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Development and validation of Quetiapine fumarate in pure and pharmaceutical formulation by UV-Spectrophotometric method

V G Prasanth *, Susamma Cicy Eapen , Sheeja Velayudhan Kutty and Jyothi T S

Department of Pharmaceutical Analysis, Grace College of Pharmacy, Kodunthirapully, Palakkad, India

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ABSTRACT

A simple, sensitive, selective, economical and reproducible UV spectrophotometric method has been developed for the quantitative determination of QTF in bulk drug and in pharmaceutical dosage forms. The methods are based on measurement of absorbance of QTF solution in ethanol at 207 nm. Beer's law is obeyed over the linear range 1-5 µg/mL of QTF for the method with apparent molar absorptivity value of 1434.41281 L $mol^{-1}cm^{-1}$. Limits of quantification (LOQ) and detection (LOD) are also reported. The methods were validated in accordance with the current ICH guidelines. The precision results, expressed by intra-day and inter-day relative standard deviation values, are satisfactory i.e % RSD 100.22% and 99.83 % respectively. The accuracy is also satisfactory (%RSD 0.39) and percentage recoveries are in the range 99.34-100.11% with the standard deviation of 0.39. Method have excellent linearity and range (r2 = 0.998).

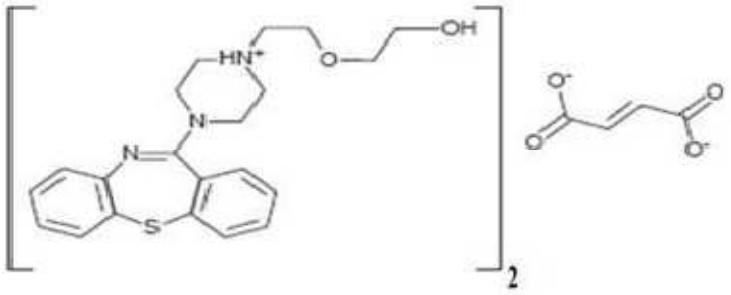
Keywords: Quetiapine Fumarate, UV spectrophotometry, molar absorptivity.

INTRODUCTION

An atypical antipsychotic, Quetiapine fumarate (2-[2-(4-dibenzo[*b*,*f*] [1,4]thiazepin-11-yl-1-piperazinyl) ethoxy] ethanol fumarate (2:1 salt)) which has a unique receptor- binding profile belonging to a new chemical class, the dibenzothiazepine derivatives [1,2]. Quetiapine is an antagonist at a broad range of neurotransmitter receptors. Quetiapine is used in the treatment of schizophrenia or manic episodes associated with bipolar disorder. As a consequence, there is an increasing demand for new analytical methods for determination of same drug in most economical way. Several HPLC methods for the determination of QUET have been reported, most of these require ultraviolet detection [3-7] as QUET is not electro active, some stability indicating[8], impurity characterizing [9]. A HPTLC method has been developed[10]. However none of these methods is sensitive enough for determination of the expected drug levels and some of them are time consuming and require complex sample pretreatment or long run times. Some gas chromatography–mass spectrometry (GC–MS) methods have also been employed, however here QUET needs to be derivatized before analysis [11]. Some HPLC–MS-MS methods

has been published for determination of QUET [9] . The goal of our work was to develop an UV spectrophotometric method for determination of QUET in solid dosage form and to use the results for analysis of drug in pharmaceuticals in most economic way, as rapid and effective ways for determination of drugs in sample matrix by spectroscopy is desirable as such no analytical paper is available for the quality control of pharmaceutical formulations containing QUET by spectroscopy.

Structure of quetiapine fumarate



MATERIALS AND METHODS

A SHIMADZU Model PHARAMASPEC-1800 UV–Vis spectrophotometer with 1.0 cm matched cells was used for the electronic spectral measurements. Quetiapine Fumarate and all other chemicals used were analytical reagent grade (AR grade). Ethanol was used as a solvent in all experimental purpose. QTF pure drug (certified to be 99.85% pure) was kindly provided by Dr. Reddy's Laboratories Ltd Hyderabad, India, as a gift and used as received. Qutipin-100 (100 mg QTF) were manufactured by Sun Pharmaceuticals Ltd, India and purchased .

I. Solutions

An accurately weighed quantity of 10 mg QUET was transferred into 100 mL volumetric flask with sufficient quantity of ethanol and sonicated. The volume was made up to the mark with ethanol. Aliquots of this standard stock solution (SSS) of QUET was diluted with ethanol and scanned over the UV range of 200-400 nm. A spectrum of drug was drawn out and selected the wavelength 207 nm for the analysis at which drug showed maximum absorbance (**Fig. No.1**).

II. Procedure

1. For calibration curve: (study of Beer- Lambert's Law)

Five mixed standards of QUE having concentrations 1, 2, 3, 4 and 5 µg/mL were prepared from SSS . Individual and overlay absorption spectra were processed at 207 nm (**Fig. No 2 and 3**). Absorbance at five different standards plotted against concentration and calibration graph forms .**(Table no 2)**

2. For absorptivity study :

From the SSS , a solution of 5 µg/ml concentration was prepared . Absorbance of such five of QUET standard solution measured and results of absorptivity study out by A1% 1cm[12]. (**Table No.1**)

3. Estimation of QUET in tablet formulation sample :

Twenty tablets were weighed accurately and powdered. Powder equivalent to 10 mg[13] (Label claim-100 mg) was taken and transferred to 100 ml volumetric flask and dissolved in ethanol, sonicate for 10 min, filtered and further diluted to get a final concentration of 5 µg/mL of QUET (label claim basis). The absorbance of solution is measured at the selected wavelength i.e 207 nm.(**Table No. 2)**

RESULTS AND DISCUSSION

The method was accurate , simple , rapid , reliable , sensitive , reproducible and economical . The wavelength 207 nm was selected which showed good linearity between concentrations .

Table No .1 Absorptivity (1%, 1cm) values of quet at 207 nm

Sl. No.	Conc. g/100mL	Abs.	A (1%, 1cm)*
1	0.0005072	0.720	1419.55836
2	0.0005683	0.734	1444.02912
3	0.0005003	0.712	1423.14611
4	0.0005126	0.743	1449.47327
5	0.0005098	0.732	1435.85721
Mean			1434.41281
± S.D.			1.06196
% RSD			0.074

Table No. 2: Estimation of quet in tablet formulation

Sl. No.	Wt. Of tablet powder taken mg (label claim 100mg)	Abs. at 207 nm	Amount of drug per tablet (mg)	% Purity
1	21.2	0.720	99.44	99.44
2	21.34	0.734	100.71	100.71
3	21.06	0.712	98.99	98.99
4	21.4	0.743	101.66	101.66
5	21.32	0.732	100.53	100.53
Mean			100.27	100.27
± SD			1.06309	1.06309
% RSD			1.06023	1.06023
Variance			1.13018	1.13018

Table no 2-Calibration Curve

Sl.no	Concentration (µg/ml)	Absorbance
1	1	0.138
2	2	0.267
3	3	0.428
4	4	0.577
5	5	0.712

Table no 3 Determination of accuracy by percentage recovery method

Drug	Tablet amount (mg)	Amount of pure drug added (mg)	Level of addition (%)	Total Drug estimated (mg)	Amount of pure drug Recovered (mg)	% recovery
QTF	21	8	80	18.13	8.09	99.34
	21	10	100	20.22	10.01	100.11
	21	12	120	22.31	11.95	99.58
Mean						99.68
±SD						0.39402
%RSD						0.39528
Variance						0.15525

Table No.4: Results of estimation in intra-day studies and inter-day studies

Sl. No	Intra-day			Inter-day		
	Hour	Wt. of tablet powder taken (mg)	% Label Claim	Day	Wt. of tablet powder taken (mg)	% of Labeled Claim
1	0 hr	21.21	99.44	Day-1	21.41	100.65
2	3 hr		100.53	Day-2		99.44
3	6 hr		100.71	Day-3		99.4
Mean			100.22	Mean		99.83
± SD			0.68724	± SD		0.72436
% RSD			0.68573	% RSD		0.72559
Variance			0.47230	Variance		0.52469

Table no-5 Validation parameters

Sl No	Parameter	Result
1	Absorption maxima (nm)	207
2	Linearity range (µg /ml)	1-5
3	Slope	0.143
4	Intercept	0.006
5	Correlation coefficient (r2)	0.999
6	Molar absorptivity	1434.41281
7	Accuracy (% recovery)	99.68
8	Precision	100.22% (intraday precision) and 99.83% (inter day precision)
9	LOD (µg /ml)	0.02
10	LOQ (µg /ml)	0.12

Figure no 1. DETERMINATION OF λmax OF QUET

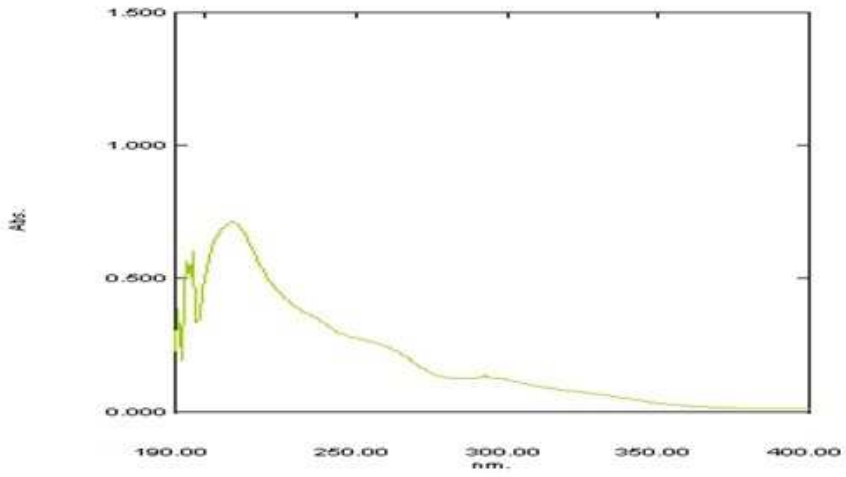


Figure no.2 PLOT OF BEERS- LAMBERT'S LAW FOR QUET AT 207 nm

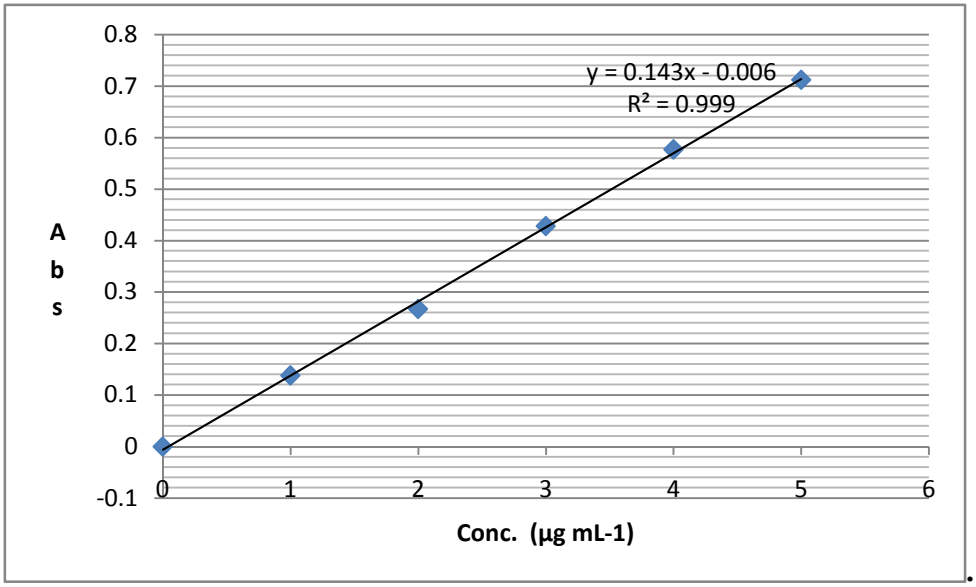
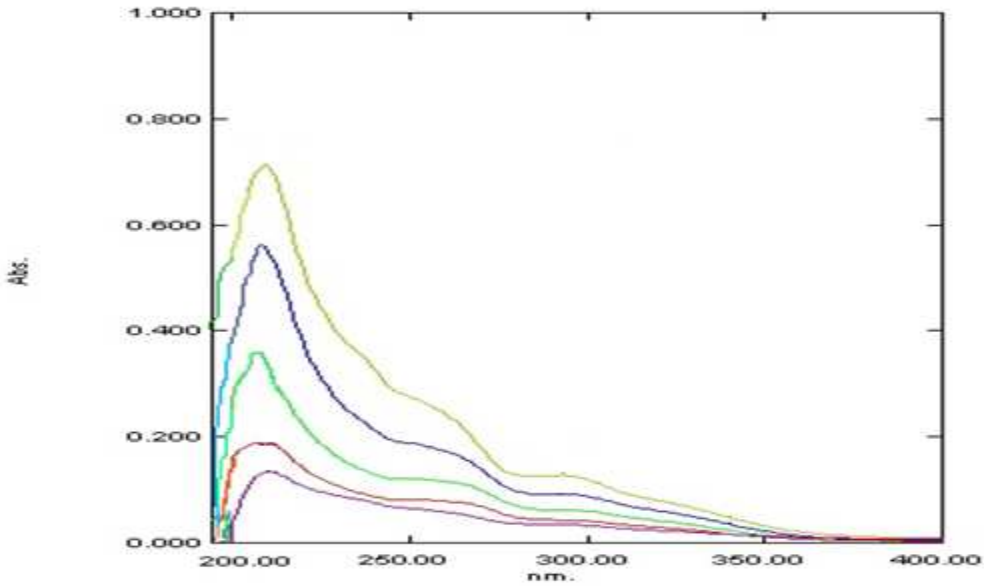


Figure no. 3 OVERLAY SPECTRA OF QUET



IV Validation of analytical data

The study of Beer's -Lambert's law was checked by preparing standard solutions at 5 different concentrations and the linearity of the calibration graphs and conformity of the UV measurements of the proposed methods to Beer's law were proven by the values of the correlation coefficient (r) of the absorptivity study. The linear range of concentrations for the analysis of QUET was found to be 1-5 µg mL^{-1} for UV spectrophotometric method . (**Figure No.2)**

The utility of this method was verified by analysis of a recovery assay in the marketed tablet sample. Tablet sample (Label claim- 100mg) QUET was prepared and processed according to the proposed method. Recoveries were determined by standard addition

method (SAM). The mean percentage recoveries of QUET by UV method were found to be 99.68 %. Results represent accuracy by study of recovery. (**Table No.3**)

The reproducibility of this developed method established by study of precision for QUET was determined by five replicates analysis on the tablet sample[14-16] . The mean relative standard deviations were found to be 100.27 % for UV spectrophotometric method. (**Table No.2**)

Correlation coefficient for UV spectrophotometric method was found to be 0.998 of QUET was found to be linear . (**Figure No.2)**

The Ruggedness of the proposed method checked by means of two parameters i.e . Intraday & Interday[17] . For intra –day inter –day study , standard deviation and relative standard deviations were found to be 0.68724, 0.685732 % and 0.72437 , 0.7255953 % respectively .(**Table No.4)**

CONCLUSION

Validation parameters complies , the applied spectrophotometric methods of analysis are simple , sensitive , accurate and satisfactorily capable for determination of QUET in tablet formulation with reproducible specific results. The linear concentration range of preordain elaborated method were observed wider (**Table no-5).** In addition , the analyses by proposed method is cheaper and economic too . Thus , proposed UV spectrophotometric method is applicable for the quality control and routine analysis and may also be proposed for determination from biological fluids or other solid dosage form containing same drugs .

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