Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Chromatography A, 1091 (2005) 118–123
JOURNAL OF CHROMATOGRAPHY A
www.elsevier.com/locate/chroma

Comparative study of the enantioselective separation of several antiulcer drugs by high-performance liquid chromatography and supercritical fluid chromatography☆

L. Toribio*, M.J. del Nozal, J.L. Bernal, C. Alonso, J.J. Jiménez

Department of Analytical Chemistry, Faculty of Science, University of Valladolid, Prado de la Magdalena s/n, 47005 Valladolid, Spain

Received 6 July 2005; accepted 7 July 2005
Available online 18 July 2005

Abstract

A comparative study of the enantiomeric separation of several antiulcer drugs such as omeprazole, lansoprazole, rabeprazole and pantoprazole using HPLC and supercritical fluid chromatography (SFC) on the Chrialpak AD column is presented in this work. The results show that employing the above mentioned column only two compounds (omeprazole and pantoprazole) could be enantiomerically resolved using HPLC, on the contrary SFC allowed the enantiomeric separation of all the compounds studied with higher resolutions and lower analysis times.

Keywords: Enantiomeric separation; Supercritical fluid chromatography; Liquid chromatography; Antiulcer drugs

1. Introduction

Since it is well known that the enantiomers of a compound can display quite different activity and toxicity profiles, the number of chiral pharmaceutical candidates has been increasing in the last few years and many of them are moving to the enantiopure formulations [1,2]. Therefore, the pharmacological evaluation of each enantiomer and the enantiomeric purity of a drug are important tasks in drug development. As a consequence, the separation of enantiomers is a subject of growing interest not only in the pharmaceutical industry but also in the analytical chemistry area.

HPLC is one of the most widely used separation techniques in this field. Although the separation is slower and shows less efficiency with regards to GC, it can be used over a vast range of compounds including those which are thermally labiles or have high molecular weights. For this reason, and because of the fact that a broad range of columns has been developed for this technique, HPLC has been the most used for the separation of chiral drugs [3–7]. However, more recently, supercritical fluid chromatography (SFC) has emerged as a powerful alternative and in some cases as a complementary technique in the area of chiral separations [8,9]. The singular properties of supercritical fluids provide several advantages such as: higher efficiencies, higher resolutions in shorter analysis time and faster column equilibration [10].

Among the different chiral stationary phases (CSPs), the polysaccharide based ones have shown a very broad applicability to different compounds, being the phenyl carbamate derivatives one of the most successful CSPs [11–15]. Concretely the Chiralpak AD and Chiralcel OD columns have demonstrated to be highly effective not only in HPLC but also in SFC [16].

In this work, a study of the enantiomeric separation of several chiral antiulcer drugs including omeprazole, lansoprazole, pantoprazole and rabeprazole, using HPLC on the Chiralpak AD column is presented. The results are compared with those obtained using SFC [17].

☆ Presented at the Fourth Scientific Meeting of the Spanish Society of Chromatography and Related Techniques, Madrid, 5–7 October 2004.

* Corresponding author. Tel.: +34 9 8342 3262; fax: +34 9 8342 3013.
E-mail address: ltoribio@qa.uva.es (L. Toribio).

0021-9673/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.chroma.2005.07.018

2. Experimental

2.1. Reagents

The organic solvents methanol, absolute ethanol, acetonitrile and hexane were purchased from Scharlau (Madrid, Spain) and 2-propanol from Lab-Scan (Deslian, Ireland). All the solvents were HPLC grade. Triethylamine (TEA) and trifluoroacetic acid (TFA) were of analytical grade from Sigma–Aldrich (Madrid, Spain).

Carbon dioxide was SFC grade and purchased from Carburos Metálicos (Barcelona, Spain).

2.2. Compounds

The compounds studied (Fig. 1) were purchased from Sigma–Aldrich (Madrid, Spain), and all of them were in their racemic form. The stock solutions of the individual drugs were prepared in ethanol at the 100 mg/L level.

2.3. Instrumentation

The supercritical fluid chromatograph used was a HP 1205 A model from Hewlett Packard (Wilmington, DE, USA) equipped with a diode array detection (DAD) system and a Rheodyne 7410 injector of 20 μL loop volume (Cotati, CA, USA), and operated in downstream mode.

The liquid chromatograph consisted of a Constantmetric II pump from Milton Roy (Madrid, Spain), a 4100 variable wavelength UV–vis detector from LDC Analytical (Madrid, Spain), a manual Rheodyne 7125 (Cotati) and a JLC 6000 software from Jones Chromatography (Littleton, USA). The detection wavelength was set at 285 nm.

A Chiralpak AD column, 250 nm × 4.6 mm, packed with the 3,5-dimethylphenylcarbamate derivative of amylose, coated on 10 μm silica-gel support, was obtained from J.T. Baker (Deventer, The Netherlands).

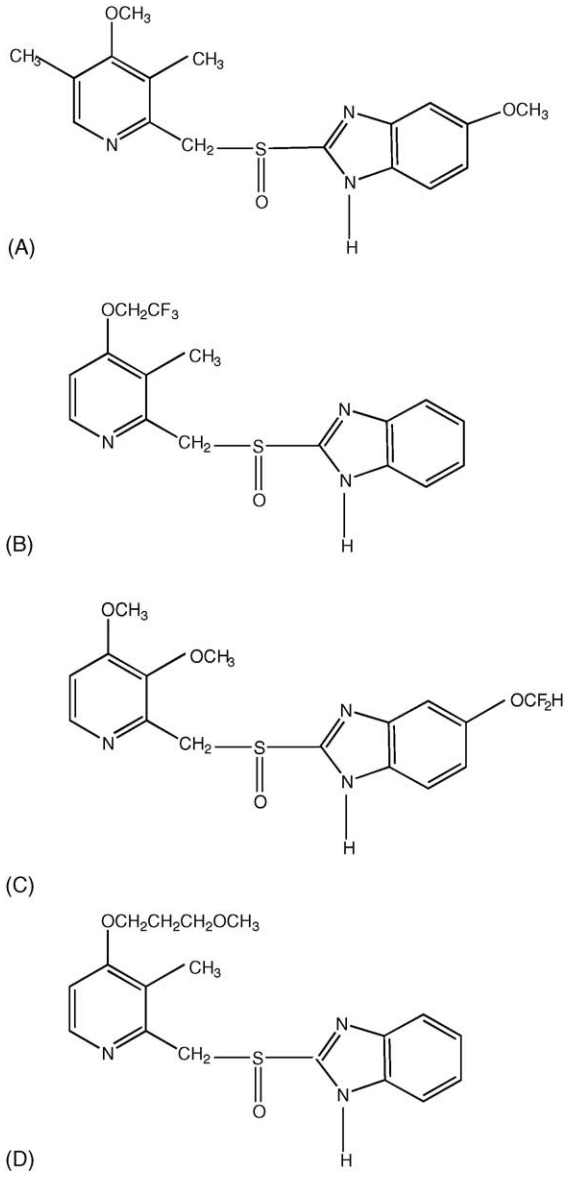

Fig. 1. Structure of the compounds: (A) omeprazole, (B) lansoprazole, (C) pantoprazole, and (D) rabeprazole.

3. Results and discussion

As the Chiralpak AD column used is design for working in normal-phase mode, the HPLC study was started using binary mixtures of hexane–ethanol or hexane/2-propanol. The percentages of organic modifier ranged from 0% to 25% in the case of 2-propanol, from 0% to 15% with ethanol, and a 60% of ethanol as a polar modifier was also used, taking into account the miscibility range of the solvents. Because most of the compounds could not be baseline resolved, the study was improved using polar organic mobile phases, which recently have attracted a lot of interest for chiral separations [18,19]. One hundred percent of methanol, ethanol and acetonitrile were the mobile phases employed. Due to the high pressure drop, a 100% of 2-propanol could not be used. Although a flow-rate of 0.2 mL/min could be possible, the compounds were highly retained.

The flow-rate was fixed at 1 mL/min, except when the pressure drop obligated to work at lower flow-rate to avoid damaging the column, as in the case of 60 and 100% of ethanol, where the flow-rate were 0.75 and 0.5 mL/min, respectively.

Working in normal-phase mode with 2-propanol as a polar modifier, the omeprazole enantiomers could not be baseline resolved in isocratic conditions. Although the effect of the temperature was studied to improve the separation, similar resolution was obtained, but the retention decreased with increasing temperature. However, the resolutions were over 1.5 when a gradient elution was used (Fig. 2). Although a baseline resolution is possible in HPLC in these conditions, the enantioresolutions were not so high as in SFC.