



METHOD DEVELOPMENT AND VALIDATION OF QUETIAPINE FUMERATE BULK AND IN TABLET DOSAGE FORM BY USING UV-SPECTROPHOTOMETRY

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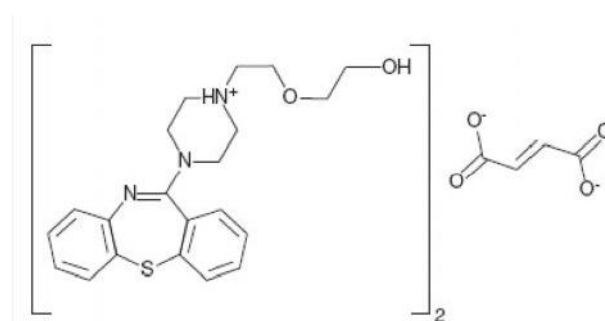
Abstract

A simple, fast and reliable Spectrophotometric method was developed for determination of Quetiapine fumarate in pharmaceutical formulation. Spectrophotometrically, Quetiapine fumarate was determined by measuring the 2D-values at 254.76nm with water as background solvent. Analytical Calibration curves were linear within a concentration range from 10 to 50µg/ml. The developed method was applied to directly and easily to the analysis of the pharmaceutical tablet preparations. %R.S.D was found to be 0.33 (Quetipin® tablet; 200 mg) respectively. The percentage recoveries werer 98 - 100% for given methods. The method was completely validated and proven to be rugged. The excipients did not interfere in the analysis. The results showed that this method can be used for rapid determination of Quetiapine fumarate in pharmaceutical tablet with linearity, precision, accuracy specificity and LOD, LOQ.

Key words: UV-Spectrophotometry, Quetiapine fumarate, Pharmaceutical dosage form.

Introduction

The chemical formula of Quetiapine fumarate is 2-[2-(4-dibenzo [b,f][1,4] thiazepin-11-yl-1-Piperazinyl) ethoxy] ethanol hemifumarate. It is Antipsychotic drug which is White or almost white powder, soluble in water and soluble in Methanol & 0.1N HCl. It is used to treat psychosis associated with Parkinson's disease and chronic schizophrenia. [1-2] The mode of action of Quetiapine fumarate, as with other drugs used to treat schizophrenia, is unknown. However, it is thought that the drug's therapeutic activity in schizophrenia is mediated through a combination of dopamine type 2 (D2) and serotonin type2 (5HT2) receptor antagonisms.



Structure of Quetiapine fumarate

Literature survey revealed that methods have been reported for a simple and accurate reverse phase liquid chromatographic method was developed for the of related substance and degradants of Quetiapine Fumarate bulk drug.[3] A simple, fast and reliable derivative Spectrophotometric methods were developed for determination of Quetiapine fumarate in pharmaceutical formulation. Second order derivative ultraviolet Spectrophotometric methods were developed. [4] A sensitive, selective, precise, and stability-indicating HPTLC method for quantitative analysis of quetiapine fumarate both as the bulk drug

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and in formulations has been established and validated.^[5] A rapid and sensitive gas chromatographic method using flame ionization detection (GC–FID) has been developed and validated for five processes related non-chromophoric impurities.^[6] A sensitive high-performance liquid chromatography-tandem mass spectrometry method was developed and validated for the quantification of quetiapine in rat plasma.^[7] A simple, sensitive isocratic rapid resolution liquid chromatographic assay method has been developed for the quantitative determination of quetiapine hemifumarate in bulk active pharmaceutical ingredient.^[8] Pharmacokinetic measurement of the psychotropic compound quetiapine and four related metabolites in human plasma was conducted using a sensitive and specific liquid–chromatography tandem mass spectrometry (LC–MS/MS).^[9] Two different analytical methods for the quality control of quetiapine in commercial formulations have been developed and compared.^[10] An original HPLC and UV method has been developed for the simultaneous determination of the atypical antipsychotic quetiapine and the geometric isomers of the second-generation antidepressant fluvoxamine.^[11]

Materials and Methods

Instrument

Absorption spectral measurements were carried out with a UV – Visible spectrophotometer (Shimadzu Model 1700, UV probe) was employed with spectral bandwidth of 1 nm and wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 5 cm matched quartz cells).

Chemicals

Quetiapine pure drug was supplied by local pharmaceutical industry, India as gift sample and used as such. Spectroscopy graded Water was used.

Preparation of standard stock solution:

Standard solution of quetiapine fumarate was prepared by dissolving 10mg of quetiapine fumarate in 10ml of water to get concentration 1000µg/ml. Different aliquots of above solution in the range 0.1 to 0.5ml were transferred into series of 10ml volumetric flask and volume made upto the mark with water to obtain the concentrations 10 to 50µg/ml. scanning

ranges was finalized for study and solutions were scanned on spectrophotometer in the uv range of 230-350nm. The spectra of was shown in Fig 2.

Preliminary solubility studies of drugs

A small quantity of standard drug were dissolved in different solvents like distilled water, methanol, ethanol, acetonitrile, isopropyl alcohol, and PH 4, 7, 9 buffer solutions. By the solubility studies we determined that the drug was dissolved in Water, 0.1N HCl for the economical study Water was taken as a solvent

Determination of λ_{max}

From the stock solutions, a working standard was prepared. The absorption spectrum for Quetiapine, the absorption spectrum was recorded using 10µg/ml solution and the maximum absorption was found to be 254nm. The Calibration curves were prepared for Quetiapine in the concentration range of 10-50 µg/ml at selected wave lengths by diluting aliquot portions of stock solution of each drug. The plots of Beer's law limit are shown in Fig.2, Fig 3.

Preparation of Sample solution:

Sample label claim 200 mg. The average weight was determined with 20 tablets, which were grounded in a mortar until fine powder. Accurately weighed amount of powder equivalent to 20mg of Quetiapine fumarate was quantitatively transferred to a 100 ml calibrated flask with the aid of Water. The volume was made up to mark, sonicate for 10 min. From above solution 1ml was transferred to 10ml calibrated flask and made up to mark with the aid of water to obtain the concentration 20 µg /ml. And filtered through whatman Filterpaper no.1. Then the solution was scanned at 254nm. The spectra of sample was shown in Fig 3.

Method Validation

The method was validated with reference to linearity, accuracy, precision, and Limit of detection & Limit of quantification.^[12]

Linearity

Linearity was performed by taking from stock solution (1mg/ml) aliquots of 0.1, 0.2, 0.3, 0.4 and 0.5 mL were taken in 10ml volumetric flasks and diluted upto

the mark with water such that the final concentration of Quetiapine fumerate in the range of 10 to 50 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.1.

Table 1: Optical characteristic and linearity data

Parameters	Quetiapine Fumerate
nm	254
Beer's law limits	10-50 µg/ ml
Correlation coefficient	0.999
Regression equation Y=mx+c	Y=0.00852-0.0026
Intercept(c)	-0.0038
Slope	0.00852
Std error	0.00894
Molar absorptivity	4021.16
Sandell sensitivity	0.117371

Accuracy

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The recovery studies were carried out by adding known amount of standard solution of three different levels. The resulting solutions were then re-analysed by proposed methods; the results are shown in table 2.

Table 2: Recovery studies

% Conc.	Amount added	Amount found	% of Recovery	%RSD
80	16	15.82	98.9	2.04
100	20	18.70	99.3	1.193
120	24	23.89	99.6	1.154
	Mean		99.2	

Precision

Precision of the methods was studied as intra-day, interday and repeatability. Intra-day study was performed by analyzing, the three different concentration of drug for three times in the same day. Inter-day precision was performed by analyzing three different concentration of the drug for three days in a week. Repeatability was performed by analyzing same concentration of drugs for six times. The results are shown in table 3.

Table 3: Results from precision

S.No	Concentration µg/ml	Inter Day		Intra day	
		S.D	%RSD	S.D	%RSD
1	10	0.001	1.23	0.0015	1.87
2	30	0.0015	0.611	0.0015	0.60
3	50	0.0025	0.595	0.00152	0.361

The limits of detection (LOD) and quantitation(LOQ)

The limits of detection (LOD) and quantitation(LOQ) calculated according to ICH guidelines¹ using the formulae: $LOD = 3.3 S/b$ and $LOQ = 10 S/b$, where S is the standard deviation of blank. The high values of molar absorptivity (ϵ), low values of Sandell sensitivity and LOD indicated the high sensitivity of the proposed methods. Absorbance values, and b is the slope of the calibration plot, are also

Fig 1: Standard curve of Quetiapine

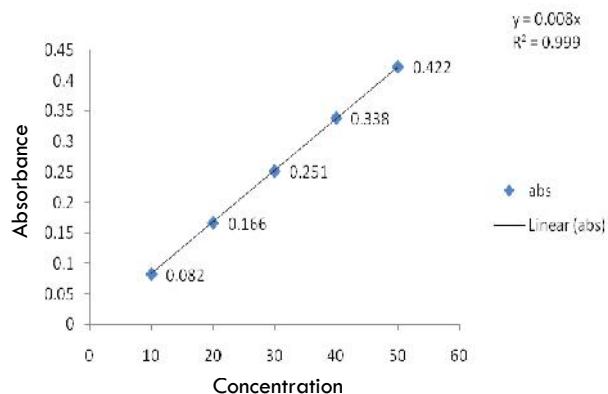
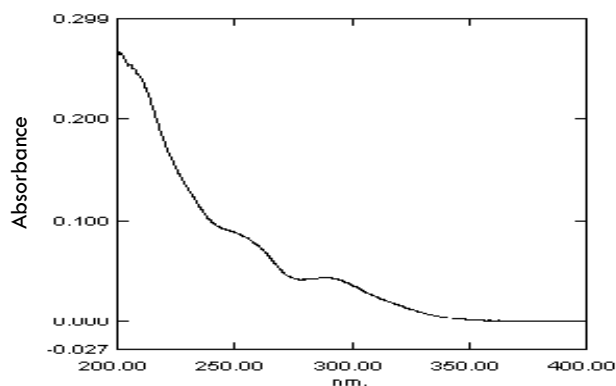


Fig 2: UV-Spectra of Quetiapine



Results and Discussion

The wavelength 254nm (λ_{max} for Quetiapine) was selected for analysis of the drugs in Water.

Linearity was observed in the range 10-50 $\mu\text{g/ml}$ ($r^2 = 0.999$) for the amount of drugs estimated by the proposed methods was in good agreement with the label claim. The proposed methods were validated. The accuracy of the methods was assessed by recovery studies at three different levels. Recovery experiments indicated the absence of interference from commonly encountered pharmaceutical additives.

Fig 3: UV-Spectra of Sample Quetiapine

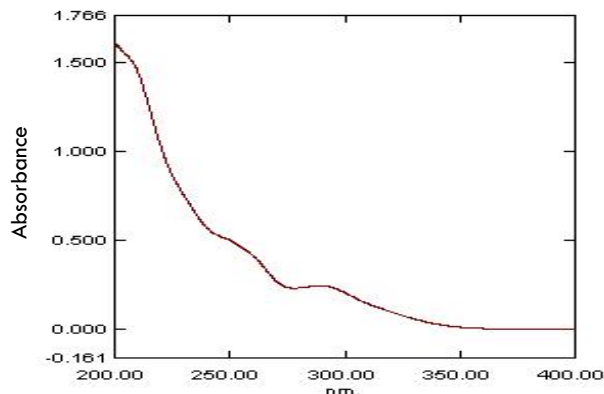


Fig 4: UV-Over line Spectra of Quetiapine

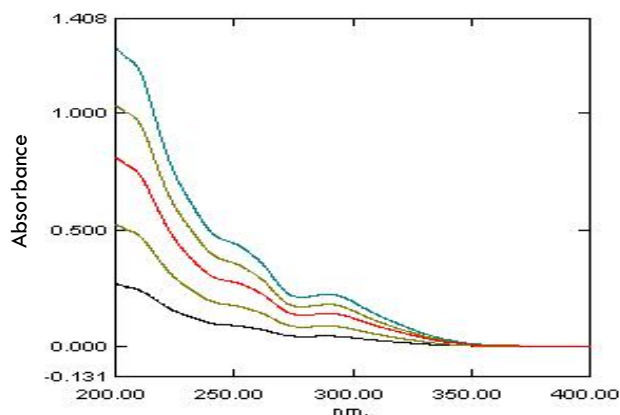


Table 5: Analysis data of Tablet formulation

Drug	Label claim mg/tab	Amount found mg/tab	Label claim (%)	S.D.*	S.E*
Quetiapine	200	197.9	98.9	0.0052	0.0026

S.D: Standard deviation, S.E: Standard error,
*Average of four estimation of tablet formulation.

The method was found to be precise as indicated by the repeatability, intra-day, inter-day analysis, showing %RSD less than 2. The results did not show any

statistical difference between operators suggesting that methods developed were rugged. The results of precision shown in table 4. All statistical data proves validity of the methods and can be used for routine analysis of pharmaceutical formulation.

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