ELSEVIER

Journal of Pharmaceutical and Biomedical Analysis
15 (1997) 581–585

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

Densitometric determination of metoprolol tartrate in pharmaceutical dosage forms[1]

Z. Vujic*, D. Radulovic, D. Agbaba

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Vojvode Stepe 450, P.O. Box 146, 11001 Belgrade, Yugoslavia

Received 14 September 1995; accepted 14 May 1996

Abstract

This paper describes a simple densitometric method for the determination of metroprolol tartrate in tablets and ampoules. After separation on silica gel GF254 plates, using acetone–methanol–triethylamine as the mobile phase for the tablets and acetone–triethylamine for ampoules, the chromatographic zones corresponding to the spots of metoprolol were scanned. Quantitation was performed using a computer-controlled Camag TLC scanner and applying five-point calibration with polynomial regression. The calibration function was established in the ranges 1–28 μg for tablets and 1–9 μg for ampoules. The results obtained are precise and reproducible, with recovery values of 99.1–99.4%.

Keywords: Ampoules; Densitometry; Metoprolol tartrate; Tablets; Thin layer chromatography

1. Introduction

Beta blockers have been in clinical use for 30 years, and have an accepted role in, for example, the treatment of high blood pressure, the secondary prevention of myocardial infarction and the treatment of arrhythmias. The drugs available in the 1970s and early 1980s have been subjected to intense investigation.

Metoprolol tartrate, (±)-(isopropylamino)-3-[4-(2-methoxyethyl)phenoxy]-2-propanol tartrate, is known as a cardioselective beta adrenergic receptor blocker. A number of articles have described spectroscopic methods for the determination of metoprolol tartrate [1–4]. The methods were based on reaction of metoprolol tartrate with analytical reagents and formation of coloured ion pairs or complexes.

Various chromatographic methods have been used for the determination of beta adrenergic receptor blockers e.g. TLC [5–7], GC [8–10], GC–MS [11,12], reversed-phase ion-pair chromatography [13,14], and HPLC [15,16].

Most beta blockers are racemic modifications and it is known that their enantiomers have different pharmacological effects. Over 100 chromatographic procedures for the separation of beta blocker enantiomers have been reviewed, includ-

* Corresponding author.

[1] Presented at the Fifth International Symposium on Drug Analysis, September 1995, Leuven, Belgium.

PII S0731-7085(96)01857-2

ing a large number for the analysis of biological samples. All the principal chiral chromatographic procedures that have found use employ chiral mobile phase additives, chiral derivatization agents [17,18] and chiral stationary phases [19,20]. Pflugmann et al. [6] described the determination of the enantiomers of metoprolol, oxprenolol and propranolol in urine by TLC (in an ammonium atmosphere) with fluorimetric detection. Sungar et al. [21] described a TLC method for simultaneous detection of six beta blockers after derivatization with dabsyl chloride. MN Polygam Sil G plates were used and chloroform–acetone–95% ethanol (2:1:1 v/v/v) was used as the mobile phase.

The majority of the published works described the determination of metoprolol tartrate in biological fluids, while only a few articles mentioned the use of TLC for determination in pharmaceutical dosage forms.

The proposed method is used for the determination of metoprolol tartrate in tablets and ampoules by "in situ" densitometry. This method is found to be suitable, accurate and time-saving (up to 36 samples can be determined simultaneously).

2. Experimental

2.1. Apparatus

Chromatoplates (20 cm × 20 cm, precoated with 0.25 mm silica gel GF254) were purchased from Merck (Darmstadt, Germany). Nanomat III was used as an application device (Camag, Muttenz, Switzerland). A TLC scanner with a computer system and CATS software (version 3.15) were provided by Camag. The experimental conditions of the measurements were: $\lambda = 275$ nm; scanning speed = 10 mm s^{-1}.

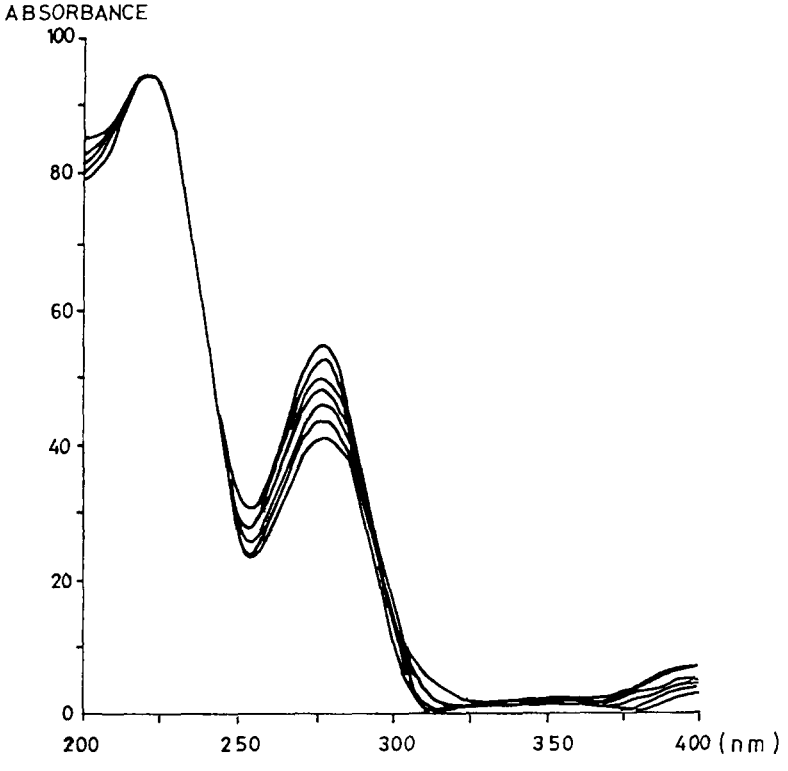

Fig. 1. Absorption spectra of metoprolol tartrate investigated "in situ" at seven different concentrations

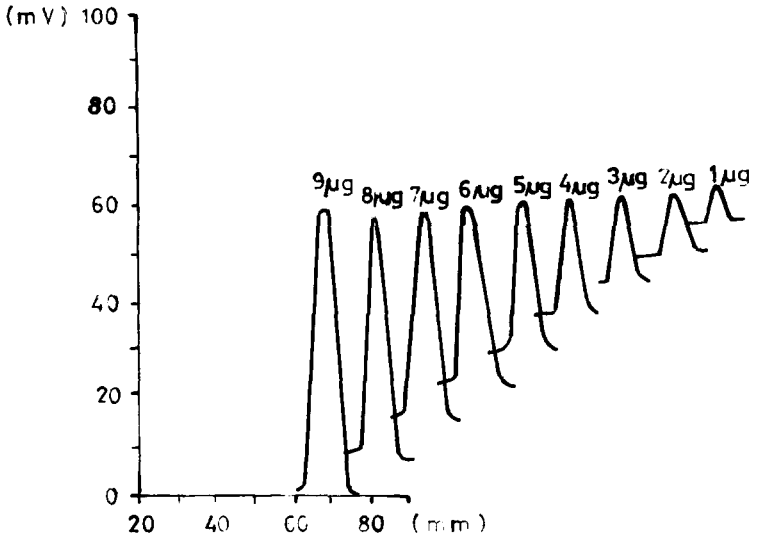

Fig. 2. Densitogram of metoprolol tartrate standard. Mobile phase: acetone–methanol–triethylamine (2:1:0.1 v/v/v); $\lambda = 275$ nm.

2.2. Reagents

Chloroform (Alkaloid, Skoplje, Macedonia), acetone (Zorka, Šabac, Yugoslavia), methanol (Zorka) and triethylamine (Merck) were used as received. All chemicals and solvents were of analytical grade.

2.3. Preparation of standards and samples

Lopresor tablets (Ciba-Geigy AG, Basle, Switzerland) containing 200 mg of metoprolol tartrate and Lopresor ampoules (Ciba-Geigy AG) containing 5 mg of metoprolol tartrate per 5 ml were used.

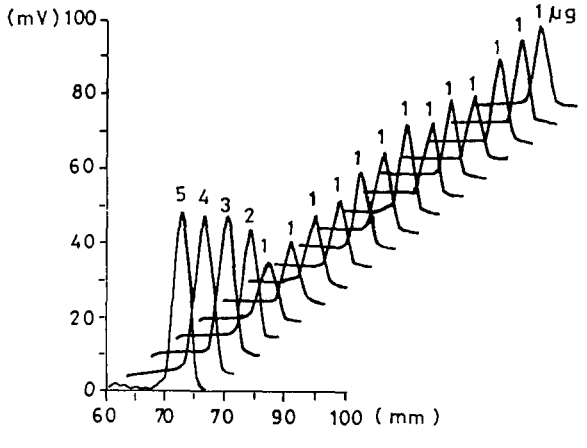

Fig. 3. Densitogram of metoprolol tartrate standard. Mobile phase: acetone–triethylamine (2.5:0.5 v/v); $\lambda = 275$ nm.

Standard solutions (**I**, **II**) were prepared by dissolving 40 mg (**I**) and 10 mg (**II**) of metoprolol tartrate in 10 ml of chloroform. Concentrations were 4 mg ml^{-1} and 1 mg ml^{-1} respectively.

Lopresor tablet solution was prepared by dissolving one tablet (average of 10 tablets) in 50 ml of chloroform. After filtering, 2.5 ml of filtrate was diluted to 10 ml with chloroform. The concentration of the solution obtained was 1 mg ml^{-1}.

2.4. Chromatography

1 μl portions of standard and sample solutions were applied to TLC plates and developed in

Table 1
Precision of "in-situ" densitometry determination

Number of determinations	Peak area (mm^2)	Mass of metoprolol (μg)	Relative error
1	442.3	0.96	2.8
2	452.2	1.01	2.2
3	450.8	1.0	1.5
4	446.2	0.98	0.9
5	448.8	0.99	0.4
6	447.6	0.99	0.4

Table 2
Recovery of metoprolol tartrate from tablets and ampoules

Sample	Number of determination	Amount added (μg)	Amount measured($\pm$SD) (μg)	Recovery efficiency (%)	RSD (%)
Lopresor tablet (200 mg)	6	1	0.99	(0.1205)	99.022.07
Lopresor ampoule	6	5	5.01(0.123)	100.31	2.45

acetone–methanol–triethylamine (2:1:0.1 v/v/v) solvent for tablets and acetone–triethylamine (2.5:0.5 v/v) for ampoules. The plates were air-dried and the spots were detected under UV light at 254 nm. The chromatographic zones corresponding to the spots of metoprolol tartrate were scanned using the reflectance/absorbance mode.

3. Results and discussion

The UV spectral study showed that metoprolol tartrate had two absorbance maxima, at 225 nm and 275 nm (Fig. 1). Quantitative measurements were taken at 275 nm because of obtaining more precise and reproducible results than measurements taken at 225 nm. Densitograms obtained after separation are shown in Figs. 2 and 3. Two calibration curves were constructed (peak area and peak height plotted against amount of substance applied). Seven different calibration standards for tablets were produced by applying 1–7 μl of standard solution **I**. For ampoules, five point-calibration was used. This was obtained by applying 1,3,5 μl of standard solution **II**. The equations for the curves were calculated by polynomial regression analysis. The first curve covered the concentration range 1–28 μg μl^{-1} and the second covered the concentration range 1–9 μg μl^{-1}.

The regression equations of the calibration functions were: $y = -1.94x^2 + 203.8x + 249.04$ and $y = -0.443x^2 + 10.669x + 8.83$ and the correlation coefficient was >0.995 on each case. The precision of the method was checked with a concentration of metoprolol tartrate of 1 μg μl^{-1}. The obtained results are SD = 0.0124, RSD = 1.28% (Table 1).

The applicability of the method for the assay of simple dosage forms was examined by analysing Lopresor tablets and Lopresor ampoules. The statistical analysis of the obtained results is shown in Table 2. The results suggest that because of its sensitivity and reproducibility, the proposed method may be used for the quantitation of metoprolol tartrate in both pure and dosage forms.

References

[1] D.M. Shingbal and S.R. Bhangle, Indian Drugs, 24 (1987) 270–271.
[2] D.M. Shingbal and G.D. Sardesai, Indian Drugs, 24 (1987) 373–374.
[3] L. Ersoy and S. Kocaman, Arch. Pharm., 324 (1991) 259–260.
[4] R.B. Patel, A.A. Patel, S.K. Patel and S.B. Patel, Indian Drugs, 25 (1988) 424–425.
[5] D.R. Jack, S. Dean and M.J. Kendall, J. Chromatogr., 196 (1980) 189–192.
[6] G. Pflugmann, H. Spalin and E. Mutschler, J. Chromatogr. 416 (1987) 331–339.
[7] J. Lewandowska, J. Tyfczynska and M. Bujak, Acta Pol. Pharm., 46 (1989) 350–353.
[8] O. Gyllenhaal, W.A. Koenig and J. Vessman, J. Chromatogr., 350 (1985) 328–331.
[9] K.-J. Hoffman, O. Gyllenhaal and J. Vessman. J. Biomed. Environ. Mass. Spectrom., 14 (1987) 543–548.
[10] M. Ervik, K.-J. Hoffman and K. Kylberg-Hanssen, Biomed. Mass. Spectrom., 8 (1981) 322–326.
[11] J. Zamecnik, J. Anal. Toxicol., 14 (1990) 132–136.
[12] F.T. Delbeke, M. Debackere, N. Desmat and F. Maertens, J. Chromatogr., 426 (1988) 194–201.
[13] C. Pettersson and C. Gioeli, Chirality, 5 (1993) 241–245.
[14] C. Pettersson and G. Schill, J. Chromatogr., 204 (1981) 179–183.
[15] H. Winkler, W. Reid and Bj. Lemmer, J. Chromatogr., 228 (1982) 223–234.
[16] K.V. Buehring and A. Garbe, J. Chromatogr., 382 (1986) 215–224.
[17] G. Pflugmann, H. Spahn and E. Mutschler, J. Chromatogr., 421 (1987) 161–164.

[18] M.M. Bhatti and R.T.J. Foster, Chromatogr. Biomed. Appl., 579 (1992) 361–365.
[19] D.R. Rutledge and C. Garrick, J. Chromatogr., 497 (1989) 181–190.
[20] B.-A. Persson, K. Balmer, P.-O. Lagerstrom and G. Schill, J. Chromatogr., 500 (1990) 629–636.
[21] S. Sungur, L. Ersoy, B. Alpertunga and M.S. Yalcin, Pharmazie, 12 (1989) 864–865.