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Research Article

Simple and sensitive extractive spectrophotometric method for the assay of Ambien in pure and pharmaceutical formulations

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ABSTRACT

Two simple, reliable, inexpensive and less time-consuming methods were developed and validated for determination of Zolpidem tartrate in bulk and pharmaceutical formulation. Both methods were based on ion-pair complexation reaction of the drug with Bromothymol blue (BTB) and Solochrome black –T (SBT). Absorbance measurement was made at 416 nm for BTB and 508 nm for SBT. Beer's law was obeyed in the concentration ranges of 5-50 µg ml^{-1} for BTB and 2-20 µg ml^{-1} for SBT with a correlation coefficient of 0.9991 and 0.9990 respectively. The proposed method may be successfully applied for the routine analysis of Zolpidem in pharmaceutical preparations as the results are on par with the reported method.

Keywords: Molar absorptivity; Ion-pair complex; Visible Spectrophotometry; Zolpidem Tartrate (ZPD); Insomnia

INTRODUCTION

Ambien (zolpidem tartrate) is a non-benzodiazepine hypnotic of the imidazopyridine class and is available in 5 mg and 10 mg strength tablets for oral administration. Zolpidem is a prescription short-acting nonbenzodiazepine hypnotic that potentiates gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter, by binding to benzodiazepine receptors which are located on the gamma-aminobutyric acid receptors. Zolpidem is used for the short-term treatment of insomnia. It works quickly (usually within 15 minutes) and has a short half-life (2-3 hours). As an anticonvulsant and muscle relaxant, the beneficial effects start to emerge at 10 and 20 times the dose required for sedation, respectively. For that reason, it has never been approved for either muscle relaxation or seizure prevention. Recently, zolpidem has been cited in various medical reports mainly in the United Kingdom as waking persistent vegetative state (PVS) patients, and dramatically improving the conditions of people with brain injuries.

Chemically, zolpidem is N,N-dimethyl-2-[6-methyl-2-(4-methylphenyl)imidazo[1,2-a]pyridin-3-yl] acetamide. Its structure is shown in figure 1.

Zolpidem tartrate is a white to off-white crystalline powder that is sparingly soluble in water, alcohol, and propylene glycol. It has a molecular weight of 307.3895.

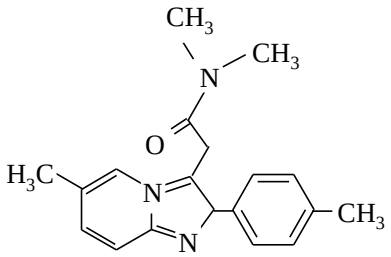

Figure 1: Chemical Structure of Zolpidem

Each Ambien (zolpidem tartrate) tablet includes the following inactive ingredients: hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide. The 5 mg tablet also contains FD&C Red No. 40, iron oxide colorant, and polysorbate 80. It is official in British Pharmacopeia (2, 2007) and Merck Index (Budavari S.12, 1996) which describes liquid chromatographic method for its quantitation. Literature survey revealed that very few HPLC methods (Nirogi RV *et al.*, 2004; Laviana L *et al*., 2004; Ring P R *et al.,* 2000; Kintz P *et al.,* 2004), Potentiometric method (Kelani K M *et al.,* 2004) and spectrophotometric methods (Rajiv Chomwal *et al.,* 2010) have been developed so far for the estimation of Zolpidem tartrate in human serum, in bulk and dosage forms. Spectrophotometric methods are popular because of their low cost and high sensitivity. This prompted us to develop more simple, sensitive and accurate extractive spectrophotometric methods for the estimation of Zolpidem in pure and dosage form.

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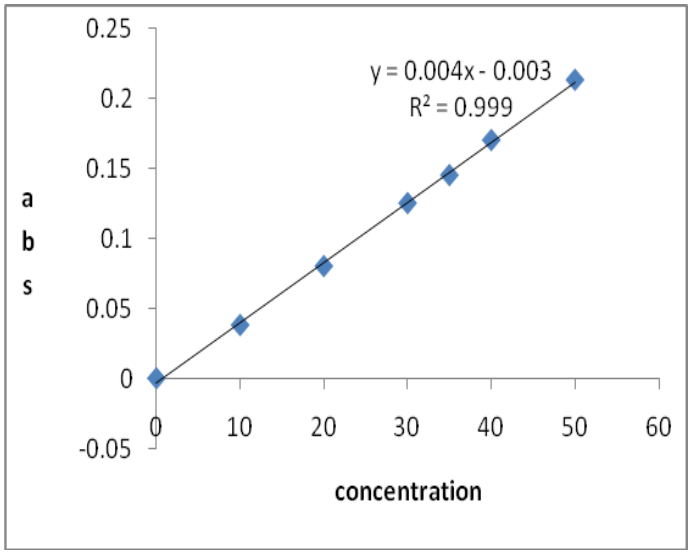

Figure 2: Calibration curve Zolpidem Tartrate with BTB

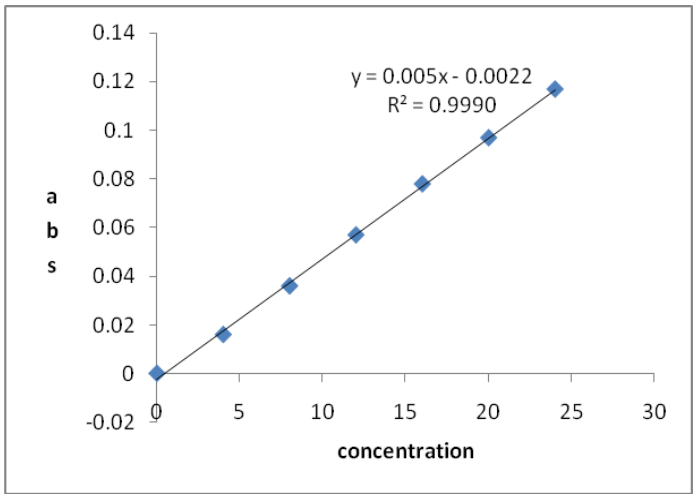

Figure 3: Calibration curve for Zolpidem Tartrate with EBT

Table 1: Spectral characteristics of Zolpidem Tartrate

Parameters	Method A	Method B
λ max (nm)	416	508
Beer's Law limits[a] (µg/ml)	5-50	4-30
Molar Absorptivity (L $mol^{-1}cm^{-1}$)	1.309×10^4	1.511×10^4
Correlation Co-efficient(r^2)	0.9991	0.9990
Regression equation	y = 0.0043x - 0.0033	y = 0.005x -0.0022
Standard Deviation	0.075103	0.04284
RSD (%)[b]	0.74	0.68
Recovery (%)[c]	99-100	99-100

[a] Data obtained from 4 determinations (n = 4). [b] and [c] For six replicates

MATERIALS AND METHODS

Apparatus

After due calibration of the instrument, spectral and absorbance measurements were made using Genesys 10 UV Spectrophotometer procured from Thermo Scientific company marketed by Merck. All the chemicals used were of analytical grade. All the solutions were freshly prepared with double distilled water. Reagents were prepared a fresh for every method.

Preparation of Standard solution

100 mg of pure Zolpidem was transferred into a 100 ml standard flask. It was dissolved in 10 ml of methanol and then diluted with double distilled water up to the mark. 10 ml of the standard solution was pipetted and diluted up to the mark in another 100ml volumetric flask, and was used for preparing a standard curve for method A and 2 ml of the standard solution was pipetted and diluted up to the mark in another 100 ml volumetric flask and used for method B.

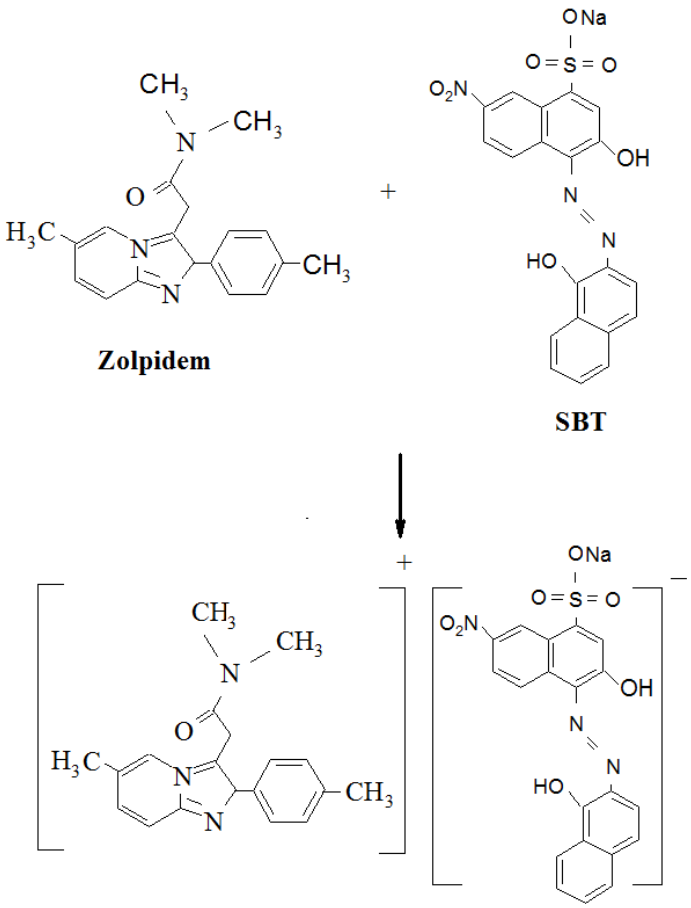

Figure 4: Scheme of Ion-association complex of ZPD with SBT

Preparation of buffer solution and reagents

Sodium acetate-acetic acid buffer solution was prepared by mixing 84.7 ml of 0.1 M acetic acid and 15.3 ml of 0.1 M sodium acetate. Its p^H was found to be 3.8 and used for method A. KCl-HCl buffer was prepared by mixing 50 ml of 0.2 M KCl and 7.8 ml of 0.2 M HCl and the solution was diluted to 200 ml with distilled water. Its p^H was found to be 2.2 and used for method B. Dye solutions were prepared by dissolving 40 mg of Bromothymol blue in 5 ml of methanol and the solution was diluted to 100 ml in a standard flask and by dissolving 100 mg of Solochrome black T in distilled water in 100 ml volumetric flask.

Recommended Procedure for the determination of Zolpidem

Method A

Aliquots of standard Zolpidem (1 ml=100 µg) solution ranging from 0.2-1.0 ml were transferred into a series of 250 ml separating funnels. To that 1 ml of BTB (0.2%) and 2 ml of buffer was added and the total volume of the aqueous phase was made up to 10 ml with distilled water. About 10 ml of chloroform was added to each funnel and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the chloroform layer was measured at 416 nm against the corresponding reagent blank.

Method B

Aliquots of standard Zolpidem (1 ml=20 µg) solution ranging from 0.2-1.2 ml were transferred into a series of 250 ml separating funnels. To that 1 ml of SBT (0.2%) and 2 ml of buffer was added and the total volume of the aqueous phase was made up to 10 ml with distilled water. About 10 ml of chloroform was added to each funnel and the contents were shaken gently for 2 min. The two phases were allowed to separate and the absorbance of the chloroform layer was measured at 508 nm against the corresponding reagent blank.

A calibration curve was prepared by plotting absorbance against concentration and the unknown was read from the calibration curve, or deduced using a regression equation, obtained from Beers' law data.

Procedure for pharmaceutical preparations

10 tablets (claiming for 10 mg of zolpidem tartrate per tablet) were finely powdered and transferred into a small conical flask. It was then dissolved in 20 ml of methanol and 50 ml of distilled water. It was filtered through Whatmann filter paper No.42 into 100 ml volumetric flask. The filtrate was diluted to mark with distilled water. The stock solution was diluted to provide theoretical concentrations as mentioned above. The content of Zolpidem tartrate was determined with the above developed methods A & B.

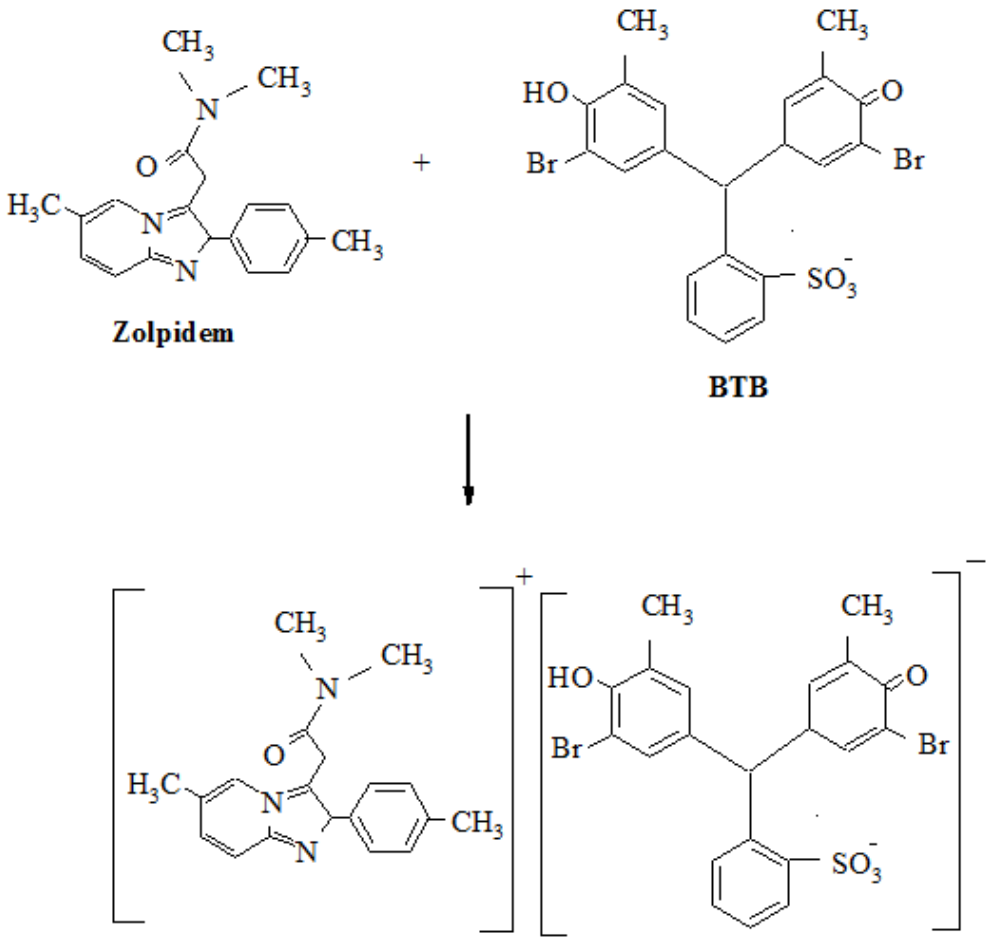

Figure 5: Scheme of Iron association complex of ZPD with BTB

Recovery studies

Recovery studies were carried out for both the developed methods by standard addition technique at three different concentration levels. The resulting solutions were analyzed by proposed methods. The recovery was in the range of 99 – 100 % for methods A and B. The results of recovery studies were reported in Table 1.

RESULTS AND DISCUSSION

The development of a new dosage form involves a number of stages and the analytical methods that are specific, accurate and precise plays an important role in many of the essential features required for an identical analytical system have been adopted in a wide range of pharmaceutical analysis. Taking into consideration these facts, two simple, reliable, economical and rapid visible spectrophotometric methods were developed for the quantitative estimation of Zolpidem tartrate in bulk and dosage form. The proposed methods can be successfully applied for the quality control of Zolpidem tartrate in pure and dosage form. The results compiled in table 1 were checked by an established UV-Visible spectrophotometric method and were found to be in close agreement between the proposed method and the reference methods. The excipients like hydroxypropyl methylcellulose, lactose, magnesium stearate, micro-crystalline cellulose, polyethylene glycol, sodium starch glycolate and titanium dioxide in the formulations did not interfere with the BTB method or with the SBT method. The proposed reaction mechanisms of Zolpidem with BTB and EBT have been given in the reaction Schemes I and II respectively.

CONCLUSION

The methods developed here are direct, simple and rapid for the analysis of zolpidem in tablets which, most frequently prescribed. Unlike UHPLC, HPLC, LC-MS, GC procedures the UV –Visible spectrophotometer is simple, is not of high cost, the reagents used are cheap, readily available and the procedures do not involve any critical conditions or tedious sample preparation. Moreover the methods are free from interference by common additives and excipients. Thus the methods can be used in the routine determination of Zolpidem tartrate in pure form and in pharmaceutical formulation.

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