International Journal of ChemTech Research
CODEN (USA): IJCRGG ISSN : 0974-4290
Vol.4, No.1, pp 403-408, Jan-Mar 2012

Validated Spectrophotometric method for the estimation of Zolpidem tartrate in Bulk and Tablet Formulation

M. P. Mahajan*, S. D. Sawant.

Department of Pharmaceutical Analysis, Sinhgad Technical Education Society's, Smt. Kashibai Navale College of Pharmacy, Kondhwa (Bk.), Pune-48 (MS),India.

Corres. Author : m_p_mahajan@yahoo.co.in

Abstract: Three simple, precise and economical UV spectrophotometric methods have been developed for the estimation of Zolpidem tartrate in bulk and tablet formulations. Zolpidem tartrate has absorbance maxima at 293 nm in zero order spectrum method (Method A) First order derivative spectra of drug, showed λ maxima = 305 nm and λ minima = 280 nm and amplitude difference was measured for the respective concentration of standard and was plotted against concentration and regression equation was calculated. (Method B). Wavelength range of 316 nm to 263 nm was considered for the calculation of area under curve (AUC) for analysis (Method C). The drug followed the Beer-Lambert's law in the concentration range of 5-30 µg/ml with correlation coefficient (R^2)=0.999, recovery of the drug was found to be more then 99.60% and relative standard deviation(SD) was found to be less than 2 % for precision studies in all the three methods. Results of the analysis, validated statistically and by recovery studies were found to be satisfactory. The newly developed methods can be used for routine analysis of zolpidem tartrate in bulk and tablet dosage forms.

Key Words: Zolpidem tartrate (ZOL); Ultraviolet spectrophotometry; Zero order spectrum; First order derivative spectroscopy and Area under curve (AUC).

Introduction:

Zolpidem tartrate (ZOL) is a non-benzodiazepine hypnotic of the imidazopyridine class and is available in 5 mg and 10 mg strength tablets for oral administration. Chemically, It is N,N,6- trimethyl-2-p-tolylimidazo[1,2-a] pyridine-3-acetamide L-(+)-tartrate. (Fig.1) The drug is official in British Pharmacopoeia[1] and Merck Index [2] .It is a white to off-white crystalline powder that is sparingly soluble in water, alcohol, and propylene glycol. It produces agonistic effect on $GABA_A$ receptors and it is used in the treatment of insomnia. Zolpidem belongs to a class of medications called sedative-hypnotics[3]. Literature survey reveals that four HPLC methods,[4–7] one potentiometric method[8] one spectrophotometric method[9] have been developed for the estimation of zolpidem tartrate in human serum and tablet formulation. The objective of the present work was to develop simple, rapid, accurate, specific and economic UV spectrophotometric methods [10] for the estimation of Zolpidem tartrate in bulk and tablet. The method was further validated as per ICH guidelines [11] for the parameters like precision, accuracy, sensitivity, and linearity. The results of analysis were validated statistically and by recovery studies. These methods of

estimation of Zolpidem were found to be simple, precise, accurate and economic.

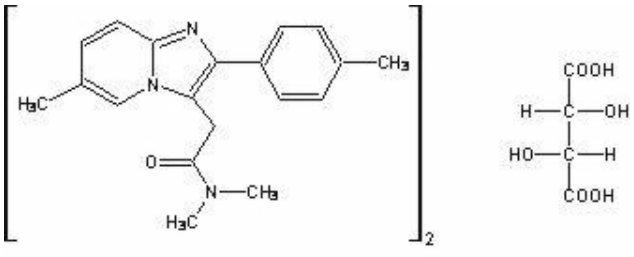


Fig.1: Structure of Zolpidem Tartrate

Materials and Method:

Instrument:

The instrument used was Jasco double beam UV/VIS spectrophotometer model V- 530. Weighing was done on electronic balance (Contech precision balance CB series).

Materials:

Standard gift sample of Zolpidem tartrate was procured from Lupin Pharmaceuticals Ltd. Jammu and Kashmir, India. Tablets of 10 mg strength were procured from local pharmacy of a commercial brand.

Solvent used:

Various solvent systems were screened for determination and 0.1 N H_2SO_4 was selected as solvent system.

Standard Stock solution:

Standard stock solutions of ZOL were prepared by dissolving 100 mg of drug in 100 ml of 0.1 N H_2SO_4 to get standard stock solution of 1000 µg/ml by sonicating for 15 min and 10 ml was pipette out and further volume was made up to 100 ml with 0.1 N H_2SO_4 to obtain concentration of 100 µg/ml. Further dilutions were made in 0.1 N H_2SO_4 from stock solution to get concentrations of 5-30 µg/ml of ZOL. The standard solutions of ZOL were scanned in the range of 400-200 nm against solvent 0.1 N H_2SO_4 and spectra were recorded. λ max of ZOL was found at 293 nm. (Fig.2)

Method A: (Zero order)

Aliquots of standard stock solution were pipette out and suitably diluted with 0.1 N H_2SO_4 to get the final concentration of 5, 10, 15, 20, 25 & 30 µg/ml of standard solutions. The solutions were scanned in the spectrum mode from 400 nm to 200 nm wavelength range and the zero order spectra was obtained (Fig.3). The maximum absorbance (λ- max) of ZOL was observed at 293 nm. The drug followed the Beer-Lambert's law in the concentration range of 5-30 µg/ml. The calibration curve was plotted as absorbance against concentration of ZOL. The coefficient of correlation (r), slope and intercept values of this method are given in Table 1. Six concentrations of sample solutions were determined from calibration curve.

Method B: (First order derivative)

In this method, standard solution of ZOL was scanned in the spectrum mode from 400 nm to 200 nm and the absorption spectra thus obtained were derivatized to first order. First order derivative spectra were selected for the analysis of drug. First order derivative spectra of drug (Fig. 4), showed λ maxima = 305 nm and λ minima = 280 nm and amplitude difference was measured for the respective concentration of standard and was plotted against concentration and regression equation was calculated. The concentration range of 5-30 µg/ml for ZOL was chosen for the derivative analysis.

Method C: (Area under curve)

The Area under curve (AUC) method involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelengths 316 and 263nm. Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which the area has to be calculated. This wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. Suitable dilutions of standard stock solution (100µg/ml) of ZOL were prepared and scanned in the spectrum mode from the wavelength range 400 nm to 200 nm (Fig. 5) and the calibration curve was plotted as AUC against concentration of ZOL. The method was checked by analyzing the samples with known concentration.

Analysis of tablet formulation:

For estimation of Zolpidem tartrate in tablet formulation by all the methods, twenty tablets were weighed and triturated to the fine powder. Tablet powder equivalent to 10 mg of ZOL was weighed and dissolved in 25 ml 0.1 N H_2SO_4 and further diluted with 0.1 N H_2SO_4. It was kept for ultrasonication for 45 min. Finally, the volume was made up to the mark with 0.1 N H_2SO_4; it was filtered through Whatman filter paper no. 41 to get tablet stock solution of concentration 100 µg/ml. Various dilutions of tablet

stock solution were prepared and analyzed for six times by all three methods and concentrations of ZOL in tablet formulation were calculated by all three methods (Table 2). All these methods were validated according to ICH guidelines. Recovery studies were carried out at three different levels i.e. 80 %, 100 % and 120 % by adding the pure drug (8 mg,10 mg and 12 mg respectively) to previously analyzed tablet powder sample (10 mg) as per ICH guidelines. Percentage recovery was calculated as shown in Table 3. All the methods A, B and C were validated for linearity, accuracy and specificity.

Validation of Methods

Validation of the UV method was done with respect to following parameters.

Linearity and range

The standard solutions were prepared by dilution of the stock solution with 0.1 N H_2SO_4 to reach a concentration range 5-30 µg/ml for Zolpidem tartrate. The Absorbance was plotted against the corresponding concentrations to obtain the calibration graphs.

Accuracy

Recovery studies was carried out by applying the method to drug sample to which known amount of Zolpidem tartrate corresponding to 80, 100, 120% of label claim has been added (standard addition method).

Precision

The standard solutions of drug sample were prepared and analyzed. The tablet assay was performed to determine reproducibility and repeatability. The percentage relative standard deviation (RSD %) was found to be within limits.

Table 1: Optical Characteristics, statistical and precision data:

Sr. No.	Parameter	Method- A	Method- B	Method- C
1	λ- max / wavelength range (nm)	293	305 to 280	316 to 263
2	Beer's law limit (µg/ml)	5-30	5-30	5-30
3	Correlation coefficient (r)	0.999	0.9996	0.9998
4	Molar absorptivity (L/mol/cm)	36957.26	482.0712	681146.25
5	Sandell's sensitivity (µg/cm^2 /0.001)	0.022696	1.5866	0.001123
6	Regression equation	Y=0.048x+0.026	Y=0.0006x+0.002	Y=0.890x-0.25
7	Slope (m)	0.0483	0.00063	0.890
8	Intercept	0.0261	-0.002283	-0.2590
9	% COV	0.05477	0.5046	0.00296
10	Confidence limit with 0.05 level	0.00029	0.000021	0.000271

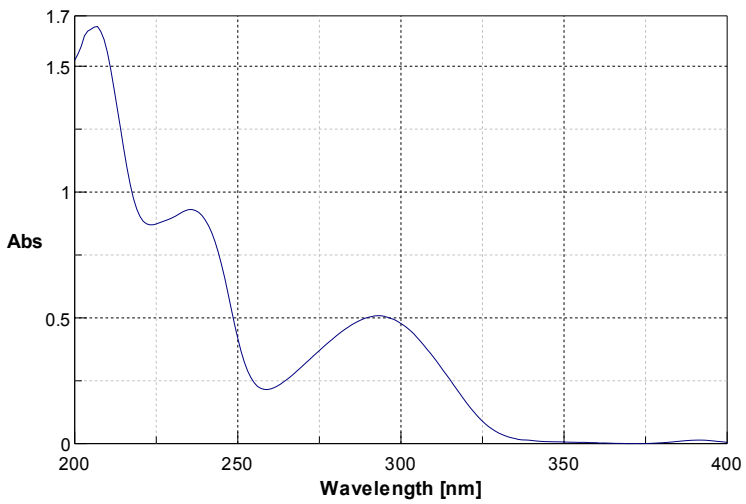


Fig. 2: λ- Max of Zolpidem tartrate

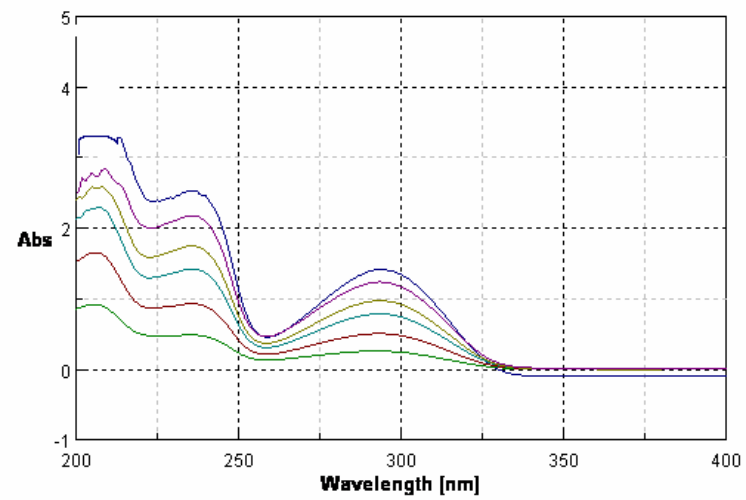


Fig. 3: Overlay spectrum of Zolpidem tartrate (zero order)

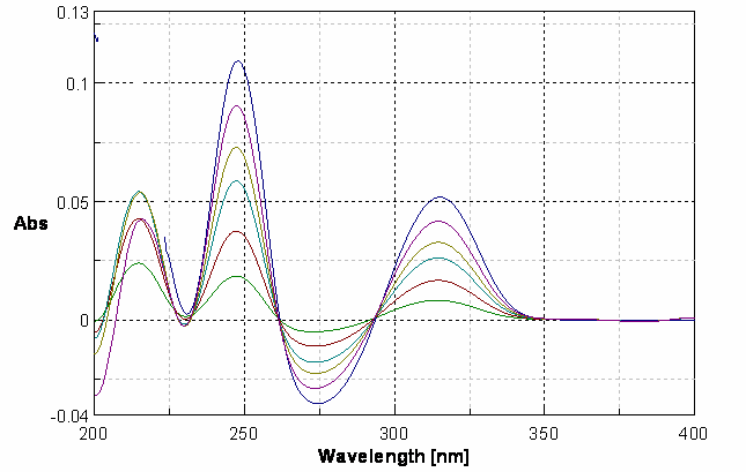


Fig. 4: Overlay spectrum of Zolpidem tartrate (First order)

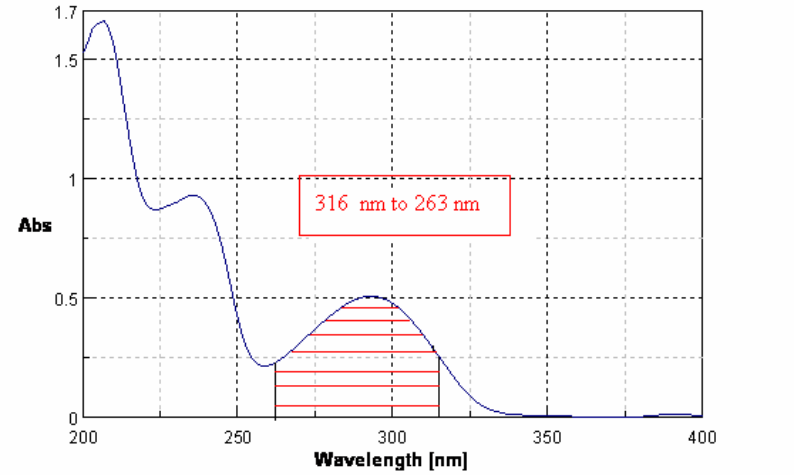
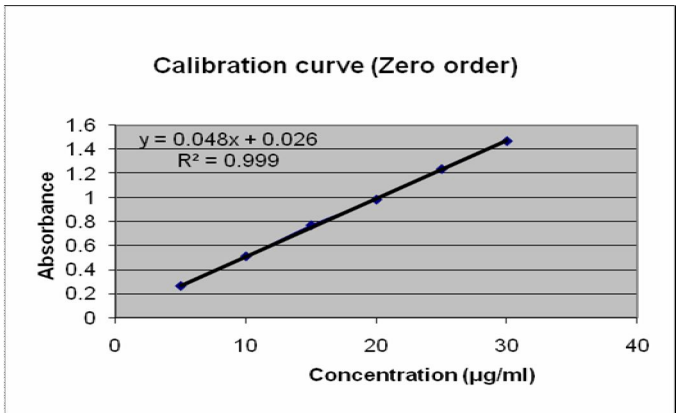
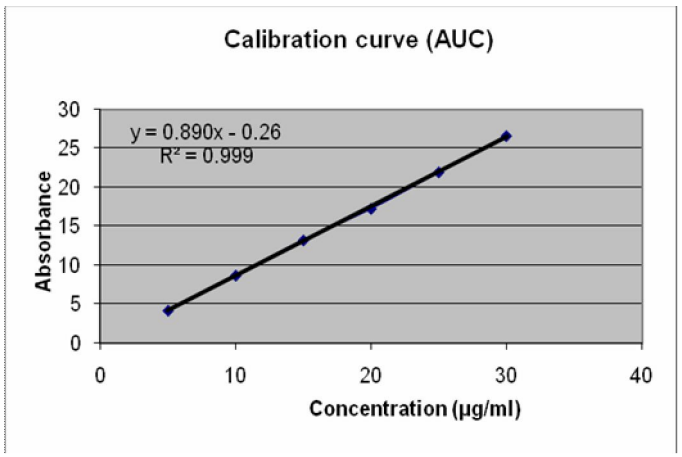


Fig. 5: Spectrum of Zolpidem tartrate (Area Under Curve)





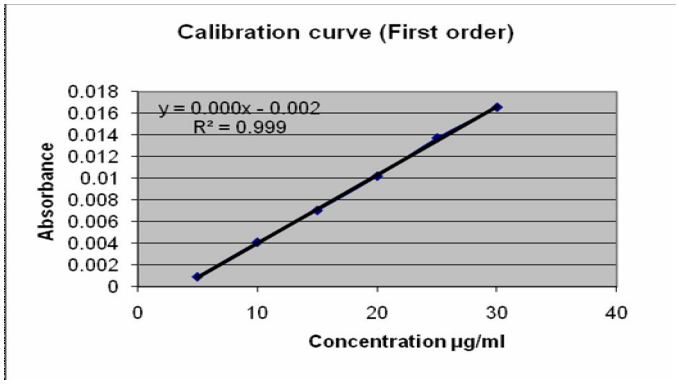


Table 2: Results Analysis of Precision Studies.

Method	Label Claim (mg)	% of drug estimated*	% Recovery	S.D	COV (%)	S.E.
A	10	99.861	100.172	0.0461	0.0419	0.0188
B	10	100.874	100.014	0.1664	0.1649	0.0679
C	10	100.63	99.749	0.0015	0.0015	0.0006

** Indicates mean of six determinations, S.D. =Standard Deviation, COV=Coefficient of Variance S.E. =Standard Error*

Table 3: Result of Recovery Studies of Zolpidem tartrate

Method	Level of Recovery	% Recovery*	S.D.	R.S.D.	S.E.
A	80	101.2015	0.00103	0.0010	0.00058
	100	99.0159	0.02350	0.0237	0.01824
	120	100.9855	0.01436	0.0142	0.00383
B	80	99.8257	0.02394	0.0239	0.00927
	100	99.7060	0.17590	0.1764	0.14330
	120	100.9704	0.47250	0.4680	0.57900
C	80	99.3362	0.00061	0.0006	0.00076
	100	99.4227	0.00032	0.0003	0.00022
	120	99.0476	0.00029	0.0002	0.00041

** Indicates mean of three determinations, S.D. =Standard Deviation, R.S.D. =Relative Standard Deviation, S.E. =Standard Error*

Result and Discussion:

All methods A, B and C for the estimation of ZOL in tablet dosage form were found to be simple, accurate, specific and reproducible. Beer-Lambert's law was obeyed in the concentration range of 5-30 µg/ml in all the methods. The values of standard deviation were satisfactory low and the recovery studies were close to 100%. ZOL showed broad spectra at zero order, the derivative spectroscopy method applied has the advantage that it locates the hidden peaks in the normal spectrum when the spectrum is not sharp and it also eliminates the interference caused by the excipients present in the formulation. The AUC method has advantage that it is applicable to be drug which shows the broad spectra without a sharp peak. Hence these methods can be useful in the routine analysis of ZOL in bulk drug and formulations.

Acknowledgement:

The authors are thankful to Lupin Pharmaceuticals Ltd. Jammu and Kashmir, India, for supplying gift sample of zolpidem tartrate and to the management, Sinhgad Technical Education Society's , Smt. Kashibai Navale College of Pharmacy, Kondhwa (Bk.), Pune-48, for providing excellent research facilities.

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