ROLE OF THE MOBILE PHASE COMPOSITION IN THE CHROMATOGRAPHIC ENANTIOSEPARATION OF PHARMACEUTICALLY RELEVANT COMPOUNDS

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Purpose. The recognition of chirality as a new asset in drug development has an enormous effect on the product pipelines of the major players in the pharmaceutical industry. Accordingly, enantioselective analytical assays play a key role in the development of chiral drug candidates throughout the entire development cycle, including the quality control of the formulated drugs. Suitable analytical procedures are indeed required to demonstrate that the manufacturing process doesn't induce unacceptable changes in enantiomer purity of the final products, and that stereochemical integrity may be maintained for the proposed shelf-lives.
Methods. A challenging way to face enantioseparation issues is to identify, with a unique chiral column, the best combination of eluent variables able to improve the degree of complementary chiral selector-analyte interactions. Barely considered aspects concerning the impact of the mobile phase components on the overall enantiorecognition process, by employing both low- and high-molecular weight chiral selectors, are discussed.
Results. With the use of a chiral ligand-exchange chromatography system operating with the O-benzyl-(*S*)-serine as the eluent chiral mobile phase additive, the best enantioresolution is provided by Cu(II) formate and Cu(II) fluoride, for the majority of the selected hydrophobic aminoacidic analytes.
The possibility to run the analyses with all the elution regimes allowed to identify the NP-based eluents as the most suitable, for the simultaneous diastereo- and enantioseparation of four non-steroidal FXR agonists, when analyzed with an anion-exchange-based chiral stationary phase incorporating a quinine derivative as the chiral selector.
In the enantioseparation of six anti-breast cancer purine derivatives, with a cellulose tris(3,5-dimethylphenylcarbamate)-based chiral stationary phase, relevant improvements of the overall chromatographic performance is obtained with the use of ''non standard'' solvents as constituents of the eluent mixture. The reliance on otherwise detrimental solvents was made possible due to the immobilized nature of the enantioresolving agent, which confers an universal solvent compatibility to this kind of stationary phase and opens the way to previously unexplored enantioselectivity profiles.
Conclusions. The mobile phase should not be regarded as a passive transporter of the analytes along the column, but it is rather an essential component inherently involved in the enantioselective chiral selector–selectand association mechanism at multiple levels.