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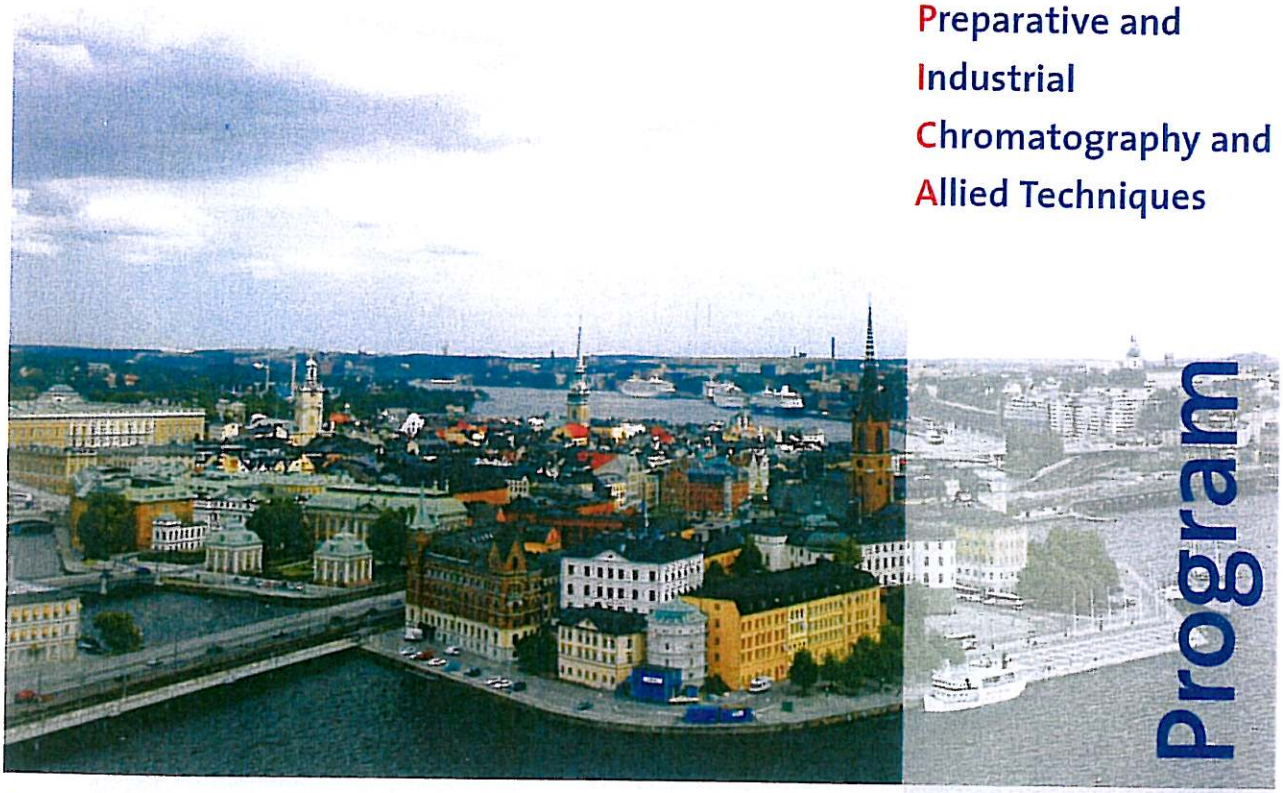

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Optimization of Mobile Phase Composition in Simulated Moving Bed Chiral Separation Processes

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ABSTRACT

In the last years, simulated moving bed (SMB) chromatography has become a more and more important separation process for the purification of pharmaceuticals and other added-value products. The optimization of SMB processes for chiral separation depends on the choice of the proper chiral stationary phase (CSP) and mobile phase combination. In this choice, a high selectivity of enantiomers should not be the only goal to be aimed, as it is frequently followed at analytical scale. Other objectives, such as, to obtain high solubility of enantiomers and low retention times should also be taken into account. In fact, SMB processes achieve high throughputs when high feed concentrations and short cycle times are applied.

This work will present two case studies; the chiral separation of ketoprofen and flurbiprofen enantiomers, both important examples of non-steroidal anti-inflammatory drugs (NSAIDs), frequently used in the treatment of arthritis and related diseases. The Chiralpak AD material (Daicel, Japan) will be used as CSP and mixtures of n-hexane, ethanol and methanol as solvent. A complete methodology concerning experimental, modeling and simulation results will be presented, including the enantiomers solubility and adsorption isotherm measurements, fixed-bed and SMB operations. The main focus will be placed on optimizing the mobile phase composition for chiral separation by SMB operation. These two comparative case studies will reveal that there are no predictive general rules for the optimization of mobile phase composition at a production scale and that an individualized study must be carried out, since compounds of the same family (profen enantiomers) can lead to different solutions.