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RESEARCH ARTICLE

New Derivative Spectrophotometric Methods for the Determination of Zolpidem Tartrate in Pharmaceutical Dosage Forms

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Abstract: Two simple, rapid and sensitive first derivative spectrophotometric methods were developed for the determination of zolpidem tartrate in pharmaceutical formulations in phosphate buffer pH 8.0 and borate buffer pH 9.0. Beer's law was obeyed in a concentration range of 1-30 µg/mL in phosphate buffer pH 8.0 and borate buffer pH 9.0 respectively with correlation coefficient of r^2 =0.999 in both the methods. The linear regression equations are found to be y=0.008x+0.001 and y = 0.0094x + 0.0033 in phosphate and borate buffer respectively. The %RSD for intra-day and inter-day precision studies were found to be 0.23 and 0.56 in phosphate buffer pH 8.0 and 0.63 and 0.68 in borate buffer pH 9.0 respectively which is less than 2.0 indicating that the methods are precise. The %RSD in accuracy studies was also found to be less than 2.0. The proposed methods are suitable for the determination of zolpidem tartrate in pharmaceutical formulations. No interferences were observed from the excipients in the formulations. The methods were validated according to ICH guidelines.

Keywords: Zolpidem Tartrate, Derivative spectrophotometry, Validation

Introduction

Zolpidem tartrate (ZLT), chemically known as *N, N*, 6-trimethyl-2-ptolyl-imidazo(1,2-a) pyridine-3-acetamide L-(+)-tartrate (2:1) (Figure 1) is an imidazopyridine derivative, is a non benzodiazepine hypnotic agent binds preferentially to one benzodiazepine receptor subtype ω-1 bezodiazepine-1 thought to mediate hypnotic effects[1]. 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. The hypnotic actions of zolpidem, like benzodiazepine hypnotics, are mediated at the benzodiazepine recognition site of the GABAA receptor complex[2-4]. 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 α5-containing GABAA –receptor subtypes[7]. Triazolam and diazepam, two benzodiazepines, bind with high affinity to these GABAA -receptor subtypes. Literature survey revealed that zolpidem was determined by liquid chromatographic methods[8-15] in biological fluids, LC-MS[16-17], GC[18-19], GC-MS[20], capillary electrophoresis[21], UV-Visible spectroscopy[22-23] and HPTLC-LC[24].

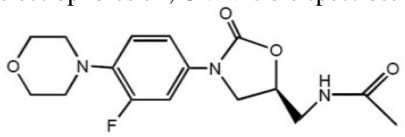

Figure 1. Chemical structure of zolpidem tartrate (ZPT)

In the present study, two novel simple, rapid and cost-effective derivative spectrophotometric methods were developed for the routine analysis of ZPT in pharmaceutical formulations in Phosphate Buffer pH 8.0 (Method A) and Borate Buffer pH 9.0 (Method B) and they are validated as per the ICH guideline[25-26].

Experimental

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe was employed with spectral bandwidth of 1 nm and wavelength accuracy of ±0.3 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (Denver, Germany). For scanning, the wavelength range selected was from 400 nm to 200 nm with medium scanning speed. All experiments were performed at room temperature (25±1) °C.

Reagents and chemicals

Analytical grade reagents were used. zolpidem tartrate was supplied as gift sample from Dr. Reddy's Labs (India) India. Zolpidem tartrate (ZPT) stock was prepared by dissolving 25 mg of the drug in 25 mL of methanol in a volumetric flask (1000 µg/mL) and working standard solutions were obtained by proper dilution of this stock solution with Phosphate Buffer pH 8.0 and Borate Buffer pH 9.0 for method A and B respectively.

Zolpidem tartrate (ZPT) is available commercially as tablets with brand names ZOLINOX ® and AMBIEN ® (containing 7.5 mg and 5 mg of the drug content) respectively and twenty tablets from each brand were procured from the local market.

Preparation of stock and sample solution

The standard solution of zolpidem tartrate was prepared by dissolving accurately about 25 mg of the zolpidem tartrate with methanol in a 25 mL volumetric flask.

Preparation of phosphate buffer (0.02 M) pH 8.0

50 mL of 0.2 M potassium dihydrogen phosphate was mixed with 46.8 mL of 0.2 M sodium hydroxide and sufficient water to make up to volume in a 500 volumetric flask.

Preparation of borate buffer pH 9.0

6.2 g of Boric acid was dissolved in 500 mL of water and pH was adjusted to 9.0 with 1.0 M sodium hydroxide and diluted with water to 1000 mL. The stock solution was further diluted with phosphate buffer pH 8.0 and borate buffer pH 9.0. The above solutions were scanned 200-400 nm against their reagent blank and the absorption spectra were recorded for both methods A and B respectively. The absorption spectra were transformed in to first derivative spectra.

Assay procedure for the commercial formulations (Tablets)

Zolpidem tartarate is available in the local market with brand names zolinox (7.5 mg of the drug per tablet; Ranbaxy Ltd.) and Ambien (5 mg; 10 mg of the drug per tablet; Dr. Reddy's Labs) were purchased. Twenty tablets were collected from the above two different brands and ZLT equivalent to 25 mg was weighed, extracted with methanol separately, sonicated and make up to volume with methanol in two different 25 mL volumetric flasks (1 mg/mL) and filtered. The dilutions were made from this stock with phosphate buffer and borate buffer for method A, B separately and analyzed according to the recommended procedure.

Precision and accuracy

The precision study was done as per the ICH guidelines by recording the absorbance of six replicates for method A, B and C (20 µg/mL) and the %RSD was calculated. Accuracy was evaluated as per the ICH guidelines by the percent recovery studies by the addition of 80%, 100% and 120% of pure sample solution to the pre-analysed formulation solution. For the present study ZLT drug solution (5 µg/mL) extracted from the formulation was taken and 80%, 100% and 120% of pure drug solution (*i.e.* 4, 5 and 6 µg/mL) were added and the %RSD was calculated.

Results and Discussion

In method A, the derivative spectrum (Figure 2) shows maxima (230.95 nm) and minima (254.25 nm) in phosphate buffer pH 8.0 and therefore the amplitude was chosen for the analytical determinations.

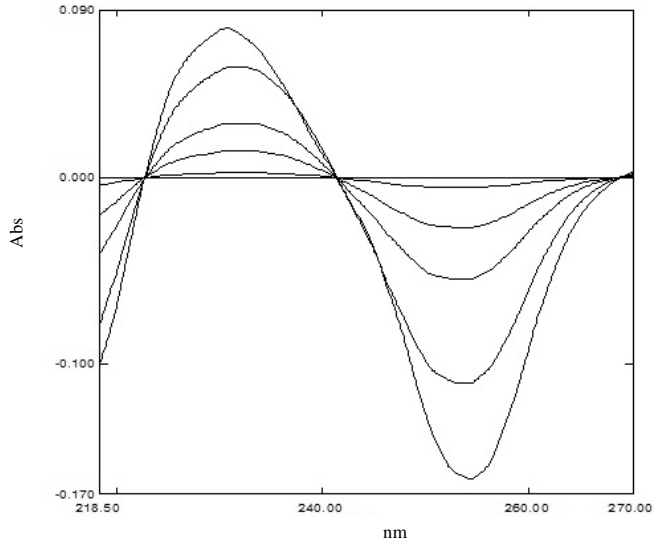

Figure 2. First order derivative overlay spectrum of zolpidem tartrate in phosphate buffer pH 8.0 (1-30 µg/mL)

In method B the derivative spectrum (Figure 3) shows maxima (231.07 nm) and minima (254.76 nm) in borate buffer pH 9.0 and hence the amplitude was chosen for the analytical study. A graph was drawn by taking the concentration on the x-axis and the corresponding derivative absorbance on the y-axis for both method A and B.

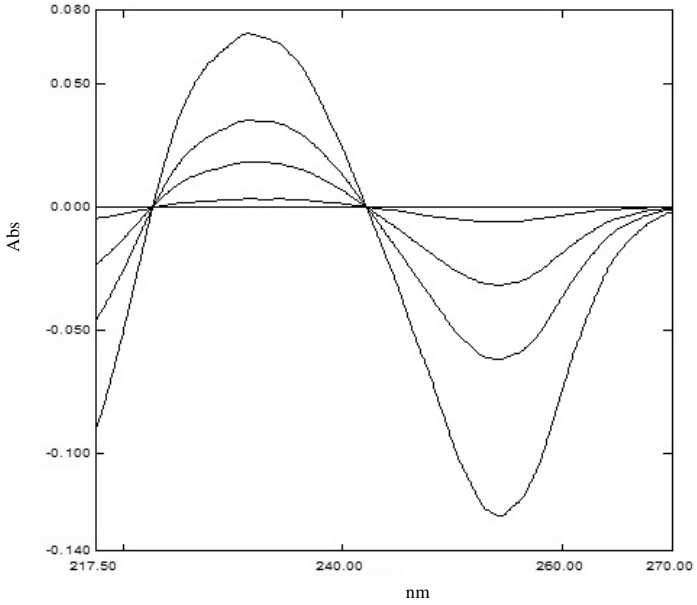

Figure 3. First order derivative spectrum of zolpidem tartrate in borate buffer pH 9.0 (1-30 µg/mL)

Beer-Lambert's law was obeyed over the concentration range of 1-30 µg/mL for both method A and B (Figure 4 and 5) respectively. The linear regression equations for method A and B were found to be y=0.008x+0.001(r^2 = 0.9999) and y = 0.0094x + 0.0033 (r^2 = 0.999) respectively.

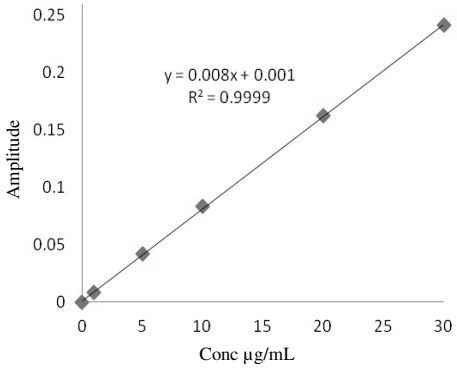

Figure 4. Linearity of zolpidem tartarate in phosphate buffer pH 8.0

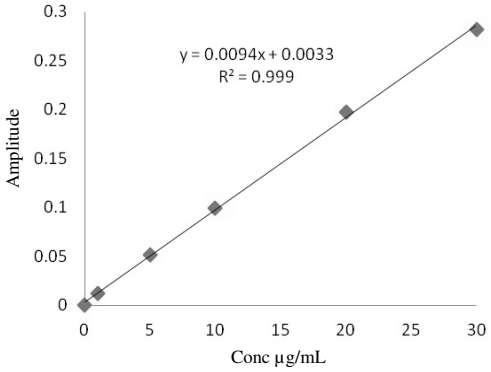

Figure 5: Linearity of zolpidem tartarate in borate buffer pH 9.0

The %RSD values in precision studies were found to be less than 2% in both methods A and B indicating that the method is more precise. The %RSD values in accuracy studies were also found to be less than 2% in both methods A and B indicating that the method is more accurate. The optical characteristics were shown in Table 1. The % recovery was found to be 99.7-99.88 and 99.46-99.91 for methods A and B respectively in marketed formulations (Table 2).

Table 1. Optical characteristics of Zolpidem Tartrate

Parameters	Method A	Method B
λ. nm (Amplitude)	230.95- 254.25	231.07-254.76
Beer-Lambert's range, µg/mL	1-30	1-30
Slope	0.008	0.0094
Intercept	0.001	0.0033
Correlation coefficient	0.9999	0.999
Precision (RSD, %)		
Intra-day (n=3)	0.23	0.63
Inter-day (n=3)	0.56	0.68
Accuracy (% recovery)	99.7-99.88	99.46-99.91

Table 2. Analysis of zolpidem tartrate commercial formulation (Tablets)

Brand	Labeled Amount, mg	*Amount Obtained, mg		% Recovery*		% RSD*	
		Method		Method		Method	
		A	B	A	B	A	B
Zolinox	7.5	7.49	7.48	99.87	99.73	0.36	0.55
Ambien	5.0	4.99	4.97	99.80	99.40	0.48	0.67

**Mean of three determinations*

Conclusion

The proposed methods are simple, precise and accurate and can be applied for the determination of zolpidem tartrate (ZPT) in pharmaceutical formulations successfully.

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