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Immobilization of Chondroitin Sulfate A onto Monolithic Epoxy Silica Column as a New Chiral Stationary Phase for High-Performance Liquid Chromatographic Enantioseparation

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Abstract: Chondroitin sulfate A was covalently immobilized onto a monolithic silica epoxy column involving a Schiff base formation in the presence of ethylenediamine as a spacer and evaluated in terms of its selectivity in enantioseparation. The obtained column was utilized as a chiral stationary phase in enantioseparation of amlodipine and verapamil using a mobile phase consisting of 50 mM phosphate buffer pH 3.5 and UV detection. Sample dilution by organic solvents (preferably 25% v/v acetonitrile-aqueous solution) was applied to achieve baseline enantioresolution ($Rs > 3.0$) of the individual drug models within 7 min, an excellent linearity ($R^2 = 0.999$) and an interday repeatability of 1.1% to 1.8% RSD. The performance of the immobilized column for quantification of racemate in commercial tablets showed a recovery of 86–98% from tablet matrices. Computational modeling by molecular docking was employed to investigate the feasible complexes between enantiomers and the chiral selector.

Keywords: amlodipine; chiral stationary phase; chondroitin sulfate A; enantioseparation; immobilization; monolithic column; Schiff base; verapamil

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1. Introduction

Polysaccharide-based chiral stationary phases (CSPs) play an important role in enantioseparations of chiral compounds by high-performance liquid chromatography (HPLC) [1]. Due to the asymmetric and long-range helical structures, polysaccharides offer high recognition capacity and enantioselectivity toward broad types of chiral substances [2,3]. As one of the most prominent separation methods in analysis and preparative purposes, HPLC using amylose-based and cellulose-based columns delivers excellent performance [4–7]. In the beginning, the utilization of polysaccharide-based CSPs faced a restriction in the enantioselectivity improvement due to their low compatibility toward polar organic modifiers [8,9]. Therefore, immobilized CSPs are developed to achieve an expansion of column compatibility with a wide range of solvent polarity [9,10]. Immobilized CSPs typically could be applied in normal phase (NP)-, reversed-phase (RP)-, and polar-elution mode with a large diversity of organic solvents as mobile phases [1,11]. On the other hand, coated CSPs can only be used as a single mode in NP or RP.

Immobilization of a chiral selector onto macroporous silica has been conducted through a radical copolymerization reaction [12] and a photochemical technique [9]. In