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Determination of Quetiapine fumarate in pharmaceutical formulations by sodium nitroprusside reagent

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ABSTRACT

A simple and sensitive visible spectrophotometric method is described for the determination of Quetiapine fumarate in bulk and pharmaceutical preparations based on the formation of light green colored molecular complex with sodium nitroprusside in presence of hydroxyl amine under alkaline conditions and exhibiting λmax at 401 nm. The Regression analysis of Beer's Law plot showed good correlation in a general concentration range of 2-10µg/ml with correlation coefficient (r^2 = 0.996). The proposed method is validated with respect to accuracy, precision, linearity and limit of detection. The suggested procedure is successfully applied to the determination of the drug in pharmaceutical preparation, with high percentage of recovery, good accuracy and precision. The results of analysis have been validated statistically by repeatability and recovery studies. The results are found satisfactory and reproducible. The method is applied successfully for the estimation Quetiapine fumarate in tablet form without the interference of excipients.

Key words: Quetiapine fumarate, Sodium nitroprusside (SNP), Pharmaceutical formulations Visible Spectrophotometry.

Introduction

Quetiapine fumarate is chemically 2-[2-(4-dibenzo [b, f] [1, 4] thiazepin-11-yl-1- piperazinyl) ethoxy] ethanol hemifumarate (figure-1). It is used to treat psychosis associated with Parkinson's disease and chronic schizophrenia. 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 type2 (D2) and serotonin type 2 (5HT) receptor antagonisms [1-3].

Literature survey revealed that some methods have been reported for Quetiapine fumarate reverse phase liquid chromatographic method [4], derivative spectrophotometric methods [5] have been developed. Chromatographic methods like HPTLC [6], GC-FID developed and validated for five processes related non-chromophoric impurities [7]. A high performance liquid chromatography- tandem spectrometry method was developed and validated for the quantification of quetiapine in rat plasma [8], isocratic resolution chromatographic assay method has been developed for the quantitative determination of quetiapine hemifumarate in bulk ingredient [9]. Pharmacokinetic measurement of the psychotropic compound quetiapine and four related metabolites in human plasma was conducted using a sensitive and specific liquid-chromatography tandem absorption mass spectrometry (LC-MS/MS) [10]. Two different analytical methods for the quality control quetiapine in commercial formulations have been developed and compared [11]. 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[12]. We now report a sensitive and flexible visible spectrophotometric method based on the complex formation reaction of drug with sodium nitroprusside and hydroxylamine hydrochloride.
(Method B).

MATERIALS AND METHODS

A Shimadzu UV/Visible spectrophotometer model -1800 with10mm matched quartz cells was used for all spectral measurements. Quetiapine pure drug was supplied by Cipla Ltd, Bangalore, India as gift sample. All the chemicals used were of analytical grade sodium nitroprusside (SD Fine Chemicals, Mumbai, 0.4%, 1.34×10^{-2}M, solution prepared by dissolving 400mg of sodium nitroprusside in 100ml distilled water), Hydroxylamine hydrochloride (Loba, 0.4%, 5.75×10^{-2}M solution prepared by dissolving 400mg of hydroxylamine hydrochloride in 100ml of distilled water), sodium carbonate (Loba,10%, 9.43×10^{-1}M solution prepared by dissolving 10g of sodium carbonate in 100ml of distilled water)were prepared.

Chemicals:

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

Standard drug solution:

Standard drug solution of was prepared by dissolving 10mg of in 100ml of distilled water to obtain 100µg/ml of solution.

Sample solution:

About 20 tablets were pulverized and the powder equivalent to 10mg of quetiapine was taken in a 100ml volumetric flask and then diluted to 100ml with distilled water to get 100µg/ml.

Assay:

Aliquots of standard solution Quetiapine (1.0ml-5.0ml, 100µg/ml) were transferred into a series of 10ml calibrated volumetric flask and the volume in each flask was brought to 5.0ml with distilled water. To this 0.5 ml of (1.324×10^{-2}M) sodium nitropruside and 1ml of (5.75×10^{-2}M) hydroxylamine hydrochloride solutions were successively added to each flask and shaken for 2 minutes. Then 1.0ml of (9.43×10^{-1}M) Na_2CO_3 solution was added and further shaken for 15 minutes. The contents were diluted to the mark with distilled water and the absorbance were measured at 401nm against a reagent blank and the absorbance spectra is

shown in the figure 4 within the stability period (immediate-120 min). The amount of quetiapine in the sample solution was computed from its calibration graph shown in figure 3.

Method Validation

The method was validated with reference to linearity; Standard solution of quetiapine fumerate was accuracy, precision, and Limit of detection& Limit of quantification. [13]

Linearity

Linearity was performed by taking from stock solution flask and volume made up to the mark with water to (100 mcg/ml) aliquots of 0.2,0.4,0.6,0.8and 1 ml obtain the concentrations 2 to 10µg/ml. were taken in 10ml volumetric flasks and diluted up to 10ml with water. To 1ml of drug solution to this add 0.5ml of SNP and 1ml of hydroxylamine hydrochloride and shake for 2min and add 0.5ml of sodium carbonate and shake for 15 min and the results are shown in table -1 an the calibration graph shown in figure-2.

Precision

Precision of the methods was studied as intra-day, interday and repeatability. Intra-day study was performed by analyzing, a homogenous sample separately 6 times for interday and intraday using the same instrument employing the same analyst evaluated the same data for standard deviation relative standard deviation and coefficient of variance and the results are summarized in Table -2.

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

LOD limits of detection is defined as lowest concentration of an analyte that analytical processes can be reliably differentiated from back ground levels. LOQ is defined as lowest concentration of a standard curve that can be measured with an accuracy precision

The limits of detection (LOD) and quantitation (LOQ) calculated according to ICH guidelines using the formulae: LOD = 3.3 S/b and LOQ = 10 S/b, where S

is the standard deviation of sample and m is the slope of the calibration plot result shown in table -1.

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 deferent levels. The resulting solutions were then reanalyzed by proposed methods; the results are shown in table 3.

Chemistry of colored species:

In the present investigation Quetiapine fumarate functions as a donor due to the presence of cyclic tertiary nitrogen. Sodium nitroprusside in the presence of hydroxylamine and alkali exists as aquoferrocyanide $[Fe(CN)_5H_2O]^{3-}$. In a general way it may be expected that the electron transfer depends upon the extent of delocalization of the donor and acceptor metal orbitals of the intervening ligands. From this stand point, ligands such as water and ammonia, which contain single bonds, are expected to be much less effective in conducting electrons between metal ions than unsaturated ligands such as CN- whose complexes are characterized by high degree of covalency and electron delocalization. Based on the analogy, the probable sequence of reactions is presented in scheme Figure2.

RESULTS AND DISCUSSION

In developing this method, a systematic study of the effects of various parameters were undertaken by varying one parameter at a time and controlling all others fixed. The effect of various parameters such as time, volume and strength of sodium nitro prusside, hydoxylamine, sodium carbonate, stability of colored species and solvent for final dilution of the colored species were studied and the optimum conditions were established. The optical characteristics such as Beer's law limit, Sandell's sensitivity molar absorptivity, percent relative standard deviation, were calculated and the results are summarized in (table-1). Regression characteristics like standard deviation of slope (b), standard deviation of intercept (a), shown in table-1. As an additional demonstration of precision were performed the SD and RSD% of interday and intraday results are summarized in Table-2 accuracy, recovery , experiments were performed by adding a fixed amount of the drug to the pre analyzed formulations at three different concentration levels. These results are summarized in Table-3. The ingredients usually present in formulations of Quetiapine fumaratedid not interfere with the proposed analytical method.

CONCLUSION

The reagents utilized in the proposed method are cheap and readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed analytical method is validated as per ICH guide lines and possess reasonable precision, accuracy, simple, sensitive and can be used as alternative method to the reported ones for the routine determination of Quetiapine fumarate depending on the need and situation.

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[13] Code Q2A, text on Validation of analytical methods ICH harmonized tripartite guidelines(1995)

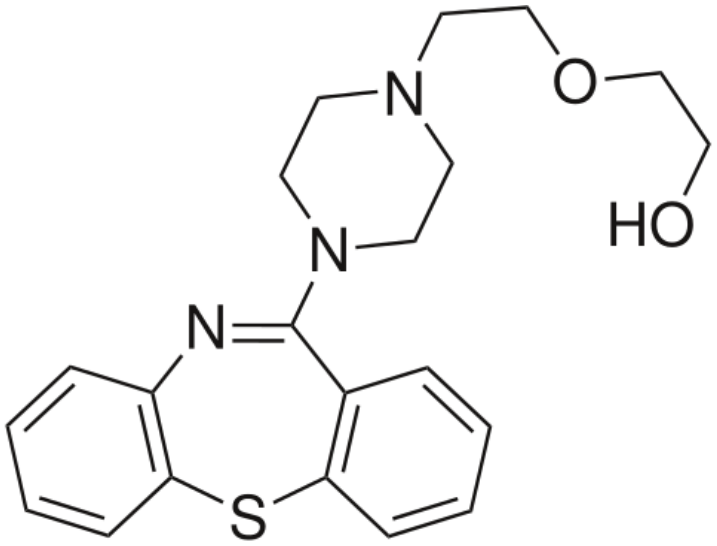
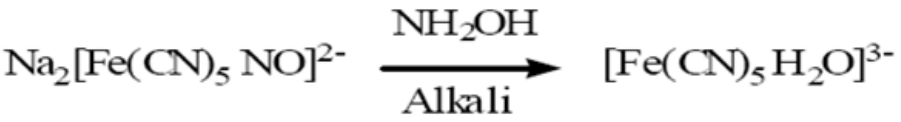
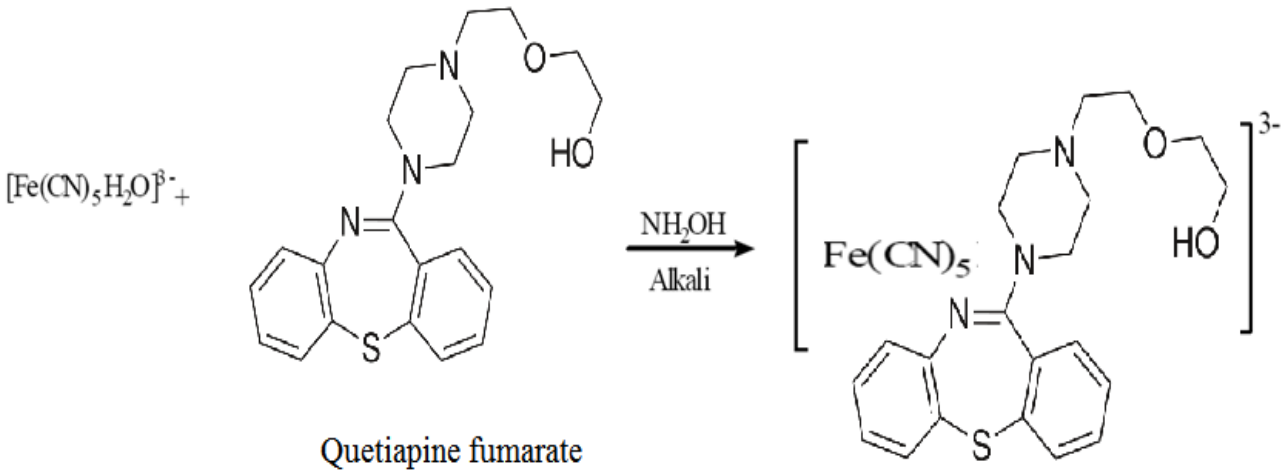


FIGURE-1 chemical structure Quetiapine fumarate

REACTION

Figure-2





Quetiapine fumarate

Green colour complex

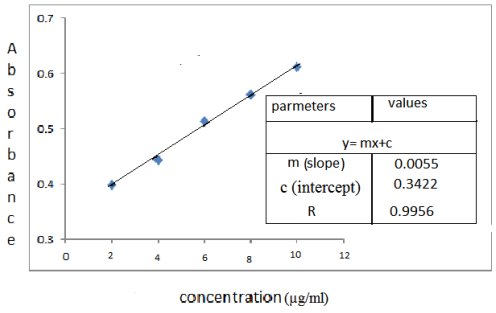


Figure-3 analytical curve determination of Quetiapine fumarate with SNP, HA

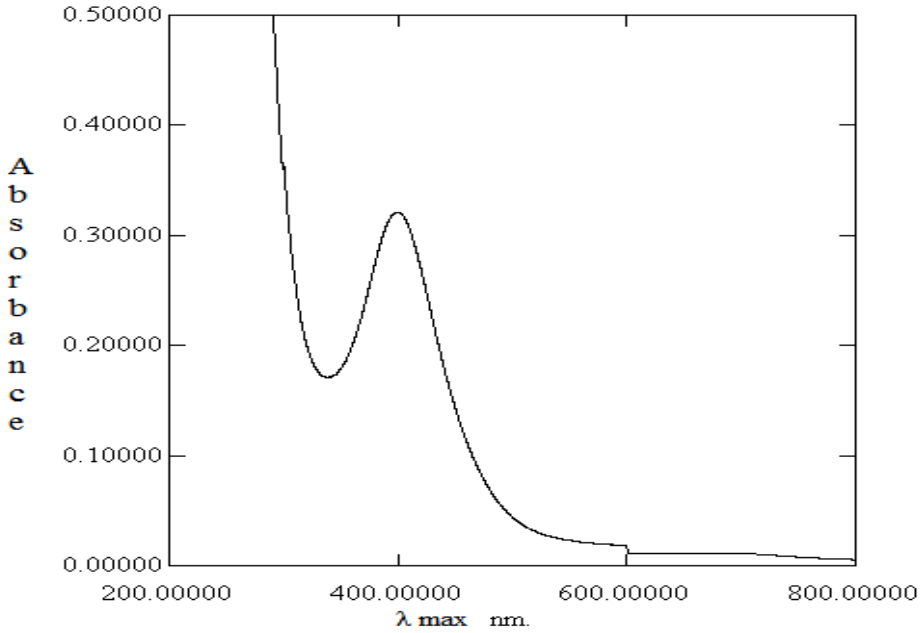


FIGURE 4-Showing Absorption Spectra of Absorption spectrum of the reaction product. Quetiapine fumarate concentration = 10µg/ml ; optical path = 1 cm. Measurements taken at 25 °C against the reagent blank after stoppered to room temperature for 30 min, as described in the recommended procedure.

Table 1: Optical Characteristics of proposed analytical Method

PARAMETERS	**VALUES**
Wavelength (nm)	401nm
Beer's law limit(µg/ml)	2-10µg/ml
Sandell's sensitivity (µg/cm/0.001 abs. unit)	0.0251
Molar absorptivity (Liter/mole/cm)	1669.25
Regression equation (Y)	
Intercept (m)	0.3422
Slope(c)	0.0055
Correlation Coefficient (R^2)	0.989
%RSD	0.77
SD	0.0046
LOD(µg/ml)	2.617
LOQ(µg/ml)	7.931

Table-2: **Precision**

INTRA DAY		**INTERDAY**	
SD (µg/ml)	**RSD%**	**SD (µg/ml)**	**RSD%**
0.004604	0.77	0.00331	0.474

Table -3 **Accuracy**

Concentration %	**Amount taken µg/ml**	**Amount added(µg/ml)**	**Amount recovered %**	**SD**	**%RSD**
80	20	12	99.8	0.005	0.91
100	20	20	99.6	0.003	0.506
120	20	28	99.9	0.0058	0.91