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Spectrophotometric Estimation of Zolpidem in Tablets

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Abstract:
A simple, sensitive, rapid, accurate and precise spectrophotometric method has been developed for the estimation of Zolpidem tartrate in bulk and pharmaceutical dosage forms. Zolpidem tartrate shows maximum absorbance at 238.5 nm with molar absorptivity of 4.4648×10^4lit/mol/cm. Beer's law was obeyed in the concentration range of 2-16 µg/ml. The limit of detection and limit of quantification were found to be 0.038152 µg/ml and 0.114577 µg/ml, respectively. Results of analysis were validated statistically and by recovery studies.
Keywords: Estimation, Tablets, UV spectroscopy, Zolpidem tartrate.

Introduction:

Zolpidem tartrate is N,N,6-Trimethyl-2-p-tolyl-imidazo(1,2-a)pyridine-3-acetamide L-(+)-tartrate (2:1), *(fig. 1)* an imidazopyridine derivative, is a nonbenzodiazepine hypnotic agent binds preferentially to one benzodiazepine receptor subtype ω-1 bezodiazepine-1 thought to mediate hypnotic effects. This combines a rapid onset with a short duration of action. Zolpidem behaves as a sleep inducer without the muscle relaxant and anticonvulsant effects of the benzodiazepines [1-2]. The hypnotic actions of Zolpidem, like benzodiazepine hypnotics, are mediated at the benzodiazepine recognition site of the $GABA_A$ receptor complex [3-4]. However, the neuropharmacological profile of Zolpidem is somewhat different from that of most benzodiazepines [5–6]. For example, Zolpidem binds with low affinity to a α_5 –containing $GABA_A$ -receptor subtypes [7]. Triazolam and diazepam, two benzodiazepines, bind with high affinity to these $GABA_A$ -receptor subtypes.

Literature survey revealed that the analytical techniques published for Zolpidem, and eventually some of its metabolites, have mainly involved HPLC [8–11], gas chromatography (GC) [12-14], capillary electrophoresis (CE) [15]. Two methods are described for the determination of Zolpidem hemitartrate in presence of its degradation product by quantitative HPTLC and LC [16]. Zolpidem has been determined by GC/MS for postmortem specimens [17]. Zolpidem has been also found to be estimated by oral fluid by liquid chromatography–tandem mass spectrometry [18]. Method was found on Simultaneous determination of Zolpidem and Zopicone in human plasma by gas chromatography-nitrogen-phosphorus detection [19] and also Zaleplon and Zolpidem can be determined by liquid chromatography– turbo-ionspray mass spectrometry for forensic cases [20]. However, no UV spectrophotometric method is available for the quantitative determination of Zolpidem in its pharmaceutical dosage forms.

The objective of the present work was to develop simple, rapid, accurate and specific UV spectrophotometric method for the estimation of Zolpidem in pharmaceutical dosage forms. The method was further validated for the parameters like precision, accuracy, sensitivity, and linearity. The limit of detection (LOD) and limit of quantification (LOQ) were also determined. The results of analysis were validated statistically and by recovery studies. This method of estimation of Zolpidem was found to be simple, precise and accurate.

Materials and Methods:

Zolpidem was obtained as a gift sample from Aurobindo Pharma Ltd., Hyderabad, India. Zolpidem tablets were procured from local pharmacy. All the reagents were of analytical grade. Glass double distilled water was used throughout the experiment. A Shimadzu UV/VIS 1700 spectrophotometer with 1 cm matched quartz cells were used for the estimation.

An accurately weighed 5 mg of Zolpidem was dissolved in 5 ml methanol in a 50 ml volumetric flask and the volume was adjusted up to the mark with distilled water to obtain a stock solution of 100 µg/ml. Aliquots of 0.2 to1.6 ml portions

Table 1: Optical Characteristics and Regression Equation for the Standard Zolpidem

Sr. No.	Parameter	Value
1.	λ_{max} (nm)	238.5
2.	Beer's range (µg/ml)	2-16
3.	Molar absorptivity (l/mol/cm)	4.4648×10^4
4.	Sandell's sensitivity (µg/cm^2/0.001AU)	0.017134
5.	Correlation coefficient (r^2)	0.9997
6.	Regression equation	$y = .058x - 0.0029$
7.	Intercept (a)	-0.002
8.	Slope (b)	0.05821
9.	Limit of detection (LOD µg/ml)	0.038
10.	Limit of quantification (LOQ µg/ml)	0.11

Table 2: Results of Analysis and Recovery Studies

Formulations	Label Claim mg	% Estimated	S.D.	C.O.V. (%)	S.E.	% Recovery
Zoldem	10	99.45	0.97	0.98	0.53	99.68
Nitrate	10	99.12	0.89	0.94	0.45	100.65
Zolfresh	10	99.89	0.75	0.75	0.33	100.10

S.D.: Standard Deviation; S.E.: Standard Error; C.O.V.: Coefficient of Variation

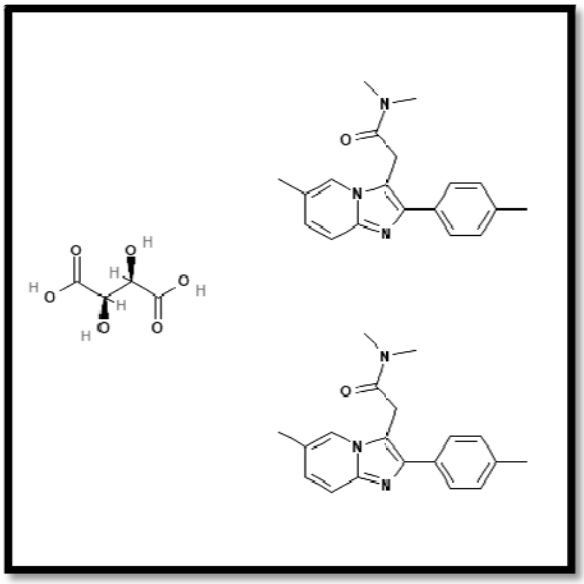

Fig. 1: **Chemical structure of Zolpidem**

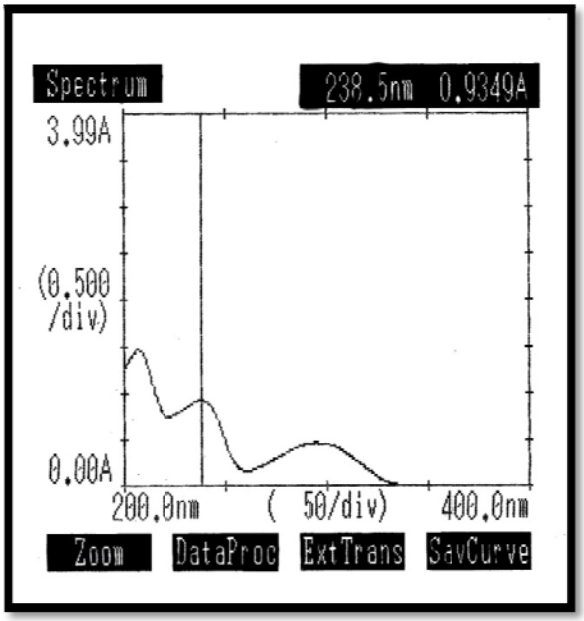

Fig. 2: **λ_{max} of Zolpidem in DMF: distilled water (1:4).**

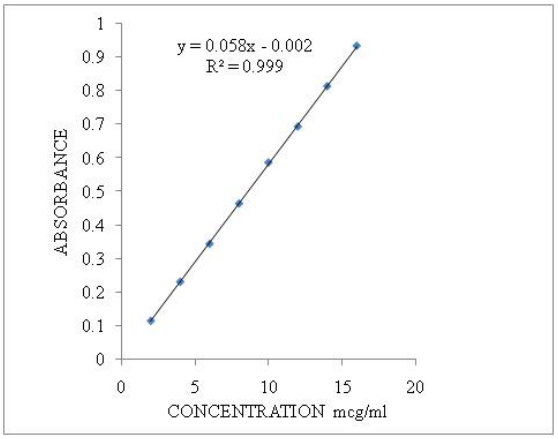

Fig. 3: **Calibration curve of Zolpidem in Methanol: distilled water (1:9) at 238.5 nm.**

of standard solution were transferred to a series of 10 ml volumetric flasks and volume in each flask were adjusted to 10 ml with distilled water to obtain a concentration of range of 2-16 µg/ml. One of the solutions was scanned in UV range using methanol: distilled water (1:9) as a blank and λ_{max} was found to be 238.5 nm. The absorbance of solutions was measured at 238.5 nm against blank and calibration curve of Zolpidem was constructed.

Twenty tablets of Zolpidem were emptied and powder was weighed. Amount equivalent to 5 mg was transferred to 50 ml volumetric flask, dissolved in 5 ml of methanol and made up the volume with distilled water to obtain a concentration of 100 µg/ml. The solution was filtered through Whatman filter paper No. 41 and filtrate was diluted to obtain concentration in between linearity range. The absorbance of sample solution was measured and amount of Zolpidem was determined by referring to the calibration curve. Recovery studies were carried out by adding a known quantity of pure drug to the preanalyzed formulation and the proposed method was followed. From the amount of drug found, percentage recovery was calculated.

Results and Discussion:

The results of optical characteristics and analysis of Zolpidem in tablets are presented in Table 1 and Table 2 respectively. The proposed method of determination of Zolpidem showed molar absorptivity of 4.4648×10^4 l/mol/cm and Sandell's sensitivity 0.017134 mcg/Sq.cm/0.001-absorbance units. Zolpidem exhibits its maximum absorption at 238.5 nm *(fig. 2)* and obeyed Beer's law in the range of 2-16 µg/ml *(fig. 3)*. Linear regression of absorbance on concentration gave equation y=0.058x-0.0029 and coefficient of correlation (R^2) = 0.9997. Relative standard deviation of 0.00067 was observed for analysis of 9 replicate samples, indicating precision and reproducibility. LOD and LOQ were calculated by Eqs. (1) LOD = $\frac{3.3\delta}{s}$ and (2) LOQ = $\frac{10\delta}{s}$, respectively, where δ is the standard deviation of blank and s is slope of calibration [21].

The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.038 µg/ml and 0.114 µg/ml respectively. The percentage recovery values 99.68%, 100.65%, 100.10% for Zoldem, Nitrate and Zolfresh respectively indicates that there is no interference from the excipients present in formulation (Table 2). The developed method was found to be sensitive, accurate, precise and reproducible and can be used for the routine quality control analysis of Zolpidem in bulk drugs and formulations.

Conclusion: The present spectroscopic method developed provides a rapid, sensitive, accurate, and reproducible determination of Zolpidem in tablets. This method can be successfully applied routine estimation of Zolpidem in bulk and pharmaceutical dosage form.

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