International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.1, No.4, pp 898-904, Oct-Dec 2009

Development and validation of UV-Spectrophotometric method for determination of Quetiapine fumarate in two different dose tablets

Bagade S.B.*, Narkhede S.P., Nikam D. S., Sachde C. K.
***Department of Pharmaceutical chemistry, School of Pharmacy and Technology Management, NMIMS University, Shirpur - 425 405, Dist: Dhule (M.S.), India.**
Corres author:sagar.pharma18@gmail.com
Mobile No: 0091 97665 08509

Abstract: 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. Spectrophotometrically, Quetiapine fumarate was determined by measuring the ^2D-values at 254.76nm with 0.1 N HCl as background solvent. Analytical Calibration curves were linear within a concentration range from 10 to 30 µg/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 0.20% (Quetipin® tablet; 200 mg) and 0.16% (Quetipin® tablet; 300 mg) respectively. The percentage recoveries were near 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 precision, accuracy and specificity.
Keywords: Derivative UV spectrophotometry; Zero crossing, Quetiapine fumarate, Pharmaceutical dosage form (tablet)

Introduction and Experimental

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, moderately soluble in water and soluble in Methanol & 0.1N HCl. 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 type 2 (D2) and serotonin type 2 ($5HT_2$) receptor antagonisms. [1-3]

Literature survey revealed that methods have been reported for the estimation of Quetiapine fumarate in plasma using high performance liquid chromatography (HPLC) method[4]. Baby et al. (2009) developed Simple and sensitive UV Spectrophotometric methods for the determination of Quetiapine as fumarate having absorption maximum at 254.7 nm[5]. Vincenzo, P. et al. (2003) developed a spectrophotometric method and a capillary zone electrophoretic (CZE) method for the quality control of quetiapine in commercial formulations[6]. Li K.Y. et al. (2004) developed a high performance liquid chromatochrophy-elecrospray mass spectrometry method for simultaneous determination of Quetiapine and its three metabolite in human plasma[7].

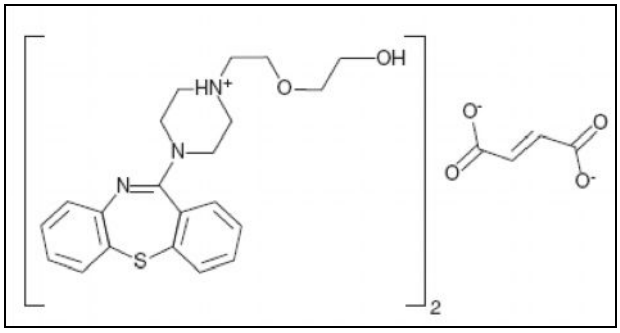


Fig 1: Chemical structure of Quetiapine fumarate

Derivative ultraviolet spectrophotometry has successfully been applied to drugs alone or in association. This technique is an alternative method to determine drugs with low specific absorptivity, substances under the influence of increased background absorption, or drugs in association, wherein overlaps and absorption addition

occur. This technique offers various advantages over the conventional absorbency methods such as the discrimination of the sharp spectral features over the large bands and the enhancement of the resolution of overlapping spectra. This outstanding feature coupled with zero crossing, least square deconvolution, or Fourier transform data processing technique has received increasing attention in single and multi-component quantitative analysis of pharmaceutical drug substances, especially in UV absorbing matrices. For example, derivative UV spectroscopy has been used for the quantification of acyclovir, celecoxib, amiloride and furosemide in the presence of degradation products and other ingredients [8-10].

There is no derivative Spectrophotometric method for the analysis of Quetiapine fumarate in pharmaceutical preparations has been reported in literature. The aim of this work was to investigate the utility of derivative spectrophotometry in the assay of Quetiapine fumarate in pharmaceutical preparations without the necessity of sample pre-treatment. In this study, three derivative UV Spectrophotometric methods were developed and validated for the determination of Quetiapine fumarate. The developed methods were applied to two different (Quetipin-200 mg and Quetipin-300 mg) commercial dose tablets. The results obtained by these two approaches were compared.

Materials

Pure sample of Quetiapine fumarate(QPF) was generous gift from Whokhardt pharmaceuticals Ltd., Aurangabad. Tablets of two strength were procured from local pharmacy i.e. Qutipin 200 mg (Sun Pharmacetical Indusries Ltd.) and Qutipin 300 mg (Sun Pharmacetical Indusries Ltd.), distilled water, 0.1 N HCl, 0.1 N NaOH, Methanol, Mortor pastle, Watman filter paper no.1, all other reagents used were of analytical grade.

Methods

Preparation of Standard solutions and calibration: Standard solution of QPF was prepared by dissolving 20 mg of Quetiapine fumarate in 20 ml of 0.1 N HCl solution to get concentration of 1000 µg/ml. Different aliquots of above solution in the range 0.2-0.6 ml were transferred into series of 20 ml volumetric flasks and the volume was made up to the mark with 0.1N HCl to obtain concentrations 10-30 µg/mL. Scanning range was finalized for study and solutions were scanned on spectrophotometer in the UV range of 230 - 350 nm.

Zero order spectrum of 10-30 µg ml−1 standard Quetiapine fumarate solution in 0.1N HCl was shown in fig. 2. After scanning of all standard solution derivative method was applied get second, third and fourth order derivative spectra which are shown in fig. 3. Working calibration curve were plotted and evaluated by least squares method.

Preparation of Sample solution:

Tablet samples A (Qutipin 200) and B (Qutipin 300), label claimed 200 mg and 300 mg of Quetiapine per dosage unit respectively. 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 20 ml calibrated flask with the aid of 0.1 N HCl. The volume was made up to mark, sonicate for 10 min and filtered through whatman Filter paper no.1. The filtrate is suitably diluted to get a final conc. of 20 µg ml−1 Quetiapine fumarate. The second, third and fourth order amplitudes at specified wavelengths were recorded and conc. of drug was worked out utilizing equations obtained from calibration graphs.

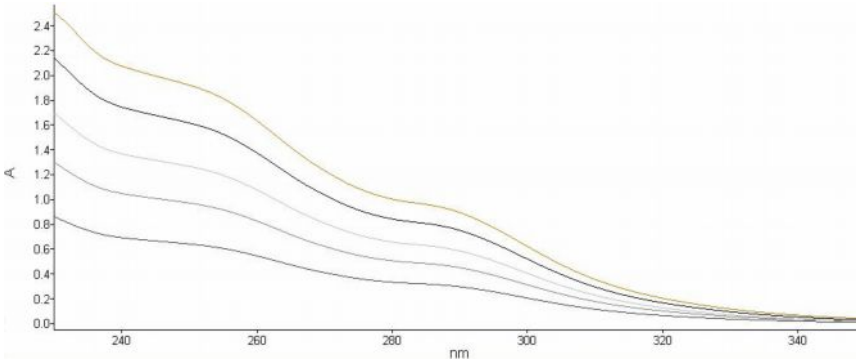
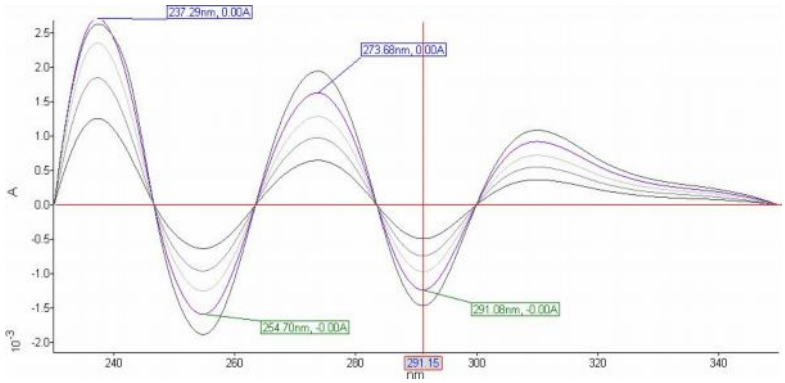
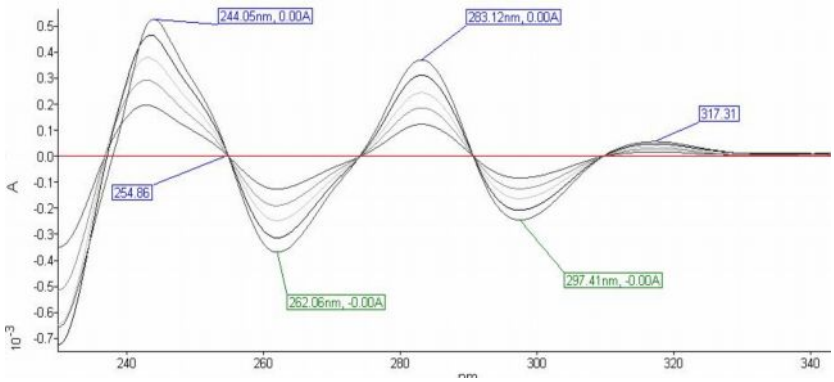


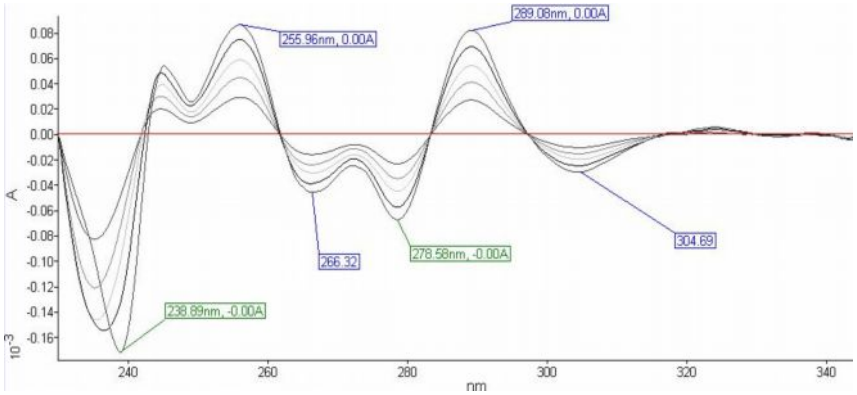
Fig. 2: Overlay of Zero order Spectrum of 10-30 ug ml-1 standard QPF in 0.1N HCl



(a)



(b)



(c)

Fig.3: Overlay of 2nd order derivative (a), 3rd order derivative (b) & 4 th order derivative curves of Standard with concentration range of 10-30 µg ml−1 of Quetiapine fumarate in 0.1 N HCl.

Results and Discussion

Solubility of Quetiapine fumarate was checked in different solvents and 0.1 N HCl was selected as the solvent for dissolving the drug. The zero-order spectrum of Quetiapine fumarate in 0.1N HCl (Fig. 1) displayed very compact absorption bands. This compacted spectrum was separated by using derivative Spectrophotometric method with 25 Δλ (smoothing factor). The ^{2}D curve displayed two sharper and well-defined peak with maximum absorption in positive region at *237.29*nm, 273.68nm and in negative region at 254.76nm and 291.08nm in the measuring wavelength,

The ^3D spectrum showed sharper and well-defined peak with maximum positive absorption at 244.05nm, 283.12nm, 317.31nm and negative absorption at 262.06nm, 297.41nm in the measuring wavelength & showed zero crossing amplitude occurs at 254.86nm, while the ^4D curve showed a maximum positive absorption at *255.96*nm, 289.08 nm and negative absorption at 266.32nm, 278.58nm, 304.69nm in the measuring wavelength different dilutions of Quetiapine fumarate in range of 10-30 µg/mL with Δλ of 25nm was recorded (Fig. 2).

Linear calibration graphs with negligible intercepts were obtained between the measured ^{2}D, ^3D and ^{4}D values and the corresponding concentrations over the range 10–30 µg/ml. The statistical parameters, regression equations, calculated from the calibration graphs along with the standard deviations of the slope (S_b) and the intercept (S_a) on the ordinate are given in Table 1. From the calibration curve linearity was found at 273.68 nm, 254.76nm, and 291.08 nm for ^{2}D, at 283.12 nm, and 262.06, 297.41nm for ^{3}D and at *255.96*nm, 266.32nm, 278.58nm, and 289.08 nm 304.69nm for ^{4}D. These wavelengths at their respective derivative order were selected for further study and other selected wavelengths were rejected.

From the obtained assay results (table 2) it was decided that at 262.06nm in 3rd order derivative spectrum (74.595% in Quetipin-200 & 77.24% in Quetipin-300) and 255.96nm in 4th order derivative spectrum (74.595% in Quetipin-200 & 77.24% in Quetipin-300) in two different dose tablets did not showed acceptable percent found.
However, at 254.76nm in 2nd order derivative spectrum of Quetiapine fumarate showed maximum estimation (99.56 % in Quetipin-200 & 99.76 % in Quetipin-300) in two different dose tablets as compare to other wavelengths. Hence, 2nd derivative mode at 254.76 nm was selected for further validation of method.

Method Validation [11-13]

Linearity range

Under the experimental conditions described the graphs obtained by plotting ^{2}D order absorbance values vs. concentration show linear relationships. Regression analysis using the method of least-squares was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curves were shown in fig.8. The linearity ranges were found to be 10–30 µg ml^{-1} for second order derivative spectrophotometric method.

Accuracy and recovery

To verify the capability of regression equations to predict the absorbance behavior of Quetiapine fumarate in dosage forms, the method was tested for precision and recovery. To study the recovery the pre-analyzed sample solutions a known amount of standard solutions of the pure drugs were added at different level i.e. 80, 90, 100, 110 and 120 %. Recovery study was determined by following formula;

% Recovery = [A-B/ C] X 100

Where, A = Total amount of drug estimated

B = Amount of drug found on pre-analyzed basis

C = Amount of drug added

The result of recovery studies are presented in Table 3. The mean recovery and relative standard deviation (RSD) were found to be 101.60 and 0.97% for first-derivative, 101.70 and 0.54% for second-derivative Spectrophotometric method, indicates very good reproducibility of these methods.

Precision

Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 15, 20 and 25 µg/ml of QPF solutions for three times in the same day. Inter-day precision was determined by analyzing the 15, 20 and 25µg/ml of QPF solutions daily for three days over the period of week. (Table 4)

Repeatability

Repeatability was determined by analyzing 20 µg/ml concentration of Quetiapine fumarate solution for six times with SD 0.06 & % RSD 0.31), indicating that the method have excellent repeatability.

Ruggedness

The ruggedness test of analytical assay method is defined as degree of reproducibility of assay results obtained by the successful applications of the assay over time and among multiple laboratories and analyst. Second-derivative UV Spectrophotometric determination of Quetiapine fumarate was carried out by two analysts and in two different instruments with the same standard. The results showed no statistical differences between different operators and instruments suggesting that the developed methods were robust and rugged (Table 5).

Specifity

According to the results obtained by interference study, the derivative Spectrophotometric method is able to access the analyte in the presence of excipients and hence, it can be considered specific. It has been concluded that there was no spectral interaction in the analysis of pharmaceutical preparation of Quetiapine fumarate. Therefore, calibration curve method was chosen for analysis of drug.
Specificity is a procedure to detect quantitatively the analyte in presence of component that may be expected to be present in the sample matrix. The analytes should have no interference from other extraneous components and be well resolved from them. Stress testing was performed by stressing the Quetiapine fumarate solution at concentration of 20ug/ml under UV light for 24 hrs, temperature 60°C for 24 hrs and under some extreme conditions such as 0.1 N HCl and 0.1 N NaOH, 3% H_2O_2 solutions for 24 hrs at 55°C. From stress testing results

(Table-7), it showed that when 3% H_2O_2 was added, Quetiapine fumarate was degraded (37.63%) while it has not been affected by other stressing conditions. No detectable changes were observed in the drug solutions when those were exposed to UV light (254 nm), different pH (acidic and basic pH), temperatures (60°C).

Comparison of results for all three derivative methods

From the above study, significant difference was found between the proposedspectrophotometric methods (table-1) but the recommended best feasible method for Quetiapine fumarate determination was second order derivative at 254.74nm ($^2D_{254.76nm}$). It showed lower R.S.D. values for intermediate precision and interference level (intercept value) for its calibration curve[14-15].

Conclusion

No derivative procedures have been described for the assay of Quetiapine fumarate therefore new derivative Spectrophotometric method has been develop for routine determination of Quetiapine fumarate. The results of the developed method have shown reliable results for estimation of QPF in tablet dosage form.

It can be concluded that the proposed methods are fully validated for 2nd derivative scan and found to be simple, sensitive, accurate, precise, reproducible, rugged and robust and relatively inexpensive. So, the developed methods can be easily applied for the routine Quality Control analysis of QPF in pharmaceutical preparations.

Table 1: Analytical data of Calibration curves by Derivative methods

Wavelength (nm)	**Linearity range**	**Regression equation (y=mx+c)[a]**	**R[b]**
$^2D_{254.76}$	10-30 µg/ml	Y = 6E-05x + 1E-05	0.999
$^2D_{273.68}$	10-30 µg/ml	Y = 6E-05x - 1E-06	0.999
$^2D_{291.08}$	10-30 µg/ml	Y = 5E-05x + 2E-06	0.999
$^3D_{262.06}$	10-30 µg/ml	Y = 1E-05x + 3E-06	0.999
$^3D_{283.12}$	10-30 µg/ml	Y = 1E-05x +52E-07	0.999
$^3D_{297.41}$	10-30 µg/ml	Y = 8E-06x + 7E-07	0.999
$^4D_{255.46}$	10-30 µg/ml	Y = 3E-06x + 1E-06	0.999
$^4D_{266.32}$	10-30 µg/ml	Y=1E-06x + 5E-07	0.998
$^4D_{278.58}$	10-30 µg/ml	Y = 2E-06x + 6E-07	0.998
$^4D_{289.08}$	10-30 µg/ml	Y = 3E-06x + 7E-08	0.999
$^4D_{304.69}$	10-30 µg/ml	Y = 1E-06x + 2E-07	0.999

Table 2: Assay results of two different dose tablets of Quetiapine Fumarate

Wavelength (nm)	Quetipine® tablet; 200mg					Quetipine® tablet; 300mg				
	Amount found (mg)	Amount found* (%)	±SD	%RSD	SE	Amount found (mg)	Amount found * (%)	±SD	%RSD	SE
	Second order derivative									
254.76	199.33	99.56	0.20	0.20	0.12	299.31	99.76	0.16	0.160	0.09
273.68	109.98	54.99	0.39	0.711	0.23	160.88	53.63	0.16	0.30	0.09
291.08	135.96	67.98	0.08	0.109	0.05	200.43	66.81	0.22	0.322	0.13
	Third order derivative									
262.06	149.19	74.595	0.15	0.196	0.09	231.73	77.24	0.28	0.359	0.16
283.12	96.38	48.19	0.28	0.596	0.16	136.93	45.64	0.15	0.32	0.09
297.41	114.93	57.47	0.04	0.062	0.02	183.99	61.33	0.16	0.25	0.09
	Fourth order derivative									
255.96	194.72	97.36	0.03	0.035	0.02	294.70	98.035	0.92	0.94	0.53
266.32	182.63	91.81	0.18	0.201	0.10	283.33	94.44	0.31	0.33	0.18
278.58	141.10	70.55	0.18	0.260	0.11	224.64	74.88	0.15	0.195	0.09
289.08	125.30	62.65	0.04	0.061	0.02	196.77	65.59	0.27	0.42	0.16
304.69	97.72	48.86	0.08	0.164	0.04	162.15	54.05	0.30	0.56	0.17

***mean of three estimation at each level**

Table 3: Accuracy of Quetiapine fumarate

Order	Level (%)	drug added (mg/ml)	Amount recovered* (mg/ml)	% Recovery	±SD	% R.S.D.	SE
$^2D_{254.76nm}$	80	2	2.02	100.89	0.075	0.467	0.043
	90	4	3.93	98.19	0.92	0.512	0.053
	100	6	6.05	100.84	0.218	0.84	0.126
	110	8	7.82	97.71	0.019	0.088	0.012
	120	10	9.91	99.12	0.051	0.213	0.029

***mean of three estimations at each level**

Accuracy(% Recovery) =(Found concentration/added concentration)*100.

Table 4: Results of Precision Studies (Intra-day and Inter-day)

Order (nm)	Concentrations (µg/mL)	Intra-day Precision*				Inter-day Precision*			
		Conc. Found	±SD	% R.S.D.	SE	Conc. Found	±SD	% R.S.D.	SE
$^2D_{254.76}$	15	15.28	0.034	0.22	0.019	15.08	0.498	0.49	0.044
	20	19.87	0.044	0.23	0.025	19.94	0.255	0.31	0.147
	25	24.49	0.284	1.15	0.164	25.22	0.255	0.31	0.147

*mean of three estimations at each level

SD: standard deviation; RSD:relative standard deviation.

Table 6: Results of Ruggedness Studies

Order (nm)	Component	Label claim (mg)	Analyst I	Analyst II				
			% Amount found*	±SD	SE	% Amount found*	±SD	SE
$^2D_{254.76}$	Quetiapine	200	99.91	0.37	0.151	98.85	0.71	0.289

* mean of three determinations

Table 7: Stress testing parameters

Medium	Conditions to be apply	%Sample estimated
0.1 N HCl, 1 ml(acid hydrolysis)	55^0 C, 24 hrs	99.48
0.1 N NaOH, 1 ml(base hydrolysis)	55^0 C, 24 hrs	95.95
3 % Hydrogen peroxide,1 ml(oxidation)	55^0 C, 24 hrs	62.35
Light (UV)	Light chamber, 1 lumens, 24 hrs	99.45
Temperature (dry heat)	60^0 C, 24 hrs	98.86

Acknowledgment

Authors are heartily thankful to Associate Dean, School of Pharmacy and Technology Management, NMIMS University, Shirpur, for providing facilities to carry out this work.

References

1) Seroquel package insert (Zeneca—US), Rev 7/97, Rec. 10/97.

2) Product Information: Seroquel®, quetiapine fumarate, Zeneca. In: Welbanks L (ed): Compendium of Pharmaceuticals and Specialties, 35th ed. Canadian Pharmaceutical Association, Ottawa, Ontario, Canada, 2000, 1451–1453.

3) www.drugbank.com

4) Mandrioli R., Fanali S., Ferranti A. and Raggi M.A., HPLC analysis of the novel antipsychotic drug quetiapine in human plasma, Journal of pharmaceutical and biomedical analysis, 2003, 30, 969-977.
5) Baby Sudha Lakshmi P., Vardhan S.V.M., Ramachandran D. and Rambabu C., UV Spectrophotometric Determination of Quetiapine and Zonisamide, Asian Journal of Chemistry, 2009, 21,1, 811-813.
6) Vincenzo P., Roberto M., Anna F., Sandra F. and Maria A.R., Journal of Pharmaceutical and Biomedical Analysis, 2003, 32, 4-5,1037-1044.
7) Li, Cheng K.Y., Li Z., Bai X., Zhang X., Wang B. and Li H., Quality control of commercial 1tablets containing the novel antipsychotic quetiapine, Acta Pharmacol Sin., 1, 2004, 25,110-114.
8) Uslu B, Özkan SA. Determination of lamivudine and zidovudine in binary mixtures using first derivative spectrophotometric, first derivative of the ratio-spectra and high-performance liquid chromatography–UV methods. Anal Chim Act 2002,466,175-185.
9) Sultan M. Spectrophotometric determination of acyclovir in some pharmaceutical formulations. Il Farmaco 2002, 57, 865-870.
10) Bebawy LI, Moustafa AA, Abo-Talib NF, Stability-indicating methods for the determination of doxazosin mezylate and celecoxib. J Pharma Biomed Anal 2002, 27,779-793.
11) The United State Pharmacopoeia/ The National Formulary, USP 28/ NF 23 edition, US Pharmacopoeial Convention, Rockville, MD, 2005, 2, 2389.
12) ICH, Q2A (R1), Validation of Analytical Procedures: Definition and terminology CPMP III/5626/94, March 1995, Geneva, Switzerland.
13) ICH, Q2B(R1), Validation of Analytical Procedures: Methodology (CPMP/281/95) Nov. 1996, Geneva, Switzerland.
14) Mehdi H., Maryam K., Mehdi B. and Hassan J., Derivative spectrophtometric method for determination of Losartan in pharmaceutical formulation, Iranian Journal of Pharmacology & Therapeutics, 3,2004, 21-25.
15) Sharma M., Mhaske D., Mahadik M., Kadam S. and Dhaneshwar S., UV and three derivative Spectrophotometric methods for determination of Ezetimibe in tablet formulation, Indian Journal Of Pharmaceutical Sciences, 2, 2006, 70. 258-260.

*****