IJPSR (2013), Vol. 4, Issue 6 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 24 January, 2013; received in revised form, 14 April, 2013; accepted, 12 May, 2013

STABILITY INDICATING HIGH-PERFORMANCE THIN-LAYER CHROMATOGRAPHIC DETERMINATION OF QUETIAPINE FUMARATE

Zarna R. Dedania*[1], Navin R. Sheth [2] and Ronak R. Dedania [1]

Bhagwan Mahavir College of Pharmacy [1], Nr. Ashriwad Villa, B/H Heena Banglows, Bharathana- Vesu, Surat- 395017, Gujarat, India
Department of Pharmaceutical Sciences, Saurashtra University [2], Rajkot, Gujarat, India

Keywords:

Quetiapine fumarate, High-performance thin-layer chromatography, Stability indicating, Stress degradation, Validation

Correspondence to Author:

Dr. Zarna R. Dedania

Bhagwan Mahavir College of Pharmacy [1], Nr. Ashriwad Villa, B/H Heena Banglows, Bharathana- Vesu, Surat- 395017, Gujarat, India

E-mail: zaroo229@yahoo.co.in

ABSTRACT: A simple, sensitive, selective, precise and stability indicating high-performance thin-layer chromatographic method for determination of quetiapine fumarate both as a bulk drug and from tablets was developed and validated as per the International Conference on Harmonization (ICH) guidelines. The HPTLC method employed aluminum plates precoated with silica gel G 60F254 as stationary phase. The solvent system consisted of methanol: butanol: ethyl acetate (2:1:1) and give compact spots for quetiapine fumarate with R*f* value 0.76 ± 0.01 cm. Densitometry analysis was carried out in the absorbance mode at 220 nm. Linear regression analysis showed good linearity (r^2 = 0.999) with respect to peak area in the concentration range of 1000–5000 ng/spot. The method was validated for precision, accuracy, specificity and robustness. The limits of detection and quantitation were 171.65 and 520.18 ng/spot, respectively. The method was validated for precision, accuracy, ruggedness and recovery. Quetiapine fumarate was subjected to acid and alkali hydrolysis, oxidation, thermal and photodegradation. The degraded products were well separated from the pure drug. The statistical analysis proves that the developed method for quantification of quetiapine fumarate as bulk drug and tablets was reproducible and selective. As the method could effectively separate the drug from its degradation products, it can be employed as stability-indicating one.

INTRODUCTION: Quetiapine fumarate, 2-(2-(4-dibenzo[b,f][1,4]thiazepine-11-yl-1-piperazinyl) ethoxy)ethanol an atypical antipsychotic drug used for the treatment of schizophrenia as well as for the treatment of acute manic episodes associated with bipolar I disorder [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.4(6).2406-14

Article can be accessed online on: www.ijpsr.com

The antipsychotic effect of quetiapine fumarate is thought by some to be mediated through antagonist activity at dopamine and serotonin receptors.

Specifically the D1, D2 dopamine, the α1, α2 adrenoreceptor and 5-HT1A, 5-HT2 serotonin receptor subtypes are antagonized. Quetiapine fumarate also has an antagonistic effect on the histamine H1 receptor. It has no significant affinity for cholinergic muscarinic or benzodiazepine receptors. Drowsiness and orthostatic hypotension associated with use may be explained by its antagonism of histamine H1 and adrenergic α1 receptors, respectively.

Quetiapine fumarate's antagonism of adrenergic α1 receptors may explain the orthostatic hypotension observed with this drug. However, it is thought that the drug's therapeutic activity in schizophrenia is mediated through a combination of dopamine type 2 (D2) and serotonin type 2 (5HT2) receptor antagonism. Although quetiapine fumarate is known to bind other receptors with similar affinity only the dopamine D2 and serotonin 5HT2 receptor binding is responsible for quetiapine fumarate's therapeutic activity in schizophrenia [2].

Several analytical methods have been reported in the literature for the analysis of quetiapine fumarate from pharmaceutical dosage form. The techniques include HPLC [3], polarographic [4], HPTLC [5, 6] and UV Spectrophotometry [7] etc. forms. There are numerous methods to quantify quetiapine fumarate in biological fluid and human plasma, including HPLC [8, 9, 10, 11], HPLC-MS/ MS [12], LC-MS/MS [13]. An ideal stability-indicating method shall quantify the drug per se and also resolves its degradation products. HPTLC has become a part of routine analytical techniques in many product development and analytical laboratories due to its advantages.

The major advantage of HPTLC is that several samples can be run simultaneously using a small quantity of mobile phase unlike HPLC, thus lowering the analysis time and cost per analysis with high sample throughput. The uniform particle size (7µm) of precoated HPTLC plates enables achievement of a greater resolution and an easy reproducible separation. Suspensions, dirty or turbid samples can be directly applied. Additionally, it permits simultaneous assay of several components in a multicomponent formulation or herbal extracts.

The aim of the present work was to develop an economic, accurate, specific, reproducible and stability-indicating HPTLC densitometric method for the determination of quetiapine fumarate in the presence of its degradation products and related impurities from a pharmaceutical dosage form. The proposed method was validated as per ICH guidelines [14].

EXPERIMENTAL

Materials: Quetiapine fumarate was received as a gift sample from Tripada Pharmaceuticals, Ahmedabad, India. All chemicals and reagents used were of analytical grade and were purchased from Merck Chemicals, India.

HPTLC instrumentation: The samples were spotted in the form of bands of width 6mm with a Camag microlitre syringe on precoated silica gel aluminium plate 60F-254 (20 cm×10 cm, 200µm thickness, E. Merck, Germany) using a Camag Linomat V (Switzerland) sample applicator. The plates were pre-washed by methanol and activated at 60 ◦C for 5 min prior to chromatography. The mobile phase consisted of methanol: butanol: ethyl acetate (2:1:1). Linear ascending development was carried out in twin-trough glass chamber saturated with the mobile phase. The optimized chamber saturation time for the mobile phase was 30 min at room temperature (25±2 ◦C).The length of chromatogram run was 80 mm. Subsequent to the development; TLC plates were dried in a current of air with help of an air-dryer. Densitometric scanning was performed on Camag TLC scanner III in the absorbance mode at 220 nm. Evaluation was done using linear regression analysis via peak areas.

Calibration curve of quetiapine fumarate: A stock solution of quetiapine fumarate (1000 ng/µl) was prepared in methanol. From this stock solution 2 ml was diluted to 10 ml with diluent methanol to give concentration 200 ng/µl. Different volumes of sub-stock solution 5, 10, 15, 20 and 25 µl were spotted on the TLC plate to obtain concentrations of 1000, 2000, 3000, 4000 and 5000 ng/µl quetiapine fumarate respectively. Each concentration was spotted three times on the TLC plate. The data of peak areas plotted against the corresponding concentrations were treated by linear least-square regression analysis.

Method validation:

1. **Precision:** Precision of the system was determined by repeatability of the sample application and measurement of peak areas for six replicates of the same spot (3000 ng/spot). For method precision, the intra- and inter-day variation for the determination of quetiapine fumaratewas carried out at three different concentration levels of 2000, 3000 and 4000 ng/spot and was expressed in terms of % R.S.D.

2. **Robustness of the method:** Robustness was studied in three replicate at a concentration level

of 3000 ng/spot. In this study, parameters (mobile phase composition, mobile phase volume, duration of saturation, activation of prewashed TLC plates and time from spotting to chromatography and from chromatography to scanning) were investigated and the effects on the results were expressed as standard deviations. The mobile phase methanol: butanol: ethyl acetate in varying ratios (1.8:1.1:1, 1.8:1:1.1, 2.2:1:1) was tried and chromatograms were run. The amount of mobile phase and duration of saturation were varied at 20 ± 2 ml (18, 20 and 22 ml) and 30 ± 10 min (20, 30 and 40 min), respectively. Time from spotting to chromatography and from chromatography to scanning was varied from 0, 10 and 20 min.

3. **Limit of detection and Limit of Quantification:** In order to estimate the limit of detection (LOD) and limit of quantitation (LOQ), blank methanol was spotted six times following the same method and the signal-to-noise ratio was determined.

4. **Recovery studies:** Recovery studies were carried out by applying the method to drug samples to which known amount of quetiapine fumarate corresponding to 50, 100 and 150% of the quetiapine fumarate label claim had been added. At each level of the amount, six determinations were performed. This was done to check for the recovery of the drug at different levels in the formulations.

5. **Specificity:** The specificity of the method was ascertained by analyzing the standard drug and sample. The spot for quetiapine fumarate in sample was confirmed by comparing the *R*f values and spectra of the spot with that of standard. The peak purity of the quetiapine fumarate was assessed by comparing the two spectra at three different levels, viz. peak start (S), peak apex (M) and peak end (E) positions of the spot.

6. **Ruggedness:** A solution of concentration 3000 ng/spot was prepared and analyzed on day 0 and after 6, 12, 24, 48 and 72 h. Data were treated to calculate % R.S.D. to assess the ruggedness of the method.

Analysis of Quetiapine fumarate from Tablet dosage form: Twenty tablets was weighed and finely powdered. The powder equivalent to 25 mg quetiapine fumarate was accurately weighed and transferred to 50 ml volumetric flask containing 25 ml of methanol. To ensure complete extraction of drug, it was sonicated for 30 min and diluted with methanol. The above solution was filtered through whatman filter paper (# 42). Volume was made up to the mark with methanol to give a solution 500 µg/ml quetiapine fumarate (stock solution).

From this Sub stock solution was prepared by diluting 4 ml of solution to 10 ml to give concentration 200 ng/µl. A 10 µl of the prepared sub stock solution was applied on pre-washed TLC plate, developed in the above mobile phase, dried in air and photometrically analyzed. From the peak area obtained in the chromatogram, the amount of drug was calculated. The analysis was repeated in triplicate and the possibility of excipient interference in the analysis was studied.

Forced degradation of Quetiapine fumarate: In order to determine the stability indication of the analytical method and assay, quetiapine fumarate API powder were stressed under various conditions to conduct forced degradation studies. All solutions used in forced degradation studies were prepared with final concentrations 200 µg/ml. A 15 µl of the prepared sub stock solution of forced degradation studies were applied on pre-washed TLC plate, developed in the above mobile phase, dried in air and photometrically analyzed as described above.

1. **Preparation of Acid-induced degradation product:** A 100 mg of quetiapine fumarate was accurately weighed and transferred to a 100 ml round bottom flask and dissolved in 50 ml of diluent methanol. The flask was sonicated for 15 min and added 10 ml of 0.1M hydrochloric acid solution. The content kept for constant stirring for 24 h at room temperature. After specified time, the content was neutralized with 10 ml 0.1 M sodium hydroxide. Then volume was made up to the mark with diluent methanol.

2. **Preparation of Alkali-induced degradation product:** A 100 mg of quetiapine fumarate was accurately weighed and transferred to a 100 ml round bottom flask and dissolved in 50 ml of diluent methanol.

The flask was sonicated for 15 min. and added 10 ml of 0.1M sodium hydroxide solution. The content kept for constant stirring for 24 h at room temperature. After specified time, the content was neutralized with 10 ml 0.1 M hydrochloric acid. Then volume was made up to the mark with diluent methanol.

3. **Preparation of hydrogen peroxide-induced degradation product:** A 100 mg of standard quetiapine fumarate was accurately weighed and transferred to a 100 ml round bottom flask and dissolved in 50 ml of diluent methanol. The flask was sonicated for 15 min. and after adding 10 ml of 3 % hydrogen peroxide solution, after 60 min volume was made up to the mark with diluent methanol.

4. **Thermal degradation product:** A quantity of 1g of quetiapine fumarate sample was taken in to a petridish and kept in oven at 80 °C for 36 h. A 100 mg of thermal stressed quetiapine fumarate was accurately weighed and transferred to a 100 ml round bottom flask and dissolved in 50 ml of diluents methanol. The flask was sonicated for 15 min and volume was made up to the mark with diluent methanol.

5. **Photo-degradation product:** A quantity of 1 g of quetiapine fumarate sample was taken in to a petridish and kept in UV light for 36 h. A 100 mg photo stressed quetiapine fumarate was accurately weighed and transferred to a 100 ml round bottom flask and dissolved in 50 ml of diluent methanol. The flask was sonicated for 15 min. and volume was made up to the mark with diluents methanol.

RESULTS AND DISCUSSION:

Development of the Optimum Mobile phase: The TLC procedure was optimized with a view to develop a stability indicating assay method to quantify the quetiapine fumarate. Both the pure drug and the degraded products were spotted on the TLC plates and run in different solvent systems. Initially methanol: toluene in varying ratio was tried but degradants products were not resolved. The mobile phase methanol: butanol: water (2:2:1) gave slightly diffused spot with tailing. Substitution of water with ethyl acetate improved the spot characteristics.

Finally the mobile phase consisting of methanol: butanol: ethyl acetate (2:1:1) gave a sharp and well defined symmetrical peak at R*f* at 0.76 ± 0.01. Well defined spots were obtained when the chamber was saturated with mobile phase for 30 min at room temperature. The developed analytical procedure can be completed in about 1.5 h, which includes the pre-analysis steps viz. washing of HPTLC plates with methanol and activation at 60 °C (30 min); preparation of mobile phase and saturation of development chamber (30 min).

Calibration curves: The linear regression data for the calibration curves (n = 3) showed a good linear relationship over concentration range 1000–5000 ng/spot with respect to the peak area as shown in **Fig. 1**. The equation for the calibration curve is y = 2.525x + 5988. The linearity of the calibration graphs and adherence of the system to Beer's law was validated by high value of correlation coefficient 0.999.

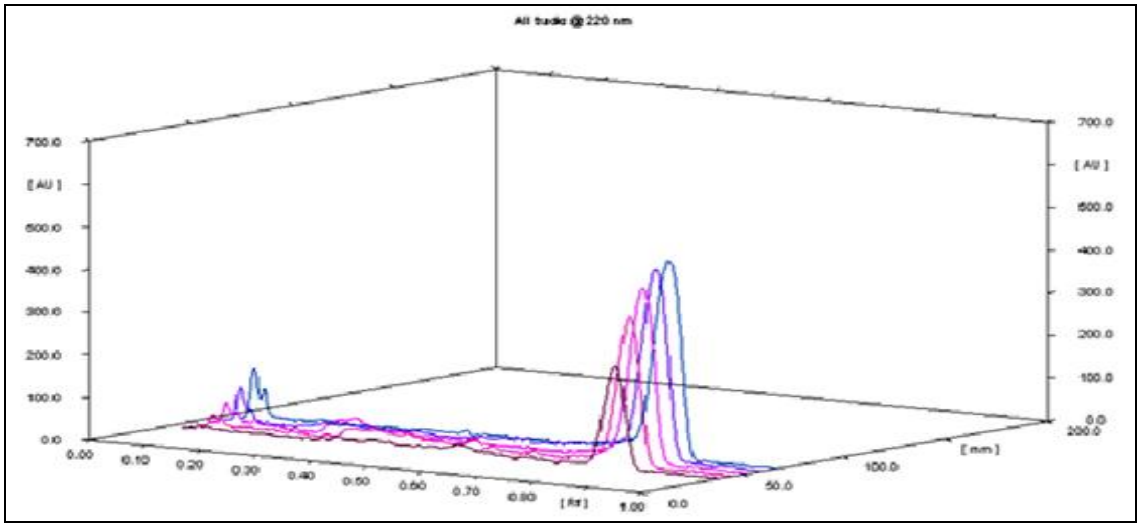

FIG. 1: 3D VIEW OF ALL TRACKS FOR CALIBRATION CURVE (1000- 5000 ng/spot) at 220 nm

Validation of the method:

1. **Precision:** The intraday and interday precisions determined as % R.S.D. of peak area, ranged between 0.38–0.57 % and 0.37–0.46 % respectively as shown in **Table 1**.

The % R.S.D. for repeatability of sample application (3000 ng/spot) and measurement of peak areas were found to be 0.74 and 0.87, respectively.

TABLE 1: INTRA AND INTER DAY PRECISION STUDY FOR QUETIAPINE FUMARATE

Conc. (ng/spot)	Intraday (n=3) Area (Mean ± SD)	CV	Interday (n=3) Area (Mean ± SD)	CV
2000	11055.68 ± 42.17	0.38	11069.14 ± 43.46	0.39
3000	13594.98 ± 77.59	0.57	13598.35 ± 50.68	0.37
4000	16122.50 ± 79.90	0.49	16128.4 ± 75.41	0.46

2. **Robustness of the method:** The S.D. and % R.S.D. of the peak areas for each parameter at a concentration level of 3000 ng/spot. The low values of % R.S.D. (≤ 0.49) obtained after introducing small deliberate changes in the developed HPTLC method indicated the robustness of the method.

3. **LOD and LOQ:** Detection limit and quantitation limit with signal-to-noise ratio of 3:1 and 10:1 were considered as LOD and LOQ and were found to be 171.65 and 520.18 ng/spot, respectively, which indicates the adequate sensitivity of the method.

4. **Recovery studies:** The proposed method when used for estimation of quetiapine fumarate from marketed formulation after spiking with 50, 100 and 150 % of additional drug, afforded mean recovery and % R.S.D. values as shown in **Table 2**. The recovery was found to be ± 2 % of amount added indicate accuracy of method.

TABLE 2: RECOVERY STUDY FOR QUETIAPINE FUMARATE

Label claim Mg/tablet	Amount added %	Total amount added (mg)	Amount recovered (mg) ± SD	% Recovery ± SD (n=3)
Quetiapine	50	12.5	12.46 ± 0.17	99.70 ± 1.36
Fumarate	100	25	24.97 ± 0.23	99.90 ± 0.92
25	150	37.5	37.53 ± 0.39	100.08 ± 1.06

5. **Specificity:** The peak purity of quetiapine fumarate was assessed by comparing the spectra at peak start, peak apex and peak end positions of the spot i.e., r^2 (S, M) = 0.9997 and r^2 (M, E) = 0.9998. Good correlation (r^2 = 0.9997) was also obtained between standard and sample spectra of quetiapine fumarate.

6. **Ruggedness:** Low % R.S.D. value of 0.84 between peak area values obtained for the same drug solution of quetiapine fumarate at a concentration of 3000 ng/spot after 48 h proved the ruggedness of the method. No indication of compound instability in the sample solution was observed.

Analysis of the prepared Formulation: A single spot at R*f* 0.76 was observed in the chromatogram of the drug samples extracted from tablets. There was no interference from the excipients commonly present in the tablet. The drug content was found to be 100.50 % with a % RSD of 0.97 for three replicate determinations.

It may therefore be inferred that degradation of quetiapine fmarate had not occurred in the marketed formulations that were analyzed by this method. The good performance of the method indicated the suitability of this method for routine analysis of quetiapine fumarate in pharmaceutical dosage form.

Stability indicating property: The chromatograms of the samples treated with acid, base, hydrogen peroxide, UV light, dry heat, showed well separated spots of pure quetiapine fumarate as well as some additional peaks at different R*f* values. The spots of the degraded products were well resolved from the drug spot. The number of degradation products with their R*f* values, content of quetiapine fumarate remained and percentage recovery were calculated and listed in **Table 3**.

TABLE 3: SUMMARY OF FORCED DEGRADATION RESULTS FOR QUETIAPINE FUMARATE BY HPTLC

Sr. no.	Exposure condition	Number of degradation products (R_f value)	Drug remained/ 3000 ng ± SD (n=3)	Recovery (%)	Degradation (%)
1	Acid degradation	3 (0.06, 0.47, 0.68)	2291 ± 19.41	76.36	23.63
2	Alkali degradation	2 (0.48, 0.68)	2140.72 ± 16.71	71.35	28.64
3	Oxidation	3 (0.16,0.23,0.48)	1296.80 ± 18.66	43.22	56.77
4	Thermal degradation	2 (0.06, 0.48, 0.60)	2660 ± 26.23	88.66	11.33
5	Photo degradation	3 (0.21, 0.47, 0.67)	2691.51 ± 26.73	89.71	10.28

1. **Acid-induced degradation product:** Drug recovery at the level of 76.36 % from acid stressed sample after 24 h suggesting that quetiapine fumarate was susceptible towards the acid induced degradation. The chromatograms of the acid degraded sample showed additional peak at R*f* value of 0.06, 0.47 and 0.68 were shown in **Fig. 2(a)**.

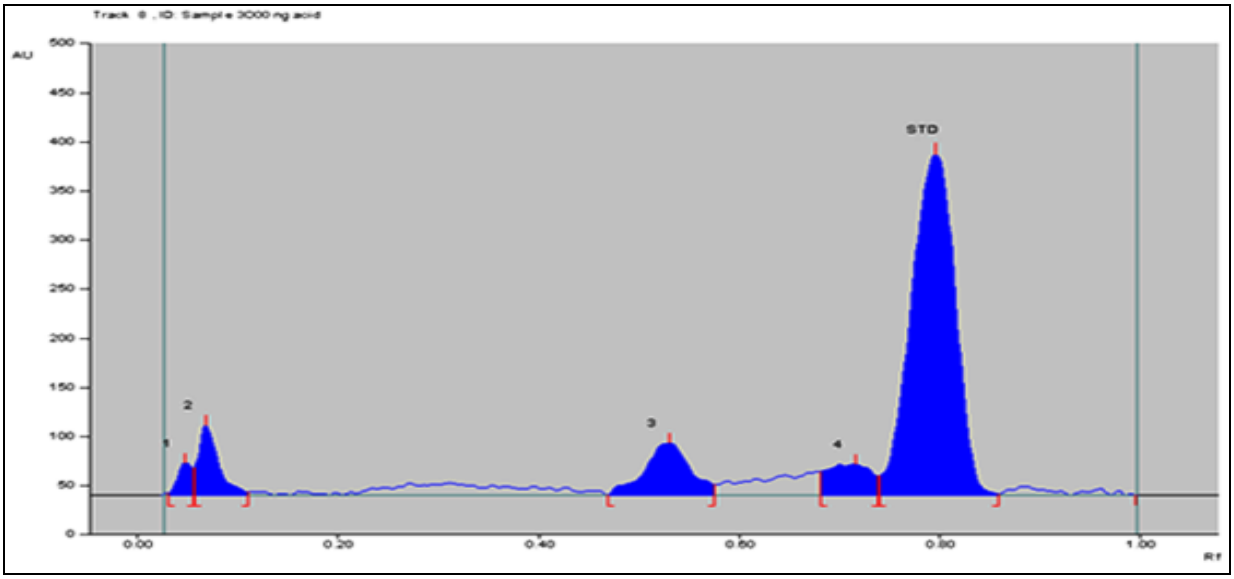

FIG. 2(A): TYPICAL HPTLC CHROMATOGRAM OF ACID-INDUCED DEGRADATION OF QUETIAPINE FUMARATE

2. **Alkali-induced degradation product:** Drug recovery at the level of 71.35 % from alkali stressed samples after 24 h suggests significant degradation of quetiapine fumarate in these conditions. The chromatograms of the base degraded sample showed additional peaks at R*f* value of 0.48 and 0.68 were shown in **Fig. 2(b).** Common peaks at R*f* 0.68 indicates that this degradant was common to both acid and base hydrolysis.

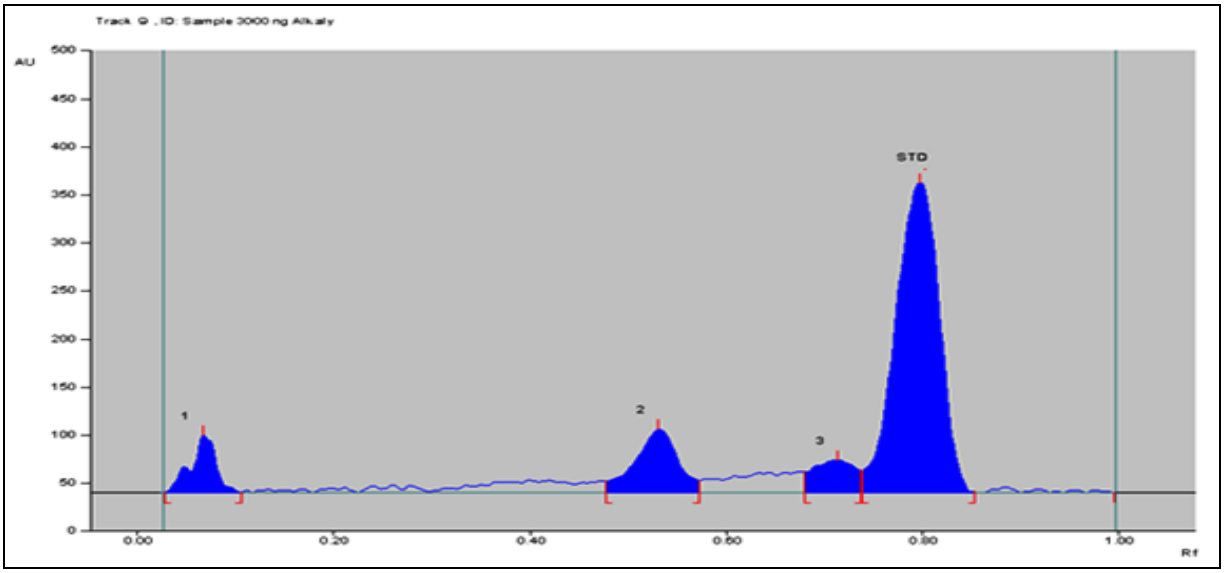

FIG. 2(B): TYPICAL HPTLC CHROMATOGRAM OF ALKALI-INDUCED DEGRADATION OF QUETIAPINE FUMARATE

Hydrogen peroxide-induced degradation product: The chromatogram of the sample of quetiapine fumarate treated with 3% (v/v) H_2O_2 showed additional peaks at R*f* values of 0.16, 0.23 and 0.48 suggesting that quetiapine fumarate was found to be susceptible towards the oxidation induced degradation as shown in **Fig. 2(c).** The area of H_2O_2 degradation product peak at R*f* value 0.16 was significant as compared to quetiapine fumarate and only 43.22 % recovery of quetiapine fumarate from the H_2O_2 stressed samples.

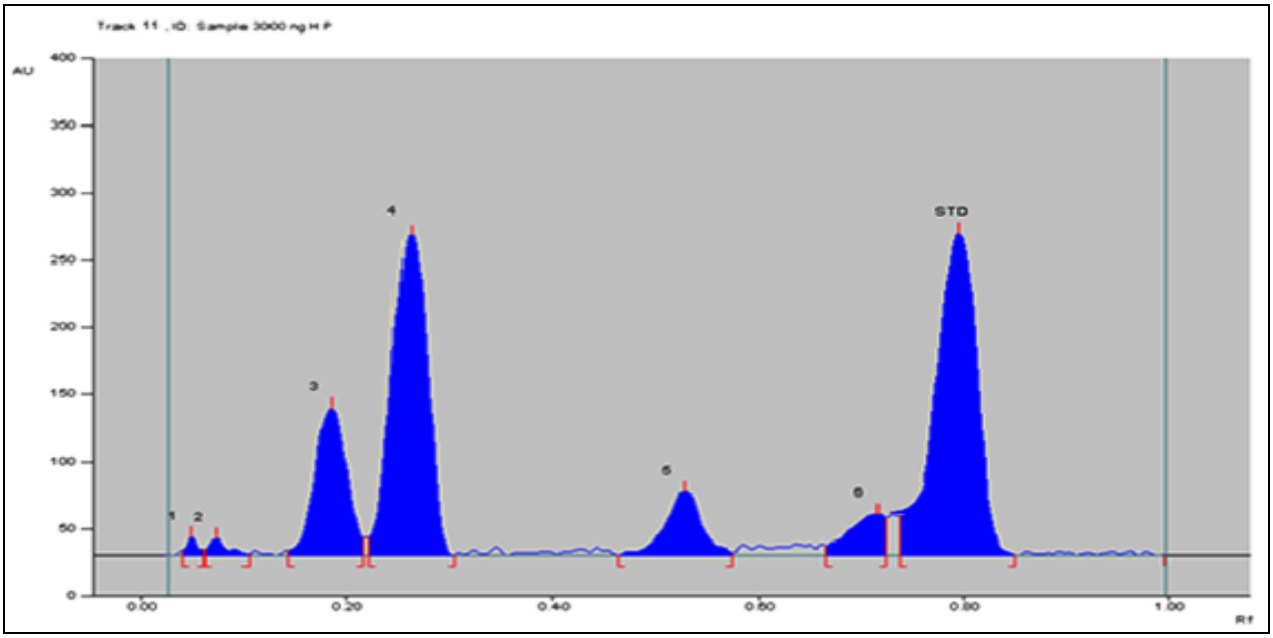

FIG. 2(C): TYPICAL HPTLC CHROMATOGRAM OF HYDROGEN PEROXIDE-INDUCED DEGRADATION OF QUETIAPINE FUMARATE

3. **Thermal-degradation product:** The dry heat stressed samples show additional peaks of degradants at R*f* values of 0.06, 0.48 and 0.60 as shown in **Fig. 2(d)** but recovery was found to be 88.66 % suggesting that quetiapine fumarate are comparatively stable towards heat. The R*f* value 0.48 suggest thermal induced oxidation of quetiapine fumarate.

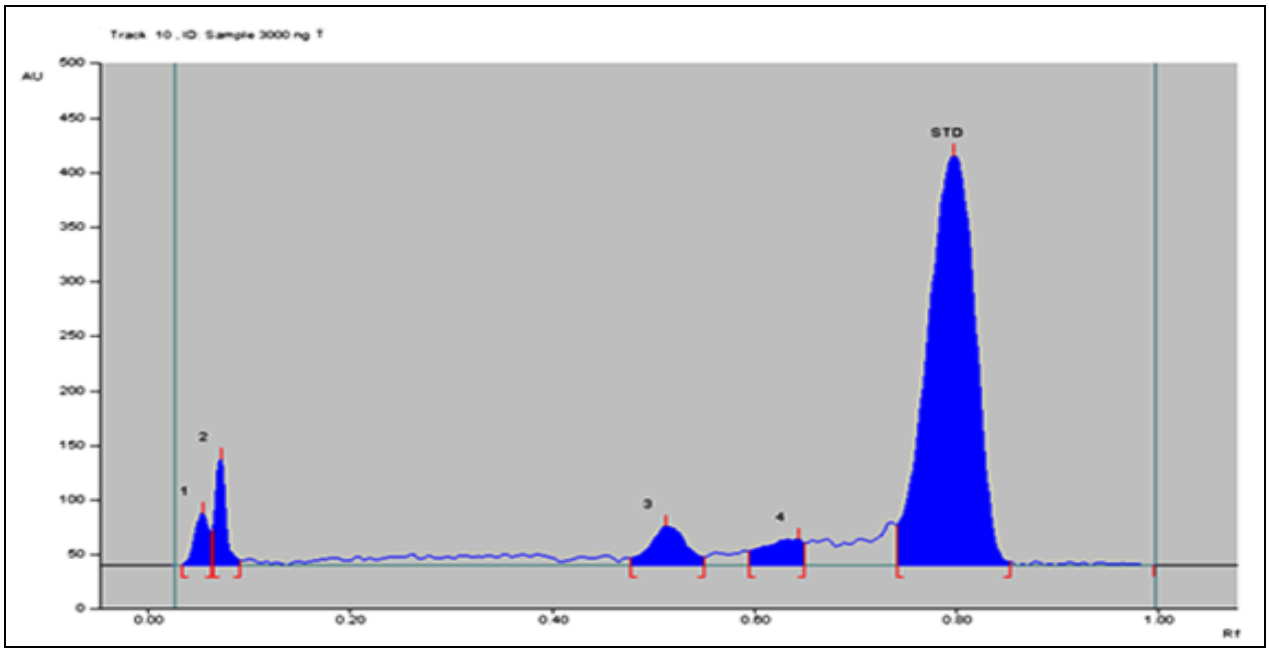

FIG. 2(D): TYPICAL HPTLC CHROMATOGRAM OF THERMAL-INDUCED DEGRADATION OF QUETIAPINE FUMARATE

4. **Photo-degradation product:** Drug recovery at the level of 89.71 % for the UV exposed samples showed that drug is comparatively stable UV irradiation. Both sun light and UV degraded sample showed additional peak at R*f* values of 0.21, 0.47 and 0.67 as shown in Fig 2(e). The R*f* value at 0.47 of the photochemical degradation products is similar to acid degradation products.

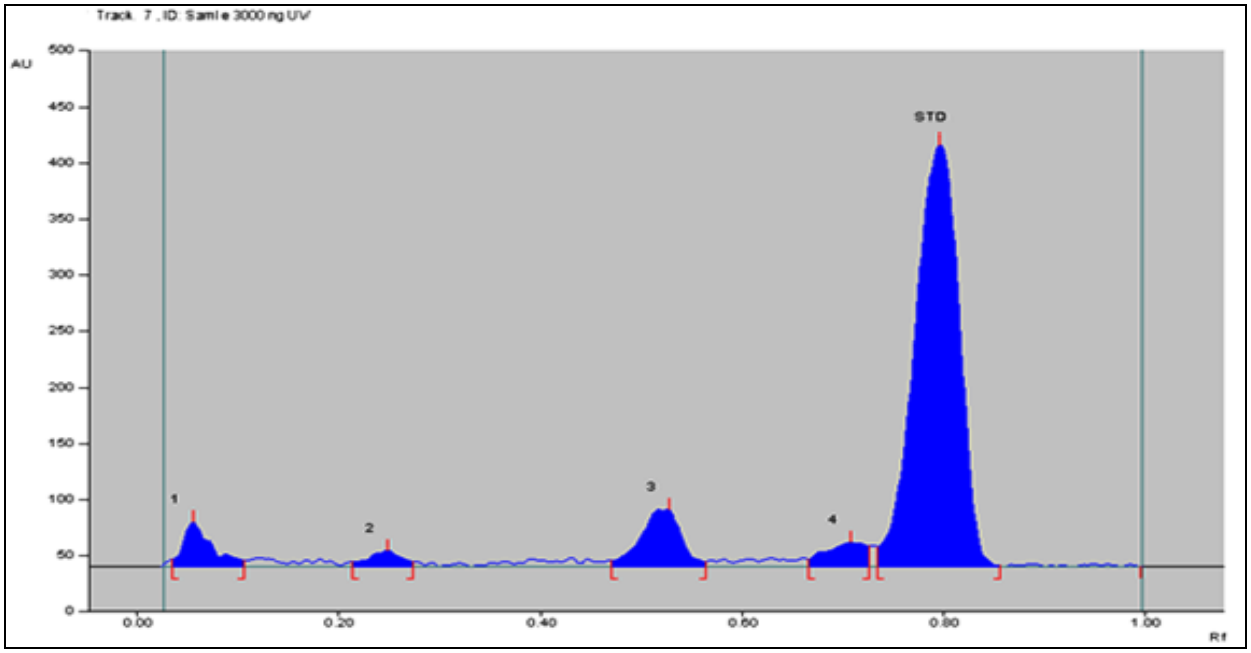

FIG 2(E): TYPICAL HPTLC CHROMATOGRAM OF PHOTO-INDUCED DEGRADATION OF QUETIAPINE FUMARATE

CONCLUSION: The developed HPTLC technique is precise, specific, accurate and stability indicating for the determination of quetiapine fumarate. Statistical analysis proves that the method is reproducible and selective for the analysis of quetiapine fumarate as bulk drug and tablet dosage form. The method can be used to determine the purity of the drug available from various sources by detecting the related impurities. It may further be extended to study the degradation kinetics of quetiapine fumarate and also for its determination in plasma and other biological fluids. As the method separated the drug from its degradation products, it can be employed as a stability indicating one.

ACKNOWLEDGMENTS: The authors are grateful to Veerayatan Institute of Pharmacy, Jakhania and Saurashtra University, Rajkot, India for providing the facilities to carry the experiment as well as Tripada Pharmaceuticals, Ahmedabad, India for providing gift sample of Quetiapine Fumarate.

REFERENCES:

1. http://www.drugbank.ca/drugs/DB01224
2. http://www.rxlist.com/seroquel-drug.htm
3. Belal F, Elbrashy A, Eid M and Nasr J: Stability-indicating HPLC method for the determination of quetiapine: Application to Tablets and Human Plasma. J Liq Chromatogr Rel Techn 2008; 31: 1283-1298.
4. El-Enany N, El-Brashy A, Belal F and El-Bahay N: Polarographic Analysis of Quetiapine in pharmaceuticals. Portugaliae Electrochimica Acta 2009; 27: 113-125.
5. Skibinski R, Komsta L and Kosztyla L: Comparative validation of quetiapine determination in tablets by NP-HPTLC and RP-HPTLC with densitometric and videodensitometric detection. J Planar Chroma 2008; 21:289-294.
6. Dhandapani B, Somasundaram A, Raseed SH, Raja M and Dhanabal K: Development and validation of HPTLC method for estimation of quetiapine in bulk drug and in tablet dosage form. Int J PharmTech Res. 2009; 1:139-141.
7. Bagade SB, Narkhede SP, Nikam DS and Sachde CK: Development and validation of UV-Spectrophotometric method for determination of quetiapine fumarate in two different dose tablets. Int J ChemTech Res 2009; 1:898-904.
8. Sachse J, Koller J, Hartter S and Hiemke C: Automated analysis of quetiapine and other antipsychotic drugs in human blood by high performance-liquid chromatography with column-switching and spectrophotometric detection. J Chromatogr B 2006; 830: 342-348.
9. Davis PC, Wong J and Gefvert O: Analysis and pharmacokinetics of quetiapine and two metabolites in

human plasma using reversed-phase HPLC with ultraviolet and electrochemical detection. J Pharma Biomed 1999; 20: 271-282.
10. Addolorata SM, Laura M, Giuseppina F, Lawrence A, Roberto M and Augusta RM: Simultaneous determination of fluvoxamine isomers and quetiapine in human plasma by means of high-performance liquid chromatography; J chromatogr Anal Tech Biomed Life Sci 2006; 843: 227-233
11. Hasselstrom J and Linnet K: Fully automated on-line quantification of quetiapine in human serum by solid phase extraction and liquid chromatography. J Chromatogr B 2003; 798: 9-16.
12. Barrett B, Holcapek M, Huclova J, Borek-Dohalsky V, Fejt P, Nemec B and Jelinek I: Validated HPLC–MS/MS method for determination of quetiapine in human plasma. J Pharma Biomed Anal 2007; 44: 498-505.
13. Nirogi R, Bhyrapuneni G, Kandikere V, Mudigonda K, Ajjala D and Mukkanti K: Sensitive liquid chromatography tandem mass spectrometry method for the quantification of quetiapine in plasma. Biomed Chromatogr 2008; 22: 1043-1055.
14. ICH, Q2 (R1), Validation of Analytical Procedures: Text and Methodology, International Conference on Harmonization, Geneva, November, 2005.

How to cite this article:
Dedania ZR, Sheth NR and Dedania RR: Stability indicating High-Performance Thin-Layer Chromatographic determination of Quetiapine fumarate. *Int J Pharm Sci Res* 2013; 4(6); 2406-2414. doi: 10.13040/IJPSR.0975-8232.4(6).2406-14