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Doctoral Dissertations Abstract

"Ternary Complexes in Liquid Chromatography"

The aim of my PhD study was to use the process of formation of the ternary complexes to optimize the enantioseparation of pharmacologically active compounds. The first part of the work contains a description of a novel method for a direct separation of the enantiomers of drugs. The enantiomers were separated by means of chromatography on reversed-phase (RP-HPLC) column with β-cyclodextrin as a chiral addition to the mobile phase and hydroxy acids as solubility enhancers. It was found that the systems with high concentrations of β-cyclodextrin in the presence of hydroxy acids, especially DL-tartaric acid, improve enantioselectivity, while the presence of citric acid aggravates it. Moreover, D-, L- and DL-tartaric acids have a positive impact on the stability and solubility of β-CD complexes with most of the test compounds. This point may be used in the production of new forms of drugs. Due to the fact that the triple complexes drug - tartaric acid - cyclodextrin have high bioavailability.

The second part of the work concerned the separation of enantiomers using cyclodextrins (β-CD or γ-CD) and the ion-pairing reagents (OPI) as components of the mobile phase in liquid chromatography. It was shown, that the combination of these two types of selectors (OPI and CD) may lead to improved enantioseparation. Studies on the effect of concentration and type of OPI allowed to perform interpretations of retention mechanism. Designated thermodynamic parameters (enthalpy, entropy, Gibbs' free energii) were used to describe the mechanism of eantioseparation. Furthermore, the significant increase in stability of complexes drug-OPI-CD was obtained. This would allow to design new forms of drugs with higher bioavailability.

Additionally, the possibility of using a two-phase extraction techniques for the separation of enantiomers of cyclopentolate was examinited. The distribution coefficients and enantioseparation of cyclopentolate were studied in a chiral extraction containing D-tartaric acid ditertbutyl ester in organic phase and 2-hydroxypropyl-β-cyclodextrin (HP-β-CD) in aqueous phase. Various parameters involved in the enantioseparation such as the type and the concentration of chiral selectors, pH value and wide range of organic solvents were investigated.Two novel chiral liquid chromatography methods have been developed for the quantification and qualitative analysis of enantiomers of cyclopentolate.