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VALIDATED SPECTROPHOTOMETRIC METHOD FOR THE QUANTITATION OF QUETIAPINE FUMARATE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

Simple, precise and accurate area under curve spectroscopic method has been developed and validated for the estimation of Quetiapine fumarate in bulk and pharmaceutical dosage form. The drug shows maximum absorption (λ_{max}) at 226nm in Methanol:1N NaOH (50:50) solution and Area under Curve [AUC] in absorption spectra were measured between the wavelength range 221 to 231nm which obeys Beer's law in the concentration range of 2-10 µg/ml. The linearity study was carried out and regression coefficient was found to be 0.9998 and it has showed good linearity, precision during this concentration range. The % recovery was found to be 99.16-100.6. The LOD and LOQ were found to be 0.0349 and 0.105µg/ml. The percentage relative standard deviation were found to be less than 2. According to ICH guidelines the method have been validated for linearity, precision, accuracy, robustness, ruggedness, LOD and LOQ. The developed and validated method can be successfully applied for routine quantitation of Quetiapine fumarate in bulk and pharmaceutical dosage form.

KEYWORDS: Quetiapine Fumarate, Area under curve spectroscopy, validation, pharmaceutical formulations.

INTRODUCTION

Quetiapine fumarate is a second-generation atypical antipsychotic medication used to treat certain mental /mood disorders (such as schizophrenia, bipolar disorder, sudden episodes of mania or depression associated with bipolar disorder)

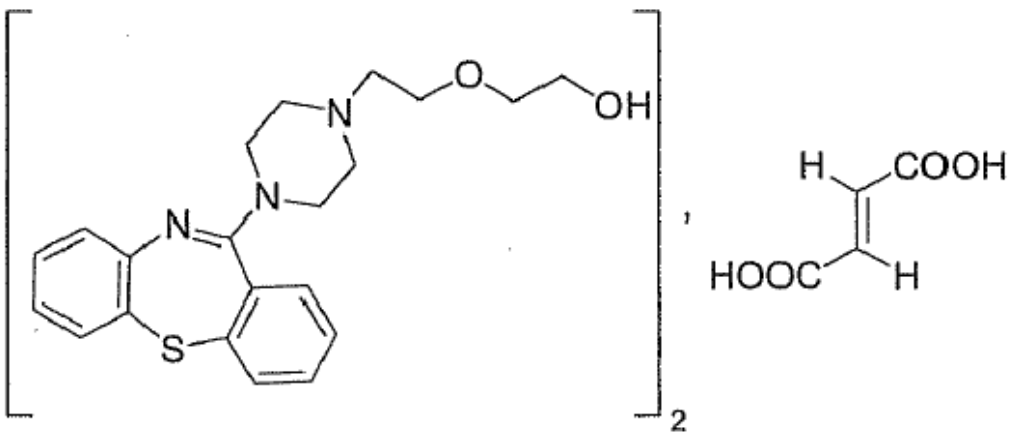

Fig. 1: Chemical structure of Quetiapine fumarate.

Literature survey revealed that there were few analytical methods have been reported for the determination of

Quetiapine fumarate in pure drug and pharmaceutical dosage forms by using UV spectrophotometric[2-7], HPLC[8-16], HPTLC[17-18] and UPLC[19-20] so far.

The aim of present work is to develop and validate a novel, rapid, simple, precise and specific Area under curve Spectrophotometric method for estimation of Quetiapine fumarate in bulk and tablet dosage form.

MATERIALS AND METHODS

Instrument: Ultraviolent-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software. All weights were taken on weighing balance.

Chemicals: Quetiapine fumarate pure drug was obtained as a gift sample from Hikal Ltd Jigani, Bengaluru and its pharmaceutical dosage form Quetiapine fumarate 20 tablet labelled claim 50mg from local pharmacy manufactured by Elite Pharma India Ltd.

Solvent: Methanol: 1N NaOH (50:50) used as a solvent.

Selection of analytical wavelength: Appropriate dilutions of Quetiapine fumarate were prepared from standard stock solution and using spectrophotometer solution was scanned in the wavelength range 200-400nm. Area under Curve [AUC] in absorption spectra were measured between the wavelength range 221 to 226nm as the wavelength for detection (Fig-2).

Preparation of 1N NaOH: 40gm of Sodium hydroxide is transferred into 1000ml volumetric flask and make up the volume up to the mark with distilled water.

Preparation of standard stock solution: 100mg of Quetiapine fumarate was weighed accurately and transferred in to 100ml volumetric flask and diluted in Methanol:1N NaOH (50:50) up to mark. From this, the solution was further diluted into 100µg/ml and pipette out 0.2, 0.4, 0.6, 0.8, and 1.0ml into 10ml individual volumetric flask and diluted in Methanol:1N NaOH (50:50) up to the mark, this gives 2, 4, 6, 8, and 10µg/ml concentration.

Preparation of sample solution: 20 tablets of Quetiapine fumarate marketed formulations were weighed and powdered. A quantity of tablet powder equivalent to 100mg of Quetiapine fumarate was transferred into a 100ml of volumetric flask then it was diluted with Methanol:1N NaOH (50:50) and made up to the mark.

METHOD AND VALIDATION: The method was validated according to ICH guidelines.

RESULTS AND DISCUSSION

Method: Area under curve spectroscopy.

Linearity: The linearity of an analytical method is its dimensions to show the test results that are directly proportional to the concentration of the analyte in the sample within the range. The linearity was established in the range of 2-10µg/ml and Area under Curve [AUC] in absorption spectra were measured between the wavelength of 221 to 231nm as absorbance values are shown in table-1 (Fig-3). The calibration curve was prepared by plotting graph against the concentration and absorbance and therefore the graph shown in (Fig-4). Statistical variables like slope, intercept, regression equation, correlation coefficient and Sandell's sensitivity were determined. (table-2).

Precision: The precision of an analytical method expresses the closeness of a series of individual analyte measurements obtained from multiple sampling of the equivalent sample. Precision is determined by intra-day and inter-day study. Intra-day precision was determined by analysing the same concentration for six times in a same day. Inter-day precision was determined by analysing the same concentration daily for six days. (table-3).

Accuracy: The accuracy of an analytical method says that closeness of test results obtained by that method to the true value. To assess the accuracy of the developed method, recovery studies were carried out at three different levels as 50%, 100% and 150%. In which the formulation concentration hold constant and varied pure drug concentration. (table-4).

Ruggedness: The ruggedness is defined as the reproducibility of results when the method is performed under the different in conditions. This includes distinct analyst, laboratories, instruments, temperature etc. Ruggedness was determined between different analyst; the value of %RSD was found to be less than 2. (table-5).

LOD and LOQ: The limit of detection is an individual analytical method is the smallest amount of analyte in a sample which can be reliably detected by the analytical method. The limit of quantitation is an individual analytical procedure is the smallest amount of analyte in a sample which can be quantitatively determined. LOD and LOQ was calculated by using following formula.

LOD = 3.3(SD)/S and LOQ = 3(LOD)

LOD and LOQ value of were found Quetiapine fumarate be 0.0349 and 0.105µg/ml.

TABLES

Table 1: Results of calibration curve at 221-231nm by Area under curve method.

Sl no	Concentration in µg/ml	Absorbance ± Standard deviation*
1	0	0
2	2	0.209±0.00279
3	4	0.401±0.000687
4	6	0.597±0.0035
5	8	0.795±0.00273
6	10	0.984±0.002608

*Average of six determinations.

Table 2: Regression parameter for Quetiapine fumarate at 221-231nm by Area under curve method.

Regression parameter	Results
Range(µg/ml)	2-10
Detection Wavelengths (nm)	221-231
Regression Equation	Y= 0.0982x+0.0067
Slope(b)	0.0982
Intercept(a)	0.0067
Correlation coefficient(r^2)	0.9998
Sandell's equation	0.010
Limit of detection(µg/ml)	0.0349
Limit of quantitation(µg/ml)	0.105

Table 3: Determination of precision results for Quetiapine fumarate at 221-231nm by Area under curve method.

Concentration (µg/ml)	Intra-day Absorbance ±Standard deviation*	%RSD**	Inter-day Absorbance ±Standard deviation*	%RSD**
2	0.209±0.00298	1.42	0.207±0.00125	0.57
4	0.401±0.00121	0.301	0.401±0.0005	0.124
6	0.598±0.00124	0.207	0.599±0.00103	0.171
8	0.797±0.00149	0.186	0.797±0.00047	0.058
10	0.986±0.00149	0.151	0.986±0.00076	0.077

*****Average of six determinations, **percentage relative standard deviation.

Table 4: Determination of Accuracy results for Quetiapine fumarate at 221-231nm by Area under curve method.

Spiked Levels	Amount of Sample (µg/ml)	Amount of Standard (µg/ml)	Amount Recovered	% Recovery ±Standard deviation*	%RSD**
50	6	3	8.91	99.16±0.271	0.273
100	6	6	12.08	100.6±0.149	0.147
150	6	9	14.96	99.9±0.326	0.326

*****Average of six determinations, **percentage relative standard deviation.

Table 5: Determination of Ruggedness results for Quetiapine fumarate at 221-231nm by Area under curve method.

Analysts	Analyst 1	Analyst 2
Mean absorbance	0.601	0.60
±Standard deviation*	0.00068	0.00089
%RSD	0.113	0.148

*Average of six determinations, **percentage relative standard deviation.

FIGURES

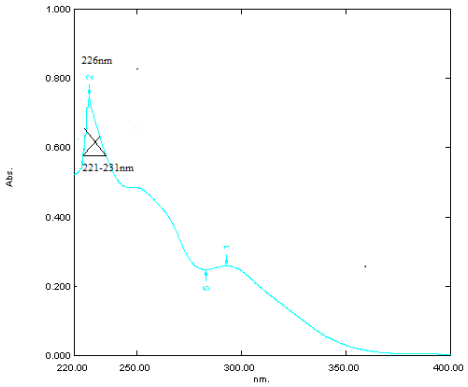

Fig. 2: Area under curve spectrum of Quetiapine fumarate at 221-231nm.

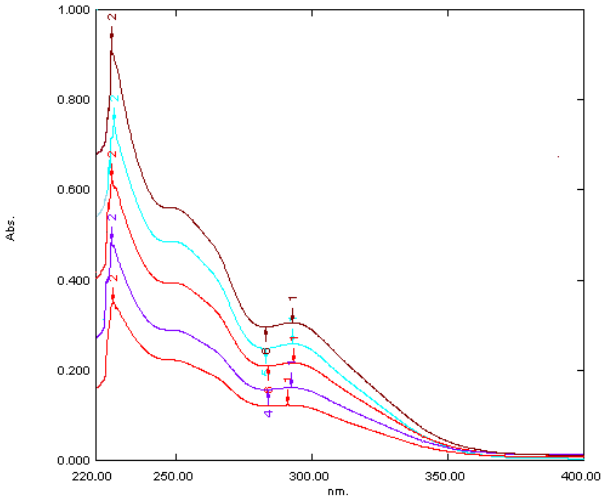

Fig. 3: Area under curve overlain spectra of Quetiapine fumarate showing absorbance at 221-231nm.

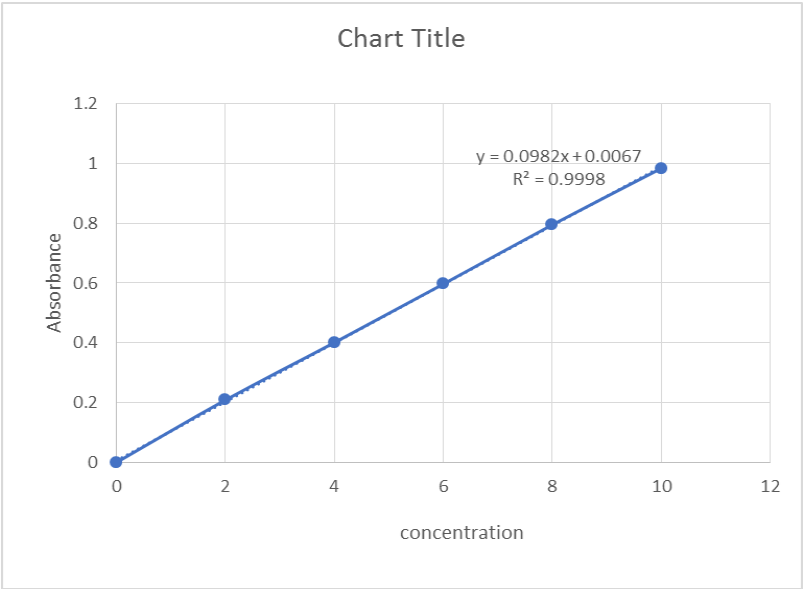

Fig. 4: Calibration curve of Quetiapine fumarate at 221-231nm by Area under curve.

CONCLUSION

As per ICH guidelines, the developed analytical method meets the acceptance criteria. It was concluded that the method is simple, specific, accurate, economical, sensitive and can be used for routine analysis of Quetiapine fumarate in bulk drug and in pharmaceutical dosage forms.

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