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Short Communication

Pharmaceutical analysis by capillary zone electrophoresis and micellar electrokinetic capillary chromatography[a]

K. D. ALTRIA*
Pharmaceutical Analysis Department, Glaxo Group Research, Ware, Herts. (U.K.)
and
N. W. SMITH
Chemical Analysis Department, Glaxo Group Research, Greenford, Middlesex (U.K.)
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ABSTRACT

The techniques of capillary zone electrophoresis and micellar electrocapillary chromatography have been found to be of use for the analysis of pharmaceuticals and separation from related impurities. The methods can give good resolutions and high separation efficiencies in many instances.

INTRODUCTION

Following its introduction in 1981 [1] capillary zone electrophoresis (CZE) is now developing into a useful and viable analytical technique. The high separation efficiencies, rapid run-times, relatively high levels of automation and low sample and solvent requirements make CZE particularily attractive to pharmaceutical analysis; and this potential use has been recognised [2]. This report gives details of some pharmaceutical applications within a commercial environment.

In CZE an electroendosmotic (EEO) flow of liquid occurs when a high voltage is applied across a capillary filled with carrier electrolyte. This EEO flow sweeps solutes along the capillary towards the detector. Therefore, the magnitude and direction of EEO flow affects the analysis times, separation efficiencies and resolution that are possible [3,4].

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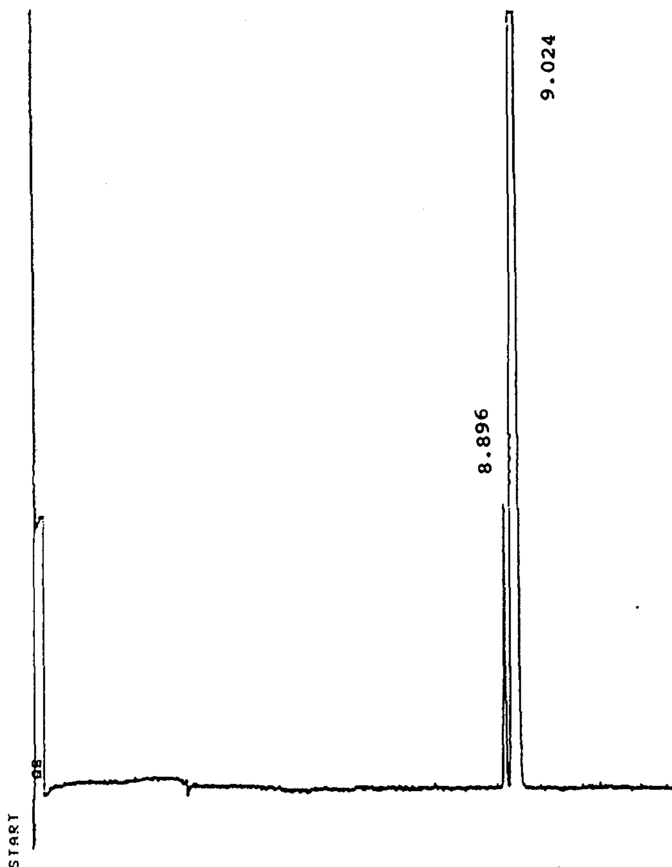
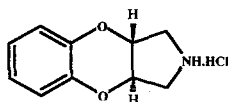


Fig. 1. Electropherogram of GR50360A and its des-5-fluoro analogue. Conditions: sample injection by vacuum for 1 s, detection by UV absorbance at 200 nm, +30 kV applied across the 100 cm × 50 μm capillary, equipment thermostatted at 30°C, 20 m*M* sodium citrate buffer (pH 2.5). Numbers at peaks indicate retention times in min.

EXPERIMENTAL

The electropherograms given in this paper were produced using an Applied Biosystems Model 270A instrument.

Des-5-fluoro analogue of GR50360A



GR50360A

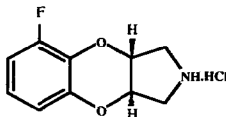


Fig. 2. Molecular structures of GR50360A and its desfluoro analogue.

RESULTS AND DISCUSSION

Fig. 1 shows the baseline separation of the anti-depressant GR50360A from a potential manufacturing impurity, the desfluoro analogue (Fig. 2). This separation is difficult to achieve by high-performance liquid chromatography (HPLC).

Equipment designed for use in CZE can also be applied to micellar electrokinetic capillary chromatographic (MECC) separations. In MECC [5] the stationary phase consists of surfactant micelles which typically move against the direction of EEO flow. Fig. 3 shows the resolution of the *syn* and *anti* isomers of a compound currently being developed for pharmaceutical use. The mobile phase was modified by the addition of 15% methanol to facilitate solubility of the test compound. This use of non-aqueous solvents has been recognised in CZE and MECC [6–8] and will become increasingly important.

A sample of peptide derived material was supplied that had previously been found to give only one peak by HPLC. Fig. 4 shows the electropherogram following

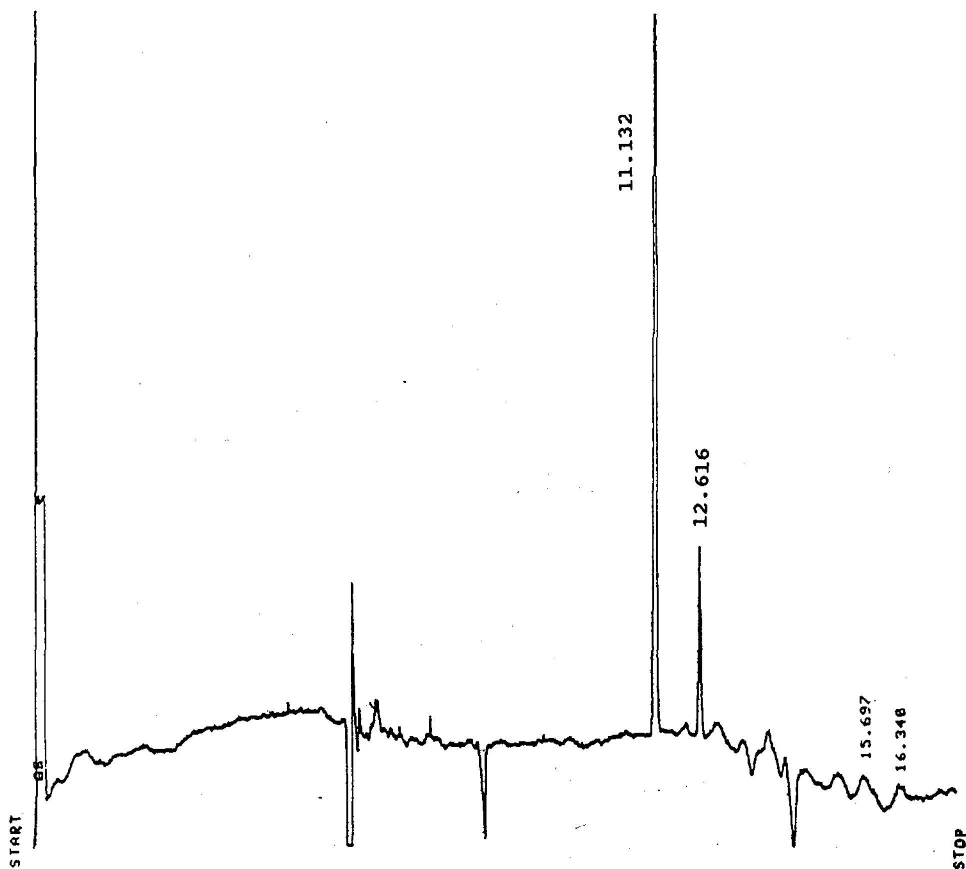


Fig. 3. MECC separation of *syn* and *anti* isomers. Conditions as in Fig. 1, except pH 11.0 [3-cyclohexyl-amino-1-propanesulfonic acid (CAPS) buffer], 50 m*M* sodium dodecyl sulphate, 15% (v/v) methanol. Numbers at peaks indicate retention times in min.

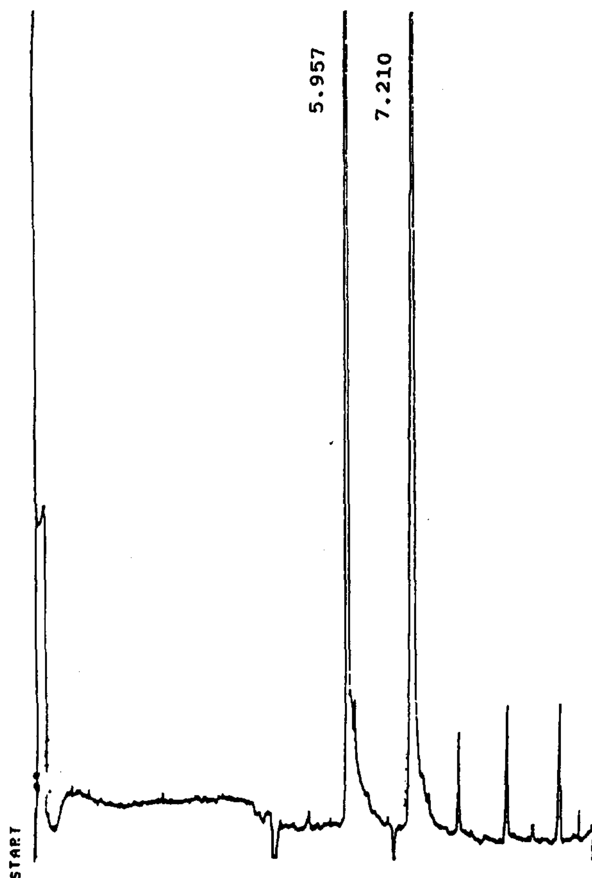


Fig. 4. MECC separation of a peptide. Conditions as in Fig. 3. Numbers at peaks indicate retention times in min.

resolution by MECC, the sample was separated into two principal components and three smaller constituents. This example highlights the alternative separation basis of MECC, compared to HPLC.

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