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Effect of the crosslinker type on the enantioseparation performance of β-cyclodextrin functionalized monoliths prepared by the one-pot approach

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ABSTRACT

Low column efficiency for enantioseparations in capillary liquid chromatography (CLC) is a major problem commonly encountered with β-cyclodextrin (β-CD) functionalized polymer-based monoliths. In order to investigate the effect of the crosslinker type on enantioseparation performance, three commonly used crosslinkers, i.e. 1,4-bis(acryloyl)piperazine (PDA), ethylene dimethacrylate (EDMA) and *N*,*N*-methylenebisacrylamide (MBA), were copolymerized using the one-pot approach with glycidyl methacrylate-mono-6-amino-6-deoxy-β-CD (GMA-NH_2-β-CD) as functional monomer. The three monolithic columns, including poly(GMA-NH_2-β-CD-*co*-PDA) and poly(GMA-NH_2-β-CD-*co*-MBA), as well as the previously reported column poly(GMA-NH_2-β-CD-*co*-EDMA) were systematically compared with respect to morphology, permeability, β-CD density, retention mechanism and efficiency. The enantioseparation ability of each column was evaluated using 14 chiral compounds, including mandelic acid derivatives, profens, *N*-derivatized amino acids, and herbicides, as test substances. The β-CD-functionalized monolith with MBA as crosslinker was found to exhibit higher polarity, higher column efficiency and better enantioseparation performance than those with PDA or EDMA as crosslinker.

1. Introduction

Since enantiomers present identical physicochemical properties in an achiral environment, but profoundly differ in biological interactions, pharmacological and toxicological effects, their separation always remains a hot research topic [1–4]. The use of chiral stationary phases (CSPs) in LC containing various kinds of chiral selectors (CSs) has proved to be one of the most efficient approaches for the direct separation and analysis of enantiomers. Cyclodextrins (CDs) and their derivatives have the ability to form inclusion complexes with a variety of chiral compounds, resulting in their enantioseparation [5–7]. In recent years, based on the chiral recognition ability of CDs and the flexibility of the monolithic material, a series of CD functionalized monolithic columns have been extensively studied and widely applied to enantioseparations in capillary liquid chromatography (CLC) [8–10] or capillary electrochromatography (CEC) [11–14], taking advantage of the interesting features of monoliths, such as high permeability, low resistance to mass transfer, and fast and simple preparation [15,16].

Compared to the technically challenging procedures for silica-based monolith preparation, CD functionalized organic polymer-based monoliths have gained increasing attention due to their distinct merits, such as diverse surface chemistry, high porosity, pH stability, and low resistance to hydrodynamic flow [17–19]. Previously, our research group developed a novel and facile "one-pot" copolymerization approach to prepare a β-CD functionalized organic polymer monolith for the first time. The synthesis of the novel monomer glycidyl methacrylate-ethylenediamine-β-CD (GMA-EDA-β-CD) and the subsequent copolymerization with the crosslinker ethylene dimethacrylate (EDMA) were realized in the same vial without any purification step of the β-CD monomer [20]. This one-pot strategy not only largely simplifies the column preparation process, but also significantly increases the β-CD loadability. More importantly, it also offers the possibility to prepare easily various β-CD functionalized monoliths using different polymerization systems and hence to study the influence of different components on column performance. More recently, the effects of the degree

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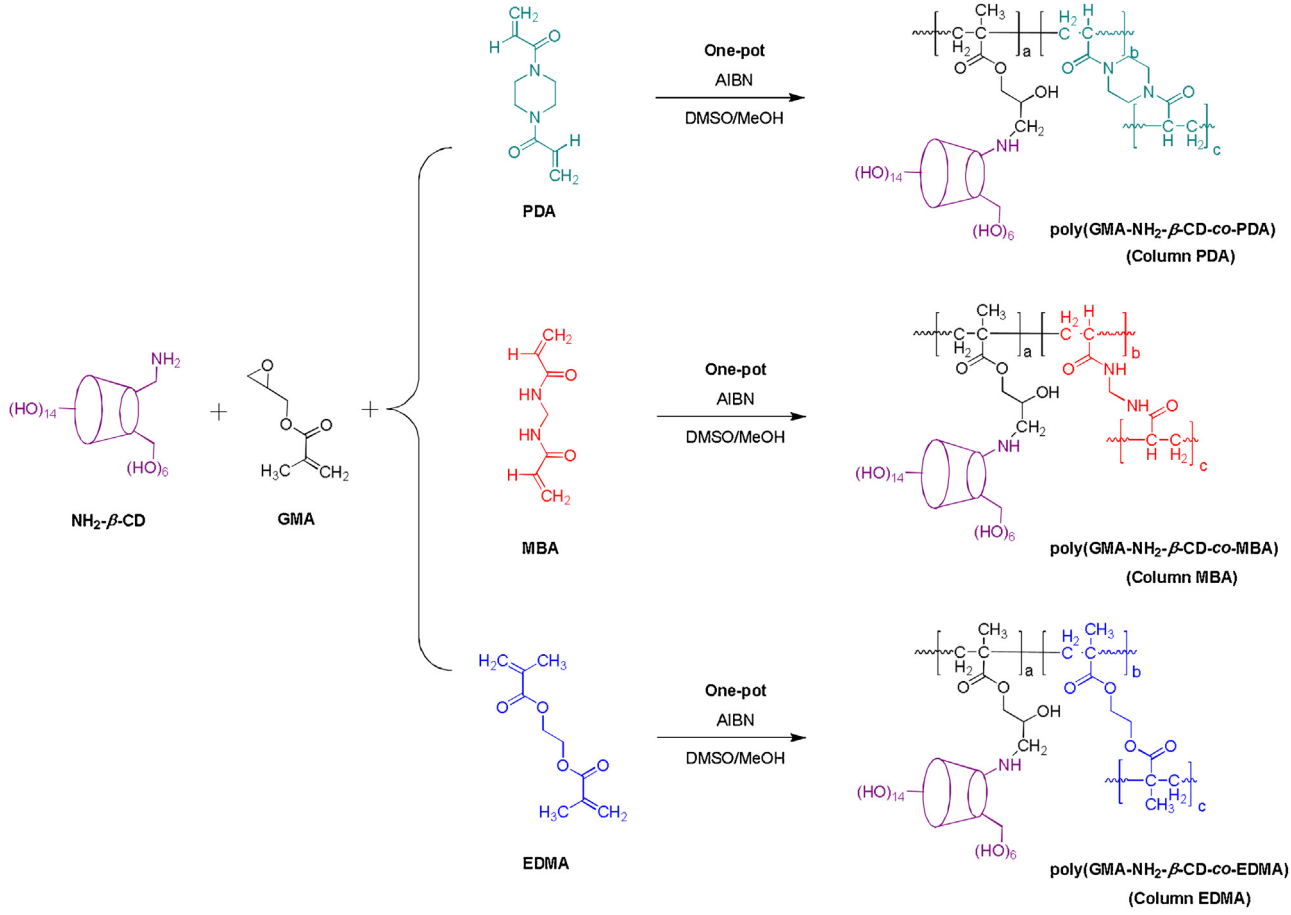

Fig. 1. Schematic preparation of the NH_2-β-CD functionalized polymeric monoliths via one-pot strategy.

of amino substitution [21] and length of linking spacer [22] on enantioseparation performance of β-CD functionalized monoliths prepared by the one-pot strategy have also been systematically studied. However, unsatisfactory column efficiency was obtained for these columns, which is a major problem commonly encountered with β-CD-based organic polymer monoliths in CLC mode.

Numerous studies focused on the development of polymer monoliths for efficient isocratic HPLC separations of small molecules have been reported through new chemistries, optimization of polymerization conditions and hyercrosslinking [16]. It is well known that the crosslinker plays an important role in the preparation of polymeric monoliths. The size, polarity and functional groups of the crosslinker and its proportion in the polymerization mixture could affect the pore size, permeability and efficiency of monolithic columns [23]. Actually, many studies demonstrated that the separation efficiency of these columns would significantly improve with the optimization of the crosslinker type and content [24–27]. Liu et al. prepared seven highly crosslinked polymeric monoliths using crosslinkers with different alkyl-bridging chains. Monoliths prepared with crosslinkers containing longer alkyl-bridging chains showed higher hydrophobicity [24]. Zou's group selected the dipentaerythritol penta-/hexaacrylate (DPEPA), which has multi-acrylate groups to participate in the polymerization, for the formation of highly crosslinked poly(lauryl methacrylate-*co*-dipentaerythritol penta-/hexaacrylate) monoliths. The resulting monolithic columns possessed remarkably high column efficiency (up to 165,000 N/m) for small molecules in CLC [25]. Later on, Liu et al. [26] found that the type of crosslinker (*N*,*N*-methylenebisacrylamide (MBA), 1,4-bis(acryloyl)piperazine (PDA) and ethylene dimethacrylate (EDMA)) also had a strong effect on the chromatographic properties of zwitterionic sulfoalkylbetaine-type monolithic columns. The polarity of the crosslinker was found to affect the selectivity and efficiency of the sulfoalkylbetaine-type monolithic columns. The results also indicated that a more polar crosslinker might be more suitable for preparing monolithic columns based on hydrophilic monomers. However, until now, few reports have studied the effect of the crosslinker type on the enantioseparation performance of β-CD functionalized monolithic columns.

To the best of our knowledge, EDMA could be considered to be one of the most popular crosslinking agents used for the preparation of organic polymer monoliths [23,28–30], including β-CD functionalized monoliths [9,11]. In order to further evaluate the effect of the crosslinker on column efficiency and enantioseparation ability, we also selected PDA and MBA as crosslinkers for the fabrication of β-CD functionalized monoliths. The three β-CD functionalized monolithic columns with different crosslinkers were prepared through one-pot *in situ* copolymerization of mono-6-amino-6-deoxy-β-CD (NH_2-β-CD), glycidyl methacrylate (GMA) and the three corresponding crosslinkers, i.e. EDMA, PDA and MBA, respectively. The permeability, CD density, efficiency and retention mechanism of the three monolithic columns were systematically and comparatively studied using elemental analysis, scanning electron microscopy (SEM) and micro-HPLC. The enantioseparation ability was evaluated for each column, using 14 chiral compounds, including mandelic acid derivatives, profens, *N*-derivatized amino acids, and herbicides, as test analytes.