HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC SEPARATION OF PHARMACEUTICALLY RELEVANT ISOPULEGOL-BASED COMPOUNDS

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The chiral separation of biologically active compounds, in the case of the synthesis of enantiomerically pure drugs, is a particularly important application area of HPLC in pharmaceutical analysis. ß-Amino lactones and ß-amino amides are pharmaceutically important molecules for several reasons. For example, water-soluble derivatives of the ß-amino lactones can exhibit cytotoxic activity through a prodrug mechanism for different human cancer cell lines [1]. ß-Amino amides are well-known subunits of biologically-important compounds such as bestatin, a potent aminopeptidase B, which is quite useful in the treatment of cancer through its ability to enhance the cytotoxic activity of known antitumor agents [2]
In this study, the separation of enantiomers of isopulegol-based ß-amino lactones and ß-amino amides was studied on seven covalently immobilized polysaccharide-based chiral stationary phases. The separation of the stereoisomers was optimized by investigating the effects of the composition of the bulk solvent and the influence of the temperature on the chromatographic behavior. Since the enantiorecognition mechanisms of the polysaccharide-based selectors are not entirely known [3], the elution orders of the enantiomers cannot be predicted. Therefore, during our work, close and thoughtful attention was paid to the elution sequences. In addition, the relationships between the compound's structure and the chromatographic parameters were also investigated. Experiments were performed in the temperature range 10–50 °C and thermodynamic parameters were calculated from plots of lnα versus 1/T. The separations were generally enthalpy-controlled, but entropy-controlled separation was also observed. Our results contribute to a better understanding of the enantiorecognition mechanism of polysaccharide-based chiral stationary phases.

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