Asian Journal of Chemistry Vol. 13, No. 4 (2001), 1535–1538

Spectrophotometric Determination of Dobutamine Hydrochloride in Pharmaceutical Formulations

K.V. KANNA RAO* and M.N. REDDY†
Roland Institute of Pharmaceutical Sciences, Berhampur-760 010, India

Two simple, sensitive and accurate visible spectrophotometric methods (A and B) have been developed for the determination of dobutamine hydrochloride either in pure form or in pharmaceutical formulations. Method A is based on the reduction of 1,2-naphthoquinone-4-sulphonate, the well-known Follin's reagent, and method B is based on the oxidataion of DBH with excess ferric chloride and determining the consumed $FeCl_3$ with $K_3Fe(CN)_6$. All of the variables have been optimized and the reactions presented.

INTRODUCTION

Dobutamine hydrochloride (DBH) is a sympathomimetic agent, used mainly in the management of heart failure[1]. Chemically it is 4-[2-[[3-(4-hydrophenyl)-1-methyl propyl] amino] ethyl] 1-benzene diol hydrochloride and is official in United States Pharmacopoeia and National Formulary[2]. Analytical literature survey revealed few spectrophotometric methods[3–5], HPLC[2, 6–9] and GC[10]. The reported spectrophotometric methods suffer deficiencies such as low λ_{max} value or low sensitivity. It is, therefore, of interest to develop simple and sensitive procedures with higher λ_{max} for the determination of DBH in pure form and from its formulations.

This paper describes two visible spectrophotometric methods for the determination of DBH making use of its ability (a) to react with an oxidant. Ferric salt converts into ferrous ions which can easily be detected by the usual reagent for divalent iron potassium ferricyanide[11]. (b) Follin's reagent was utilised for the reduction of many compounds[12–14] and now it was extended to determine the DBH.

EXPERIMENTAL

A Systronics UV-VIS spectrophotometer model 117 with 1 cm matched glass cells was used. All chemicals were of analytical grade and all of the solutions were freshly prepared with distilled water and used. Aqueous solutions of $FeCl_3$ (0.2%) $K_3Fe(CN)_6$ (0.1%), glycerol 5% (method B), borax (1%) and Follin's reagent (0.5%) (method A) were prepared. The pharmaceutical formulations of DBH (injections) were procured from the local market.

†Dept. of Pharmaceutical Sciences, Andhra University, Visakhapatnam-530 003, India.

Preparation of standard and sample drug solution: 100 mg of DBH (pure drug or formulation) was dissolved in water and diluted to 100 mL with distilled water. This stock solution was further diluted with distilled water to get 500 μg mL^{-1} and 25 μg mL^{-1} for methods A and B respectively.

Analysis of pure samples: Method A: Aliquots of standard DBH solution (0.4–2.0 mL of 500 μg mL^{-1}) were placed in a series of 10 mL calibrated test tubes. Then 1 mL of borax and 1 mL of Follin's reagent were added and diluted up to 10 mL with distilled water. The absorbance of each solution was measured at 608 nm against a reagent blank.

$$\text{DBH} + \text{Follin's reagent} \rightarrow \text{Reduced Follin's reagent (green)} + \text{Oxidation product of DBH}$$

Method B: To each 10 mL graduated test tubes containing standard DBH solution (0.2–1.6 mL of 25 μg mL^{-1}), 1 mL of $FeCl_3$ (2%) and 1.0 mL of 1% $K_3Fe(CN)_6$ were added and immediately diluted to 10 mL with 5% glycerol solution. The absorbances of bluish green species were measured at 735 nm against a reagent blank.

$$\text{DBH} + Fe^{3+} \rightarrow \text{Products of oxidation} + Fe^{2+} \xrightarrow{+ K_3Fe(CN)_6} Fe_3[Fe(CN)_6]_2 \text{ (blue)}$$

RESULTS AND DISCUSSION

In method A, DBH upon treatment with Follin's reagent in presence of alkaline media forms green coloured species measured at 608 nm whereas in method B, DBH is oxidised by ferric chloride and the ferrous ions thus obtained can easily be detected by the usual reagent for divalent iron, potassium ferricyanide. The resulting bluish-green species were measured at λ_{max} 735 nm. The resulting coloured species are stable in the 5% glycerol solution, which would otherwise precipitate in distilled water.

The Beer's law limits, molar absorptivity, Sandell's sensitivity, detection limits, regression equation, correlation coefficient, stability of coloured species, % relative standard deviation, and the per cent range of error at 95 and 99 confidence levels of each method are summarized in Table-1.

Commercial formulations (injections) containing DBH were successfully analysed by the proposed methods. The values obtained by the proposed and reference methods[5] for formulations were compared and given in Table-2. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the preanalysed formulations. These results are given in Table-2. The ingredients usually present in formulations of DBH did not interfere with the proposed analytical methods.

TABLE-1
OPTICAL AND REGRESSION CHARACTERISTICS, PRECISION AND ACCURACY OF THE PROPOSED METHODS

Parameters	Methods	
	A	B
λ_{max}	608	735
Beer's law limits ($\mu g\ mL^{-1}$)	4–100	0.4–3.2
Molar absorptivity ($1\ mol^{-1}\ cm^{-1}$)	2.85×10^4	9.88×10^4
Sandell's sensitivity ($\mu g\ cm^{-2}$/0.001 absorbance unit)	0.1185	0.0034
Regression equation (I + aC)		
Slope (a)	0.0175	0.0310
Intercept (b)	0.5867	–0.0169
% Relative standard deviation	0.833	0.756
% Range of error		
(95% confidence limit)	0.496	0.6321
(99% confidence limit)	0.603	0.9350

TABLE-2
ESTIMATION OF DBH FROM PHARMACEUTICAL FORMULATIONS AND PERCENTAGE RECOVERY

S.No.	Formulations (Injections) (50 mg/mL)	Proposed methods		Reported method[5]	% Recovery	
		Method A	Method B		Method A	Method B
1.	Brand-I	49.09	49.87	49.12	99.80	98.98
2.	Brand-II	49.24	49.96	49.39	99.90	99.85

Method A and B possess higher λ_{max} and ε_{max} values than the reported visible spectrophotometric methods and have the advantages like wider Beer's law limits and sensitivity. Thus both the proposed methods are simple, selective and useful for the routine determination of DBH in pure sample and pharmaceutical dosage forms.

ACKNOWLEDGEMENTS

The authors are grateful to Troikaa Pharmaceuticals, Gujarat, India for providing gift sample of dobutamine hydrochloride and also to Department of Pharmaceutical Sciences, Andhra University, Visakhapatnam and Roland Institute of Pharmaceutical Sciences, Berhampur, India for providing the necessary facilities of carrying out the present investigation.

REFERENCES

1. Reynolds, E.F. James and B.A. Prasad, Martindale: the Extra Pharmacopoeia, 31st Edn., The Pharmaceutical Press, London, p. 1573 (1996).
2. The United States Pharmacopoeia, 24: The National Formulary, 19th United Sates Pharmacopoeial Convention, Inc., 12601, Twinbook Parkway, p. 483 (2000).
3. E.L. Kommas, *Analyst*, **108**, 380 (1983).
4. ———, *Analyst*, **112**, 101 (1987).
5. G. Ramana Rao, A.B. Avadhanulu and R. Giridhar, *Indian Drugs*, **25**, 382 (1988).
6. D.W. McKennon and R.E. Kates, *J. Pharm. Sci.*, **67**, 1756 (1978).
7. H. Husseini, V. Mitrovic and M. Schlepper., *J. Chromatogr.*, **131**, 164 (1993).
8. G. Alberts, F. Boomsma, A.J. Man In't Veid and M.A. Schale Kamp, *J. Chromatogr.*, **121**, 236 (1992).
9. J. Zimmer Mann, R. Dennhardt and H.J. Gramm, *J. Chromatogr.*, **567**, 240 (1991).
10. P.J. Murphy, T.L. Williams and D.L. Kau, *J. Pharmacol. Exp. Ther.*, **199**, 423 (1976).
11. A. Besada *Anal. Lett.*, **20**, 247 (1987).
12. J.P.S. Sarin, R.B. Chakravarthy and G.K. Roy, *Indian J. Pharm.*, **26**, 165 (1964).
13. M. Schmall and E.G. Wollish, *Anal. Chem.*, **29**, 1509 (1957).
14. M.Z. Barakat, S.K. Shehab and M.M. Elsadr, *Analyst*, **80**, 828 (1955).

(*Received:* 26 May 2001; *Accepted:* 30 August 2001) AJC-2409