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NOTE

UV Spectrophotometric Determination of Quetiapine and Zonisamide

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Simple and sensitive UV spectrophotometric methods have been developed for the determination of quetiapine as fumarate and zonisamide having absorption maximum at 254.7 and 238.12 nm, respectively. These methods are extended to pharmaceuticals formulations. There is no interference from any common pharmaceutical additives and diluents. The methods have been statistically evaluated and found to be precise and accurate.

Key Words: Spectrophotometric determination, Quetiapine, Zonisamide.

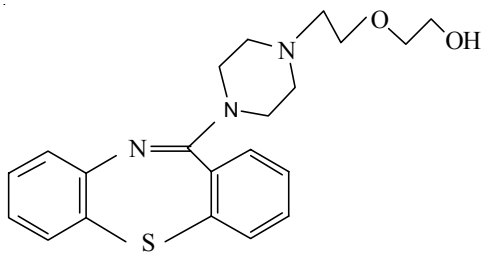
Quetiapine as fumarate (QTP) is an antipsychotic drug belonging to a new chemical class, the dibenzothiazepine derivatives. Quetiapine is intended for the treatment of schnizophrenia and other psychotic syndromes in human[1]. Benzothiazepine with mixed serotonin ($5HT_2$) and dopamine (D_2) receptor antagonistic properties[2]. QTP induces a lower incidence of extrapyramidal side effects. Chemically known as 2-[2-(4-dibenzo[b,f]-[1,4] thiazepin-1,1-yl-1-piperazinyl)ethoxy]ethanol. The chemical formula is $C_{42}H_{50}N_6O_4S_2$. $C_4H_4O_4$ having molecular weight 883.11. Zonisamide (ZSA) is a new epileptic drug to be effective in the treatment of patients with refractory partial seizures[3]. Zonisamide inhibits the sustained, repetitive firing of spinal cord neurons and tonic hind limb extension evoked by maximal electroshock[4]. Chemically, it is 1,2-benzisoxazole-3-methane sulfonamide having molecular formula $C_8H_8N_2O_3S$. Literature survey reveals that no UV-visible methods are reported for the estimation of QTP and ZSA. The authors have developed simple, accurate and reliable UV spectrophotometric methods for the estimation of QTP and ZSA in pure as well as in pharmaceutical dosage forms.

All the chemicals were used of analytical grade. Spectral and absorbance measurements were made on Elico UV-visible spectrophotometer S-159 with 10 mm matched quartz cells.

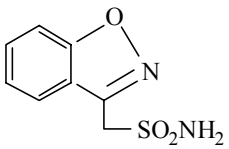
Preparation of standard solutions: Accurately weighed 100 mg of quetiapine was dissolved in 100 mL of distilled water and the solutions

were diluted quantitatively with distilled water to obtain a final concentration of 10 µg/mL.

100 mg of zonisamide was dissolved in methanol then diluted with methanol to obtain working standard solution 50 µg/mL.



Quetiapine



Zonisamide

Proposed method for QTP and ZSA: Aliquots of solution 0.5-2.5 mL were transferred into a series of 10 mL volumetric flasks and the volume was brought to 10 mL with distilled water for QTP and with methanol for ZSA. The absorbance was measured at 254.7 for QTP and 238.12 nm for ZSA against a reagent blank. The amount of QTP and ZSA present in the sample solution was computed from its calibration curve.

Procedure for the assay of QTP and ZSA in formulations: The tablet powder equivalent to 100 mg of QTP was taken and treated with (3 mL × 25 mL) portions of chloroform. The combined chloroform extract was made upto 100 mL with the same solvent to get mg/mL stock solution. From one portion of chloroform extract (20 mL), $CHCl_3$ was gently evaporated. The residue was dissolved in minimum volume of 0.1 N HCl and subsequently the solution was diluted with distilled water to get 10 µg/mL. The absorbance of the solution was determined at λ_{max} 254.7 nm. The quantity of drug was computed from the Beer's law plot of the standard drug in distilled water.

An accurately weighed portion of the capsule powder equivalent to 100 mg of drug was dissolved in 20 mL of methanol (MeOH), shaken well and filtered. The filtrate was diluted to 100 mL with MeOH to get 1 mg/mL solution of drug in formulations.

5 mL of this solution was further diluted to 100 mL to get 50 µg/mL solution. The absorbance of the solution was determined at λ_{max} 238.12 nm. The quantity of drug was computed from the Beer's law plot of the standard drug in MeOH.

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, per cent relative standard deviation, regression equation, correlation coefficients, % range of error were calculated and the results are summarized in Table-1. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to previous pharmaceutical preparations and the mixtures were analyzed by the proposed

methods and the results are presented in Table-2. These results indicate that the methods are simple, rapid with reasonable precision and accuracy and applicable to various formulations of quetiapine and zonisamide.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION OF THE PROPOSED METHOD

Parameter		Quetiapine	Zonisamide
λ_{max} (nm)		254.7	238.12
Beer's law limit (µg/mL)		5.0-20	2.0-8.0
Molar absorptivity (L mol^{-1} cm^{-1})		1.27×10^4	4.71×10^3
Sandell's sensitivity (µg cm^{-2}/0.001 absorbance unit)		0.037	0.126
Regression equation (Y = a + bC)	Slope (b)	0.014	0.028
	Intercept (a)	-2×10^{-4}	-1.4×10^{-3}
Correlation coefficient (r)		0.9999	0.9998
Relative standard deviation (%)*		0.910	0.841
% Range of error (Confidence limits)*	0.05 level	0.957	0.882
	0.01 level	1.500	1.385

*Average of six determinations considered.

TABLE-2
ESTIMATION OF QUETIAPINE AND ZONISAMIDE IN PHARMACEUTICAL FORMULATIONS

Sample	Labelled amount (mg)	Amount found (mg) Proposed method	% Recovery amount
Quetiapine			
Tablets I	25	24.91	99.64
Tablets II	25	24.96	99.84
Zonisamide			
Tablets I	100	99.89	99.90
Tablets II	100	99.94	99.94

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