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Original Scientific Article

Extractive Spectrophotometric Determination of Quetiapine Fumarate in Pharmaceuticals and Spiked Human Urine

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Abstract A simple, sensitive and selective extractive spectrophotometric method for the determination of quetiapine fumarate (QTF) in bulk drug, tablets and spiked human urine sample is described. The method is based on the formation of a chloroform extractable yellow ion-pair complex between basic nitrogen of the drug (QTF) and the dye quinoline yellow (QY) in acetate-hydrochloride buffer (pH 2.56) medium. The formed ion-pair complex exhibited an absorption maximum at 420 nm. Beer's law is obeyed over the concentration range 2.5–25 μg mL^{-1} with an apparent molar absorptivity value of 2.02×10^4 L mol^{-1} cm^{-1}. The Sandell sensitivity, limits of detection (LOD) and quantification values are also reported. The composition of the ion-pair was established by Job's continuous variations method and it was found to be 1:1 (QTF:QY). The proposed method was successfully applied for the determination of QTF in bulk drug, tablets and spiked human urine without any interference. (doi: 10.5562/cca1770)

Keywords: quetiapine fumarate, determination, spectrophotometry, quinoline yellow, pharmaceuticals

INTRODUCTION

Quetiapine fumarate (QTF) is an atypical antipsychotic drug.[1] It is a dibenzothiazepine derivative chemically known as {2-(2-(4-dibenzo[*b,f*] [1,4]thiazepine-11-yl-1-piperazinyl)ethoxy)ethanol, fumaric acid (1:2 salt; formula $C_{29}H_{33}N_3O_{10}S$; molecular weight: 615.66)} (Figure 1). QTF is prescribed for treatment of schizophrenia and other psychotic or schizoactive disorders.[2–4] QTF was approved by the FDA for the treatment of Bipolar I (Bipolar II) disorder as a monotherapeutic agent.[5]

QTF is not official in any pharmacopoeia. Several analytical methods such as HPLC,[6–13] chemiluminescence spectrometry,[14] electrospray ionization MS,[15–18] tandem MS/MS detection,[19–22] UPLC with tandem MS detection,[23,24] GC[25,26] and voltammetry[27] are found in the literature for the determination of QTF in biological materials.

Various techniques such as polarography,[28] capillary zone electrophoresis,[29,30] HPTLC,[31–33] HPLC[34–37] and UV spectrophotometry[29,38] have been reported for the estimation of QTF in pharmaceutical preparations. In the UV spectrophotometric method[29] reported by Pucci *et al*., QTF was assayed in methanol after converting the drug into its free base using a buffer of pH 2.5 and the absorbance was measured at 246 nm. This method is applicable to determine the QTF in the concentration range 5–25 μg mL^{-1}. Another UV method reported by Fursule *et al.*[38] involves measurement of absorbance of QTF solution in water at 290 nm and in this method Beer's law is obeyed in the range, 6–54 μg mL^{-1}. Since the buffer was used to convert QTF into its free base,[29] due to incomplete conversion and extraction of base; and at shorter analytical wavelength used, erratic results may obtained[29,38] in addition to the method being less sensitive.[38] Arulappa *et al.*[39] have reported a visible spectrophotometric method based on ion-pair complexation reaction with bromocresol green as reagent. The ion-pair formed in acid medium was extracted into chloroform and measured at 415 nm over a concentration range of 5–25 μg mL^{-1} QTF. The method was applied to the determination of QTF in pharmaceuticals with narrow linear dynamic range and it was not applied to urine. Present authors have also reported two extraction-free spectrophotometric methods[40] for the determination of QTF in pure form and in its dosage forms. The procedures are applicable over the ranges of 1–20 (method A) and 1.5–30 μg mL^{-1} (method B) QTF with molar absorptivity values of 2.97×10^4 and 1.97×10^4 L mol^{-1} cm^{-1}. Though these methods are more sensitive, are applicable only for pure drug and tablets but not applied for spiked

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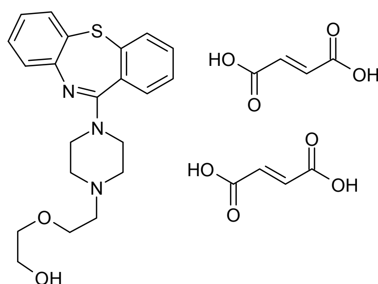


Figure 1. Chemical structure of QTF.

human urine sample. Besides, the absorbance measurements were made at 410 and 380 nm, which are some what shorter where the interferences from the excipients will be more.

In the present investigation, the authors report the development and validation[41] of an accurate, reproducible and sensitive extractive spectrophotometric method based on the formation of chloroform soluble ion-pair complex between QTF and quinoline yellow (QY; IUPAC Name: disodium 2-(1,3-dioxoinden-2-yl)quinoline-6,8-disulfonate) (Figure 2) at pH 2.56. The method was applied to the determination of QTF in pure drug, tablets and spiked human urine. No interference was observed in the assay of QTF from common excipients present in tablets and other basic substances present in urine.

EXPERIMENTAL

Apparatus

A Systronics model 106 digital spectrophotometer (Systronics India Ltd, Ahmedabad, India) with 1 cm path length quartz cells and an Elico model L1-120 pH meter were used for the measurement of absorbance and pH values, respectively.

Reagents and Solutions

All chemicals used were of analytical reagent grade and solutions were prepared in distilled water. Chloroform (spectroscopic grade) was purchased form Merck, Mumbai, India.

Quetiapine Fumarate (QTF) and its Tablets
Pharmaceutical grade of QTF was kindly gifted by Cipla Ltd, Bangalore, India, and is certified to be 99.5 % pure. It was used without further purification. Qutipin-200 and Qutipin-100 (both from Sun Pharmaceuticals Ltd, India) tablets were purchased from local market.

Sulphuric Acid (H_2SO_4; 0.1 mol L^{-1})
Concentrated acid (S.D. Fine Chem, Mumbai, India, Sp. gr. 1.84) was appropriately diluted with water to get 0.1 mol L^{-1}.

Hydrochloric Acid (HCl; 1 mol L^{-1})
Concentrated acid (S.d. Fine Chem, Mumbai, India, Sp. gr. 1.18) was diluted appropriately with water to get 1 mol L^{-1}.

Sodium Acetate (NaOAc; 1 mol L^{-1})
A 1 mol L^{-1} solution was prepared by dissolving an accurately weighed amount of 13.6 g of pure sodium acetate trihydrate (S.D. Fine Chem Ltd, Mumbai, India) in 100 mL of water in a volumetric flask.

Acetate-hydrochloride Buffer (pH 2.56)
Fifty mL each of 1 mol L^{-1} NaOAc and 1 mol L^{-1} HCl were transferred into a 250 mL volumetric flask and the volume was made upto the mark with water. The pH of this solution was adjusted using HCl/NaOAc.

Quinoline Yellow (QY) solution (500 µg mL^{-1})
A 500 µg mL^{-1} solution of dye was prepared just before use by dissolving an accurately weighed quantity of QY (Loba Chemie Ltd, Mumbai, India, certified to be 70 % pure) in water and it was filtered.

Urine Sample
Drug-free human urine was obtained from a healthy male aged about 28 years.

QTF Solution (100 and 50 µg mL^{-1})
A stock standard solution of QTF was prepared by dissolving an accurately weighed 10 mg of pure drug in 0.1 mol L^{-1} H_2SO_4 and the volume was made up to 100 mL in a volumetric flask with the same acid to get 100 µg mL^{-1} QTF. This solution was diluted appropriately with 0.1 mol L^{-1} H_2SO_4 to get 50 µg mL^{-1} QTF and used for the assay.

General Recommended Procedures

Into a series of 125 mL separating funnels, 0.5–5.0 mL aliquots of 50 µg mL^{-1} QTF standard solution were transferred by means of a microburette. The total volume in each separating funnel was adjusted to 5 mL by adding 0.1 mol L^{-1} H_2SO_4. To each funnel were added 10 mL of water, 1 mL of 1 mol L^{-1} NaOAc, 4 mL buffer of pH 2.56 and 5 mL of dye solution. The content was mixed thoroughly, and after 5 min, the ion-pair complex was extracted with 10 mL of chloroform by shaking for 30 seconds and the layers were allowed to separate. The organic layer was then passed over anhydrous sodium

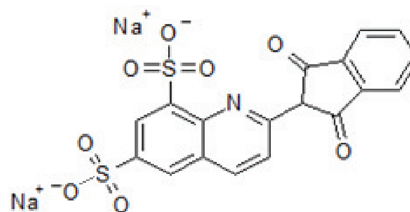


Figure 2. Structure of quinoline yellow (QY).

sulphate and absorbance was measured at 420 nm against the reagent blank similarly prepared in the absence of QTF. The procedure was repeated three times and standard graph was prepared by plotting the absorbance *versus* drug concentration. The concentration of the unknown was read from the calibration graph or computed from the regression equation derived using the absorbance-concentration data.

Procedure for Tablets

Twenty tablets were weighed and pulverized. An amount of the tablet powder equivalent to 5 mg of QTF was weighed and transferred into a clean 100 mL volumetric flask containing ~70 mL 0.1 mol L^{-1} H_2SO_4. After shaking the content for 20 min, the volume was brought upto the mark with the same acid and filtered through Whatman No 42 filter paper. A suitable aliquot (say 3 mL) of this solution (50 μg mL^{-1} QTF) was subjected to analysis by using the general procedure described earlier.

Procedure for Spiked Human Urine

A 12.5 mL aliquot of 100 μg mL^{-1} QTF solution was mixed with 3 mL of urine and 2 mL of acetonitrile in a 25 mL volumetric flask and the volume was made upto the mark with 0.1 mol L^{-1} H_2SO_4. The resulting solution was filtered through Whatman No 42 filter paper and three different aliquots of the filtered solution were subjected to analysis by following the general procedure. The concentration of QTF in urine was found using standard graph or from the regression equation.

Procedure for the Analysis of Placebo Blank and Synthetic Mixture

A placebo blank containing starch (10 mg), acacia (15 mg), hydroxyl cellulose (10 mg), sodium citrate (10 mg), talc (20 mg), magnesium stearate (15 mg) and sodium alginate (10 mg) was made and its solution was prepared as described under tablets and then subjected to analysis. The absorbance of the placebo solution was almost equal to the absorbance of the blank which revealed no interference from the excipients added to pure drug.

A synthetic mixture was prepared by adding pure QTF (100 mg) to the above mentioned placebo blank and the mixture was homogenised. Synthetic mixture containing 5 mg of QTF was weighed and its solution in a 100 mL volumetric flask was prepared as described for tablets. Three different aliquots were subjected to analysis by following the general procedure. The concentration of QTF was found from the calibration graph or from the regression equation.

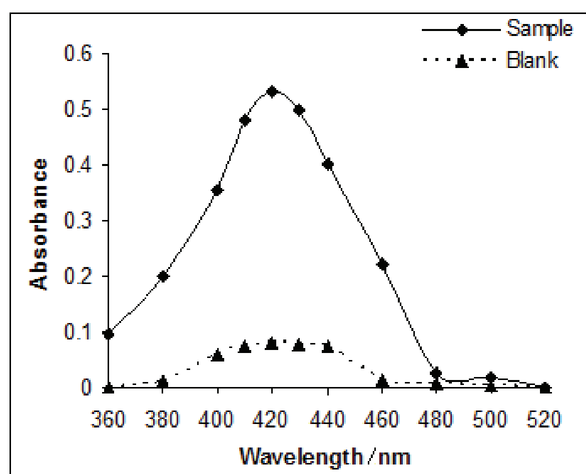


Figure 3. Absorption spectra of QTF-QY ion-pair complex (15 μg mL^{-1} QTF) and blank.

RESULTS AND DISCUSSION

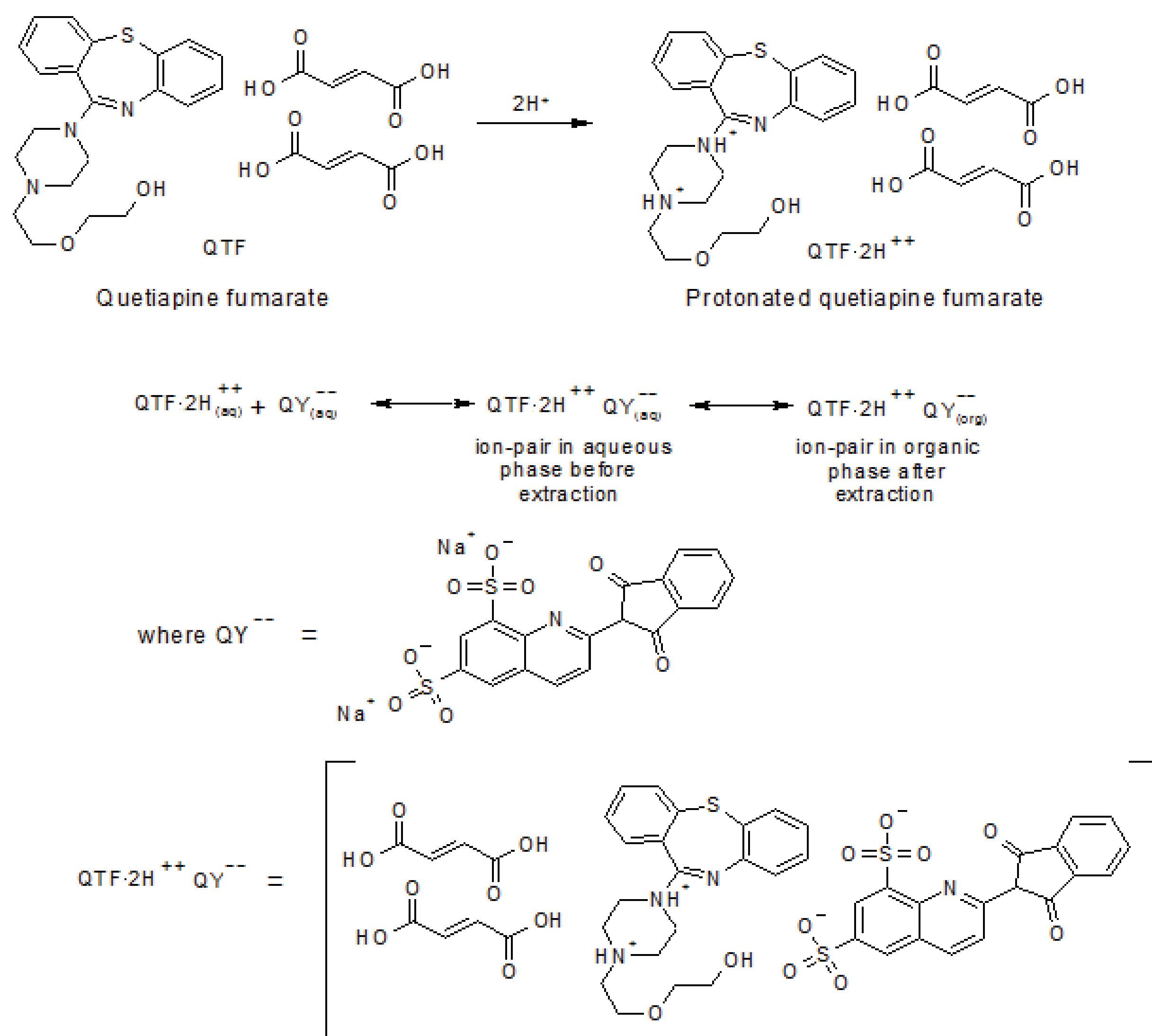
The nitrogenous drugs are present in a positively charged protonated forms and anionic dyes are present mainly in anionic form at acidic pH. So, in acidic medium (pH 2.56) the protonated QTF (QTF. $2H^{++}$), forms an ion-pair complex with the anionic dye QY ($QY^{-\,-}$) which is soluble in chloroform and showed maximum absorbance at 420 nm (Figure 3). Therefore, this wavelength was fixed as analytical λ and all absorbance measurements were made at this wavelength. The possible reaction pathway for the formation of QTF-QY ion-pair complex is shown in Scheme 1.

Optimisation of Reaction Conditions for Complex Formation

Preliminary investigations were carried out to establish the most favourable conditions to give a highly intense colour which could be used for the quantitative determination of the drug. Optimum conditions were fixed by varying one parameter at a time while keeping other parameters constant and observing its effect on the absorbance at 420 nm against respective blank. The influence of each of the following variables on the reaction was tested.

Effect of pH of Aqueous Phase and Volume of Buffer Solution

The effect of pH of the aqueous phase on the absorbance of QTF-QY ion-pair complex was studied by adding different volumes of 1 mol L^{-1} NaOAc (0–5 mL) to the aqueous phase before adding dye solution and the effective pH of the aqueous phase was recorded. It was noticed that the maximum colour intensity and highest absorbance value for QTF-QY ion-pair complex were observed in the presence of 1 mL of 1 mol L^{-1} NaOAc. The effective pH of the aqueous phase in the presence of 1 mL of 1 mol L^{-1} NaOAc was measured to be 2.56 ± 0.02. At lower and higher pH, the absorbance of the QTF-QY ion-pair complex started decreasing



Scheme 1. Probable reaction pathway for the formation of 1:1 ion-pair complex between QTF and QY.

(Figure 4a). Hence, pH 2.56 was fixed as optimum for complete formation of QTF-QY ion-pair complex. Various amounts of acetate-HCl buffer solution of pH 2.56 were used in the investigation to establish its effect on absorbance. There was almost no influence on the absorbance from 3 to 6 mL of buffer but an amount less than 3 mL resulted in unsatisfactory separation of the organic phase during the extraction and lower absorbance values (Figure 4b). So, 4 mL of buffer was used in the investigation.

Effect of Reagent Concentration

The influence of dye concentration on the absorbance of ion-pair complex was investigated by adding different volumes of 500 µg mL^{-1} QY solution (2–8 mL) to 3 mL QTF (50 µg mL^{-1}) solution. With volumes less than 4 mL, lower absorbance values were obtained and when the volume was greater than 6 mL, blank showed higher absorbance values and there was no clear separation of the two phases. A constant and maximum absorbance was obtained in the range of 4–6 mL of QY (Figure 5). Therefore, a 5 ml of 500 µg mL^{-1} QY solution in a total volume of 25 mL of aqueous phase was chosen as optimal for complete complexation.

Effect of Extraction Solvent

The effect of several organic solvents viz., chloroform, dichloromethane, carbon tetrachloride, 1,2-dichloroethane, hexane, ether, ethyl acetate and benzene was studied for the effective extraction of colored species from aqueous phase. Chloroform was found to be the most suitable for the extraction of colored complex, yielding maximum absorbance and considerably lower extraction ability for the reagent blank.

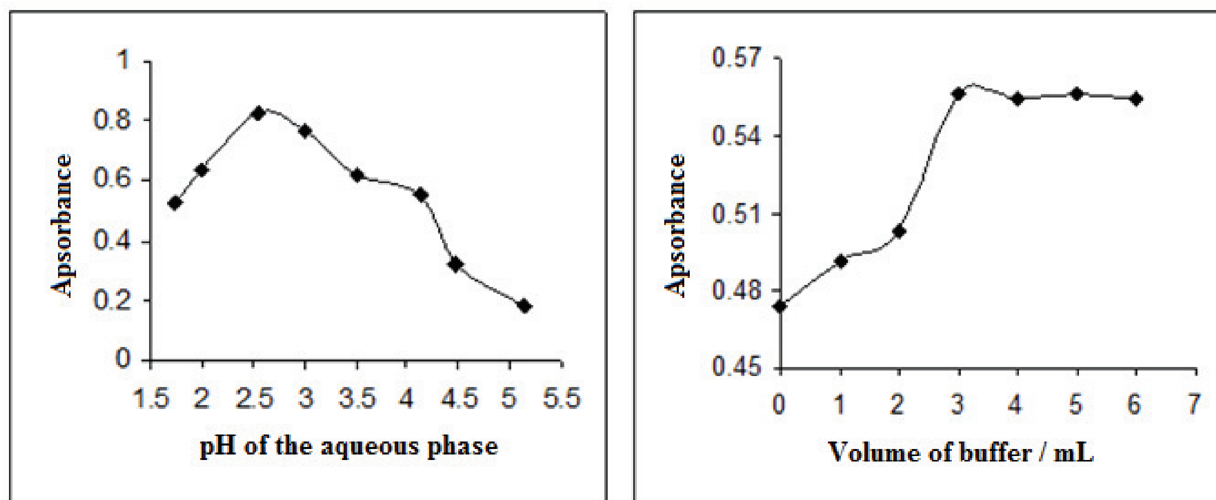


Figure 4. Effect of: a) pH and b) volume of buffer on the absorbance of QTF-QY ion-pair complex.

Effect of Ratio of Aqueous to Organic Phases

The effect of ratio of aqueous to organic phases was examined by adding 5–25 mL of water to 5 mL of QTF solution before the addition of dye solution. The extraction was performed in the presence of different volumes of chloroform (5–20 mL). Maximum and constant absorbance values were obtained with quick separation of two phases in the presence of 10–20 mL of water and 10 mL of chloroform. Therefore, aqueous to organic phase ratio of 2.5:1 was used in the investigation.

Number of Extractions

It was observed that only one extraction with 10 mL portion of chloroform was adequate to achieve a quantitative recovery of the complex and the shortest time to reach equilibrium between two phases.

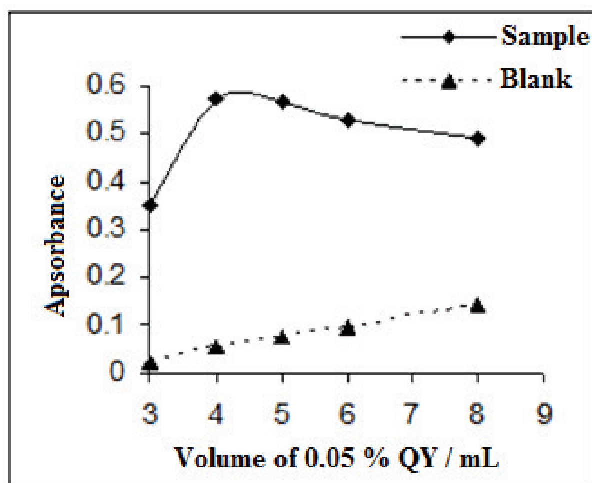


Figure 5. Effect of volume of dye on the absorbance of ion-pair complex (15 µg mL^{-1}).

Reaction Time

After the addition of dye, the effect of standing time on the complex formation was studied from 5 to 30 min before extraction. A contact time of 5 min was found adequate for full complex formation.

Effect of Shaking Time

The effect of shaking time on the extraction of QTF-QY ion-pair was studied by shaking separating funnel for different times ranging from 30 to 180 s after adding chloroform. Constant absorbance readings were obtained from 45 s and onwards and, hence a 60 s shaking time was fixed.

Equilibration Time and Stability of the Coloured Complexes

The organic and aqueous phases were clearly separated in less than 1 min. The drug-dye ion-pair complex was stable for more than 2 h at laboratory temperature (30 ± 2 ºC).

Effect of Order of Addition of Reactants

The sequence of order of addition of reactants prior to extraction had very little effect on the absorbance. So the order of addition of reactants should be in the described manner.

Composition of Ion-pair Complex

The composition of the ion-pair complex was established by Job's method of continuous variations[42] using equimolar concentrations of drug and dye (5.52×10^{-4} mol L^{-1}). The results indicated that 1:1 (drug:dye) ion-pair is formed through the electrostatic attraction between the positive protonated drug and

anionic dye. Seven solutions containing QTF and QY in various molar ratios, with a total volume of 5 mL, in addition to 10 mL of H_2O, 1 mL of 1 mol L^{-1} NaOAc and 4 mL of buffer solution, were prepared. The extraction was performed using 10 mL of chloroform and the absorbance was subsequently measured at 420 nm. The graph of the results obtained (Figure 6) gave a maximum at a molar ratio of X_{max} = 0.5 which indicated the formation of 1:1 QTF:QY ion-pair complex.

Conditional Stability Constant (K_f) of the Ion-pair Complex

The conditional stability constant (K_f) of the ion-pair formed by QTF with QY was calculated from the continuous variation data using the following equation:[43]

$$K_f = \frac{\dfrac{A}{A_m}}{\left[1-\dfrac{A}{A_m}\right]^{n+2} C_M\,(n)^n}$$

where A is the maximum observed absorbance and A_m is the absorbance value when whole amount of drug is associated. C_M is the mole concentration of drug at the maximum absorbance and n is the combination ratio of ion-pair considered. The log K_f value obtained for the QTF-QY ion-pair, on three determinations is 5.12 ± 0.56.

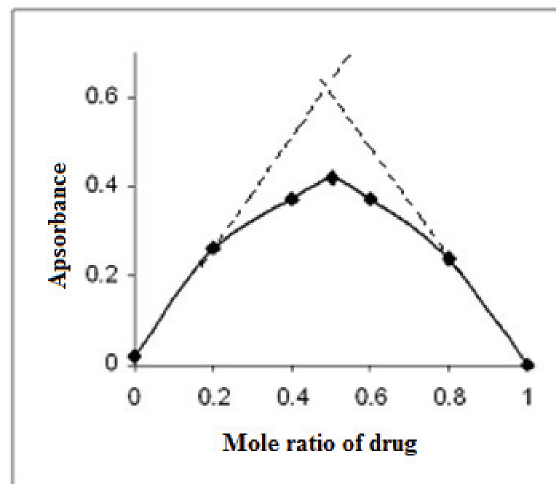


Figure 6. Job's method of continuous variation graph for the ion-pair complexation reaction of QTF with QY. [QTF] = [QY] = 5.52×10^{-4} mol L^{-1}.

METHOD VALIDATION

Linearity, Sensitivity, Limits of Detection and Quantification

Calibration graph was constructed from six points covering the concentration range 2.5–25.0 µg mL^{-1}. Regression analysis of the Beer's law data indicated a linear relationship between absorbance and concentration, (Table 1) which is corroborated by high value (close to unity) of the correlation coefficient. A plot of log absorbance and log concentration yielded a straight line with slope equal to 1.1, further establishing the linear relation between the two variables. The calculated molar absorptivity and Sandell sensitivity[44] values are summarized in Table 1. The limits of detection (LOD) and quantification (LOQ) were calculated using the formulae: LOD = 3.3 S/b and LOQ = 10 S/b, (where S is the standard deviation of blank absorbance values, and b is the slope of the calibration plot), calculated according to the ICH guidelines[41] are also summarized in Table 1. The high value of ε and low value of Sandell sensitivity and LOD indicates the high sensitivity of the proposed method.

Precision and Accuracy

The assay described under "General Procedure" was repeated seven times within the day to determine the repeatability (intra-day precision) and five times on different days to determine the intermediate precision (inter-day precision) of the method. The assay was performed on three levels of analyte. The results of this study are summarized in Table 2. The percentage relative standard deviation (RSD / %) values were ≤ 2.55 % (intra-day) and ≤ 2.88 % (inter-day) indicating high

Table 1. Sensitivity and regression parameters

Parameter	Value
λ_{max} / nm	420
Linear range / µg mL^{-1}	2.5–25.0
Molar absorptivity (ε) / L mol^{-1} cm^{-1}	2.02×10^4
Sandell sensitivity* / µg cm^{-2}	0.0304
Limit of detection (LOD) / µg mL^{-1}	0.11
Limit of quantification (LOQ) / µg mL^{-1}	0.33
Regression equation, Y**	
Intercept (a)	–0.013
Slope (b)	0.0346
Standard deviation of a (S_a)	0.0284
Standard deviation of b (S_b)	0.0020
Variance (S_a^2)	8.1×10^{-4}
Regression coefficient (r)	0.9990

*Limit of determination as the weight in µg per mL of solution, which corresponds to an absorbance of A = 0.001 measured in a cuvette of cross-sectional area 1 cm^2 and l = 1 cm.
**$A = bx + a$, Where A is the absorbance, x is concentration in µg mL^{-1}, a is intercept and b is slope.

Table 2. Evaluation of intra-day and inter-day accuracy and precision

QTF taken / μg mL^{-1}	Intra-day accuracy and precision (n = 7)			Inter-day accuracy and precision (n = 5)		
	QTF found ± CL / μg mL^{-1}	RE / %	RSD / %	QTF found ± CL / μg mL^{-1}	RE / %	RSD / %
10.0	10.27±0.19	2.67	1.97	10.36±0.27	3.60	2.08
15.0	15.51±0.37	3.40	2.55	15.48±0.55	3.20	2.88
20.0	19.69±0.20	1.53	1.10	20.15±0.49	0.75	1.98

RE / % − percent relative error; RSD / % − relative standard deviation and CL − confidence limits were calculated from: CL = ± $tS/\sqrt{n}$. (The tabulated value of t is 2.45 and 2.77 for six and four degrees of freedom respectively, at the 95 % confidence level; S = standard deviation and n = number of measurements).

precision of the method. The accuracy of the method was determined by the percent mean deviation from known concentration, bias % = [(concentration found – known concentration) × 100 / known concentration]. Bias was calculated at each concentration and these results are also presented in Table 2. Percent relative error (RE / %) values ≤ 3.60 % demonstrate the high accuracy of the proposed method.

Selectivity

The results obtained from placebo blank and synthetic mixture analyses revealed that the inactive ingredients used in the preparation did not interfere in the assay of active ingredient. The absorbance values obtained from the placebo blank solution were almost equal to the absorbance of the blank which revealed no interference from the adjuvants. To study the role of additives added to the synthetic sample, 3 mL of the resulting solution prepared by using synthetic mixture containing 50 μg mL^{-1} of QTF was assayed (n = 4). The yielded recoveries of 94.00–102.7 % with RSD values in the range 0.99–2.83 % demonstrated the accuracy as well as the precision of the proposed method and complement the findings of the placebo blank analysis with respect to selectivity.

Robustness and Ruggedness

The robustness of the method was evaluated by making small incremental changes in volume of dye, buffer and contact time, and the effect of these changes on the absorbance of the colored systems was studied. The changes had negligible influence on the results as revealed by small intermediate precision values expressed as RSD (≤ 2.55 %). Method ruggedness was demonstrated by having the analysis done by four analysts, and also by a single analyst performing analysis on four different instruments in the same laboratory. Intermediate precision values (RSD) of this study were in the range 1.89–3.21 % indicating acceptable ruggedness. The results are presented in Table 3.

Application to Tablets

The proposed method was applied for the quantification of QTF in commercial tablets. The results obtained were compared with those obtained using a conventional UV spectrophotometric method,[29] where the absorbance of the methanolic solution of QTF was measured at 246 nm. Statistical analysis of the results did not detect any significant difference in the performance of the proposed method to the reference method with respect

Table 3. Method robustness and ruggedness expressed as intermediate precision (RSD / %)

QTF taken / μg mL^{-1}	Robustness			Ruggedness	
	Parameters altered			Inter-analysts (RSD / %), (n = 4)	Inter-instruments (RSD / %), (n = 4)
	Volume of Dye*	Volume of buffer**	Reaction time#		
10.0	2.34	2.55	2.26	2.45	3.21
15.0	1.40	1.86	1.95	3.10	1.89
20.0	0.85	2.10	1.55	2.85	2.11

*The volumes of dye used were 5 ± 1.0 ml.
**The volumes of buffer used were 4 ± 0.5 mL.
#The reaction times were 5 ± 1.0 min.

Table 4. Results of analysis of tablets by the proposed method and statistical comparison of the results with the reference method

Tablet brand name[Ψ]	Nominal amount (mg/tablet)	Found[*] (Percent of label claim ± SD)	
		Reference method	Proposed method
Qutipin-200	200	97.16±1.28	98.36±0.86 ***t*** = 1.77 ***F*** = 2.22
Qutipin-100	100	100.6±1.27	101.3±0.54 ***t*** = 1.22 ***F*** = 5.53

[*]Mean value of 5 determinations.
(Tabulated *t*-value at the 95 % confidence level and for four degrees of freedom is 2.77). (Tabulated *F*-value at the 95 % confidence level and for four degrees of freedom is 6.39).
[Ψ]Marketed by: Sun Pharmaceuticals Ltd, India.

to accuracy and precision as revealed by the Student's *t*-value and variance ratio *F*-value.[45] The results of this study are given in Table 4.

Application to Spiked Human Urine

The proposed method was applied to the determination of QTF in spiked human urine by following the general procedure described above. The recovery of the drug from spiked urine analysis was calculated by triplicate analysis of urine sample containing 10, 15 and 20 μg mL^{-1} QTF separately. The percentage recovery values of 98.40–103.1 with standard deviation 0.84–1.48 % showed the non-interference of other materials present in urine to the assay of QTF with considerable accuracy. The analytical results obtained for QTF in human urine sample are presented in Table 5.

Recovery Study

To further assess the accuracy of the proposed method, recovery experiment was performed by applying the standard-addition technique. The recovery was assessed by determining the agreement between the measured standard concentration and added known concentration to the sample. The test was done by spiking the pre-analysed tablet powder with pure QTF at three different levels (50, 100 and 150 % of the content present in the tablet powder (taken) and the total was found by the proposed method. Each test was repeated three times. From this test the percentage recovery values were found in the range of 95.95–104.2 with standard deviation values from 0.26 to 1.2 %. Closeness of the results to 100 % showed the fairly good accuracy of the method. These results are shown in Table 6.

Table 5. Application of the proposed method to QTF concentration measurements in spiked human urine

QTF added / μg mL^{-1}	QTF found[*] / μg mL^{-1}	Recovery of QTF / %
10	9.91	99.1±1.25
15	14.76	98.40±0.84
20	20.61	103.1±1.48

[*]Mean value of three determinations.

Table 6. Results of recovery study *via* standard-addition method

Tablets studied	QTF in tablet / μg mL^{-1}	Pure QTF added / μg mL^{-1}	Total found / μg mL^{-1}	Pure QTF recovered[*] / %
Qutipin-200	9.72	5.0	14.93	104.2±1.20
	9.72	10.0	19.32	95.95±0.26
	9.72	15.0	24.86	100.9±0.87

[*]Mean value of three determinations.

CONCLUSIONS

The dye, quinoline yellow has been utilized as ion-pair reagent for the determination of quetiapine fumarate in pure drug, tablets and spiked human urine sample. The proposed method is simple and the maximum color development of QTF-QY ion-pair complex is instantaneous. No heating or long standing time was needed. The method does not involve procedural steps, do not take more operator time and expertise like HPLC and other methods. In terms of simplicity, rapidity, sensitivity and cost, the method can be considered superior to the previously reported methods, especially with those based on chromatography.[31–37] The reagent utilized in the proposed method is cheaper, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The method is unaffected by slight variations in experimental conditions such as time and reagent concentration. The proposed method gave results with good accuracy to permit determination of low concentration even down to 0.11 μg mL^{-1} QTF. Since there was no interference from the tablet excipients and numerous substances present in urine, the method is highly selective for the determination of QTF in quality control laboratories and physiotherapeutic analysis.

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