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Derivative Spectrophotometric Methods for the Determination of Zolpidem Tartrate in Tablets

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ABSTRACT

Two simple, precise and accurate first derivative spectrophotometric methods were developed for the determination of Zolpidem Tartrate in pharmaceutical formulations in phosphate buffer pH 6.8 and acetate buffer pH 4.0. Beer's law was obeyed over the concentration range 0.5-20 µg/ml in both phosphate buffer (pH 6.8) (Method A) and acetate buffer (pH 4.0) (Method B). The regression equations were found to be y = 0.101x+0.012 (r^2 = 0.999) and y = 0.064x+0.009 (r^2 = 0.999) in Method A and B respectively. The % RSD in precision studies was found to be 0.28-0.69 (Intra-day) and 0.31-0.73 (Inter-day) for Method A and 0.25-0.82 (Intra-day) and 0.26-0.57 (Inter-day) for Method B respectively. The % RSD in accuracy studies was also found to be 0.14-0.19 (Method A) and 0.18-0.23 (Method B) with percentage recovery 98.67-99.78 and 98.56-99.83 Method A and B respectively.

INTRODUCTION

Chemically, Zolpidem tartrate (ZPT) is 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, Zolpidem behaves as a sleep inducer without the muscle relaxant and anticonvulsant effects of the benzodiazepines. Zolpidem tartrate is a non benzodiazepine hypnotic agent binds preferentially to one benzodiazepine receptor subtype ω-1 bezodiazepine-1thought to mediate hypnotic effects (Budavri 2006). The hypnotic actions of Zolpidem, like benzodiazepine hypnotics, are mediated at the benzodiazepine recognition site of the GABAA receptor complex (Walker *et al.*, 1999, Haefely *et al.*, 1989, Sauvanet *et al.*, 1988). However, the neuropharmacological profile of Zolpidem is somewhat different from that of most benzodiazepines (Arbilla *et al.*, 1985, Benavides *et al.*, 1989, Besnard *et al.*, 1996). For example, Zolpidem binds with low affinity to a α5 –containing GABAA –receptor subtypes (Besnard *et al.*, 1996). Triazolam and diazepam, two benzodiazepines, bind with high affinity to these GABA A-receptor subtypes. Literature survey revealed that Zolpidem was determined by liquid chromatographic methods (Lavianaa *et al.*, 2004, Paula *et al.*, 2000, Tracqui *et al.*, 2003, Ascalone *et al.*, 1992, Gock *et al.*, 1999, Ptáček *et al.*, 1997, Qiao *et al.*, 1999, Guinebault *et al.*, 1986) in biological fluids, LC-MS (Kintz *et al.*, 2004, Giroud *et al.*, 2003), GC (Gaillard *et al.*, 1993, Stanke *et al.*, 1996), GC-MS (Keller *et al.*, 1999), capillary electrophoresis (Hempel *et al.*, 1996), UV-Visible spectroscopy (Patil *et al.*, 2010, Rajiv *et al.*, 2010, M. Mathrusri Annapurna *et al.*, 2012) and HPTLC (El Zeany *et al.*, 2003).

In the present study, two simple derivative spectrophotometric methods were developed for the routine analysis of ZPT in tablets in phosphate buffer pH 6.8 (Method A) and acetate buffer pH 4.0 (Method B) and they were validated as per the ICH guidelines (ICH 1996, ICH 2005).

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MATERIALS AND METHODS

Instrumentation

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 1nm 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

Zolpidem tartrate was obtained as gift sample from Sun Pharmaceuticals (India). Zolpidem tartrate is available with brand names ZOLPID ® (Micro Synapse, India) (Label claim: 10 mg) and NITREST ® (Sun Pharmaceuticals, India) (Label claim: 5 mg and 10 mg) as tablets.

Preparation of phosphate buffer ph 6.8

Dissolve 28.80g of disodium hydrogen phosphate and 11.45g of potassium di hydrogen phosphate and sufficient water to make up to volume in a 1000ml volumetric flask.

Preparation of acetate buffer ph 4.0

2.86 ml of glacial acetic acid and 1.0 ml of a 50% w/v solution of sodium hydroxide in a 100 ml volumetric flask make up the volume with water and mix adjusted the pH, if necessary.

Preparation of stock and sample solution

Zolpidem tartrate stock solution was prepared by dissolving 25 mg of the drug in methanol in a 25 ml volumetric flask (1000 µg/ml). The stock solution was diluted with phosphate buffer pH 6.8 (Method A) and acetate buffer pH 4.0 (Method B) respectively as per the requirement. Twenty tablets from each brand were procured from the local pharmacy store and ZPT 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 these stock solutions and diluted with phosphate buffer and acetate buffer for method A and B as per the requirement.

Preparation of calibration curve

A series of solutions (0.5-20 µg/ml) were prepared with phosphate buffer (Method A) and acetate buffer (Method B) and scanned 200-400 nm against their reagent blank and the absorption spectra were recorded. The absorption spectra obtained were transformed in to first derivative spectra by the inbuilt software.

The derivative spectrum shows maxima at 231.64 nm and minima at 253.57nm in phosphate buffer (pH 6.8) (Method A) and therefore the amplitude was chosen for all the analytical determinations. Similarly the derivative spectrum in acetate buffer (pH 4.0) (Method B) shows maxima at 229.93 nm and minima at 249.03 nm and therefore the amplitude was chosen for all the analytical determinations. Calibration curves were constructed by plotting the concentration on the x-axis and the corresponding $dA/d\lambda$ values on the y-axis and the regression equations were calculated (n=3).

RESULTS AND DISCUSSION

Zolpidem is used to treat insomnia. Two derivative spectrophotometric methods were developed for the determination of Zolpiden tartrate. Method A was developed in phosphate buffer (pH 6.8) in which the amplitude (231.64 nm - 253.57 nm) was chosen for all the analytical determinations. Similarly the amplitude (229.93 nm - 249.03 nm) was chosen even for Method B (Acetate buffer, pH 4.0). The overlay derivative spectra observed in method A and B were shown in Figure 2 and Figure 3. Zolpidem tartrate obeys Beer-Lambert's law over the concentration 0.5-20 µg/ml for both method A and B with regression equations $y = 0.101x + 0.012$ ($r^2 = 0.999$) and $y = 0.064 x + 0.009$ ($r^2 = 0.999$) respectively. The % RSD in precision studies was found to be 0.28-0.69 (Intra-day) and 0.31-0.73 (Inter-day) for Method A and 0.25-0.82 (Intra-day) and 0.26-0.57 (Inter-day) for Method B respectively. The % RSD in accuracy studies was also found to be 0.14-0.19 (Method A) and 0.18-0.23 (Method B) with percentage recovery 98.67-99.78 and 98.56-99.83 Method A and B respectively. The percentage RSD in precision and accuracy studies was less than 2.0 indicating that the proposed methods were more precise and accurate and the methods can be applied for the determination of Zolmitriptan tartrate in pharmaceutical dosage forms. The percentage recovery in marketed formulations (Table 1) was found to be 99.65-99.84 with percentage RSD less than 2.0 (0.57-0.91).

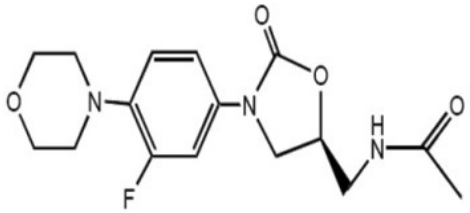

Fig. 1: Chemical structure of Zolpidem tartrate (ZPT)

Table. 1: 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
Brand I	10	9.978	9.965	99.78	99.65	0.91	0.65
Brand II	10	9.984	9.971	99.84	99.71	0.82	0.57

*Mean of three determinations

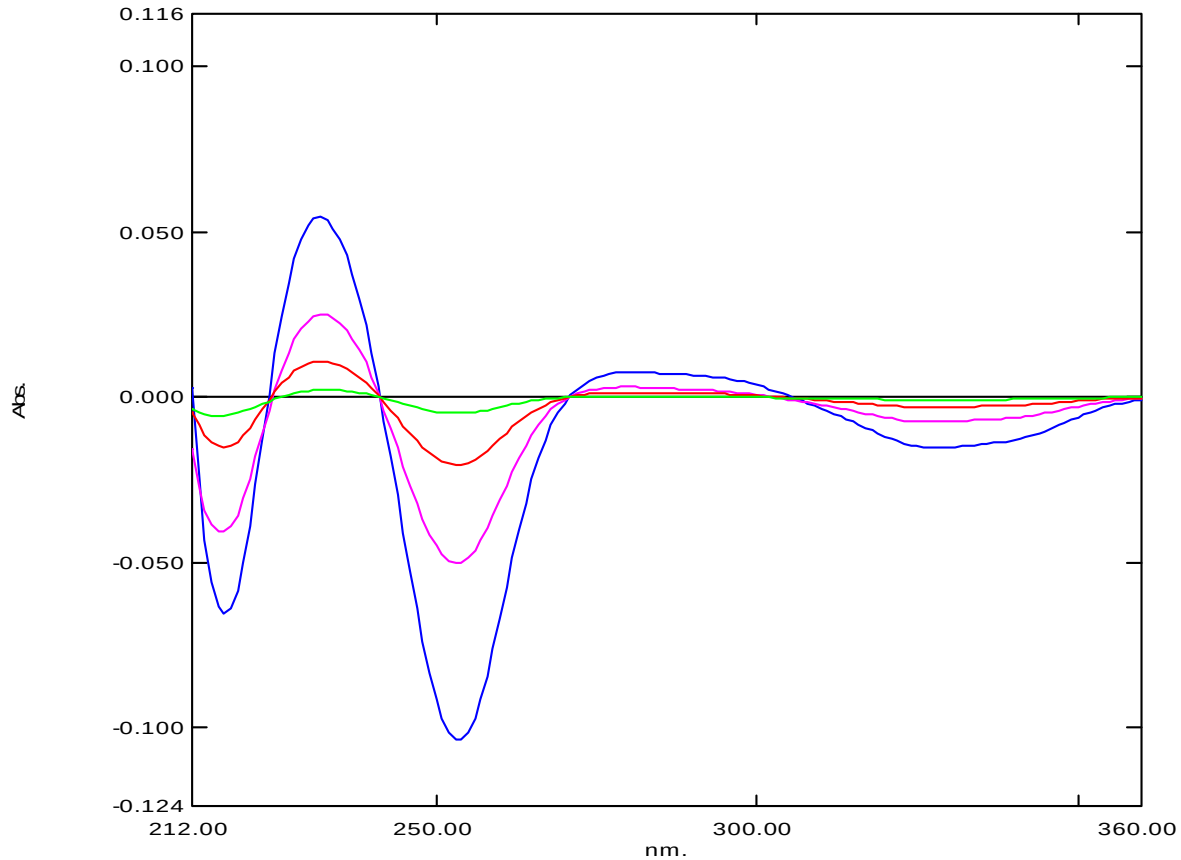

Fig. 2: Overlay first order derivative spectrum of Zolpidem tartrate in phosphate buffer (pH 6.8) (Method A).

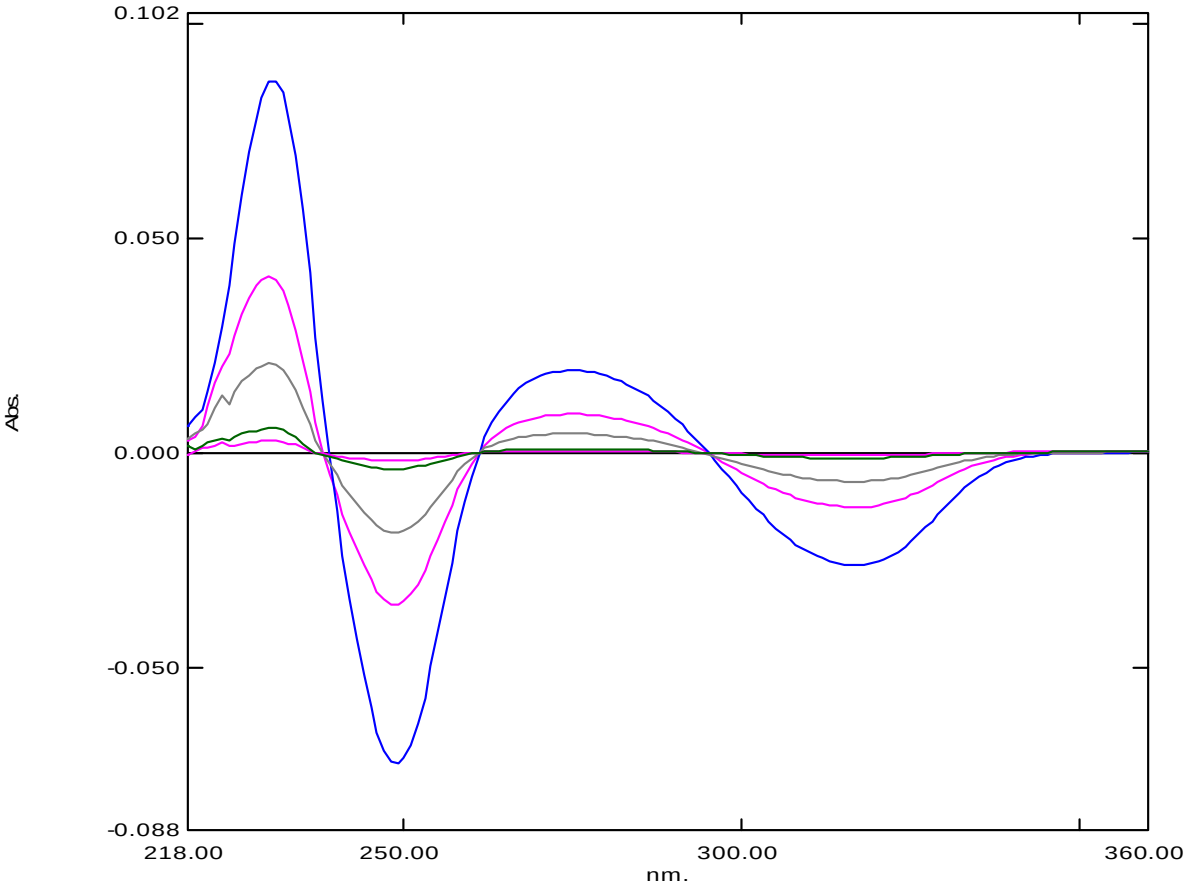

Fig. 3: Overlay first order derivative spectrum of Zolpidem tartrate in acetate buffer (pH 4.0) (Method B)

CONCLUSION

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

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