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Original Paper

Simultaneous determination of celecoxib, meloxicam, and rofecoxib using capillary electrophoresis with surfactant and application in drug formulations

A simple and selective CE using surfactant with UV detection is described for the simultaneous determination of selective cyclooxygenase-2 inhibitors, celecoxib, meloxicam, and rofecoxib. The simultaneous analysis of celecoxib, meloxicam, and rofecoxib was performed in Tris buffer (10 mM; pH 11) with 60 mM sodium octanesulfonate and 20% ACN as an anionic surfactant and organic modifier, respectively. Under this condition, good separation with high efficiency and the required short analysis time is achieved. The linear ranges of the method for the determination of celecoxib, meloxicam, and rofecoxib were over 5 – 100 μg/mL; the detection limits at 200 nm (S/N = 3; injection 3.45 kPa, 5 s) were 2, 1, and 1 μg/mL, respectively. The small amount of sample required and the expeditiousness of the procedure allow content uniformity to be determined in individual pharmaceutical products.

Keywords: Capillary electrophoresis / Celecoxib, meloxicam and rofecoxib / Pharmaceutical products

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1 Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely prescribed drugs in clinical practice for the treatment of osteoarthritis (OA), rheumatoid arthritis (RA), and other painful conditions [1 – 3]. RA is an autoimmune disease that causes chronic inflammation of the joints. OA is a type of arthritis that is caused by the breakdown and eventual loss of the cartilage of one or more joints. NSAIDs inhibit the cyclooxygenase (COX): COX-1 is generally considered a constitutive form that is responsible for maintaining normal physiologic function, and COX-2 is an inducible form that is found in increased levels in inflammatory states and in many cancers and their associated premalignant lesions [4]. All available NSAIDs can inhibit both COX-1 and COX-2 enzymes. NSAIDs side effects are mostly caused by COX-1 inhibition in the stomach, kidney, and platelets leading to many clinically undesirable side effects. The selectivity of a given NSAID can be expressed by the ratio of the concentration of drug required to reduce enzyme activity of COX-2 and COX-1. A new class of drugs, the selective COX-2 inhibitors, has recently been marketed as an alternative to conventional NSAIDs for the treatment of OA and RA [5 – 8] on the basis of the low risk of adverse gastrointestinal effects. Moreover, overexpression of COX-2 enzyme is not only limited to the inflammatory process but also has been observed in various types of cancer [4, 9, 10]. The potential use of COX-2 selective NSAIDs in the prevention of colon cancer is suggested from the distribution of COX-2 enzyme in adenomatous polyps and colon cancer [4, 9].

Recently, several reports have been published which indicate that the use of high-dose COX-2 selective NSAIDs is possibly associated with an increased risk of myocardial infarction [11 – 13]. The class of selective COX-2 inhibitors, celecoxib (Celebrex®, marketed by Pfizer/Pharmacia) and meloxicam (Mobic®, marketed by Boehringer), is the most widely prescribed long-term medication presently used for the treatment of OA, RA, and other painful conditions. Rofecoxib (Vioxx®, marketed by Merck) has been withdrawn from the market since 2004, owing to increased adverse cardiovascular events compared to

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Abbreviations: COX, cyclooxygenase; **IS**, internal standard; **NSADs**, nonsteroidal anti-inflammatory drugs; **OA**, osteoarthritis; **RA**, rheumatoid arthritis; **RE**, relative error; **SHS**, sodium hexanesulfonate; **SOS**, sodium octanesulfonate; **SPS**, sodium pentanesulfonate

placebos at higher doses. Therefore, it is essential to assure the potency and content uniformity of the selective COX-2 inhibitors in the pharmaceutical preparations for certification to ensure therapeutic efficacy, and to avoid the possible risk of toxicity.

Numerous methods are available for the determination of NSAIDs including the spectrofluorimetric [14, 15], thin layer chromatographic [16], and HPLC methods [17 – 23], as well as LC-MS [24] and CE [25 – 28]. HPLC techniques are the most widely used and accurate techniques for the analysis of the NSAIDs in various matrices. However, the HPLC separations generally necessitate a large amount of solvent waste. Recently, CE has been increasingly viewed as an alternative technique to HPLC for determination of pharmaceutics due to its high separation efficiency, speed, and minimal consumption of reagents. There are several reports for the separation of NSAIDs chemicals standards by CZE or MEKC [25 – 28]. However, all the simultaneous estimations have dealt with classical or preferential but not specific COX-2 inhibitors. As the use of selective COX-2 inhibitors is rapidly increasing, it is essential to develop simple and suitable analytical methods for its estimation in bulk and in formulations, which could be easily adapted for routine quality control analysis. There are no CE methods concerning simultaneous determination of selective COX-2 inhibitors, celecoxib, meloxicam, and rofecoxib, in bulk drug and in pharmaceutical dosage forms. The aim of the present study is to develop and validate an efficient, reliable, accurate, and sensitive CE method for the simultaneous determination of commonly used selective COX-2 inhibitors, celecoxib, meloxicam, and rofecoxib (structures shown as in Fig. 1). Application of the proposed method of analysis of celecoxib and meloxicam in commercial preparations is demonstrated and proven to be satisfactory.

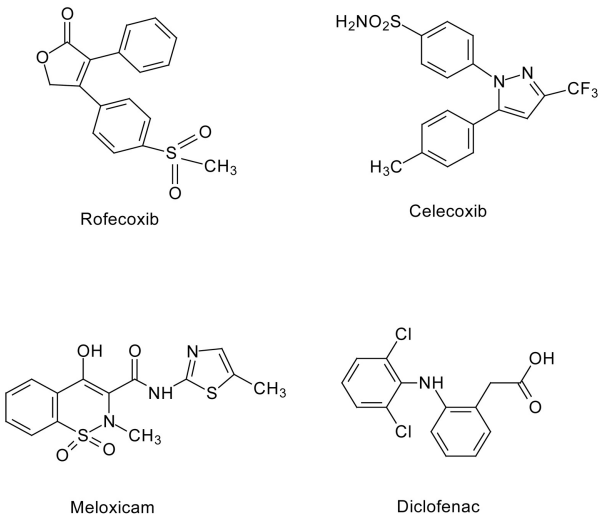

Figure 1. Chemical structures of rofecoxib, celecoxib, meloxicam, and diclofenac (IS).

2 Materials and methods

2.1 Chemicals and reagents

Celecoxib and rofecoxib were kindly supplied by Pfizer (USA) and Merck Sharp & Dohme (USA), respectively. Meloxicam, diclofenac (internal standard, IS), SDS, sodium hexanesulfonate (SHS), and sodium pentanesulfonate (SPS) were from Sigma (St. Louis, MO, USA). Sodium hydroxide, sodium octanesulfonate (SOS), Tris, phosphoric acid (H_3PO_4, 85%), and ACN were supplied by E. Merck (Darmstadt, Germany). Milli-Q (Millipore, Bedford, MA, USA) treated water was used for the preparation of buffer and related chemicals. Solutions of various Tris buffers at different pH levels were prepared by neutralizing the related Tris solution with H_3PO_4. Solutions of SOS as surfactant at various levels were obtained by dissolving different amounts of SOS in Tris buffer.

2.2 CE conditions

A Beckman P/ACE MDQ system (Fullerton, CA, USA) equipped with UV detector and a liquid-cooling device were used. CE was performed in an uncoated fused-silica capillary (Polymicro Technologies, Phoenix, AZ, USA) of 40.2 cm (effective length 30 cm) × 50 μm id. Samples were injected by pressure (3.45 kPa) for 5 s, and the applied voltage for separation was 17 kV. Separations were performed at 25°C in Tris buffer (10 mM; pH 11.0) with SOS (60 mM) and 20% ACN. Detection was carried out by the on-column measurement of UV absorption at 200 nm (cathode at the detection side). Capillary conditioning before startup is methanol for 10 min, 1 M HCl aqueous solution for 10 min, deionized water for 2 min, 1 M NaOH aqueous solution for 10 min, and deionized water for 2 min. The conditioning between runs was carried out by rinsing with 0.1 M NaOH (3 min), deionized water (2 min), and running buffer (3 min), under positive pressure applied at the injection end. A Beckman P/ACE MDQ Microsoft software system was used for data processing.

2.3 Reference and sample solutions

Stock solutions of analytes were prepared in 25% ACN aqueous solution and suitably diluted with 25% ACN aqueous solution at 50 μg/mL of celecoxib, rofecoxib, and meloxicam, and at 25 μg/mL of diclofenac (IS), respectively, as reference solutions and IS. For the assay of celecoxib in commercial capsules and meloxicam in commercial tablets, the sample solutions were prepared as follows: An accurate portion of the celecoxib (Celebrex labeled amount 200 mg/capsule) equivalent to each capsule of about 8 mg of celecoxib was transferred to a 200-

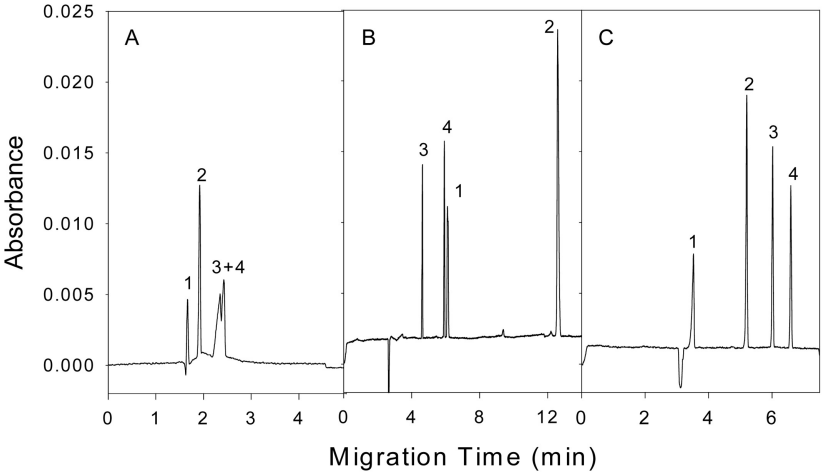

Figure 2. Electropherograms for the determination of selective COX-2 inhibitors using different modes. (A) CZE, Tris buffer (10 mM, pH 11.0) with 20% ACN; (B) MEKC, Tris (10 mM, pH 11.0) with 60 mM SDS and 20% ACN; (C) Tris (10 mM, pH 11.0) with 60 mM SOS and 20% ACN. Peaks: 1, rofecoxib; 2, celecoxib; 3, meloxicam; 4, diclofenac (IS). CE conditions: applied voltage, 17 kV (detector at cathode side); uncoated fused-silica capillary, 40.2 cm (effective length 30 cm) × 50 μm id; injection, 3.45 kPa, 5 s; wavelength, 200 nm.

mL volumetric flask that contained 20 mL of 250 μg/mL of diclofenac (IS). For the assay of meloxicam in commercial tablets (Mobic labeled amount 7.5 mg/tablet), an accurately weighed portion of the powder equivalent to 4 mg of meloxicam was transferred to 100-mL volumetric flask that contained 10 mL of 250 μg/mL of diclofenac (IS). Then the solutions were sonicated for 5 min and diluted to volume with 25% ACN aqueous solution. The solution was transferred into a 0.2-mL minivial that could be placed into the autosampler for CE analyses. For the assay of celecoxib in capsules or meloxicam in tablet, the content solutions were directed as for CE analysis. In 2004, rofecoxib was withdrawn from the market after the postmarket study had shown a two-fold increased risk of cardiovascular morbidities in rofecoxib patients compared to those receiving placebo [12], so we did not test the Vioxx tablet in this study.

2.4 Method validation

Calibration curves were prepared by simultaneously adding celecoxib, rofecoxib, and meloxicam at five different concentrations and a fixed concentration of diclofenac (IS) in 25% ACN aqueous solution to make the final concentrations 25 μg/mL for diclofenac and 5.0, 10.0, 20.0, 50.0, and 100.0 μg/mL for the tested chemicals. The calibration graphs were established with the peak-area ratio of the tested chemicals to diclofenac (IS) as ordinate (*y*) *versus* the concentration of these drugs in μg/mL as abscissa (*x*). Intraday precision and accuracy were calculated from five consecutive days, and were based on five replicate analyses for three concentration levels, at 5.0, 20.0, and 50 μg/mL for the tested chemicals. Interday precision and accuracy were calculated from five consecutive days for these concentration levels of the tested chemicals. The recovery study of the method was performed at three levels of amounts of tested chemicals added, 1, 4, and 8 mg of celecoxib and 1, 2, and 4 mg of meloxicam, spiked in pharmaceutical samples.

3 Results and discussion

Preliminary testing of celecoxib, rofecoxib, and meloxicam standards by CZE was briefly studied at 17 kV with Tris buffer without ACN and surfactant under various pHs and the tested drugs did not achieve resolution in these backgrounds. Then varied concentrations of organic modifier, 5–20% ACN, were added to test the resolution in the absence of surfactants. Celecoxib, rofecoxib, meloxicam, and diclofenac also did not achieve resolution under various concentrations of Tris buffers with 20% ACN; the typical CZE electropherogram is shown in Fig. 2A. Rofecoxib migrated closely to EOF, and a broadened peak of meloxicam overlapping with diclofenac was observed. This indicates that simple separation mode of CZE based mainly on the differences of charge to mass ratios of the analytes in the tested conditions does not effectively and simultaneously determine the ionized compounds, celecoxib and meloxicam, and the neutral compound, rofecoxib. The pK_a values of celecoxib, diclofenac, and meloxicam are 11.1, 4.5, and 4.2, respectively [29, 30] (http//www.usp.org/pdf/EN/reterinary/meloxicam.pdf). The very commonly used anionic surfactant, SDS (CMC, 8.1 mM), as a micellar source with Tris buffer was used to study the resolution of the analytes. The SDS at various concentrations in Tris buffer in the pH range 8.0–11.0 was tested to separate the ana-

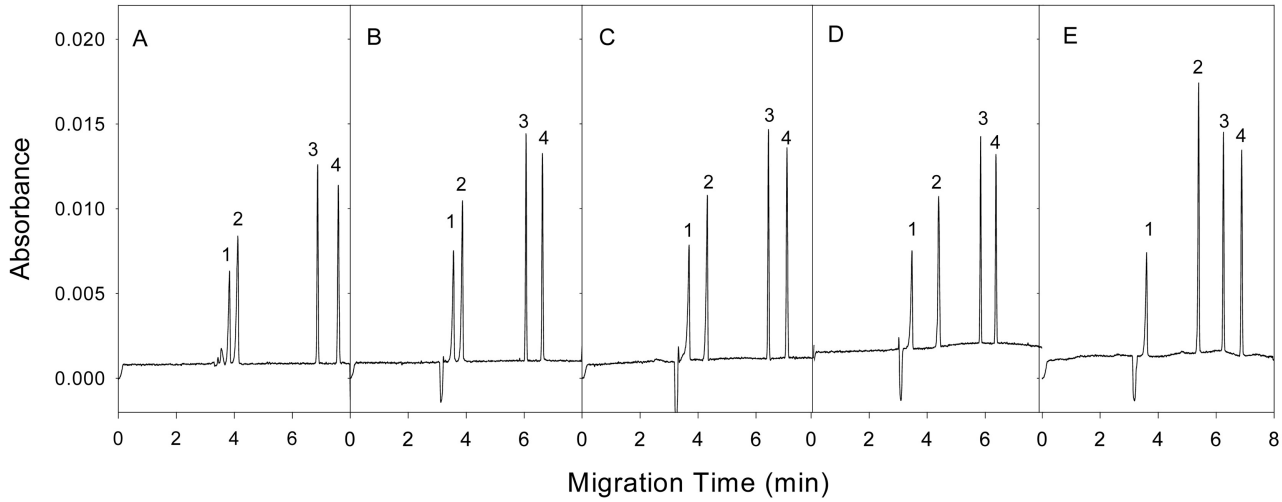

Figure 3. Effect of pH of Tris buffer (10 mM) with 60 mM SOS and 20% ACN on the migration of rofecoxib, celecoxib, meloxicam, and diclofenac (IS). (A) pH 8.0, (B) pH 9.0, (C) pH 10.0, (D) pH 10.5, (E) pH 11.0. Peaks: 1, rofecoxib; 2, celecoxib; 3, meloxicam; 4, diclofenac (IS). For other conditions and symbols see Fig. 2.

lytes. Although celecoxib, rofecoxib, and meloxicam can differentiate in 10 mM of Tris buffer with 60 mM SDS and 20% ACN as BGE, a longer migration time of celecoxib and close migration between diclofenac and rofecoxib were observed in the tested conditions (Fig. 2B). Peaks 3 and 4 represent meloxicam and diclofenac, respectively. They have the same charge as SDS micelles in the test electrolyte background and interact weakly with micelles through repulsive forces resulting in fast migration. Therefore, compounds with carbon number less than SDS such as SOS, SHS, and SPS were investigated. These anionic surfactants in Tris buffer yielded improvement of selectivity, better resolution between the analytes especially SOS, and shorter migration times than SDS as surfactant. Under the pH 11.0 of Tris buffer with 20% ACN and 60 mM SPS or 60 mM SHS system, rofecoxib migrated at near the EOF marker and could not be analyzed reliably. SOS as a surfactant has better separation efficiency as shown in Fig. 2C, indicating that ionic surfactant SOS provided a suitable carbon chain length to retain the analytes. As a consequence, simple parameters affecting the CE separation using SOS as surfactant for celecoxib, rofecoxib, and meloxicam separation were studied, including concentrations of the buffer, SOS, and pH. After CE separation of celecoxib, rofecoxib, and meloxicam in Tris buffer, the eluted compounds were monitored at 200 nm.

3.1 Optimization of the experimental conditions

Ionic strength or concentration of buffer has significant effects on solute mobilities and separation efficiency. The retention behavior of celecoxib, rofecoxib, and meloxicam in Tris buffer (pH 11.0) at the concentration range of 10–50 mM with 60 mM SOS and 20% ACN as an anionic surfactant and organic modifier, respectively, was studied. CE of the celecoxib, rofecoxib, and meloxicam in Tris buffer (pH 11.0) in the concentration range of 10–50 mM can provide complete separation. To prevent generation of too much Joule heating and to achieve shorter migration time, 10 mM of Tris buffer was chosen. The 10 mM Tris buffers with SOS (60 mM) at different pH levels (8.0, 9.0, 10.0, 10.5, and 11.0) were studied. The peak shape of the tested drugs: rofecoxib, meloxicam, and diclofenac, showed no significant changes at various pH values, but a significant effect of the peak efficiency of celecoxib was obtained at pH >10.5. On the other hand, below pH 10 Tris buffer system, rofecoxib migrated at near the EOF marker as shown in Fig. 3. Methanol is used as an EOF marker. The higher theoretical plate number N of celecoxib (as shown in Table 1) and narrower peak width were observed in pH 11.0. Regarding the pH effect on the separation efficiency of the studied analytes, obviously, celecoxib is mostly affected by pH. The efficiency of the electrophoretic system is gauged by the number of theoretical plates N. Compar-

Table 1. pH effect on theoretical plate number

Variables	Mean theoretical plate (N)[a] investigated				
	pH 8.0	pH 9.0	pH 10.0	pH 10.5	pH 11.0
Rofecoxib	21525	20165	19970	18544	18332
Celecoxib	22076	26274	28646	30063	75947
Meloxicam	129604	131936	131752	132676	130247
Diclofenac (IS)	124803	131861	127775	128889	130410

[a] All RSD <0.9% (n = 3)

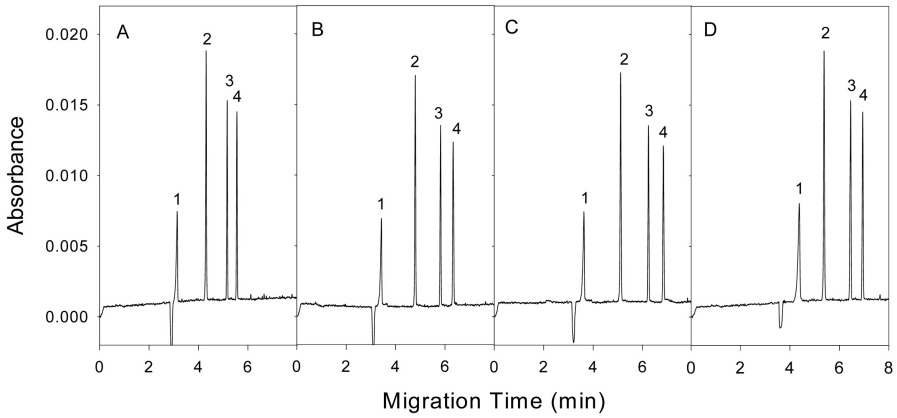

Figure 4. Effect of SOS concentration (40–70 mM) with 10 mM Tris buffer (pH 11.0) and ACN (20%) on the migration of rofecoxib, celecoxib, meloxicam, and diclofenac at 50, 50, 50, and 25 μg/mL, respectively. (A) 40, (B) 50, (C) 60, and (D) 70 mM. Peaks: 1, rofecoxib; 2, celecoxib; 3, meloxicam; 4, diclofenac (IS). For other conditions and symbols see Fig. 2.

ing pH 8.0–11.0 on the separation efficiency for celecoxib, the theoretical plate number of about three times was obtained at pH 11.0 (Table 1). Therefore, the 10 mM and pH 11.0 of Tris buffer was the choice for optimal buffer concentration and pH for simultaneous determination of celecoxib, rofecoxib, and meloxicam. The effects of SOS at concentration range 40–70 mM in Tris buffer (10 mM; pH 11.0) with 20% ACN on the separation are shown in Fig. 4. Under the 40–50 mM SOS in Tris buffer with 20% ACN, rofecoxib migrated at near the EOF marker. However, significant improvement of separation from EOF can be obtained by increasing the concentration of SOS, leading to more retention in surfactant. With the concentration of SOS ≥60 mM, a baseline resolution electropherogram of rofecoxib from EOF was observed. The surfactant concentration is set at 60 mM, which can effectively retain and have the shortest retention time of the tested drugs. Sixty millimolar SOS was used in this study, which is lower than the corresponding CMC, 160 mM [31]. No micelle is formed under this tested condition; the retention behavior of the analytes was affected not only by surfactant but also by CZE mode based on differences in the charge-to-mass ratio. The rofecoxib and celecoxib are neutral analytes, the meloxicam and diclofenac will be bearing negative charges in the structure under the tested pH buffer condition. The more lipophilic property of celebrex (having three fluorine atoms; M_r 381.38) and rofecoxib (M_r 314.36) made it more retained on the surfactant surface and then slower migration of celebrex in this running buffer was observed. Other components meloxicam (M_r 351.51) and diclofenac (M_r 296.15) are negatively charged within the tested pH and thus have negative mobilities when they migrate toward the positive electrode. Therefore, the migration orders of the tested drugs are rofecoxib, celebrex, meloxicam, and diclofenac. Electrophoresis of the drugs in the absence of ACN as an additive results in partial overlapping of meloxicam and diclofenac (Fig. 5A). Furthermore, rofecoxib migrated at near the EOF marker in the absence of organic modifier. Organic solvents miscible with water are widely used as mobile-phase modifiers to adjust the retention factor. The use of organic solvents can contribute to the improvement of resolution or to the alteration of selectivity [32]. In general, the addition of organic modifiers reduces the EOF and expands the migration time window. Owing to good solubility of the tested drugs in ACN than in methanol, better separation efficiency is obtained in Tris buffer with SOS (60 mM) and ACN. Therefore, the effects of concentrations of 0, 10, 15, 20, and 25% ACN as organic modifier added in Tris buffer (10 mM; pH 11.0) with 60 mM SOS on separation of celecoxib, meloxicam, rofecoxib, and diclofenac (IS) were studied as shown in Fig. 5A–E, respectively. Baseline resolution for rofecoxib from EOF was obtainable at ACN concentrations ≥10%. The optimization of the CE conditions for simultaneous analysis of celecoxib, meloxicam, rofecoxib, and diclofenac was set at 10 mM Tris buffer (pH 11.0) with 60 mM SOS and 20% ACN as running buffer and the analytes were monitored at 200 nm. Different voltages, including 10, 15, and 17 kV, were tested. A shorter migration time and higher theoretical plate number were observed at 17 kV; the resulting current was 35 μA in this BGE. Figure 6B and A present the typical electropherograms of the CE separation of celecoxib, meloxicam, rofecoxib, and diclofenac (IS) reference standard and blank. The reproducibility of migration time of analytes was investigated; the observed migration times of EOF, rofecoxib, celecoxib, meloxicam, and diclofenac were 3.20 ± 0.04, 3.62 ± 0.05, 5.06 ± 0.13, 6.26 ± 0.12, and 6.86 ± 0.15 min, respectively, and RSDs (n = 20) of migration times were found to be less than 2.5%. Under the optimum conditions, the plate

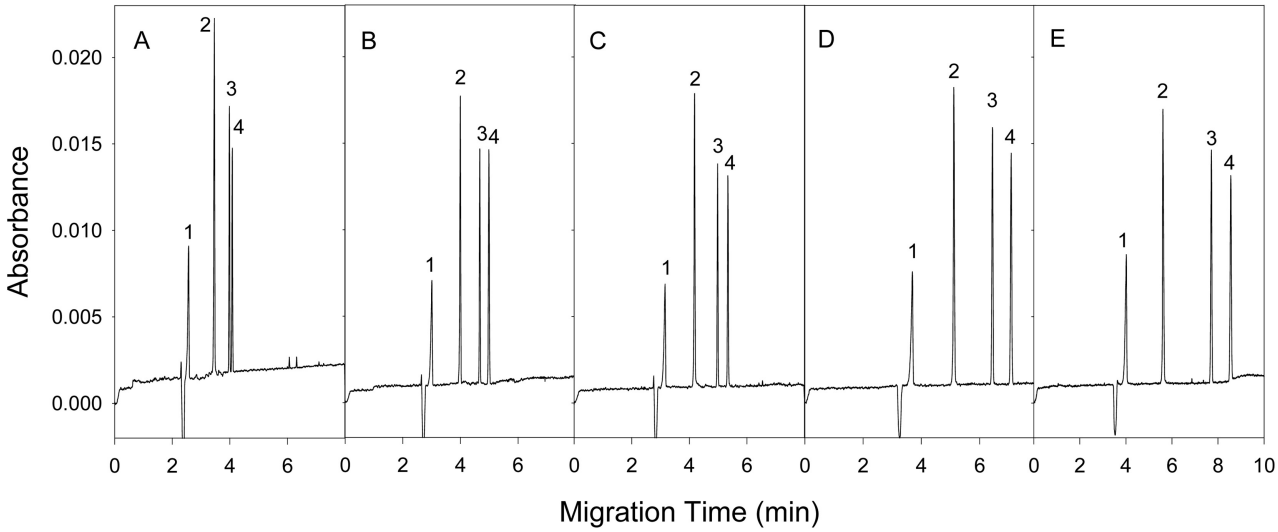

Figure 5. Effect of concentration of ACN (0–25%) with 10 mM Tris buffer (pH 11.0), SOS (60 mM) on the migration of rofecoxib, celecoxib, meloxicam, and diclofenac at 50, 50, 50, and 25 μg/mL, respectively. (A) 0, (B) 10, (C) 15, (D) 20, and (E) 25%. Peaks: 1, rofecoxib; 2, celecoxib; 3, meloxicam; 4, diclofenac (IS). For other conditions and symbols see Fig. 2.

height was calculated by the following equation: $H = L/N$, where H is the plate height, N is the number of theoretical plates (calculated by software supplied by instrument designed), and L is the length of the capillary. The plate heights (cm) were 3.17×10^{-3}, 7.92×10^{-4}, and 4.74×10^{-4} for rofecoxib, celecoxib, and meloxicam, respectively.

3.2 Analytical calibration

For evaluating the quantitative applicability of the method, five different concentrations of rofecoxib, celecoxib, and meloxicam over the range of 5–100 μg/mL were analyzed using diclofenac (25 μg/mL) as an IS. The linearity between the peak-area ratios (y) of the related analytes to IS and the concentration (x, μg/mL) of the analytes was investigated. The linear regression equations are listed in Table 2. The data indicate good linearity of the proposed method. The LOQ is the minimum injected amount that gives precise measurements and is defined as the sample concentration that generates a peak height ten times the level of the baseline noise. The LOQs for rofecoxib, celecoxib, and meloxicam (S/N = 3; 3.45 kPa, 5 s) were 5, 3, and 3 μg/mL, respectively, and the RSD (n = 5) for LOQs are all less than 2.9%. The detection limits for rofecoxib, celecoxib, and meloxicam (S/N = 3; 3.45 kPa, 5 s) were 2, 1, and 1 μg/mL, respectively. The reproducibility and reliability of the proposed method were assessed at three different concentrations of rofecoxib, celecoxib, and meloxicam and evaluated as RSD and relative error (RE). As shown in Table 3, the precision of the method for rofecoxib, celecoxib, and meloxicam for both intraday and interday analyses at three concentrations are all less than 2.3% for RSD and 6.6% for RE. The selectivity of the proposed method was briefly tested on the separation of selective COX-2 inhibitors with conventional NSAIDs including acetylsalicylic acid, lysine acetylsalicylate, flubiprofen, mefenamic acid, sulindac, and tiaprofenic acid. Under the present CE with SOS sur-

Table 2. Regression analyses for simultaneous determination of rofecoxib, celecoxib, and meloxicam

Concentration range (μg/mL)	Regression equation	Correlation coefficient (r)
Rofecoxib		
Intraday[a)] 5–100	$Y = (0.0146 \pm 0.0006)x + (0.0118 \pm 0.0059)$	0.999
Interday[a)] 5–100	$Y = (0.0146 \pm 0.0001)x + (0.0124 \pm 0.0128)$	0.999
Celecoxib		
Intraday[a)] 5–100	$Y = (0.0254 \pm 0.0010)x + (0.0279 \pm 0.0260)$	0.999
Interday[a)] 5–100	$Y = (0.0254 \pm 0.0003)x + (0.0043 \pm 0.0281)$	0.999
Meloxicam		
Intraday[a)] 5–100	$Y = (0.0191 \pm 0.0001)x + (0.0115 \pm 0.0026)$	0.999
Interday[a)] 5–100	$Y = (0.0190 \pm 0.0002)x + (0.0037 \pm 0.0061)$	0.999

[a)] Intraday data were based on five replicate analyses and interday data were taken from five consecutive days.

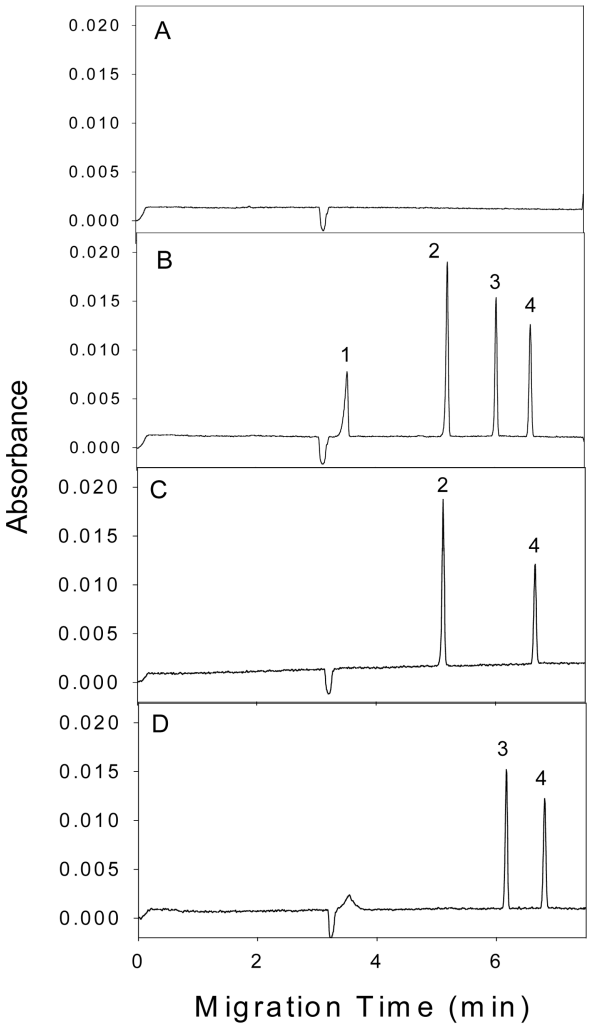

Figure 6. Typical electropherograms of (A) blank, (B) simultaneous determination of analytes standard at 50, 50, 50, and 25 μg/mL, respectively, (C) celecoxib in commercial capsule, (D) meloxicam in commercial tablet. CE conditions: 10 mM Tris buffer (pH 11.0) with 60 mM SOS and 20% ACN. Peaks: 1, rofecoxib; 2, celecoxib; 3, meloxicam; 4, diclofenac (IS). For other conditions and symbols see Fig. 2.

factant condition, a complete separation of rofecoxib, celecoxib, and meloxicam, and other NSAIDs was obtained as shown in Fig. 7.

3.3 Application

The application of the proposed method to the assay of celecoxib in capsules and meloxicam in tablets was studied. The uniformity test (a test to evaluate the content variation of the drug in formulations) is usually required by an official pharmacopoeia for quality control of the drug in formulation. The results of percentage of claimed content (%) are 100–103% for celecoxib in capsules and 108–115% for meloxicam in tablets as shown in Table 4. All the analytical values fell within 85–115% of the label claim for content uniformity test usually required by the USP27 [33]. The recoveries of tested drugs in pharmaceutical samples were obtained from the calibration graph constructed from different amounts of tested chemical at low, medium, and high concentration levels. All recoveries of the tested chemicals were >95% (data not shown). Typical electropherograms for analysis of celecoxib in capsules and meloxicam in tablets are shown in Fig. 6C and D, respectively. Many formulations contain excipient components, which may unduly affect the chromatographic performance of analytical columns. Therefore, it is often necessary to pretreat sample solutions prior to analysis by methods including SPE and liquid–liquid extraction. However, in the CE analysis of a formulation containing drugs, after the separation, the majority of excipients will be removed during a rinse step.

Table 3. Precision and accuracy for the analyses of selective COX-2 inhibitors

Concentration known (μg/mL)	Concentration found (μg/mL)	RSD (%)	RE (%)
Rofecoxib (n = 5)			
Intraday			
5.0	4.67 ± 0.09	1.95	−6.57
20.0	19.75 ± 0.44	2.21	−1.24
50.0	49.63 ± 0.26	0.53	−0.74
Interday			
5.0	4.78 ± 0.08	1.77	−4.40
20.0	20.02 ± 0.29	1.47	0.09
50.0	50.06 ± 0.34	0.68	0.13
Celecoxib (n = 5)			
Intraday			
5.0	5.12 ± 0.11	2.18	2.42
20.0	19.91 ± 0.29	1.47	−0.47
50.0	51.02 ± 0.66	1.29	2.04
Interday			
5.0	5.02 ± 0.08	1.69	0.41
20.0	19.77 ± 0.36	1.81	−1.14
50.0	49.94 ± 0.87	1.74	−0.13
Meloxicam (n = 5)			
Intraday			
5.0	4.98 ± 0.05	0.99	−0.45
20.0	20.28 ± 0.08	0.40	1.42
50.0	50.23 ± 0.17	0.34	0.47
Interday			
5.0	4.97 ± 0.04	0.80	−0.61
20.0	20.06 ± 0.17	0.84	0.31
50.0	50.27 ± 0.13	0.26	0.53

4 Concluding remarks

In conclusion, we demonstrated a simple, speedy, and specific CE method for the simultaneous determination of rofecoxib, celecoxib, and meloxicam. The CE method is based on the anionic surfactant SOS as a surfactant to differentiate the tested drugs and detect at 200 nm. The

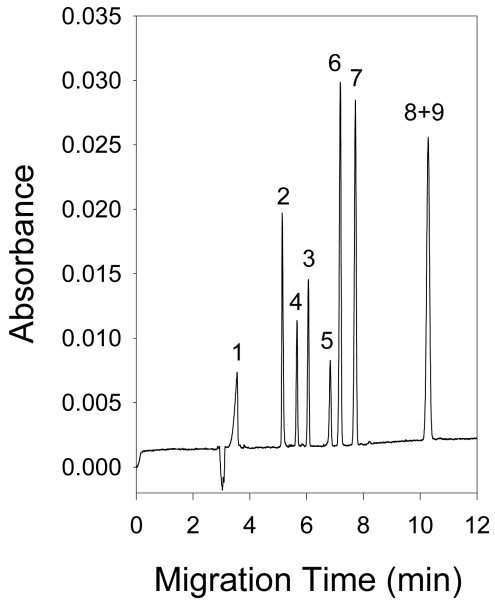

Figure 7. Electropherogram of the selectivity study of NSAIDs. Peaks: 1, rofecoxib; 2, celecoxib; 3, sulindac; 4, meloxicam; 5, tiaprofenic acid; 6, flubiprofen; 7, mefenamic acid; 8, acetylsalicylic acid; 9, lysine acetylsalicylate. CE conditions see Fig. 2. Buffer system: Tris (10 mM, pH 11.0) with SOS 60 mM and 20% ACN.

Table 4. Analytical results for content uniformity of COX-2 inhibitors in preparations obtained from commercial sources

	Concentration found[a)]	Percentage of claimed content[b)] (%)
Celecoxib capsule (Celebrex) (mg/capsule)[c)]		
1	205.7 ± 1.4	103
2	205.4 ± 0.9	103
3	203.5 ± 1.9	102
4	202.9 ± 3.2	102
5	200.6 ± 0.3	100
6	203.1 ± 2.0	102
Meloxicam tablet (Mobic) (mg/tablet)[c)]		
1	8.1 ± 0.1	108
2	8.4 ± 0.1	112
3	8.5 ± 0.1	113
4	8.5 ± 0.1	113
5	8.6 ± 0.1	115
6	8.6 ± 0.2	115

a) Mean ± SD of three replicate analyses.

b) Content uniformity test is used to check the variation of drug in each dosage form.

c) Labeled amounts of celecoxib in each capsule and meloxicam in each tablet are 200 mg/capsule and 7.5 mg/tablet, respectively.

CE method has been successfully demonstrated for the assay of celecoxib in capsules and meloxicam in tablets. We offer a completely different selectivity and simpler method for separation of selective COX-2 inhibitors of tested analytes and it is a complementary and alternative technique to HPLC in pharmaceutical assays.

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