Stationary phase optimized selectivity chiral liquid chromatography (SOS-CLC) as a novel perspective for the separation of stereoisomers.

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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 therapeutically used as racemates. Therapeutic effects and side effects of eutomer and distomer are well known and their quantitative analysis and assessment is extremely challenging as it is only separated under chiral environment.[1]

Stationary phase optimized selectivity liquid chromatography (SOSLC) has been successfully further developed and increasingly used in the last decade as a novel tool for the separation of solutes in a predictable way on combined stationary phases. The approach has been used for gradient analysis[2] and the model also proves applicable on the compressible phases used in supercritical fluid chromatography.[3] Thus far the potential of this approach to facilitate the separation and purification of stereoisomers has not been investigated, although especially in the latter case chiral SOSLC could offer significant benefits to speed up the purification process or to obtain improved chiral screening of complex mixtures. The challenge of this work is to evaluate and implement the SOSLC approach for baseline separation of enantiomers by using conventional chiral columns. A representative test mixture composed of 4 chiral pairs (Trans stilbene oxide (TSO), 1,2,3,4 Tetrahydro phenol -1- napthol (TPN), Hexobarbital (HXL) and 4-Phenyl 1,3 dioxane (PDX)) was selected presenting particular challenges on all chiral columns (Lux 3u Amylose 2, Cellulose 1, Cellulose 2, Cellulose 3 and Cellulose 4) individually. Therefore, the optimization and separation of enantiomers in the isocratic mode was done using standard commercially available chiral columns and with the classical isocratic SOSLC algorithm. Further optimization was accomplished by in-house developed gradient algorithm, which was written in Microsoft visual basic. The potential of this method is demonstrated via the prediction of the optimal chiral column combination for the baseline separation of 4 chiral pairs (Figure 1.). The methodology represents prospective for faster analytical and preparative separation of optical isomers for various applications.

References

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