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Enantiomer separation of acidic chiral compounds on a quinine-silica/zirconia hybrid monolith by capillary electrochromatography

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ABSTRACT

A weak anion-exchanger chiral selector, quinine-incorporated silica/zirconia hybrid monolithic (QUI-S/ZHM) capillary column was prepared by sol–gel technology. The performance of the QUI-S/ZHM column was investigated for enantioresolution of a set of acidic chiral drugs and dinitrobenzoyl (DNB)-amino acids by capillary electrochromatography in aqueous organic mobile phases composed of acetonitrile (ACN) and triethylammonium acetate (TEAA) buffer. Effects of several parameters including the ACN content, concentration and pH of the mobile phase on the chiral separation were examined. Baseline resolutions of all the compounds were obtained in the mobile phase consisting of 70:30 ACN/TEAA (10 mM, pH 6) under applied voltage of −10 kV at 25 °C within 20 min.

1. Introduction

The organic–inorganic hybrid monolithic columns have received great attention since the organic functional moieties can be incorporated into the inorganic monolith matrixes by the sol–gel technology to attain desirable properties such as good mechanical stability and solvent resistance. Literature reveals that polymer-based monoliths (PM) and organic-silica hybrid monoliths (OSHM) have been successfully employed as stationary phases in capillary electrochromatography (CEC). The organic-silica hybrid materials have been investigated as CEC stationary phases, which contain different functionalities, e.g. allyl [1], octadecyl [2], phenyl [3], octyl [4] and amino groups [5]. However, these monoliths showed some problems, i.e. tendency to swell in organic solvents leading to undesirable changes in the pore structure and mechanical instability (in case of PM) and a narrow working pH range (2–8) and lengthy preparation process (in case of OSHM), which have inspired scientists to explore new possibilities.

Silica-based phases with improved hydrolytic stability at extreme pH were introduced [6]. However, careful choices of operating conditions, such as the use of acetonitrile instead of methanol, the use of boric acid or organic buffers in low concentration and low temperature, are still required to achieve acceptable column lifetimes [7,8]. Zirconia has emerged as an attractive alternative to silica as the base material due to its good mechanical stability, resistance to high temperature and extreme pH [9,10]. Zirconia is an amphoteric material with anion-exchange properties in neutral and acidic solutions and cation-exchange properties in alkaline solutions [11], which can be used to generate and control the electroosmotic flow inside capillary by changing the pH and the mobile phase composition [11,12]. Recently, we reported clindamycin phosphate-incorporated zirconia hybrid monoliths for CEC enantioseparation [13].

Quinine (QUI) derivative-immobilized silica particle-packed columns (QUI-SP) have been successfully used in enantioseparations of various kinds of acidic analytes such as N-protected amino acids [14–21] and profens [16,17]. Although excellent resolution of N-protected amino acids were obtained on the QUI-SP columns, certain limitations were observed with these columns, which include long retention time, limited choices of mobile phase in view of the solubility of chiral selector (SO) as the mobile phase additive in a number of solvents [14] and limited stability in the case of particle-packed column [14]. In recent years, Lämmerhofer and co-workers developed several quinine-incorporated silica [22], and polymeric monolithic columns for chiral separation in CEC such as 9-(tert-butylcarbamoyl)-11-[2-(methacryloyloxy)ethylthio]-10,11-dihydroquinine copolymerized with 2-hydroxyethyl methacrylate and ethylene dimethacrylate [23], 9-tert-butylcarbamoylquinine (t-BuCQN)–poly(glycidyl methacrylate-co-ethylene dimethacrylate) [24] and t-BuCQN–poly-3-mercaptopropyl methylsiloxane–poly(glycidyl methacrylate-co-ethylene dimethacrylate) monolith [25]. Those

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macroporous monoliths exhibited baseline resolution of DNB-amino acids with short retention times [25]. However, enantioseparations of profens in CEC have been seldom reported on the quinine-based CSPs and one reported enantioseparation of profens showed low resolutions [16].

In this work we prepared quinine-incorporated silica/zirconia hybrid monolith (QUI-S/ZHM) in fused silica capillaries in a single step by sol–gel technology and used them in CEC enantioseparation of profens and DNB-amino acids. The preliminary results of the chiral separations on the QUI-ZHM are reported and its performance compared with those on other types of quinine-based chiral stationary phases in CEC.

2. Experimental

2.1. Chemicals and reagents

Fused silica capillaries (75 μm I.D., 365 μm O.D.) were from Polymicro Technologies (Phoenix, AZ, USA). Quinine, 3-triethoxysilylpropyl isocyanate, zirconium tetrabutoxide (Zr-Bu) in *n*-butanol, acetic acid (AcOH), triethylamine (TEA) and polyethylene glycol (PEG) (MW = 10,000 g/mol) were purchased from Aldrich (Milwaukee, WI, USA). HPLC-grade acetonitrile (ACN) was from J.T. Baker (Phillipsburg, NJ, USA). Water was purified with an Elgastat UHQ water purification system (Bucks, UK). Chiral compounds were obtained from Aldrich (Milwaukee, WI, USA) (Fig. 1).

2.2. Instrumentation

Agilent HP ^{3D}CE system (Palo Alto, CA, USA) equipped with a diode-array UV detector, a ±30 kV power supply, an external nitrogen pressure, and ChemStation software was used. A scanning electron microscope (Hitachi, FE-SEM S-4100, Japan) was used to examine the morphology of zirconia monoliths in the capillaries (Fig. 2).

2.3. Preparation of zirconia hybrid monolith

3-Triethoxysilylpropylcarbamate derivative of quinine (QUI-TEOSPC) was prepared and characterized as per the literature [26]. QUI-S/ZHMs were prepared by sol–gel method. A hydrolysis solution was prepared by dissolving 0.06 g of PEG in a solution consisting of 18 μL of water, 114 μL of acetic acid and 430 μL of *n*-butanol with ultrasonication. After complete dissolution of PEG

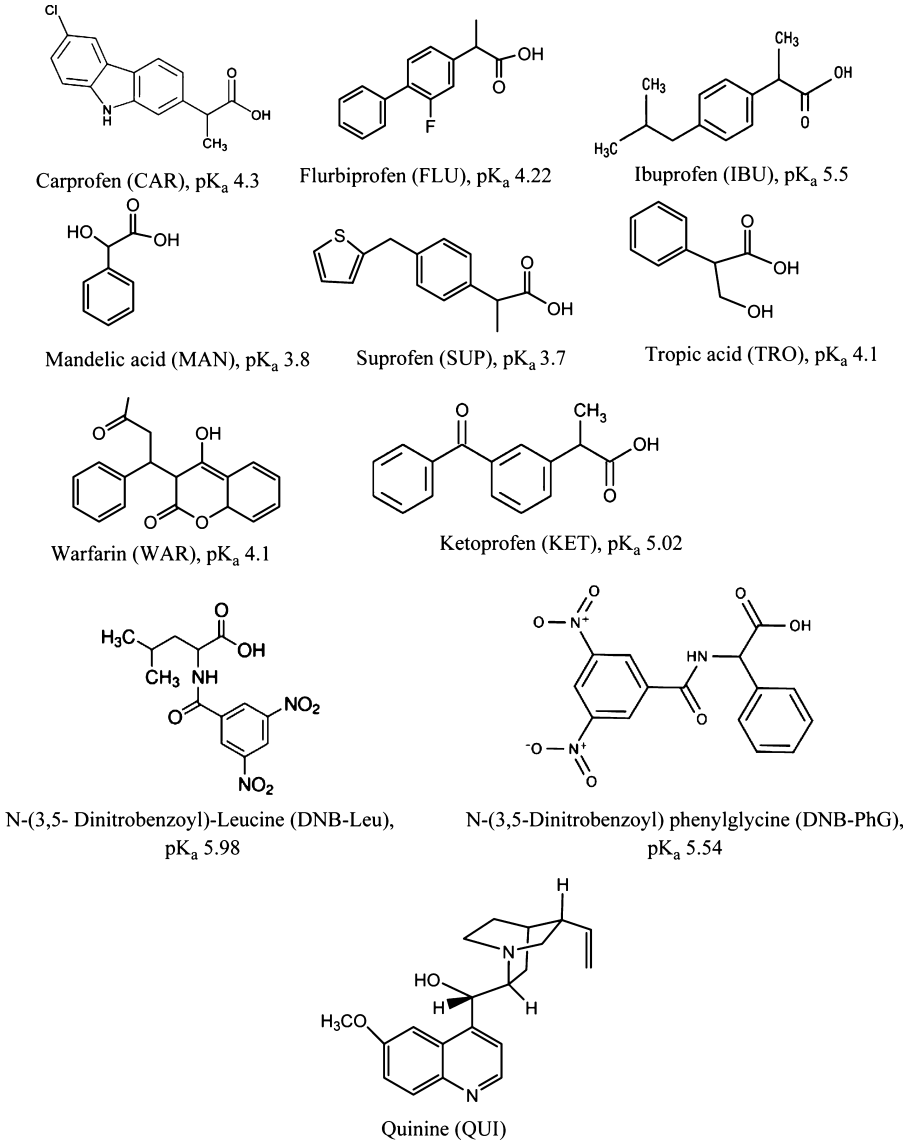

Fig. 1. Structures of chiral compounds and quinine.