Enhanced resolution of stereoisomers through Stationary phase optimized selectivity liquid and supercritical fluid chromatography (SOS-LC and SOS-SFC).

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The development of method(s) for the analysis of chiral molecules and recognition of its enantiomeric purity is crucial as the enantiomers have the same physical properties but differ in pharmacokinetic and pharmacological behavior which leads to discrimination and separation is a very difficult issue. About 56% of the drugs currently in use are chiral compounds, and 88% of these are used as racemates.1 Quantitative analysis of the active pharmaceutical ingredient (API) and of the corresponding chiral and achiral drug impurities, requires the use of chiral stationary phases. When complex samples (increasingly containing several APIs) are at hand, the availability of single chiral columns allowing the resolution of individual enantiomers proves, however, often insufficient. In this context the concept of Stationary Phase Optimized Selectivity Liquid Chromatography (SOS-LC), a novel tool for the separation of solutes in a predictable way on combined stationary phases, is particularly promising of the separation of mixtures of chiral solutes.

This approach allows now both isocratic2 and gradient analysis3, while it also proves applicable on the compressible phases such as used in supercritical fluid chromatography.4 Thus far the potential of Stationary Phase Optimized Selectivity Liquid Chromatography for the separation and purification of stereoisomers has not been fully investigated, although especially in the latter case both chiral SOS-LC and SFC could offer significant benefits to speed up the purification process or to obtain improved chiral screening of complex mixtures. Therefore in this work the possibilities offered by chiral SOS-LC and SOS-SFC for the separation of mixtures of pharmaceutical enantiomers are explored, whereby emphasis is also set on the combination of chiral and achiral columns. Optimization and separation of enantiomers in the isocratic mode was done using standard commercially available chiral columns and with the classical isocratic SOS-LC algorithm. Gradient predictions are accomplished by in-house developed Visual Basic algorithm. The methodology offers new potential for faster analytical and preparative separation of optical isomers for various applications.

References


