

Metal oxide monolithic columns

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Abstract

Metal oxide monoliths composed of ZrO_2 and HfO_2 have been synthesized in situ inside capillary columns. The material shows globular-like structure and through pores. Capillary electrochromatography and capillary liquid chromatography were performed in a monolithic column with the HfO_2 material. Separation of a simple sample mixture showed the potential of the new metal oxide monolithic columns.

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1. Introduction

A monolithic column consists of an interconnected skeletal structure inside of a tube (or channel), that forms a continuous bed of chromatographic material with flow through paths. This concept of a chromatographic column has been identified as an alternative to particle-packed columns for more than a decade [1–3] and offers several advantages over the other column formats [4–6]. The chromatographic monolithic structures are very attractive for HPLC as they reduce considerably the pressure requirements to drive the mobile phase through the column, allowing the use of higher than usual mobile phase linear velocities, providing a route for fast separations, while maintaining column performance. The reduced inlet pressures have also allowed the possibility of exploring the use of peristaltic pumps to push the mobile phase through the chromatographic bed for simple and portable HPLC systems [7]. Monolithic columns have attracted considerable attention in capillary electrochromatography (CEC) [8–11] searching for new column technology that avoided the problems associated with packed beds in CEC. The monolithic structure simplifies column technology by eliminating difficulties encountered with frit fabrication in packed capillary columns for CEC and capillary liquid chromatography (cLC) [12]. The two most

common support materials used for monolithic columns are based on organic polymers or silica [1–11]. The monolithic columns based on silica support, however, are the most popular. Monolithic columns have been prepared in both small (50–100 μm) and large (1–4.6 mm) inner diameter columns.

A research area of great interest is the development of metal oxides particulates (e.g., zirconia, alumina, and titania) as support materials for chromatography, since in most cases they offer a more pronounced chemical and thermal stability than silica and organic polymers. Two excellent and very recent reviews by Nawrocki et al., show the current state-of-the-art of stable metal oxides for HPLC [13,14]. Zirconia (ZrO_2) has been the most widely and systematically studied metal oxide for chromatographic applications and a variety of stationary phases using this support media are now commercially available [13–16]. Recent work with supports containing titania is also emerging [17–19]. Zirconia-based support materials, in particular, have two very distinct advantages over silica-based stationary phases. First, the zirconia is more stable towards extremes of pH while silica-based stationary phases are not, and second, zirconia is also more thermally stable than silica-based phases. The benefits of these stabilities allow one to obtain separations at pH values that are not common with silica-based stationary phases. Furthermore, faster separations are possible by an increase in operating temperature.

The benefits of the monolithic format as a chromatographic column, as well as the use of metal oxide materi-

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als (mainly zirconia-based) have been established. It follows that a significant advancement in HPLC column technology would be the development of monolithic structures based on metal oxide supports. Despite the imminent use of metal oxides as monolithic columns very few initial attempts towards the development of metal oxide monoliths have been reported. Tang et al. [20], prepared a monolithic structure by packing a capillary column with zirconia particles and then “gluing” or entrapping them in a polybutadiene matrix. A different approach to metal oxide monoliths is to initially fabricate a silica monolith and then coat the monolith with the metal oxide; this approach is just beginning to be explored. For example, Shi et al. [21], prepared silica-based monolithic columns in capillary columns and then coated the monolithic columns with membrane-like zirconia; the columns were tested for electrochromatography. Miyazaki et al. have used the same concept to prepare HPLC monolithic columns coated with titania to separate adenosine and adenosine phosphates (i.e., AMP, ADP, ATP) [22]. To the best of our knowledge, a monolithic chromatographic column based completely on a metal oxide has not been reported. In this short communication, we report the in situ synthesis of a metal oxide monolithic column.

2. Experimental

2.1. Materials and instrumentation

Zirconium tetrachloride and hafnium tetrachloride were purchased from Strem Chemicals (Newburyport, MA, USA). Pyridine, imidazole, pyrazole, *N*-methylformamide and propylene oxide were obtained from Aldrich (Milwaukee, WI, USA). Distilled water was purified using a Milli-Q UV Plus water purification system (Millipore, Bedford, MA, USA). Fused silica capillary columns were obtained from Polymicro Technologies (Phoenix, AZ, USA). Sodium dihydrogen phosphate was purchased from Fisher Scientific (Fair Lawn, NJ, USA).

The micrometer-range morphology of the monolithic material was observed by a S-4000 field emission scanning electron microscope (Hitachi, Japan). Both LC and CEC analyses were performed on a P/ACE MDQ capillary electrophoresis system (Beckman-Coulter, Fullerton, CA, USA). Instrument control and data collection were performed with the P/ACE station software (version 1.0) supplied by Beckman-Coulter. Test analytes were monitored by UV at 214 nm. A phosphate buffer with pH 7.1 was used as the mobile phase. For both CEC and cLC, the sample was injected hydrodynamically (15 s, 1.7 bar) and separation was carried out at 25 °C, using 25 kV for CEC and 6.9 bar for cLC. The capillary had dimensions of 31.1 cm (effective length 22.5 cm) × 50 μm I.D.

2.2. Column preparation

Prior to the synthesis of the monolithic column, the fused silica capillary was rinsed with 1.0 M NaOH for 1 h and wa-

ter for another hour. Then, it was flushed with 0.1 M HCl for 1 h, and water for 30 min. The drying step was performed using a nitrogen gas flow overnight at 120 °C. To synthesize the metal oxide monoliths, an aqueous solution of metal chloride was reacted with eight equivalents of *N*-methylformamide. Propylene oxide (166 μL) was added to induce the polycondensation reactions leading to polymerization. The resultant solution was injected into a pretreated 50 μm I.D. fused silica capillary column. The capillary was sealed and kept in an oven at 50 °C for gelation. After aging, the capillary was washed using water.

3. Results and discussion

Chromatographic monoliths based on a purely inorganic material, other than silica, have not been reported. Zirconia is the most broadly and systematically studied metal oxide for chromatographic applications and a wide variety of stationary phases on particulate media have been implemented [13–16]. While zirconia has been studied as a chromatographic support material for separations, hafnia has not been investigated. In Group IV of the Periodic Table, hafnium is situated directly below zirconium. Despite the larger atomic mass and atomic number of hafnium, the properties of these elements and the reactivities and structures of their complexes are virtually identical, due to the lanthanide contraction [23]. Monolithic columns of both zirconia and hafnia should possess the desirable qualities of silica-based monolithic columns with the added properties of the better pH and thermal stabilities.

Many of the synthetic approaches to fabricate metal oxide bulk materials utilize sol–gel chemistry, focusing on the use of metal alkoxide precursors of the form $M(OR)_n$ (where M is the metal, R is an alkyl group and $n = 2–5$) [24]. These precursors tend to be air sensitive, undergoing hydrolysis to form an alcohol and precipitating metal oxide particulates, which makes them not readily handled in air in most cases. Furthermore, preparation of metal oxide monoliths inside a column can be limited by the rapid rate of the reactions that form the monolithic structure – hydrolysis and polycondensation leading to polymerization. The monolithic gel may form too quickly, preventing the easy handling of the reaction solution to be introduced into the “mold” that will eventually form the chromatographic monolithic structure. In fact, it has been suggested that one of the main reasons why the synthesis of metal oxide monolithic structures of Group IV elements has been elusive is due to the fast hydrolysis/polycondensation rates of the alkoxides of these metals [25].

We have circumvented the use of alkoxides by using the tetrachloride salt of Hf and Zr. Metal salts of the form MX_n (where X = anionic ligand and $n = 2–6$) are more readily available, less expensive and they are more air stable than the alkoxides. Metal salts have been investigated as potential precursors to synthesize bulk metal-oxide materials [30]. With

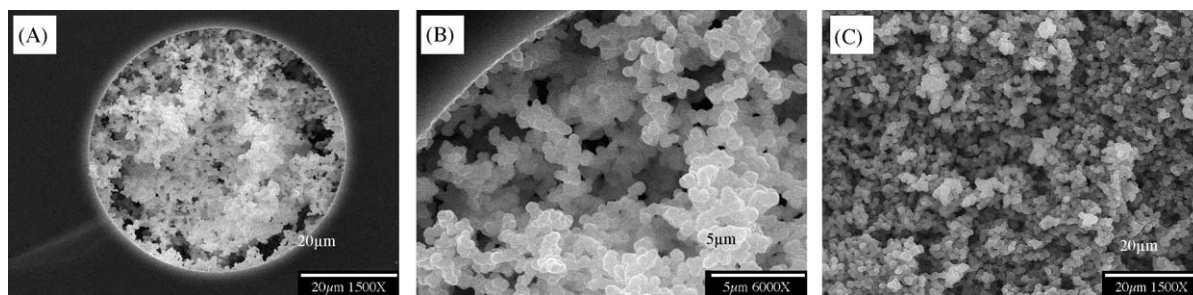
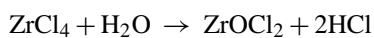
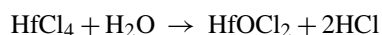


Fig. 1. Scanning electron microscopy (SEM) images of a hafnia-monolith inside a 50 μm I.D. column at two different magnifications (A) and (B), and of a zirconia monolithic pellet (C).

such a precursor, we have identified reaction conditions leading to monolithic structures of both hafnia and zirconia according to the following schemes:



polymerization-condensation \rightarrow zirconia



polymerization-condensation \rightarrow hafnia

The addition of the epoxide drives the second reaction towards the right, forming the hafnia or zirconia monolithic structure. Through condensation and polycondensation reac-

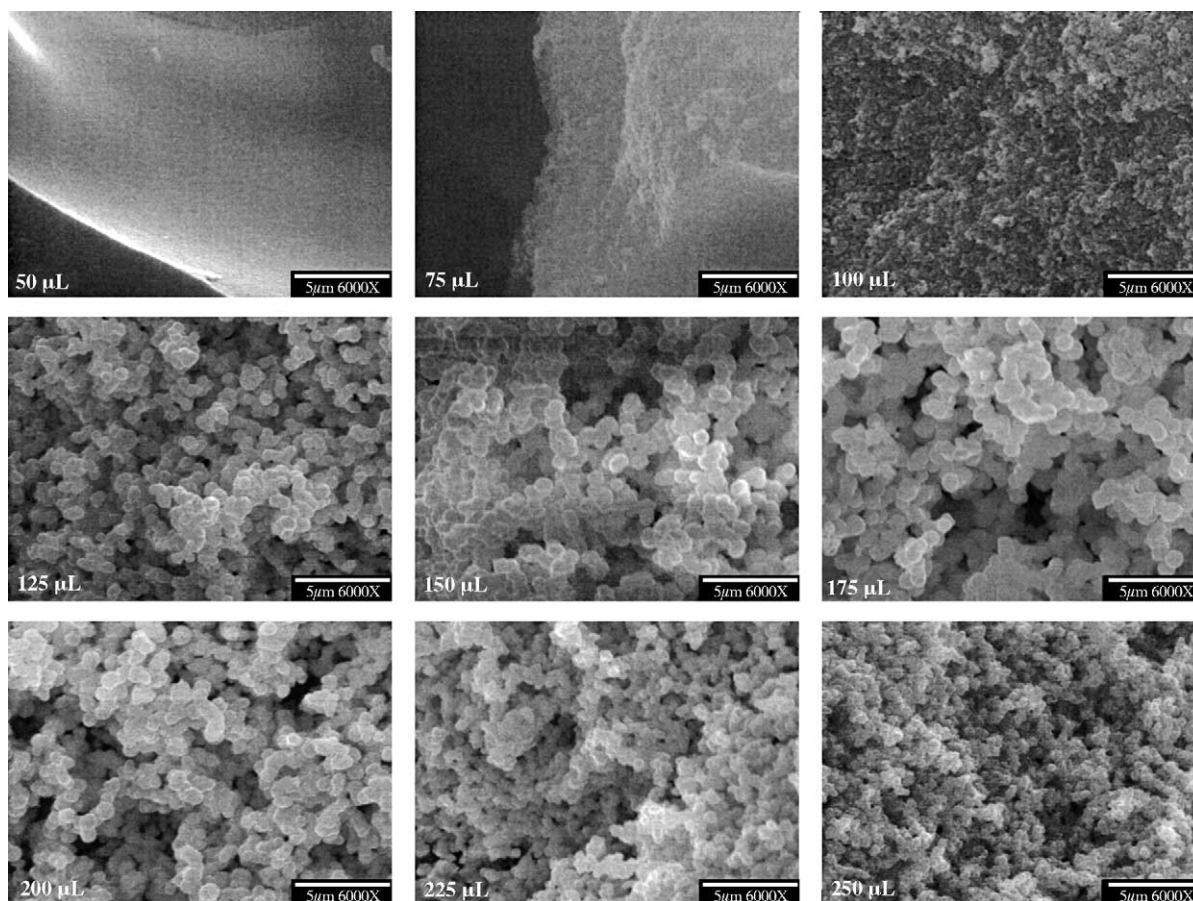


Fig. 2. SEM of hafnia material prepared using different amounts of *N*-methylformamide in the reaction mixture, as indicated on each micrograph.

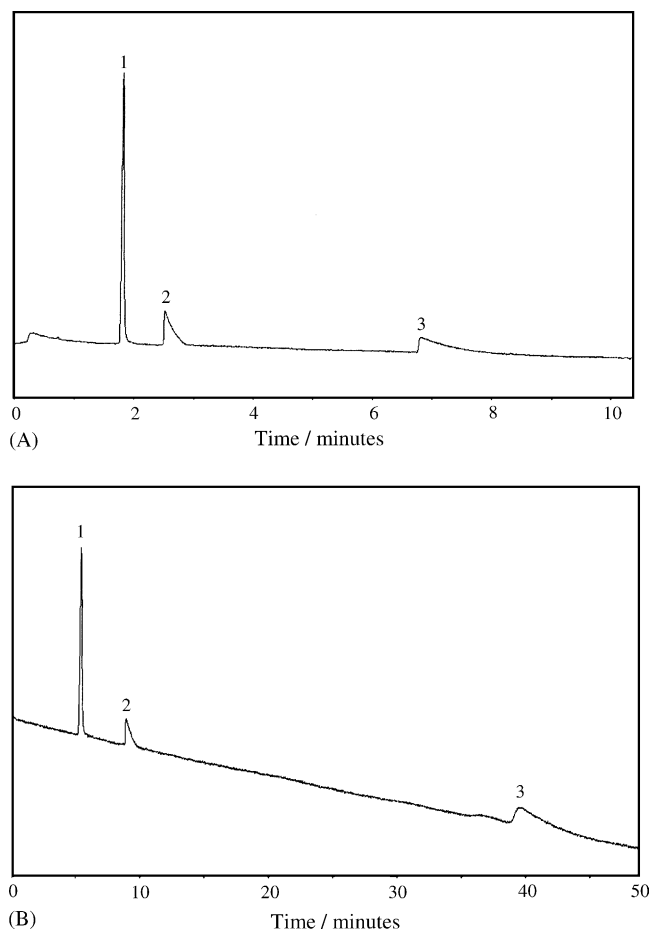


Fig. 3. (A) Separation of three components using CEC and (B) cLC using the hafnia monolithic column. Column: 29 cm length, 50 μm capillary I.D. (21 cm effective length); mobile phase: 5 mM phosphate buffer pH 7.1; UV detection at 214 nm; hydrodynamic injection (15 s, 1.7 bar); in the CEC format, separation voltage of 25 kV; in the cLC format, 6.9 bar (690 kPa) applied pressure; at 25 $^{\circ}\text{C}$ in both cases. The separated compounds are (1) pyridine, (2) pyrazole, and (3) imidazole.

tions the material gels, forming a wet structure. To make it mechanically stronger, the material is aged following gelation and then the solvent removed. The monoliths have been synthesized in situ in capillary columns as well as in the bulk pellet format. Scanning electron micrographs of a hafnia monolith inside of a capillary column are shown in Fig. 1A and B, while Fig. 1C shows an SEM of a zirconia monolith in a pellet format. From the figures, a globular interconnected microstructure as well as through pores can be observed. *N*-Methylformamide in the reaction provides for through pore formation. Fig. 2 shows different scanning electron micrographs showing the effect of different amounts of *N*-methylformamide in the reaction mixture. For the structures shown in Fig. 1, we used 150 μL of *N*-methylformamide.

We tested the suitability of the hafnia monolithic capillary column under ligand-exchange chromatographic conditions to separate three small molecules: pyridine, pyrazole and imidazole, using CEC and cLC. Under the CEC condi-

tions used, a relatively fast EOF was obtained and the three components were separated in less than 8 min (see Fig. 3A). The components eluted according to their $\text{p}K_{\text{a}}$ values, which indicate potential chromatographic interactions through the Lewis acid sites. Under the pressure driven mode of cLC, we used 6.9 bar (690 kPa) to drive the mobile phase through the monolithic column, the upper limit provided by the capillary electrophoresis (CE) unit used to perform the CEC experiment. This led to a longer analysis time (see Fig. 3B). What is important, however, is the fact that the species were separated chromatographically with the hafnia monolithic material. These results are indeed encouraging and set the stage for further investigations of in situ fabricated monolithic columns of metal oxides.

There is no doubt that our synthetic and processing parameters require optimization and that further chromatographic characterization is required. In this short communication, however, we wanted to demonstrate that it is possible to fabricate the metal oxide monoliths inside of capillary columns in situ and that they can be used in CEC and cLC.

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