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Separation of profen enantiomers by capillary electrophoresis using cyclodextrins as chiral selectors

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Abstract

A method for resolving the enantiomers of various 2-arylpropionic acids (viz. ketoprofen, ibuprofen and fenoprofen) by capillary zone electrophoresis (CZE) using a background electrolyte (BGE) containing a cyclodextrin as chiral selector is proposed. The effects of the type of cyclodextrin used and its concentration on resolution were studied and heptakis-2,3,6-tri-*O*-methyl-β-cyclodextrin was found to be the sole effective choice for the quantitative enantiomeric resolution of all the compounds tested. The influence of pH, BGE concentration, capillary temperature and addition of methanol to the BGE on resolution and other separation-related parameters was also studied. The three compounds studied can be enantiomerically resolved with a high efficiency in a short time (less than 20 min) with no capillary treatment. This makes the proposed method suitable for assessing the enantiomeric purity of commercially available pharmaceuticals. © 1998 Elsevier Science B.V.

Keywords: Enantiomeric separation; Pharmaceutical analysis; Buffer composition; Arylpropionic acids; Ketoprofen; Ibuprofen; Fenoprofen; Profens

1. Introduction

The determination of optically active substances is a subject of great interest in analytical chemistry, particularly in the pharmaceutical domain. The fact that the enantiomers of chiral compounds frequently exhibit differential pharmacological and toxicological properties has fostered the use of enantiomerically pure products; this has raised the need for enantiomeric purity controls of pharmaceuticals based on rapid, selective, sensitive techniques. Such controls are primarily done by using chromatographic techniques (HPLC or GC [1,2]) that require chiral columns. These are expensive and not very efficient, and lose resolving power with time; in addition, determining a fairly small range of compounds entails using several columns. The recently introduced high-performance capillary electrophoresis (HPCE) is an interesting alternative to chromatographic techniques for this purpose, which it surpasses in simplicity, analytical expeditiousness, efficiency and resolution; also, HPCE is highly flexible and versatile, and employs samples and background electrolytes sparingly, which enables the use of expensive chiral selectors.

Capillary zone electrophoresis (CZE) with a background electrolyte (BGE) containing a cyclodextrin as chiral selector is the most frequently used oper-

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ating mode of capillary electrophoresis [3,4] in resolving enantiomers. Cyclodextrins are cyclic oligosaccharides consisting of 6, 7 or 8 D-(+)-glucose units (named α-, β- and γ-cyclodextrins, respectively) linked by α-(1,4) bonds. Their geometry resembles a truncated cone with open ends that bounds a relatively hydrophobic cavity enveloped by a hydrophilic outer surface. The five asymmetric carbon atoms in each glucose unit endow cyclodextrins with their chiral properties. Resolving their enantiomers requires including an alkyl or aryl function in the cavity and the formation of additional hydrogen bonds between secondary hydroxyl groups in the cyclodextrin and substituents in the guest molecule. These cyclodextrins can be derivatized at positions 2, 3 and 6 to obtain new products with an altered enantioselective capacity. Some examples of compounds whose enantiomers were resolved by CZE by using cyclodextrins as chiral selectors are ephedrine and related compounds [5], β-blockers [6], tryptophan [7], ergot alkaloids [8] or ticonazole [9], among others.

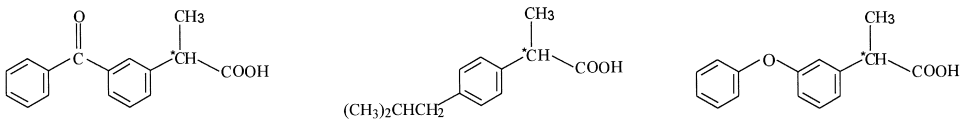
In this work we optimized the experimental conditions for the enantiomeric resolution of various profens (2-arylpropionic acids) that are used as active principles in non-steroidal anti-inflammatory pharmaceuticals. The structures of the profens studied are shown in Fig. 1. There are several references to the separation of profen enantiomers by HPCE in different operating modes. Some [10–13] report on the enantiomeric resolution of profen mixtures by CZE using linear oligosaccharides as chiral selectors; ibuprofen was quantitatively resolved in all cases, whereas fenoprofen [11,12] and ketoprofen [10,11,13] could be resolved only partly into their enantiomers. Micellar electrokinetic chromatography (MEKC) in combination with various cyclodextrins proved ineffective for separating these three profens [14].

Capillary electrochromatography (CEC) with a Chirasil-Dex stationary phase as chiral selector [15,16] was used to resolve ibuprofen enantiomers; the resolution was achieved after a fairly long time (over 20 min). Ibuprofen enantiomers were also partly resolved by using electrokinetic chromatography (EKC) and the protein bovine serum albumin as chiral selector [17]. Switching to avidin [18] as selector allowed ibuprofen and ketoprofen enantiomers to be resolved within 18 min – however, both required coating the inside of the capillary with polyacrylamide in order to avoid adsorption of the protein.

Rawjee and co-workers [19–22] studied the separation of profens from a theoretical perspective. They resolved fenoprofen and ibuprofen enantiomers in 23 and 33 min, respectively, by using β-cyclodextrin as chiral selector and hydroxymethylcellulose as reductant for electroosmotic flow (EOF). Hydroxypropyl-β-cyclodextrin allowed the enantiomeric resolution of fenoprofen and naproxen in 11 and 5 min, respectively.

Fanali and Aturki [23] carried out the study of some parameters that affect to enantiomeric separation of four profens by CZE by using an internally polyacrylamide-coated capillary. Heptakis-2,3,6-tri-*O*-methyl-β-cyclodextrin was found to be the best cyclodextrin among those tested, and total resolution of enantiomers of all compounds was achieved in a time not greater than 35 min. In a recent work [24], Lelièvre and Gareil determined the acidity constants of six profens and apparent formation constants of their inclusion complexes with five different cyclodextrins, heptakis-2,3,6-tri-*O*-methyl-β-cyclodextrin being among these, concluding that a larger complexation constant does not involve a larger enantioselectivity. As in the preceding reference, heptakis-2,3,6-tri-*O*-methyl-β-cyclodextrin was found again to be the best chiral selector among those assayed.

More recent applications use glycopeptide macrocyclic antibiotics such as vancomycin, ristocetin A



KETOPROFEN IBUPROFEN FENOPROFEN

Fig. 1. Chemical structure of the profens studied.

and teicoplanin as chiral selectors in the enantiomeric resolution of a large number of substances including ketoprofen and fenoprofen [25]. Vancomycin was found to be the most effective selector of all tested: it provided a resolution of 6.2 for ketoprofen and 3.0 for fenoprofen, both within 30 min. However, in spite of the excellent separations achieved, these chiral selectors show stability problems in solution, especially vancomycin.

The above-described enantiomeric separations demonstrate some disadvantages, such as, for example, an incomplete separation of the enantiomers or the need of altering the inside of the capillary or the existence of stability problems of the chiral selector, which make difficult its routine application in analytical controls.

The aim of this work was to develop a simple, fast method for highly efficient enantiomeric resolution involving minimal preparation of the sample, capillary and background electrolyte with a view to its routine use. Resolution was optimized by examining the influence on various experimental variables (viz. pH and concentration of the BGE, type of cyclodextrin and its concentration, and temperature). The results are presented and discussed below.

2. Experimental

2.1. Apparatus

Measurements were made on a Hewlett-Packard model ^{3D}CE instrument (Waldbronn, Germany) equipped with a diode array detector, automatic injector and sampler, and a system for thermostating the capillary to within ±0.1°C over the range 4–60°C. Hydrodynamic injection at the anode end (accomplished by applying pressure to the injection vial) was used throughout. An HP fused-silica capillary 50 μm I.D. with a lightpath extended ×3 and a length of 64.5 cm (effective length 56 cm) was used in all experiments. The experimental set-up was governed, and data acquired and processed, by using an HP ^{3D}CE Chemstation.

pH measurements were made by means of a Crison micropH 2001 pH-meter (Alella, Spain).

2.2. Reagents

The reagents used included racemic ketoprofen, *R* and *S* enantiomers, all from Laboratorios Menarini (Badalona, Spain); heptakis-2,6-di-*O*-methyl-β-cyclodextrin (di-OMe-β-CD), heptakis- 2,3,6-tri-*O*-methyl-β-cyclodextrin (tri-OMe-β-CD), racemic ibuprofen and racemic fenoprofen (as its hydrated calcium salt), all from Sigma (St. Louis, MO, USA); α-, β- and γ-cyclodextrin, triethanolamine and nitromethane, all from Merck (Darmstadt, Germany); 50% PA orthophosphoric acid from Panreac (Montcada i Reixac, Spain); and sodium hydroxide from Carlo Erba (Milan, Italy). The optical purity of *R*-(−) and *S*-(+)-ketoprofen was higher than 99.5%. Milli-Q water from a Millipore Water Purification System (Molsheim, France) was used throughout.

2.3. Procedure

A phosphate–triethanolamine solution of variable concentration was used as the BGE. Appropriate volumes of aqueous 0.2 *M* orthophosphoric acid and 0.2 *M* triethanolamine were mixed and the pH adjusted as desired with dilute NaOH. The resulting solution was passed through a filter of 0.2 μm pore size and vacuum-degassed prior to insertion into the capillary.

When the BGE was to contain a cyclodextrin, an appropriate amount of the additive was dissolved in the electrolyte. The solution was filtered and degassed as in the previous case.

Ketoprofen, ibuprofen and fenoprofen solutions were made by dissolving an appropriate amount of solid in water containing 20% methanol to facilitate dissolution. The solutions were also filtered and degassed as described above.

Unless otherwise noted, all experiments were carried out by using a BGE consisting of 20 m*M* phosphate–20 m*M* triethanolamine at pH 5, 25 m*M* tri-OMe-β-CD, at a temperature of 35°C, a voltage of 20 kV, an injection at 75 mbar·s (injected volume ca. 5 nl) and detection at λ=253 nm.

Prior to each experimental batch, the capillary was successively flushed with 1 *M* NaOH, 0.1 *M* NaOH and BGE for 10, 10 and 15 min, respectively, and then equilibrated at an applied voltage of 20 kV for 20 min. For BGE changeovers, 0.1 *M* NaOH and the

new BGE were circulated through the capillary for 5 and 15 min, respectively, which was then allowed to equilibrated at 20 kV for 20 min. Finally, prior to each injection, the capillary was flushed with 0.1 *M* NaOH for 3 min, then with BGE for 8 min and equilibration at 20 kV for 6 min.

2.4. Calculations

Electroosmotic mobility, μ_{eo}, was calculated from the following expression

$$\mu_{eo} = \frac{lL}{t_{eo}V} \quad (1)$$

where l is the capillary length between the injection end and the detector, L the capillary's overall length, t_{eo} the migration time for a neutral marker (nitromethane) and V the applied voltage. The apparent mobilities μ_{ap} of the analytes were also calculated from Eq. (1), using the migration time for each compound as t_{eo}. The apparent mobility is related to the electrophoretic mobility for the ion and the electroosmotic mobility by the following expression

$$\mu_{ap} = \mu_{ep} + \mu_{eo} \quad (2)$$

The resolution R_S and efficiency (as number of theoretical plates, N) were calculated from

$$R_S = \frac{1.175(T_{R(b)} - T_{R(a)})}{W_{50(b)} - W_{50(a)}} \quad (3)$$

where $T_{R(x)}$ is the migration time for peak x, $W_{50(x)}$ the width at half-height for that peak, and

$$N = 5.54\frac{T_R}{W_{50}} \quad (4)$$

T_R being the migration time and W_{50} the width at half-height.

Chiral selectivity, $A_{S/R}$, was calculated from [19]

$$A_{S/R} = \frac{\mu_S}{\mu_R} \quad (5)$$

where μ_S and μ_R are the electrophoretic mobilities of enantiomers *S* and *R*, respectively.

3. Results

3.1. Behaviour of the analytes as a function of pH in the absence of chiral selector

The variation of the migration time with pH in the absence of the chiral selector was studied by injecting ketoprofen, ibuprofen and fenoprofen racemates at concentrations between 0.14 and 0.2 m*M* into a BGE at pH 5, 6 or 7. The samples also contained nitromethane at a concentration about 1 m*M* as EOF marker. As expected, the electropherograms thus obtained revealed no enantiomeric separation since the enantiomer pairs could not be distinguished in a BGE containing no chiral selector. In the pH range studied, the carboxyl group of the analytes was fully or partly dissociated, so the analytes migrated as anions (i.e. upstream from the electroosmotic flow). μ_{eo} was found to exceed μ_{ep} in every case. Table 1 shows the results obtained for the three analytes. Their electrophoretic mobilities ($\mu_{ep} = \mu^0\alpha$, where μ^0 is the ionic mobility of the analyte and α the fraction of analyte present in ionic form) increased with increasing pH by effect of the increased deprotonated fraction; also, μ_{eo} increased markedly from pH 5 to 6 and then remained virtually constant up to pH 7. The slight decrease in μ_{eo} from pH 6 to

Table 1
Variation of electrophoretic parameters as a function of pH in the absence of a chiral selector

pH	μ_{eo} ($cm^2/V\,s$)	Ketoprofen		Ibuprofen		Fenoprofen	
		t_{mig} (min)	μ_{ep} ($cm^2/V\,s$)	t_{mig} (min)	μ_{ep} ($cm^2/V\,s$)	t_{mig} (min)	μ_{ep} ($cm^2/V\,s$)
5.0	4.08×10^{-4}	16.08	-2.20×10^{-4}	15.19	-2.11×10^{-4}	16.08	-2.20×10^{-4}
6.0	5.34×10^{-4}	10.20	-2.37×10^{-4}	10.46	-2.44×10^{-4}	10.46	-2.44×10^{-4}
7.0	5.08×10^{-4}	11.31	-2.40×10^{-4}	11.67	-2.50×10^{-4}	11.76	-2.48×10^{-4}

BGE, 20 m*M* phosphate–20 m*M* triethanolamine; temperature, 35°C; voltage, 20 kV, 8.7–15.1 μA.

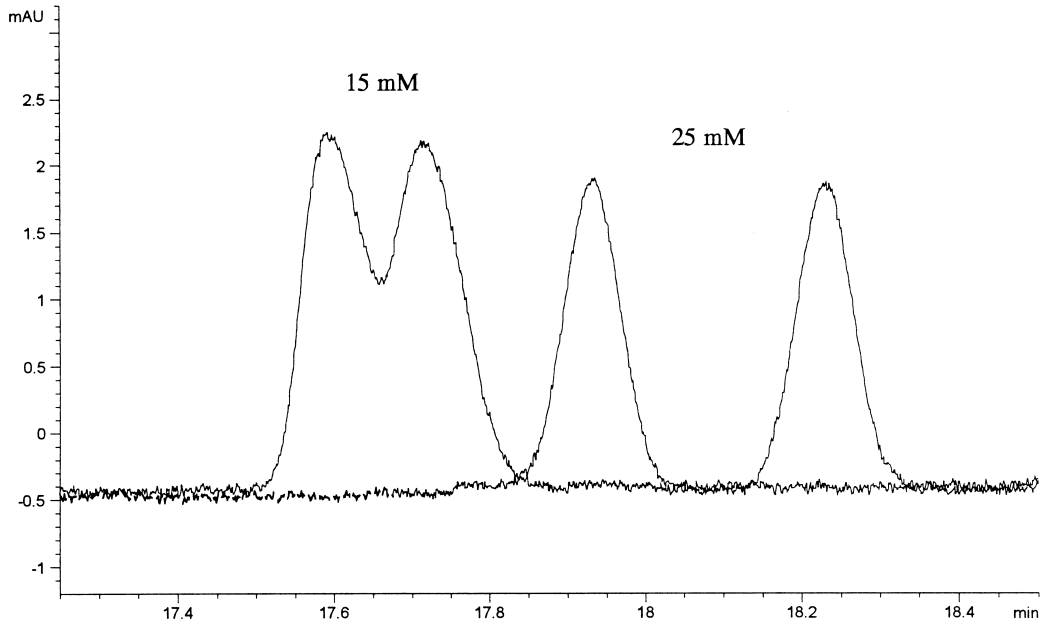


Fig. 2. Resolution of racemic ketoprofen by use of tri-OMe-β-CD. BGE, 20 m*M* phosphate–20 m*M* triethanolamine, pH 5.0; temperature, 25°C; voltage, 20 kV, 6.7 μA.

7 can be ascribed to the way the buffer was prepared. In fact, the pH of the BGE was adjusted with an NaOH solution, which altered the concentration of Na^+ ion and hence the ionic strength of the solution (and the magnitude of electroosmotic flow). The effective mobility of the analytes can also be affected by the presence of greater or lesser amounts of Na^+ in the BGE [20]. As can also be seen from Table 1, the migration sequence of the analytes changed with pH.

3.2. Influence of the type of cyclodextrin (CD) and its concentration on resolution

The resolution of ketoprofen enantiomers was assayed by adding various cyclodextrins to the BGE.

Table 2
Variation of electrophoretic parameters for ketoprofen, ibuprofen and fenoprofen as a function of the tri-OMe-β-CD concentration

[CD] (mmol/l)	T (°C)	μ_{eo} ($cm^2/V\,s$)	Compound	t_{mig1}/t_{mig2} (min)	μ_{ep1}/μ_{ep2} ($cm^2/V\,s$)	$A_{S/R}$	R_S
15	25	2.83×10^{-4}	Ketoprofen	17.59/17.71	$1.12\times10^{-4}/1.13\times10^{-4}$	1.01	0.68
25	25	2.77×10^{-4}	Ketoprofen	17.94/18.23	$1.10\times10^{-4}/1.12\times10^{-4}$	1.03	2.14
			Ketoprofen	14.09/14.41	$1.01\times10^{-4}/1.06\times10^{-4}$	1.05	2.81
25	35	3.17×10^{-4}	Ibuprofen	10.70/10.91	$0.37\times10^{-4}/0.43\times10^{-4}$	1.15	2.99
			Fenoprofen	11.21/11.54	$0.50\times10^{-4}/0.58\times10^{-4}$	1.15	3.76
			Ketoprofen	15.92/16.48	$0.84\times10^{-4}/0.90\times10^{-4}$	1.08	3.86
50	35	2.73×10^{-4}	Ibuprofen	12.66/13.04	$0.35\times10^{-4}/0.42\times10^{-4}$	1.20	4.17
			Fenoprofen	13.24/13.76	$0.45\times10^{-4}/0.54\times10^{-4}$	1.19	4.76

Subscripts 1 and 2 denote enantiomers *R*-(−) and *S*-(+), respectively.
BGE 20 m*M* phosphate–20 m*M* triethanolamine, pH 5.0; voltage, 20 kV, 6.7–8.4 μA.

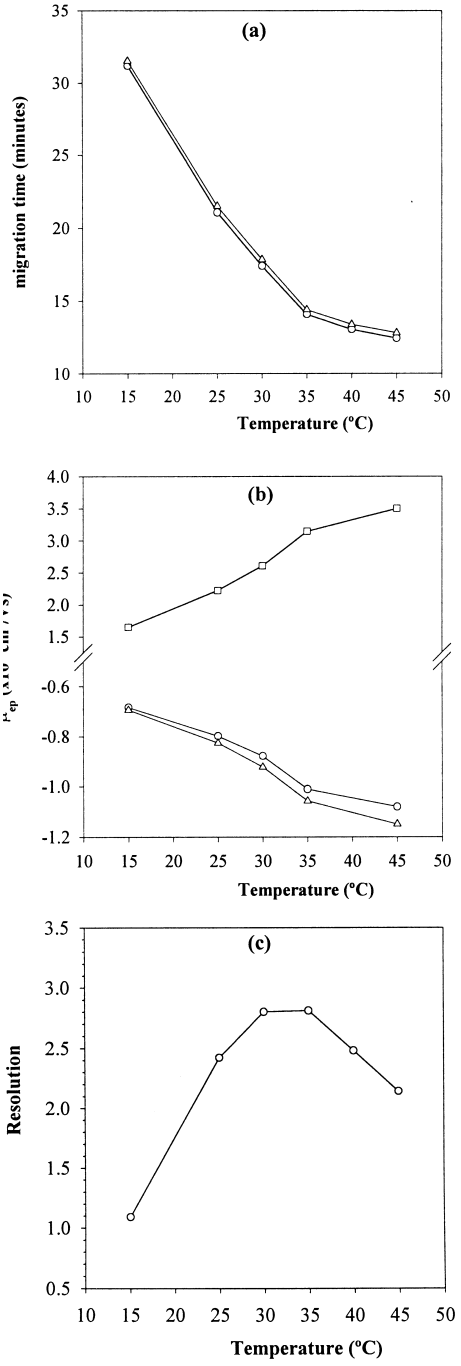


Fig. 3. Effect of temperature on (a) migration time, (b) electrophoretic mobility and (c) resolution. BGE, 20 m*M* phosphate–20 m*M* triethanolamine, pH 5.0, 25 m*M* tri-OMe-β-CD; voltage, 20 kV, 5.5–9.1 μA. ○, *R*-(−)-ketoprofen; △, *S*-(+)-ketoprofen, □, electroosmotic flow.

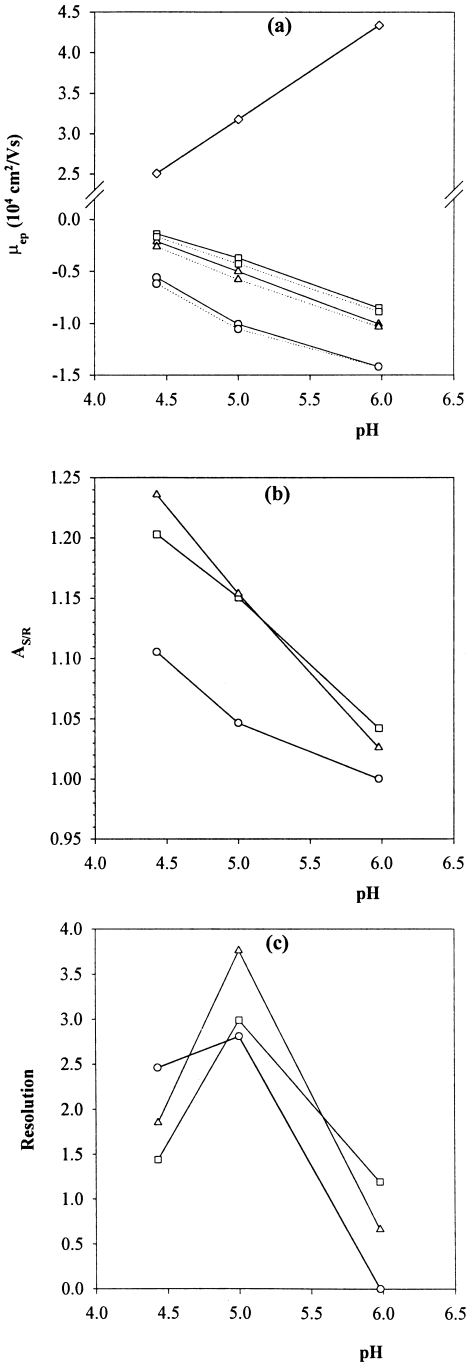


Fig. 4. Effect of pH on (a) electrophoretic mobility, (b) chiral selectivity and (c) resolution. BGE, 20 m*M* phosphate–20 m*M* triethanolamine, 25 m*M* tri-OMe-β-CD; temperature, 35°C; voltage, 20 kV, 8.0–9.9 μA. ○, ketoprofen; △, fenoprofen; □, ibuprofen; ◇, electroosmotic flow. Solid line, enantiomer *R*-(−); dotted line, enantiomer *S*-(+).

Initially, the three natural cyclodextrins, viz. α, β and γ-CD, were tested; a 0.3 m*M* racemic ketoprofen solution was injected into a BGE containing variable cyclodextrin concentrations at pH 4–6. The results were negative in every case. Then, di-OMe-β-CD and tri-OMe-β-CD were assayed in the hope that they would improve on the low selectivity of the natural cyclodextrins by virtue of their higher symmetry – which should reduce interactions between chiral sites of the host and guest [26]. Tests performed with di-OMe-β-CD at three different concentrations (15, 35 and 50 m*M*) were also negative; however, very slight resolution was observed at 35 and 50 m*M*. Tri-OMe-β-CD was used at 15, 25 and 50 m*M*, and two different temperatures (25 and 35°C). Fig. 2 shows the enantiomeric resolution of ketoprofen achieved at different tri-OMe-β-CD concentrations. Table 2 gives the results obtained for the three analytes studied. In all instances, μ_{eo} decreased with increasing cyclodextrin concentration at both temperatures by effect of the increased viscosity of the BGE. Similarly, μ_{ep} decreased as a result of the stronger interaction between the analytes and the cyclodextrin (reflected in increased $A_{S/R}$ values). The net effect was increased migration time and resolution. Ketoprofen always exhibited the lowest selectivity, which suggests that it was the analyte with the least affinity for the cyclodextrin used.

The migration sequence for ketoprofen enantiomers was established by spiking racemic mixtures with the pure enantiomers under the working conditions described in Section 2.3. Isomer *R*-(−) exhibited the lower μ_{ep}, so it presumably forms a more stable complex with cyclodextrin than does the other isomer. Based on the model of Rawjee et al. [19], profens belong to a kind of weak acids in

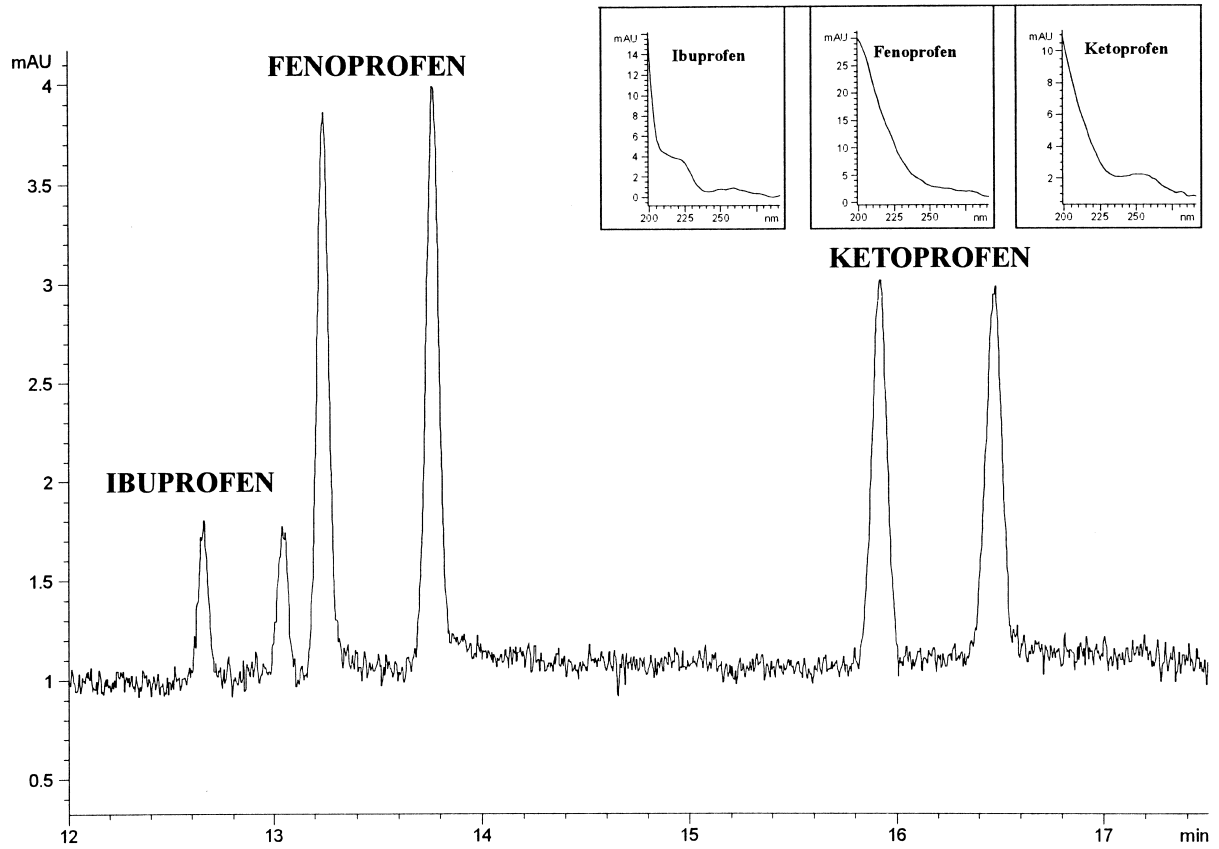


Fig. 5. Electropherogram showing the enantiomeric separation of ibuprofen, fenoprofen and ketoprofen. BGE, 20 m*M* phosphate–20 m*M* triethanolamine, pH 5.0, 50 m*M* tri-OMe-β-CD; temperature, 35°C; voltage, 20 kV, 8.1 μA.

which the complexation with the cyclodextrin is only selective in their undissociated forms (type I). In these acids, the enantiomer migration sequence cannot be altered by changing the cyclodextrin concentration or pH.

3.3. Influence of temperature on ketoprofen resolution

Changes in the capillary temperature can alter the BGE viscosity, its pH and the affinity of the analyte for the cyclodextrin – the stability constant for an inclusion complex decreases with increasing temperature [27]. As can be seen from Fig. 3b, increasing temperatures raised the electroosmotic flow and electrophoretic mobility of the enantiomers as the likely result of the two-fold effect of the decreased BGE viscosity and the also decreased equilibrium constants for the analyte–cyclodextrin complexes. The net effect was decreased migration times (Fig. 3a) and a resolution peak at 35°C (Fig. 3c), where the separation efficiency was also maximal. This temperature was thus chosen as optimal because it resulted in the maximum possible resolution and a fairly short analysis time. The decrease of resolution at temperatures higher than 35°C can be explained by a decrease in the efficiency of separation due to an increase of the band-broadening caused by the larger diffusion of the analyte.

3.4. Influence of the BGE pH on resolution

The effect of pH on the enantiomeric resolution of the three profens was examined by injecting individual solutions containing 0.3 m*M* ketoprofen, ibuprofen or fenoprofen at pH 4.5, 5.0 or 6.0. As can be seen from Fig. 4, the electrophoretic mobilities of the analytes increased in absolute terms with increasing pH (Fig. 4a); however, the increase was small relative to that in μ_{eo}, so the net effect was decreased migration times.

Chiral selectivity increased with decreasing pH (Fig. 4b) because non-selective complexation (that of the ionic forms of the enantiomers) diminished as the ionic species were gradually converted into their non-ionic counterparts, which are selectively complexed. However, resolution did not conform to the same variation pattern because it also depends on the effective charge of the enantiomers [20], which decreases markedly with decreasing pH. The net result was that resolution peaked at a pH very similar to the pK_a for the analyte and an abrupt fall on both sides of the peak; thus, resolution decreased at low pH values because the effective enantiomer charge tended to zero and was zero at a high enough pH because $A_{S/R}$ was unity. As can be seen in Fig. 4c, resolution peaked at pH 5.0 for the three analytes. These results are consistent with those previously reported by Rawjee.

By way of example, Fig. 5 shows the elec-

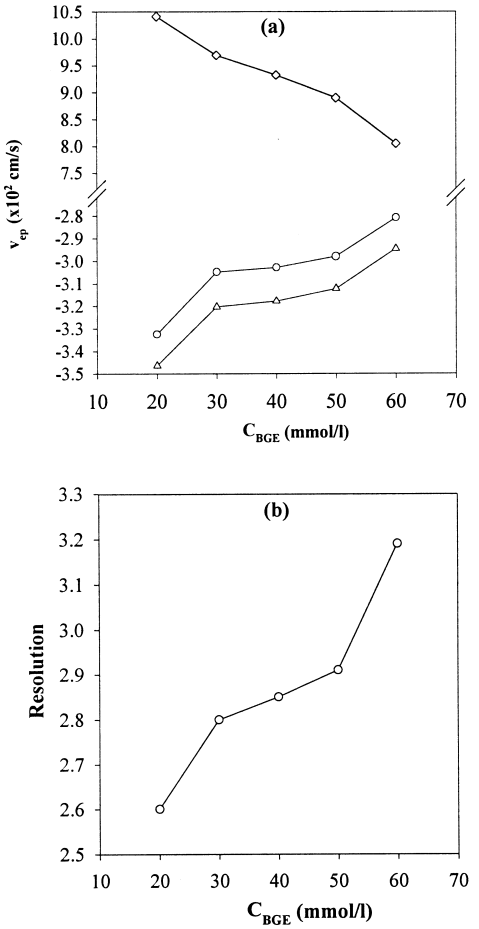


Fig. 6. Effect of the BGE concentration on (a) electrophoretic velocity and (b) resolution. BGE, 20 m*M* phosphate–20 m*M* triethanolamine, pH 5.0, 25 m*M* tri-OMe-β-CD; temperature, 35°C; voltage, 20 kV, 8.4–20.7 μA. ○, *R*-(−)-ketoprofen; △, *S*-(+)-ketoprofen; ◇, electroosmotic flow.

tropherogram for a solution of ketoprofen, ibuprofen and fenoprofen in a BGE containing 50 m*M* tri-OMe-β-CD at the optimum pH. As can be seen, all three compounds were quantitatively resolved within 17 min, which should allow us to analyze these three analytes in a single run if they were all in a hypothetical sample.

3.5. Influence of the BGE concentration on resolution

The effect of the concentration of the phosphate–triethanolamine background electrolyte (C_{BGE}) on ketoprofen resolution was studied by injecting a 0.3 m*M* racemic solution of the analyte. The results of the experiments conducted at five different BGE concentrations are shown in Figs. 6 and 7. As can be seen from Fig. 6a, the electroosmotic rate decreased with increase in the BGE concentration. The increased ionic strength of the medium had a compressive effect on the electrical double layer that decreased the potential ζ and hence μ_{eo}; this effect was combined with the resulting increased viscosity of the medium. Fig. 6a also shows the variation of the electrophoretic velocity (v_{ep}) of the enantiomers. The reason for the decrease in v_{ep} with increase in C_{BGE} is more complex; in fact, it involves terms that affect electrophoretic mobility (e.g. the viscosity of the medium and the reduced effective size of the ion) and others that influence the effective electrical field that acts on the ion (e.g. the effect of charge asymmetry, electrophoretic effects from ions with charge of opposite sign) [28]. The net result was a decrease in the apparent electrophoretic velocity of the enantiomers, i.e. increased migration times. Raising C_{BGE} strengthens hydrophobic interactions between the analyte and the cyclodextrin and increases enantioselectivity and hence resolution.

3.6. Effect of the addition of methanol to the BGE on resolution

The effect of adding methanol to the BGE on resolution was examined by injecting individual solutions of racemic ketoprofen, fenoprofen and ibuprofen into a BGE containing 10% methanol at 25°C. In all cases the presence of methanol led to a decrease of the resolution between 30 and 40%, an increase of the peak asymmetry and a considerable increase in migration times for fenoprofen and ibuprofen and, in lesser magnitude, for ketoprofen. This behavior can be attributed to a decrease in the

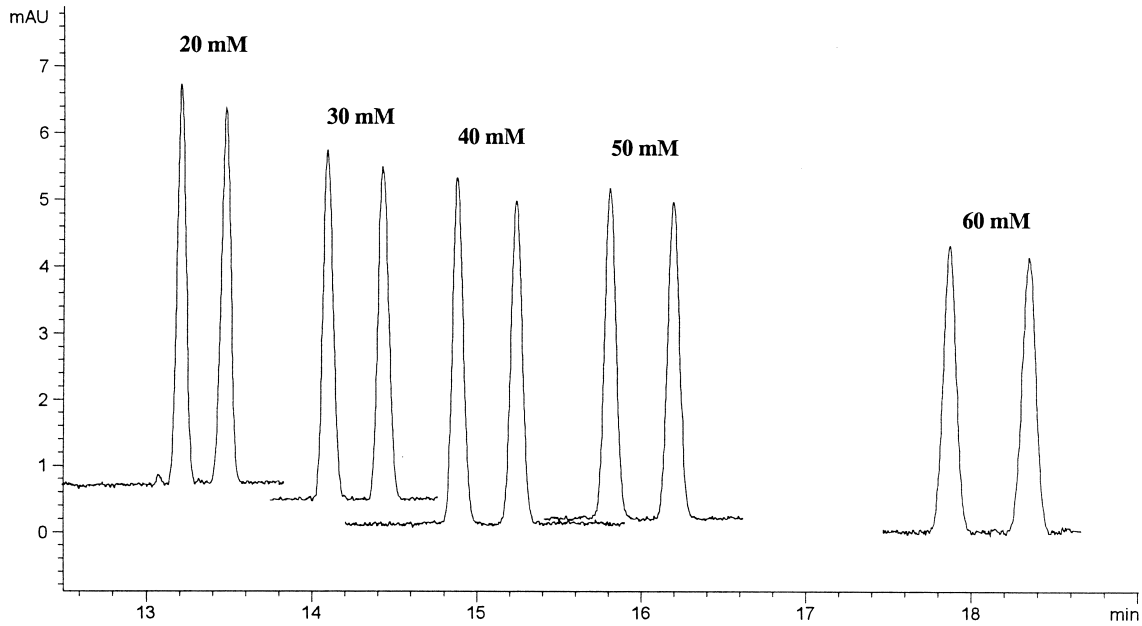


Fig. 7. Variation of the enantiomeric resolution of ketoprofen with the BGE concentration. Conditions as in Fig. 6.

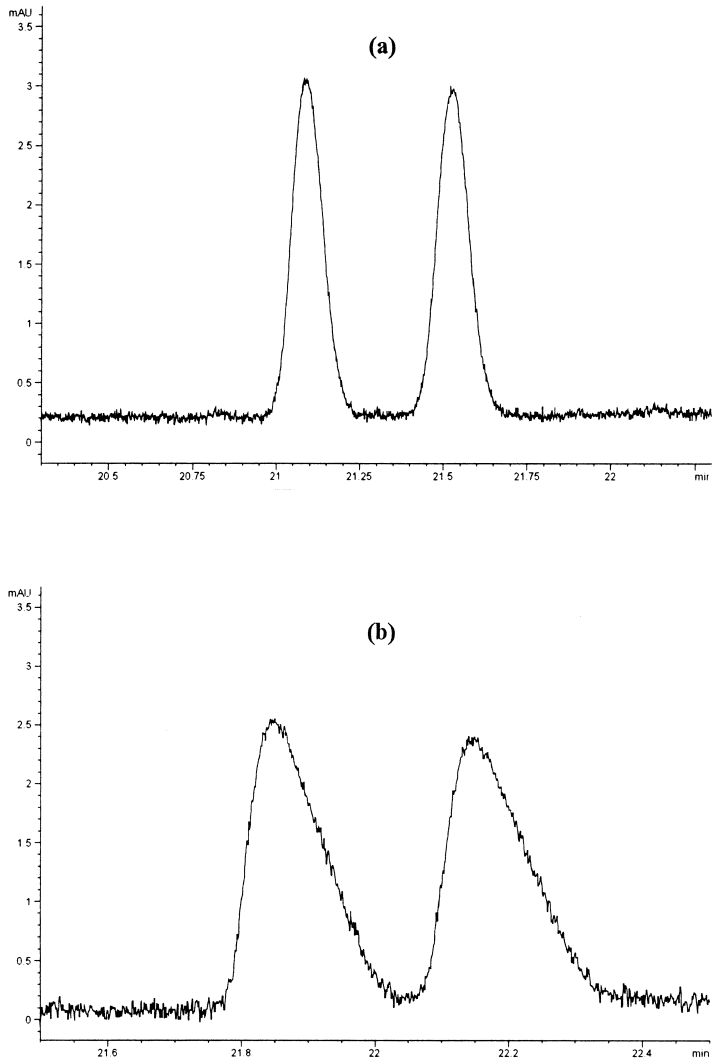


Fig. 8. Enantiomeric resolution of ketoprofen in the absence (a) and presence of 10% methanol in the BGE (b). BGE, 20 m*M* phosphate–20 m*M* triethanolamine, pH 5.0, 25 m*M* tri-OMe-β-CD; temperature, 25°C; voltage, 20 kV, 6.2 μA.

polarity of the medium, that led to a reduction of the affinity of the enantiomers by the cyclodextrin, and to a considerable decrease in μ_{eo}, such as we have observed. These results are opposite to the results of Fanali and Aturki [23], who obtained a slight improvement in the resolution of fenoprofen by adding 40% methanol in the BGE. By way of example, Fig. 8 shows the effect of adding 10% methanol in the resolution of racemic ketoprofen. Using 20% led to even poorer resolution.

4. Conclusions

The CZE technique in combination with a BGE containing a cyclodextrin was successfully used to separate the enantiomers of three 2-arylpropionic acids. The ensuing method has the advantage that it requires no capillary treatment. Ketoprofen enantiomers can be quantitatively resolved within a relatively short time (less than 20 min) by using tri-OMe-β-CD as chiral selector, and ibuprofen and

fenoprofen enantiomers can be resolved within an even shorter time. Alternative cyclodextrins produce incomplete enantiomeric resolution.

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