

## PREPARATIVE ENANTIOSELECTIVE CHROMATOGRAPHY

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In the last years, preparative chiral chromatography has become a more and more important separation process for the purification of pharmaceuticals and other added-value products. One reason chromatography is preferred is that the process allows both high yields and purities of both enantiomers. On the other hand, this technique is applicable to a wide variety of racemic mixtures, since chromatographic stationary phases for enantiomer separation are now available.

The optimization of preparative liquid chromatography and simulated moving bed (SMB) processes for enantioseparation depends on the choice of the proper stationary phase-mobile phase combination. In this choice, a high resolution (or 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.

The optimization of chiral separations is frequently a complex task that requires, at a preparative scale, a careful selection of its operating conditions. In the case of binary or multicomponent mixtures, an additional complexity results from the competition between the different components in the interaction with the stationary phase. Therefore, one of the first steps of the preliminary study of a chromatographic separation process is the determination of the equilibrium competitive adsorption isotherms of the two enantiomers that will contribute to explain the retention mechanism and allow the prediction of the production rate recoveries and separation costs. Additionally, solubility of the racemate, selectivity and retention times are separation parameters very sensitive to changes in mobile phase composition. In fact, the use of continuous separation processes, such as SMB technology, has achieved high throughputs when high feed concentrations and short cycle times were applied.

This lecture will present the experimental and simulation tools for the optimization of preparative enantioseparation chromatographic processes, including simulated moving bed operation. Experimental results will be shown to illustrate that different conclusions can be obtained at analytical and preparative scales and depending on the enantiomer system in study.