Asian Journal of Chemistry Vol. 13, No. 1 (2001), 315–318

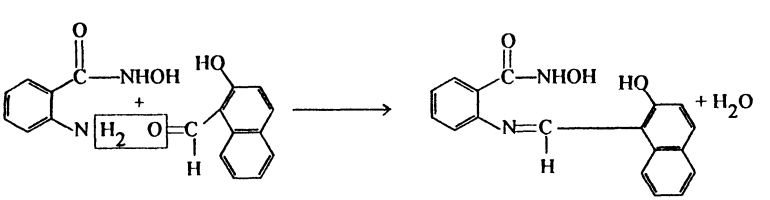
Visible Spectrophotometric Methods for Estimation of Tizanidine from Bulk Drug and Formulation

DUBBAKA RAVI, S.M. MALLI PATIL and S. APPALA RAJU*
H.K.E.S. College of Pharmacy, Gulbarga-585 105, India

Three simple acid-dye colorimetric methods for estimation of tizanidine, 5-chloro-N-(4,5-dihydro-1H-imidazol-2-yl) 2,1,3-benzothiadiazol derivative which is mainly used as a centrally acting skeletal muscle relaxant, have been developed. The developed methods involve formation of coloured chloroform extractable complexes of drug with bromocresol purple, bromocresol green and bromophenol blue in acidic medium. Extracted complexes showed absorption maxima at 417 nm, 415 nm and 414 nm and showed linearity in concentration ranges of 2–10 mcg/mL, 4–20 mcg/mL and 2–10 mcg/mL respectively. Results were validated statistically and were found to be reproducible.

INTRODUCTION

Tizanidine[1], chemically 5-chloro-N-(4,5-dihydro-1H-imidazol-2-yl) 2,1,3-benzothiadiazol-4-amine, is a benzothiadiazol derivative which is mainly used as centrally acting skeletal muscle relaxant. It is not official in any pharmacopoeia. Literature survey reveals that a few methods like electrochemical behaviour of tizanidine at solid electrodes[2], polarographics[3] and comparative study of three polymetric membrane electrodes[4], have been reported for its analytical monitoring in formulation. In the present work three simple visible spectrophotometric methods for estimation of tizanidine from bulk drug and formulations using bromocresol purple, bromocresol green and bromophenol blue have been developed. The yellow coloured complex produced using bromocresol purple shows absorption maxima at 417 nm and linearity in the concentration range 2–10 mcg/mL, the yellow coloured complex produced using bromocresol green shows absorption maxima at 415 nm and linearity in the concentration range of 4–20 mcg/mL and the yellow coloured complex produced using bromophenol blue shows absorption maxima at 414 nm and linearity in the concentration range of 2–10 mcg/mL. In all cases colour is stable for more than 2 h.



EXPERIMENTAL

Systronics UV/visible spectrophotometer (Model 119) with 1 cm matched quartz cells was used. All reagents used were of analytical grade. Following reagents and solutions were used:

1. *Buffer solution:* pH 2.2 buffer solution was prepared as per I.P.[5] 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 a mixture of 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 of bromocresol green in a mixture of 0.72 mL of 0.1 M NaOH and 20 mL of alcohol (95%) and made up to 100 mL with water.
4. *Bromophenol blue solution:* 0.05% solution was prepared by dissolving 50 mg of bromophenol blue with gentle heating in a mixture of 1.5 mL of 0.1 M NaOH and 20 mL of alcohol (95%) and made up to 100 mL with water.
5. *Chloroform*

Standard drug solution

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

B. 10 mL of above solution was diluted with chloroform to 100 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. This was filtered, and the volume was made upto 100 mL with chloroform (1 mg/mL). From this 10 mL was pipetted out in to a 100 mL volumetric flask and made up to the mark with chloroform (100 mcg/mL).

Procedure

Method I (Using Bromocresol purple): From standard solution B. 0.5, 1, 1.5, 2 and 2.5 mL were pipetted separately into 5 separating funnels; the volume was adjusted to 5 mL with chloroform to each separating funnel. 5 mL of buffer (pH 2.2) and 5 mL of (0.05%) dye solution were added. The funnel was shaken for 2 min. The contents were allowed to separate. The lower chloroform layer was collected in separate 25 mL volumetric flasks. The aqueous layer was extracted twice with 5 mL portions of chloroform; the chloroform layers were combined and the volume was made up with chloroform. So, the concentration of the drug would be 2, 4, 6, 8 and 10 mcg/mL. Absorbance was measured at 417 nm against reagent blank solution obtained in the same way omitting the drug.

The amount of tizanidine 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 B, 1, 2, 3, 4 and 5 mL were pipetted separately into 5 separating funnels. The volume was adjusted to 5 mL with chloroform to each separating funnel. 5 mL of buffer (pH 2.2) and 5 mL of (0.05%) dye solution were added. The funnel was shaken for 2 min. The contents were allowed to separate. The lower chloroform layer was collected in a separate 25 mL volumetric flask. The aqueous layer was extracted twice with 5 mL portions of chloroform. The chloroform layers were combined and the volume was made up with chloroform. So, the concentration of the drug would be 4, 8, 12, 16 and 20 mcg/mL. Absorbance was measured at 415 nm against reagent blank solution obtained in the same way omitting the drug. The amount of tizanidine present in the sample was computed from the calibration curve. Results are reported in Tables 1 and 2.

Method III (Using bromophenol blue): From standard solution B, 0.5, 1, 1.5, 2 and 2.5 mL were pipetted separately into 5 separating funnels, The volume was adjusted to 5 mL with chloroform in each separating funnel. 5 mL of buffer (pH 2.2) and 5 mL of (0.05%) dye solution were added. The funnel was shaken for 2 min. The contents were allowed to separate. The lower chloroform layer was collected in a separate 25 mL volumetric flask. The aqueous layer was extracted twice with 5 mL portions of chloroform. The chloroform layers were combined and the volume was made up with chloroform. So, the concentration of the drug would be 2, 4, 6, 8 and 10 mcg/mL. Absorbance was measured at 414 nm against reagent blank solution obtained in the same way omitting the drug. The amount of tizanidine present in the sample was computed from the calibration curve. Results are reported in Tables 1 and 2.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

	Method I	Method II	Method III
λ_{max} (nm)	417	415	414
Beer's law limits (μg/mL)	2–10	4–20	2–10
Sandell's sensitivity			
(μg/cm^2-0.001 absorbance units)	0.051	0.096	0.028
Molar absorptivity (lit. moles^{-1} cm^{-1})	1.68717×10^5	1.55397×10^5	1.96817×10^5
Regression equation (I + aC)			
Slope (a)	6.805×10^{-2}	0.084625	0.4155
Intercept (I)	-3.7×10^{-3}	−0.3079	−2.027
Correlation co-efficient (r)	0.999	1.4192	1.006
% RSD	0.8944	0.7677	0.43911
Range of errors			
Confidence limits with 0.05 level	±0.9445	±0.812	±0.4644
Confidence limits with 0.01 level	±1.39	±1.20	±1.57

TABLE-2
RESULTS OF THE ESTIMATION OF TIZANIDINE IN TABLETS

Formulation*	Claim (mg/tab)	Found by present method (mg/tab)	% recovery†
		Method-I	
T_1	2 mg	1.984	99.75
T_2	2 mg	1.979	99.43
		Method-II	
T_1	2 mg	1.988	98.86
T_2	2 mg	1.981	98.76
		Method-III	
T_1	2 mg	1.98	98.83
T_2	2 mg	1.95	98.77

*Tablets from different manufacturers

†Average of three determinations

RESULTS AND DISCUSSION

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

ACKNOWLEDGEMENTS

The authors wish to thank M/s Sun Pharmacutical Industries Ltd, Baroda and German Remedies Estate, Goa for providing drug samples.

REFERENCES

1. CIMS-53, *Drug Profile* (Biogard Pvt. Ltd., Bangalore), **17** (Sep-Dec. 1995).
2. J.M. Kauffmann, B. Lopez-Ruiz, M. Ferrandis Gotor and G.J. Patriarche, *J. Pharm. Biomed. Anal.*, **10**, 763 (1992).
3. M. Tuncel, *D. Anal. Left.*, **25**, 1087 (1992).
4. A.A. Bouklouze, A. El-Jamma, J.C. Vire and G.J. Patriarche, *Anal. Chim. Acta*, **257**, 41 (1992).
5. *Indian Pharmacopoeia* (The controller of Publications Delhi), **2**, A144 and A202 (1996).

(*Received*: 19 September 2000; *Accepted*: 16 November 2000) AJC-2173