ELSEVIER

International Journal of Pharmaceutics 123 (1995) 149–151

international journal of pharmaceutics

Rapid Communication

Determination of β-adrenoceptor blocking agents in tablets using reversed-phase high-performance liquid chromatography

A. Gustavo González *, M. Angeles Herrador, Agustín G. Asuero

Department of Analytical Chemistry, University of Seville, Seville 41012, Spain

Received 26 January 1995; accepted 20 March 1995

Abstract

An HPLC assay for determining β-blocking agents in tablets using methanol-Tris buffer as mobile phase and spectrophotometric detection is proposed. The content of these active ingredients in several samples of tablet formulations was quantitated by the proposed method yielding excellent results.

Keywords: β-Blocking agent; Tablet formulation; HPLC assay

β-Adrenoceptor blocking agents are commonly used in the treatment of hypertension, angina pectoris and cardiac arrhythmias. HPLC methods for their quality control have been proposed in the last decade (Metha, 1982; El-Yazigi, 1983; Szumilo et al., 1989; Alpertunga et al., 1990). They have been recently introduced in the pharmacopoeias. However, in the USP NF XXII current edition, only three β-blocking agents are assayed from HPLC, namely, metoprolol tartrate, pindolol and timolol maleate (oxprenolol tablets are assayed by spectrophotometry). In each case, different mobile phases and chromatographic conditions are required for their quantitation, which is an important handicap in quality control. The present paper describes a straightforward HPLC method for determining atenolol, alprenolol hydrochloride, oxprenolol hydrochloride, metoprolol tartrate, acebutolol hydrochloride, pindolol, propranolol hydrochloride and timolol maleate by using the same mobile phase and chromatographic conditions.

For the HPLC assay the following instrumentation was used: an isocratic pump Shimadzu LC-9A, a Rheodyne type injector with a 20 *l* loop, a Waters 486 tunable absorbance detector and a Hewlett Packard HP 3394A integrator. Two reversed-phase columns were utilized: Tracer 150 × 4.0 mm Spherisorb ODS2 5 m and LKB 250 × 4.0 mm Spherisorb ODS 5 m.

Operational conditions: flow rate 0.5 (tracer), 1 and 2 (LKB) ml/min depending on the analyte, selected in order to ensure analysis times less than 10 min (vide supra). Each β-blocking agent was detected at its maximum wavelength closest to the visible zone (González et al., 1995): 265 nm (pindolol), 290 nm (propanolol and timolol), 274 nm (oxprenolol), 326 nm (acebutolol), 271 nm

* Corresponding author.

SSDI 0378-5173(95)00106-9

(alprenolol) and 275 nm (atenolol and metoprolol). AUFS or attenuation was varied in calibration depending on the sensitivity of the analyte.

Methanol (Romil, HPLC quality solvent) and Milli-Q (Millipore) treated water were used throughout.

Alprenolol hydrochloride, oxprenolol hydrochloride, metoprolol tartrate (Sigma), acebutolol hydrochloride, timilol maleate, propanolol hydrochloride, pindolol (ICN) were used as received. Atenolol was kindly provided by Roig-Farma (Barcelona). All these β-blocking agents showed HPLC purity after assay. Tris (Merck analytical reagent grade) was used as received.

The solvent employed for preparing standards in calibrations was methanol. The quantitation was carried out by using the method of internal standard (Mehta, 1982). Propranolol was used as internal standard for the assay of atenolol, pindolol, acebutolol and metoprolol. Otherwise (oxprenolol, alprenolol, propranolol and timolol), atenolol was used as internal standard.

Calibration graphs: analyte to internal standard peak area ratios were rectilinear in the selected useful ranges of 50–500 mg/l for all drugs except for pindolol (25–250 mg/l; beyond this concentration, the graph became non-linear). The final concentration of internal standard in aliquots was always 150 mg/l.

Standard preparation: dissolve an accurately weighed quantity of drug in methanolic solution of internal standard (300 mg/l) to obtain a solution having a known concentration of drug of 400 mg/l. Transfer 50 ml of this solution to a 100 ml volumetric flask, dilute with methanol to the mark and mix.

Assay preparation: Weight and powder not less than 20 tablets. Transfer an amount of the powder equivalent to 20 mg of drug (according to the label claimed), to a 50 ml volumetric flask. Add about 30 ml of methanol, heat in a steam bath and sonicate for 10 min. Cool the solution at room temperature, dilute with methanol to the mark and mix. Centrifuge a portion of this solution and transfer 25 ml of the supernatant liquid to a suitable flask, add 25 ml of methanolic solution of internal standard (300 mg/l), mix and allow to come to room temperature. Filter a portion through a disposable 0.45 m filter unit into a vial and inject.

Table 1
Retention times for the studied β-blocking agents in the two columns used (tracer and LKB)

Drug	Tracer [a]	LKB
Atenolol	2.86	6.68 [b]
Pindolol	3.24	7.81 [b]
Acebutolol	3.60	9.84 [b]
Metoprolol	4.32	5.81 [c]
Timolol	4.52	6.31 [c]
Oxprenolol	4.96	7.47 [c]
Alprenolol	6.32	8.80 [c]
Propanolol	6.40	8.93 [c]

[a] 0.5 ml/min; [b] 1 ml/min; [c] 2 ml/min.

Calculations: According to this technique, the percentage of drug in the tablet with respect to the label claimed (% drug) is easily calculated as:

$$\% \text{ drug} = 100\ R_a/R_s$$

where R_a and R_s are the peak response ratio (from the recorded chromatogram) of drug to internal standard in the assay preparation and in the standard preparation, respectively.

The retention times for the assayed β-blocking agents using the two columns are depicted in Table 1. As can be observed, in all cases the flow rate was selected to ensure analysis times less than 10 min.

Table 2
Content of the β-blocking agent (as % of drug with respect the label claim) in several tablet formulations

Brand (β-blocking agent)	mg/tablet	% drug [a]
Brand 1 (atenolol)	100	97.9
	50	101.2
Brand 2 (alprenolol)	50	98.5
Brand 3 (metoprolol tartrate)	100	100.7
Brand 4 (acebutolol hydrochloride)	400	99.8
	200	102.1
Brand 5 (metoprolol hydrochloride)	200	101.0
	100	98.8
Brand 6 (propranolol hydrochloride)	40	100.9
	10	97.8
Brand 7 (oxprenolol hydrochloride)	160	103.0
	80	99.2
Brand 8 (timolol maleate)	10	98.6

[a] With respect to label claimed.

When the method was applied to the samples of tablet formulations, no peaks from non-active ingredients were observed at the retention times of the drug or the internal standard. In our research, only in the case of a very coloured tablet formulation (Sumial), a very short peak appeared before the peak corresponding to the drug (propanolol) but completely resolved.

Several tablet formulations were analyzed using the proposed procedure and the results are collected in Table 2. The percent of label claim for each formulation tested was within 97.8–103.0.

The proposed method is fast, feasible and reliable. It enables us to determine any β-blocking agent in tablet formulations (as well as in injections and collyria) with the same chromatographic conditions and mobile phase.

Acknowledgements

The authors thank Roig-Farma (Barcelona) for kindly providing atenolol. Financial support from Dirección General de Investigación Científica y Técnica de España through project PB92-0678 is gratefully acknowledged.

References

Alpertunga, B., Sungur, S., Ersoy, L. and Manav, Y., Determination of some beta blockers as dabsyl derivatives by HPLC. *Arch. Pharm. Weinheim*, 323 (1990) 587–589.

El-Yazigi, A., Analysis of oxprenolol in formulations by high performance liquid chromatography. *J. Pharm. Sci.*, 73 (1983) 751–754.

González, A.G., Herrador, M.A. and Asuero, A.G., Hydrophobicity of beta adrenoceptor blocking agents: Study of correlations between retention in reversed-phase HPLC systems and octanol-water partition constants. *Int. J. Pharm.*, (1995) in press.

Metha, A.C., High performance liquid chromatographic determination of oxprenolol hydrochloride and metoprolol tartrate in tablets and injections. *Analyst*, 107 (1982) 1379–1382.

Szumilo, H. and Przyborowska, M., Determination of some beta-adrenolytic drugs by high performance liquid chromatography. *Farm. Pol.*, 45 (1989) 304–307.