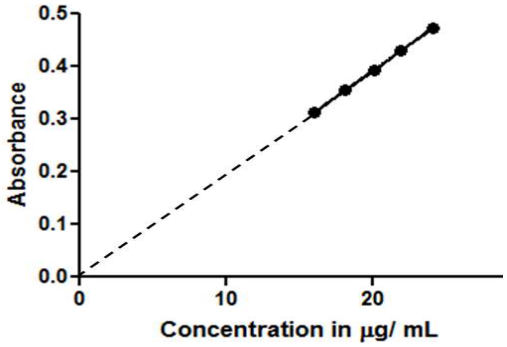



**Table 1:** Linearity profile of QTF

| S. No. | Concentration in µg/mL | Absorbance at 290nm |
|---|---|---|
| 1. | 15.968 | 0.313 |
| 2. | 18.112 | 0.355 |
| 3. | 20.128 | 0.393 |
| 4. | 21.89 | 0.430 |
| 5. | 24.068 | 0.474 |
| Correlation coefficient | | 0.9997 |

**Preparation of Sample Solution**

Tablet samples A and B , label claimed 25 mg of Quetiapine per dosage unit . The average weight was determined with 20 tablets, which were grounded in a mortar until fine powder. Accurately weighed amount of powder equivalent to 29 mg of Quetiapine fumarate was quantitatively transferred to a 25 ml calibrated flask with the aid of methanol. The volume was made up to mark, sonicate for 10 min and filtered through whatman Filter paper no.1. The filtrate is suitably diluted to get a final conc. of 20 µg /ml Quetiapine fumarate. Then the solution was scanned at 290 nm.The spectra of sample was shown in Fig. 3&4.

**Fig 3:** Absorbtion Spectra of QTF formulation (Brand A)

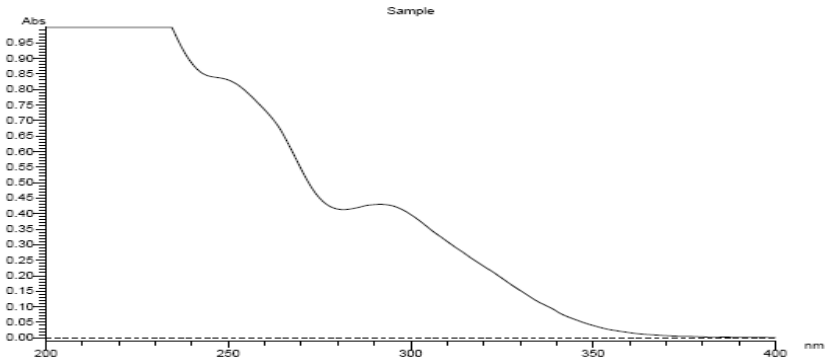


**Fig. 4:** Absorbtion Spectra of QTF formulation (Brand B)

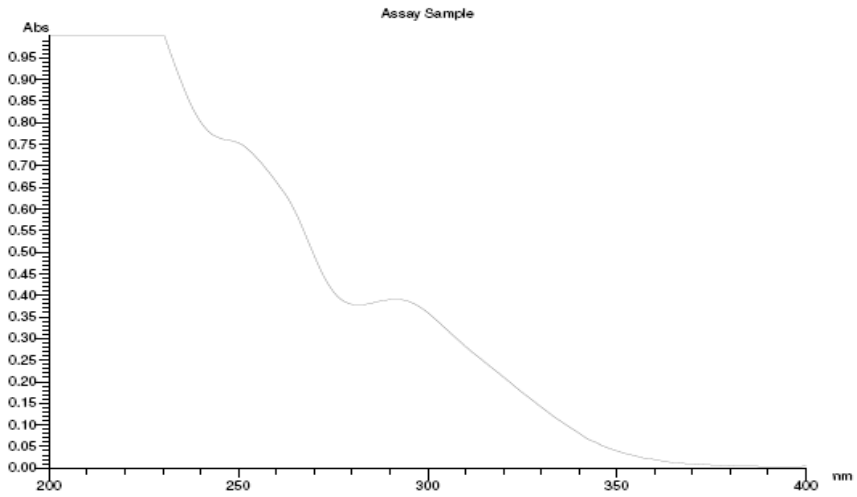



**Table 2:** Estimation of QTF in marketed formulations (Brand A & Brand B)

| S. o | Actual Amount present. (mg / tab) | Standard absorbance at 290 nm | Sample absorbance at 290 nm | | Amount found (mg/tab) | | Percentage (%) | |
|---|---|---|---|---|---|---|---|---|
| | | | Brand A | Brand B | Brand A | Brand B | Brand A | Brand B |
| 1 | 25 | 0.387 | 0.391 | 0.392 | 25.02 | 24.83 | 100.09 | 99.32 |
| 2 | | 0.383 | 0.390 | 0.391 | 25.15 | 25.02 | 100.60 | 100.09 |
| 3 | | 0.390 | 0.392 | 0.391 | 24.83 | 25.02 | 99.32 | 100.09 |
| | | | | | | **Mean** | 100.00 | 99.83 |

**Method Validation**

Validation of the analytical method for the determination of Quetiapine fumerate bulk and its tablet dosage form was carried out as per ICH guidelines.

**Linearity Range**

Linearity was performed by taking aliquots from stock solution (1mg/ml) in 25ml volumetric flasks and diluted up to the mark with methanol: water in the ratio 50:50v/v such that the final concentration of Quetiapine fumerate in the range of 16 to 24 µg/ml. Under the experimental conditions described the graphs obtained by plotting concentration Vs absorbance .The observations and calibration curve is shown in Table 1 and Fig. 2.

**Accuracy and Recovery**

Accuracy is the percent of analyses recovered from the assay from a known added amount. Data from nine determinants from three concentration levels covering the specified range were obtained. To verify the capability of regression equations to predict the absorbance behavior of Quetiapine fumarate in dosage forms, the method was tested for accuracy and recovery. To study the recovery of the pre-analyzed sample solutions, a known amount of standard solutions of the pure drugs were added at different level i.e. 110, 120 and 130 %. Recovery study was determined by following formula;

**% Recovery = [A-B/ C] X 100**

Where, A = Total amount of drug estimated

B = Amount of drug found on pre-analyzed basis

C = Amount of drug added

The result of recovery studies are presented in Table 3.

The mean recovery of the two brands (A & B) were found to be 100.41% and 99.77% respectively, indicates very good reproducibility of these methods.

**Table 3:** Recovery studies of QTF formulation (Brand A & Brand B)

| S No | Level % | Drug added in mg/mL | Brand A* | | Brand B* | |
|---|---|---|---|---|---|---|
| | | | Amount recovered in mg/mL | Mean % Recovery | Amount recovered in mg/mL | Mean % Recovery |
| 1. | 110 | 10 | 10.04 | 100.40 | 10.00 | 100.04 |
| 2. | 120 | 20 | 20.08 | 100.40 | 20.00 | 100.04 |
| 3. | 130 | 30 | 30.13 | 100.43 | 29.77 | 99.23 |

**Mean value of 3 determinants*

**Precision**

Precision is the degree of repeatability of an analytical method under optimal conditions. The precision were determined with standard quality control samples (in addition to linearity standards) prepared in triplicate at different concentration levels covering the entire linearity range. The precision of the method was determined by repeatability and reported as % RSD for a statistically significant number of replicate measurements.

**Table 4:** Precision data for QTF formulation (Brand A & Brand B)

| S. No | Brand A | | Brand B | |
|---|---|---|---|---|
| | Absorbance | % Amount | Absorbance | % Amount |
| 1. | 394 | 99.91 | 395 | 99.95 |
| 2. | 397 | 100.18 | 396 | 100.20 |
| 3. | 391 | 100.09 | 397 | 100.12 |
| 4. | 407 | 100.29 | 394 | 99.91 |
| 5. | 401 | 100.17 | 408 | 100.32 |
| 6. | 409 | 100.38 | 406 | 100.25 |
| Parameters | % Mean | 100.19 | % Mean | 100.12 |
| | SD | 0.1 | SD | 0.1 |
| | % RSD | 0.12 | % RSD | 0.09 |

**RESULTS AND DISCUSSION**

The developed method of spectrophotometric determination of QTF in tablet formulation was found to be absolute and persuading for the routine analysis of drug. In our study, QTF was analyzed using UV Spectrophotometric method where the UV Spectra of QTF were recorded over the range 200 – 400 nm in Methanol : water in the ratio of 50: 50v/v at 290 nm.

Linearity studies were carried out in the concentration range of 16 - 24 µg/mL and the sample solution is obtained from the stock solution. The readings are obtained by measuring the absorbance at 290 nm presented in Table 1 and curve was shown in Fig.2.

The proposed method can be successfully applied for the assay of QTF in tablet dosage forms without any interference. The assay showed the drug content of this product to be in concordance with the labeled claim 25 mg. the values are given in the Table 2.

The utility of this method was determined by means of the recovery assay in marketed tablet samples (Brand A & Brand B of same strength). Recoveries were determined by standard addition method (SAM). The mean percentage recoveries of QTF of Brand A & B by UV method were found to be 100.41% & 99.77% respectively. The results of the recovery studies were given in Table 3.

Performing replicate analyses of standard solution was used to assess the precision, repeatability and reproducibility of the proposed method. The selected concentration within the linearity range was prepared by using methanol : water in the ratio of 50:50 and analyzed with the relevant calibration curves to determine the variability. The precision was determined as the % RSD. The results of the precision are given in the Table 4, which demonstrate a good precision.

**CONCLUSION**

The developed UV spectrophotometric method are accurate, simple, rapid, precise, reliable, sensitive, reproducible and economical for the

determination of QTF and its pharmaceutical tablet dosage forms. The reagents utilized in the proposed methods are cheap, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The methods are more selective than many of the reported spectrophotometric methods and employs higher wavelength to measure absorbance readings where the errors due to inactive ingredients are minimized to a large extent. The methods are free from interferences from the common excipients. The statistical parameters and the recovery data reveal good accuracy and precision of the methods. These methods can be used as general methods for the determination of QTF in bulk powder and dosage forms. The methods have many advantages over the separation techniques such as HPLC and include reduced cost, and speed with high accuracy. Hence, the methods can be used in routine analysis of drug in quality control laboratories.

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