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Optimization of analytical and preparative separation of Nadolol stereoisomers by liquid chromatography

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The direct chromatographic resolution of enantiomers using chiral stationary phases (CSPs) is actually a very well established separation technique. Several reasons were responsible for the growing success of this technique. The continuous technical development of new chiral stationary phases (CSPs) combined with their commercial availability has been, probably, the most relevant leverage issue. The chiral separation process is a complex task, governed by several different interactions between the chiral solutes, the solvent and the CSP. In a preparative point of view, and when considering the choice of the solvent composition, a high selectivity of the enantiomers should not be the only goal to be aimed, as it is frequently followed at analytical scale. Besides the choice of a CSP with high loading capacity, a high solubility of the solutes in the solvent and low retention times should also be taken into account, in order to improve the preparative process performance. This work will extend the study of these topics to multicomponent chiral separations. The separation of nadolol stereoisomers will be used as case study.

The separation of nadolol stereoisomers on Chiralpak[®] AD at both analytical and preparative scales was recently reported by Ribeiro et al. The Chiralpak[®] AD is, nowadays, the most used commercially available CSP. It is an amylose-based CSP and is produced by physical coating of the chiral polymer on a matrix. However, due to their coated nature, this CSP can only be used with a limited range of solvents such as the polar solvents or non-polar solvents in combination with some polar components as modifiers. Immobilization of a polysaccharide-derivative on the support is an evolutionary strategy to make a CSP compatible with the whole range of organic solvents, which will consequently extend its application scope.

This work presents the main results obtained from the complete solvent screening using both the coated Chiralpak[®] AD and the immobilized Chiralpak[®] IA stationary phases. The selection of the proper CSP/solvent combination for analytical and preparative operations is fully studied taking into account the screening strategy proposed by Zhang et al. The selection is carried out by studying the effect of different CSP/solvent combinations on the solubility, retention and resolution of the nadolol stereoisomers. The obtained results show different possibilities to perform the separation of nadolol stereoisomers, depending on the target component or target components to be obtained. The choice of mobile phase composition is also taken based on future preparative multicomponent separations using a technology such as the Simulated Moving Bed (SMB) adsorption process.