New Derivative Spectrophotometric Methods for the Analysis of Zolpidem Tartrate in Tablets

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Key words: Zolpidem tartrate, Derivative spectrophotometry, Validation.

INTRODUCTION

Zolpidem tartrate behaves as a sleep inducer without the muscle relaxant and anticonvulsant effects of the benzodiazepines. Zolpidem tartrate (ZPT), chemically known as N, N, 6-Trimethyl-2-picolyl-imidazo (1,2-a) pyridine-3-acetamide L- (+)-tartrate (2:1) (Fig 1) is an imidazo pyidine derivative, is a non benzodiazepine hypnotic agent binds preferentially to one benzodiazepine receptor subtype α₁bezodiazepine-1thought to mediate hypnotic effects [6]. This combines a rapid onset with a short duration of action. The hypnotic actions of Zolpidem, like benzodiazepine hypnotics, are mediated at the benzodiazepine recognition site of the GABAA receptor complex [2-4]. However, the neuro pharmacological profile of Zolpidem tartrate is somewhat different from that of most benzodiazepines [5-8]. Zolpidem binds with low affinity to a α5-containing GABA A receptor subtypes [7], Triazolam and diazepam, two benzodiazepines, bind with high affinity to these GABA A receptor subtypes.

Zolpidem tartrate was determined by liquid chromatographic methods [9-15] in biological fluids, LC-MS [16-17], GC [18-19], GC-MS [20], capillary electrophoresis [21], UV-Visible spectroscopy [22-25] and HPTLC-LC [26].

Zolpidem tartrate 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 in methanol in a volumetric flask.

Preparation of sodium hydroxide (0.1 N)

4.0 grams of sodium hydroxide was dissolved in distilled water in a 1000 mL volumetric flask.

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Received 14-10-2012; Accepted 26-11-2012
Preparation of hydrochloric acid (0.1 N)  
8.5 mL of conc. hydrochloric acid was diluted with distilled water in a 1000 mL volumetric flask.

The stock solution was further diluted with sodium hydroxide and hydrochloric acid. 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 tartrate 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 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⁻¹) and filtered. The dilutions were made from this stock with sodium hydroxide and hydrochloric acid 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⁻¹) 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 ZPT drug solution (5 µg mL⁻¹) extracted from the formulation was taken and 80%, 100%, and 120% of pure drug solution (i.e. 4, 5 and 6 µg mL⁻¹) were added and the % RSD was calculated.

RESULTS AND DISCUSSION  
In method A, the derivative spectrum (Fig 2) shows minima at 255.18 nm in sodium hydroxide and therefore the derivative absorbance at minima was chosen for all analytical determinations.

![Fig. 2. Overlay first order derivative spectrum of Zolpidem tartrate in sodium hydroxide.](image_url)

In method B, the derivative spectrum (Fig 3) shows minima at 249.08 nm in hydrochloric acid and therefore the derivative absorbance at minima was chosen for all analytical determinations.

![Fig. 3. Overlay first order derivative spectrum of Zolpidem tartrate in hydrochloric acid.](image_url)

A graph was drawn by taking the concentration of the drug solutions on the x-axis and the corresponding derivative absorbance on the y-axis for both the methods A and B.

![Fig. 4. Calibration curve of Zolpidem tartrate in sodium hydroxide.](image_url)

Beer-Lambert’s law was obeyed in a concentration range of 1-30 µg mL⁻¹ in sodium hydroxide (r² =0.9996) (Fig 4) and 5-40 µg mL⁻¹ in hydrochloric acid (r² =0.9989) (Fig 5) respectively. The linear regression equations are found to be y=0.0061 x + 0.0009 and y = 0.0048 x + 0.0018 in sodium hydroxide and hydrochloric acid respectively.

![Fig. 5. Calibration curve of Zolpidem tartrate in hydrochloric acid.](image_url)

The % RSD for intra-day and inter-day precision studies were found to be 0.35 and 0.69 in sodium hydroxide and 0.71 and 0.79 in hydrochloric acid respectively which is less than 2% indicating that the methods are precise. The % RSD values in accuracy studies were also found to be less than 2% with a recovery of 99.64-99.78 and 99.65-99.81 method A and B indicating that the methods are more accurate. The optical characteristics were shown in Table 1. The % recovery was found to be 99.60 and 99.20-99.47 for methods A and B respectively in marketed formulations (Table 2).
Table 1: Optical characteristics of Zolpidem tartrate

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Method A</th>
<th>Method B</th>
</tr>
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<tbody>
<tr>
<td>( \lambda ) (nm) (minima)</td>
<td>255.18</td>
<td>249.08</td>
</tr>
<tr>
<td>Beer-Lambert’s range (( \mu )g mL(^{-1} ))</td>
<td>1-30</td>
<td>5-40</td>
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<tr>
<td>Slope</td>
<td>0.0061</td>
<td>0.0048</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.0009</td>
<td>0.0018</td>
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<tr>
<td>Correlation coefficient</td>
<td>0.9996</td>
<td>0.9989</td>
</tr>
<tr>
<td>Precision (RSD, %)</td>
<td></td>
<td></td>
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<tr>
<td>Intra-day (n=3)</td>
<td>0.35</td>
<td>0.71</td>
</tr>
<tr>
<td>Inter-day (n=3)</td>
<td>0.69</td>
<td>0.79</td>
</tr>
<tr>
<td>Accuracy (% recovery)</td>
<td>99.64-99.78</td>
<td>99.65-99.81</td>
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</table>

Table 2: Analysis of Zolpidem tartrate in commercial formulation (Tablets)

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Labeled Amount (mg)</th>
<th>*Amount obtained (mg) A</th>
<th>% Recovery* A</th>
<th>*% RSD A</th>
<th>Method</th>
<th>Method</th>
<th>Method</th>
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<tr>
<td>Brand I</td>
<td>7.5</td>
<td>7.47</td>
<td>99.60</td>
<td>0.36</td>
<td>0.55</td>
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<tr>
<td>Brand II</td>
<td>5.0</td>
<td>4.96</td>
<td>99.60</td>
<td>0.48</td>
<td>0.67</td>
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<td></td>
</tr>
</tbody>
</table>

CONCLUSION

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

ACKNOWLEDGEMENT

The authors are grateful to M/s GITAM University for providing necessary research facilities and to Dr. Reddy’s Labs (India) for providing the gift samples of the drug.

REFERENCES


Source of support: Nil,
Conflict of interest: None Declared