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Development and Validation of HPTLC Method for Estimation of Quetiapine in Bulk Drug and in Tablet Dosage form

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Abstract: Quetiapine is a potent Serotonin and Dopamine receptor antagonist used to treat major depressive disorders. The present work describes a simple, precise and accurate HPTLC method for its estimation as bulk and in tablet dosage form. The chromatographic separation was carried out on precoated silica gel 60 F_{254} aluminium plates using mixture of methanol and toluene (4:3%v/v) as mobile phase and densitometric evaluation of spots were carried out at 235nm using Camag TLC scanner – 3 with WINCAT 1.3.4 version software. The experimental parameters like band size of spot applied, chamber saturation time, solvent front migration, slit width etc were critically studied and optimum conditions were evolved. The drug was satisfactorily resolved with R_f value 0.41 ± 0.01. The accuracy and reliability of the proposed method was ascertained by evaluating various validation parameters like linearity (100-500ng/spot), precision (intra day 0.53 – 0.78, inter day 0.53-1.62), accuracy (98.87±0.2) and specificity according to ICH guide lines. The proposed method provides a faster and cost effective quality control tool for routine analysis of quetiapine as bulk drug and in tablet formulation.

Key words: Quetiapine (QTP), HPTLC, densitometric estimation, method development and validation.

Introduction

Quetiapine (QTP), chemically 2-[2-(4-dibenzo (b,f) (1,4) thiazepine-11yl-1-piperazinyl) ethoxy] ethanol (E)- 2-butanediote [1] is a serotonin and dopamine receptor antagonist used to treat Schizophrenia [2-5] . Literature survey reveals that few HPLC, UV and GC-MS have been reported for estimation of quetiapine [6-9] but no HPTLC method is reported so far. The present study illustrates development and validation of a simple, accurate, economical and reproducible procedure for determination of quetiapine by HPTLC as bulk and in tablet dosage form.

Materials and Methods

Pharmaceutical grade quetiapine (99.18%) working standard was a generous gift from Indo biotech labs, Hyderabad. Fixed dose tablets (Socalm-50mg) containing 50mg of quetiapine procured from local pharmacy store. Silica gel 60 $F_{254,}$ TLC plates (10X10cm, layer thickness 0.2mm, E-Merck, Germany) were used as stationary phase. All chemicals and reagents used were of analytical grade and purchased from Merck Chemicals Corporation Ltd, Mumbai, India. A Camag HPTLC system containing Camag Linomet IV semiautomatic sample applicator, Hamilton syringe(100µl), Camag TLC scanner – 3 with WINCAT software version 1.3.4, Camag twin trough chamber (20X10cm) were used for present study.

Quetiapine 25mg were weighed accurately dissolved and diluted with methanol to obtain the final concentration of 100µg /ml. Twenty tablets were weighed accurately and ground to fine powder. Weight equivalent to 25mg of quetiapine was transferred to conical flask and mixed with methanol. The solution was sonicated for 15min. the extracts were filled through Whatmann filter paper No. 41 and residue washed thoroughly with methanol. The extracts and washings were transferred to 25ml volumetric flask and volume was made up to 25ml with methanol. Required dilutions were made to get 100µg/ml.

Various solvent system were tried to separate and resolve spot of quetiapine from its impurities and other excipients of formulations. The mixture of Methanol and Toluene (4:3%v/v) could resolve QTP spot with better peak shape (Fig-1) with R_f value of 0.41 ± 0.01.

TLC plates were prewashed with methanol. Activation of plates was done in an oven at 115° C for 10 minutes. The chromatographic conditions maintained were precoated silica gel 60 F_{254} aluminium plates (10X10cm) as stationary phase, methanol and toluene

(4:3%v/v) as mobile phase and plate saturation time of 30min, migration distance allowed was 72mm, wavelength scanning was done at 235nm, keeping the slit dimension at 5X0.45mm, temperature 26.5^{0}C and humidity 61%l. A deuterium lamp provided the source of radiation.

Three µl standard solution of quetiapine was spotted and developed. Photometric measurements were performed at 235nm in reflectance mode with Camag TLC scanner 3 using WINCAT software version 1.3.4 incorporating track optimization position. For the preparation of Calibration curve aliquots of 1-5µl of standard solution of quetiapine (100µl/ml) were applied on TLC plate using semi automatic spotter. TLC plate were dried, developed and densitometrically analyzed as described earlier.

Results and Discussion

The method was validated as per ICH guidelines[10] in terms of linearity, accuracy, specificity, intraday and interday precision, repeatability of measurement of peak area as well as repeatability of sample application **(Table – 1).** The method was fount to be linear in the range of 100-500ng/spot, (Y=10.02X + 8.467), (r = 0.9915) in six replicates. The signal to noise ratios of 3 and 10 were considered as LOD and LOQ respectively. LOD and LOQ of quetiapine found to be 30 and 100ng/spot. The intraday precision was determined by analyzing standard of quetiapine solution in the concentration range of 200ng/spot and 500ng/spot for three times on same day while interday precision was determined by analyzing corresponding standards daily for five days over a period of one week. The percentile RSD of intraday and interday precision of quetiapine the range of 0.53 – 1.62. The value indicates the method is precise. Repeatability sample application was assessed by spotting 3µl of drug solution six times on TLC plate followed by development of plate and recording the peak area of spots. The percentile RSD peak area values of quetiapine were found to be 0.32. Repeatability measurement of peak area was determined by spotting 3µl quetiapine solution TLC plate and developed. The separated spot was scanned six times without changing the position of plate and the percentile RSD measurement of peak area value of quetiapine was found to be 0.19.

To confirm the specificity of proposed method the solution of formulation was spotted on TLC plate which was then developed and scanned. It was observed that the excipients present in the formulation did not interfere with peak of quetiapine.

Recovery studies of the drug were carried out for the accuracy parameters. These studies carried out at three different levels namely 80, 100 and 120%. The result of recovery study indicates the proposed method is accurate for estimation of quetiapine in tablet dosage form. **(Table-2**).

In conclusion the proposed HPTLC method was found to be rapid, specific, precise and accurate can be used routinely for the estimation of quetipine in bulk drug and tablet dosage form.

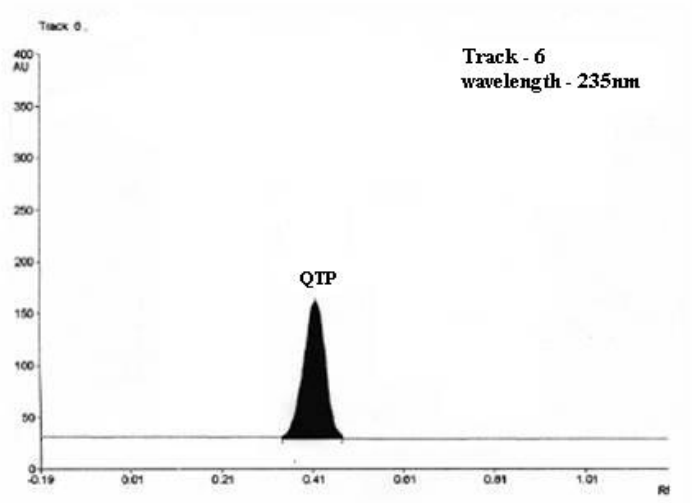

Fig – 1 HPTLC Chromatogram of Quetiapine (QTP) standard solution

Table – 1: Summary of Validation Parameters

Parameters	Range
Linearity range (ng/spot)	100 - 500
r	0.9995
Slope (m)	10.02
Intercept (c)	8.467
LOD (ng/spot)	30
LOQ (ng/spot)	100
Precision* (%RSD) - Intraday - Interday - Repeatability of sample application (n=6) - Repeatability of sample application (n=6)	 0.53 – 0.78 0.53 – 1.62 0.32 0.19

* Each value is a mean of six observations

Table – 2: Recovery studies

Label Claim (mg/tablet)	Amount added (%)	Total amount added (mg)	Amount Recovered (mg)	% Recovery*
Quetiapine (50)	80	40	39.15	97.87±0.23
	100	50	49.70	99.40±0.24
	120	60	59.62	99.36±0.13
Average % Recovery				98.87±0.2

***** Average value ± Standard deviation of six determinations.

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