Visible Spectrophotometric Methods for Estimation of Zopiclone from Bulk Drug and Formulations

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Two simple extractive colorimetric methods for estimation of zopiclone, 6-(5-chloro-2-pyridyl)-6,7-dihydro-7-oxo-5H-pyrrolo-[3,4-b]-pyrazin-5-yl-4-methyl piperazine-1-carboxylate, a non- benzodiazepine derivative which is mainly used as a hypnotic for short term management of insomnia, have been developed. The developed methods involve formation of coloured chloroform extractable complexes of drug wth bromocresol purple and bromocresol green in neutral and acidic medium. Extracted complexes showed absorption maxima at 410 nm and 420 nm respectively. Results were validated statistically and were found to be reproducible.

INTRODUCTION

Zopiclone[1], chemically 6-(5-chloro-2-pyridyl)-6,7-dihydro-7-oxo-5H-pyrrolo-[3,4-b]-pyrazin-5-yl-4-methyl-piperazine-1-carboxylate, is a non-benzodiazepine derivative which is mainly used as hypnotic for short term management of insomnia. Zopiclone is official in B.P. Literature survey reveals that a few polarographic,[2–4] HPLC[5] and HPTLC[6] methods were reported for its analytical monitoring in formulation. In the present work two simple visible spectrophotometric methods for estimation of zopiclone from bulk drug and formulations using bromocresol green and Bromocresol purple have been developed. The yellow coloured complex produced usin Bromocresol purple shows absorbance maxima at 410 nm and linearity in the concentration range 20–70 mcg/mL while yellow coloured complex produced using bromocresol green shows absorbance maxima at 420 nm and linearity in the concentration range of 10–60 mcg/mL. In both cases colour is stable for more than 5 h.

EXPERIMENTAL

Systronics uv/visible spectrophotometer (model 118) with 1 cm matched quartz cells.

All reagents used were of analytical grade. Following reagents and solutions were used:

1. *Preparation of Buffer:* pH 7.2 and 6.0 buffer solutions were prepared as

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per IP[7] by mixing appropriate quantities of 0.2 M potassium hydrogen phthalate and 0.2 M sodium hydroxide.

2. *Bromocresol purple solution:* 0.05% solution was prepared by dissolving 50 mg Bromocresol purple in 0.92 mL of 0.1 M NaOH and 20 mL of alcohol (95%) and made up to 100 mL with water.

3. *Bromocresol green solution:* 0.05% solution was prepared by dissolving 50 mg bromocresol green in 0.72 mL of 0.1 M NaOH and 20 mL of alcohol (95%) and made up to 100 mL with water.

4. Chloroform A.R. grade.

Standard Drug Solution

A. 100 mg of zopiclone was accurately weighed and transferred to a 100 mL volumetric flask. This was dissolved in chloroform and the volume made up to 100 mL mark with chloroform so as to give the stock solution A of concentration 1 mg/mL.

B. 5 mL of above solution was diluted with chloroform to 50 mL so as to give stock solution B of concentration 100 mcg/mL.

C. *Sample solution (tablets):* Twenty tablets were taken and average weight was calculated. The tablets were powdered in a glass mortar. Tablet powder equivalent to 100 mg of the drug was weighed accurately and transferred to a 100 mL volumetric flask. Chloroform was added to dissolve the drug. The flask was shaken well for complete dissolution of the drug. Volume was made upto 100 mL with chloroform. This was filtered, from this 5 mL was pipetted out into a 50 mL volumetric flask and made up to the mark with chloroform (100 mcg/mL).

Procedure

Method I (using Bromocresol purple): From standard solution A, 20 mL was pipetted out into 100 mL volumetric flask and volume was made up using chloroform. From this solution 5, 7.5, 10, 12.5, 15 and 17.5 mL were pipetted out into 6 separate separating funnels, and the volume was adjusted to 10 mL with chloroform. To each separating funnel 5 mL of buffer (pH 7.2) and 5 mL of 0.05% dye solution were added. The contents were allowed to separate. The lower chloroform layer was collected in separate 50 mL volumetric flasks. The chloroform layers were combined and the volume was made up with chloroform. So the concentration of the drug would be 20, 30, 40, 50, 60 and 70 mcg/mL. Absorbance was measured at 410 nm against blank solution obtained in the same way omitting the drug. The amount of zopiclone present in the sample was computed from the calibration curve. Results are reported in Tables 1 and 2.

Method II (Using Bromocresol green): From standard solution A, 20 mL was pipetted out into 100 mL volumetric flask and volume was made up using chloroform. From this solution 2.5, 5, 7.5, 10, 12.5 and 15 mL were pipetted out into 6 separate separating funnels, and the volume was adjusted to 10 mL with chloroform. To each separating funnel 5 mL of buffer (pH 6) and 10 mL of 0.05% dye solution were added. The contents were allowed to separate. The lower chloroform layer was collected in separate 50 mL volumetric flasks. The

chloroform layers were combined and the volume was made up with chioroform. So the concentration of the drug would be 10, 20, 30, 40, 50 and 60 mcg/mL. Absorbance was measured at 420 nm against blank solution obtained in the same way omitting the drug. The amount of zopiclone present in the sample was computed from the calibration curve. Results are reported in Tables 1 and 2.

TABLE-1
OPTICAL CHARACTERISTICS AND OTHER PARAMETERS

	Method-I	Method-II
$\lambda_{max(nm)}$	410	420
Beer's Law limits (mcg/mL)	20–70	10–60
Molar absorptivity	3.848×10^3	1.83×10^4
Standard deviation	0.983	0.342
Coefficient variation (%)	0.989	0.343

TABLE-2
RESULTS OF THE ESTIMATION OF ZOPICLONE IN TABLETS

Formulation*	Claim (mg/tab)	Found by present method (mg/tab)	Found by official method (mg/tab)	% recovery†
		Method-I		
A	7.5	7.468	7.47	99.60
B	7.5	7.452	7.32	99.30
C	7.5	7.431	7.22	99.00
		Method-II		
A	7.5	7.32	7.47	97.60
B	7.5	7.42	7.32	98.90
C	7.5	7.46	7.22	99.46

*Tablets from different manufacturers.
†Average of five determinations.

RESULTS AND DISCUSSION

The proposed methods are colorimetric methods for determination of zopiclone from bulk powder and formulations. These methods are very simple and accurate. Method I was found to be more sensitive, accurate as compared to method II and official method. Both methods give reproducible results. Proposed methods can be used for determination of zopiclone in bulk powder and formulations in a routine manner.

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