Journal of Pharmaceutical & Biomedical Analysis
Vol. 8, No. 7, pp. 569–571, 1990
Printed in Great Britain

0731–7085/90 $3.00 + 0.00

Kinetic determination of sotalol by oxidation with sodium vanadate

SALAH M. SULTAN,* A.M. BUKHARI and HERMAN PERZANOWSKI

Department of Chemistry, King Fahd University of Petroleum and Minerals, KFUPM Box 2026, Dhahran 31261, Saudi Arabia

Abstract: A kinetic method is described for the determination of sotalol. The method uses 0.033 M sodium vanadate to oxidize sotalol in 4 M sulphuric acid. The solution is heated at 90°C and the absorbance is measured at 750 nm at a fixed time of 30 min. The concentration (c) of sotalol is calculated from the absorbance (A) by the equation: $A = 0.04 + 0.0015625\ c$.

Keywords: *Drugs; sotalol; sodium vanadate; kinetic method; fixed-time method.*

Introduction

Sotalol is a non-cardioselective beta-adrenergic blocking agent [1, 2]. It is currently under review for approval by the Food and Drug Administration as an anti-arrhythmic drug. Numerous methods for the determination of sotalol in blood are available; the techniques include spectrofluorimetry [3, 4], GC [5] and most commonly HPLC [6–13]. This paper describes a kinetic method for the determination of sotalol. The drug is oxidized by sodium vanadate in sulphuric acid and the resultant coloured species formed at a preselected fixed time is measured at 750 nm; the concentration of sotalol is calculated from the corresponding calibration equation.

Experimental

Apparatus

Cary model 2300 UV-visible-NIR and Beckman model 35 spectrophotometers were used for spectrophotometric measurements. Matched sets of cells (10.00 mm) were used.

Reagents and samples

Analytical grade chemicals were employed together with high-purity distilled water.

Sotalol hydrochloride was kindly supplied by Bristol-Myers, Pharmaceutical Research and Development Section, (Paris) batch ref. No. 138/76060/10910; the drug was 100.4% pure and was used before the expiry date.

Stock solutions

Solution sotalol. A 1 mg ml^{-1} solution was prepared by dissolving 0.500 g of sotalol in about 200 ml of warm water; the solution was stirred for 5 min, cooled with tap water and diluted to volume with water in a 500-ml standard flask.

Sulphuric acid. A 10 M solution was prepared.

Sodium vanadate solution. A 0.0485 M solution was prepared in 5 M sulphuric acid.

Procedure

To 17 ml of sodium vanadate solution a 25-ml standard flask was added 1.5 ml of sulphuric acid and the appropriate amount of sotalol solution. The mixture was diluted to 25 ml with water; the flask was shaken gently and kept on a water-bath at 90 ± °C for 30 min. The reaction was quenched by cooling with tap water for 2 min and the absorbance (A) of the solution was measured at 750 nm. The concentration (c) of sotalol ($\mu g\ ml^{-1}$) was calculated using the calibration equation: $A = 0.04 + 0.0015625\ c$.

Results and Discussion

Kinetics and optimization

The oxidation reaction of sotalol with sodium vanadate was found to be slow and led to the formation of Vandium Blue that absorbs

* Author to whom correspondence should be addressed.

at 750 nm. For direct spectrophotometric measurements, several hours are required to complete the reaction and thus to attain maximum absorbance. For this reason, a kinetic method was considered as an alternative.

It was found that an increase in temperature and an increase in the concentrations of sodium vanadate and sulphuric acid enhanced the rate of the reaction. 90°C was chosen as an optimum temperature since it could be easily monitored with an ordinary thermostatically controlled water-bath. Above this temperature chemical changes of the drug may occur.

In 4 M sulphuric acid the reaction rate is measurable and is easily followed. The addition of more acid would limit the upper concentration of sotalol that could be determined.

The use of high concentrations of sodium vanadate is limited by the difficulty in dissolution and the final dilution volume in the flask; 17 ml of a 60 mg ml^{-1} solution in a 25-ml standard flask is acceptable.

With such high concentrations of sulphuric acid and sodium vanadate, the reaction rate is dependent only upon changes in the initial concentration of sotalol in accordance with the following equation:

$$\text{Rate} = k' [\text{sotalol}]^n,$$

where k' is the pseudo-nth order rate constant and n is the order of the reaction with respect to sotalol.

In the method, the reaction rate is followed by measuring the change of absorbance at different time intervals; thus at a fixed time, the absorbance varies with different initial concentrations of sotalol:

$$A = k' [\text{sotalol}]^n.$$

Calibration equation

Solutions were prepared using 4 M sulphuric acid, 0.033 M sodium vanadate and different concentrations of sotalol of 10–240 μg ml^{-1}. Reaction rates were determined for several replicates and the absorbance values were measured at pre-selected times. The regression of absorbance against initial sotalol concentration was examined for different fixed times. It was found that linearity was best at sotalol concentrations of 40–200 μg ml^{-1}. Typical results are shown in Table 1. On the basis of the intercept and the correlation coefficient, a fixed time of 30 min was chosen for absorbance measurements. The following calibration equation was followed for calculating unknown concentrations of sotalol in μg ml^{-1}: $A = 0.04 + 0.0015625\ c$.

Analysis of sotalol solutions

The fixed-time method was applied to the determination of different known concentrations of sotalol in the range of 40–200 μg ml^{-1}. The results (Table 2) indicate the high accuracy of the method.

Table 2
Results of the analysis of sotalol solutions by the fixed-time method using the equation: $A = 0.04 + 0.0015625\ c$

Sotalol taken (μg ml^{-1})	Sotalol found (μg ml^{-1})	% Error	SD*
40	39	−0.3	0.11
60	60	+0.2	0.14
80	79	−0.1	0.04
100	99	−0.1	0.20
140	140	0.1	0.10
170	170	0.0	0.03
180	180	0.1	0.01

*Standard deviation for five replicates.

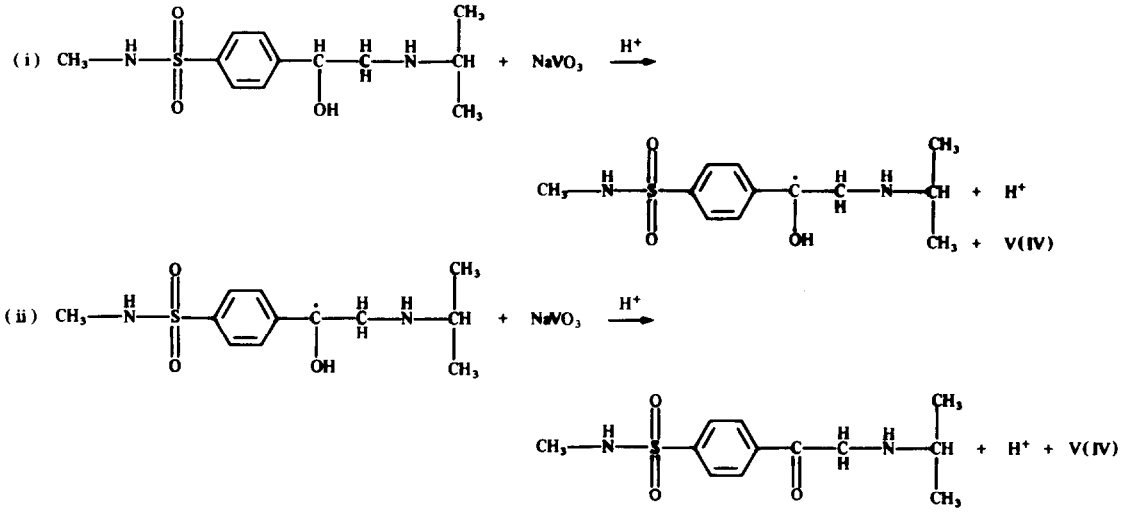
Table 1
Calibration equations obtained by the fixed-time method for 0.003 M sodium vanadate, 4 M sulphuric acid and different concentrations (c) of sotalol. Solutions were heated at 90°C and the absorbance (A) was measured at different fixed times

[Sotalol] μg ml^{-1}	Absorbance at 30 min	Absorbance at 45 min	Absorbance at 60 min
40	0.102	0.103	0.112
80	0.165	0.184	0.192
120	0.226	0.248	0.255
160	0.290	0.317	0.328
200	0.350	0.384	0.392
Calibration equation	$A = 0.04 + 0.0015625\ c$	$A = 0.04 + 0.0017375\ c$	$A = 0.05 + 0.00174\ c$
r	1.0	0.980	0.988

The method might be suitable for the determination of sotalol in drug formulations. However, since proprietary preparations of the drug such as Sotalex, Beta-cardone or Sotacor, quoted in Martindale [14], were not registered in Saudi Arabia, the method was not applied to formulated products of sotalol.

Proposed mechanism

The active site that is prone to oxidation in sotalol and similar compounds is the *N*-isopropylethanolamine group. Oxidation with sodium vanadate of the hydroxyl function gives a ketone as the final product via formation of an intermediate radical, similar to that suggested earlier [15, 16]. The two steps of the reaction could be represented by:



Acknowledgement — Thanks are due to Bristol-Myers (Paris) for the gift of a standard sample of sotalol.

References

[1] B.N. Singh and E.M. Vaughan Williams, *Br. J. Pharmacol.* **39**, 675–680 (1970).
[2] H.C. Strauss, J.T. Bigger Jr and B.F. Hoffman, *Circ. Res.* **26**, 661–664 (1970).
[3] H. Sundquist, M. Antilla and M. Arstila, *Clin. Pharmacol. Ther.* **16**, 465–470 (1974).
[4] E.R. Garrett and K. Schnelle, *J. Pharm. Sci.* **60**, 833–838 (1971).
[5] T. Walle, *J. Pharm. Sci.* **63**, 1885–1891 (1974).
[6] S. Karkkainen, *J. Chromatogr.* **336**, 313–320 (1984).
[7] M.A. Lefebvre, J. Girault, M.Cl. Saux and J.B. Fourtillan, *J. Pharm. Sci.* **69**, 1216–1220 (1980).
[8] M.A. Lefebvre, J. Girault and J.B. Fourtillan, *J. Liq. Chromatogr.* **4**, 483–490 (1981).
[9] B. Lemmer, T. Ohm and H. Winkler, *J. Chromatogr.* **309**, 187–191 (1984).
[10] D.G. Gallo, Mead Johnson Pharmaceutical Division Report, Gall-DG-0777 (1979).
[11] M.B. Boarman, Bristol-Myers Pharmaceutical Research and Development Division Report, BOAR-MP-09758m (1983).
[12] G.L. Hoyer, *J. Chromatogr.* **427**, 181–187 (1988).
[13] W.P. Gluth, F. Soergel and M. Von Mallinckrodt, *Anal. Chem. Symp. Ser.* **20**, 113–118 (1984).
[14] *Martindale*, London, 28th edn, 1300–1360 (1984).
[15] S.M. Sultan, *Analyst* **113**, 149–152 (1988).
[16] S.M. Sultan, S.A. Altamrah, A.M.A. Alrahman, I.Z. Alzamil and M.O. Karrar, *J. Pharm. Biomed. Anal.* **7**, 279–286 (1989).

[*Received for review 16 June 1989; revised manuscript received 6 March 1990*]