

The effect of temperature on the separation of enantiomers with cellulose-based chiral stationary phases.

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It has been widely accepted that a pair of enantiomers may exhibit quite different bioactivities, pharmacological and toxicological behaviors. Therefore, their preparation and analysis have been becoming increasingly important in many fields of science dealing with drugs, natural products, synthetic intermediates, and agrochemicals. For more than 3 decades, chromatographic techniques and especially high-performance liquid chromatography (HPLC) has been extensively developed for the separation of enantiomers. HPLC has become essential for the research and development of chiral drug. In the separation of enantiomers one of the most important role has temperature. Temperature can directly affect thermodynamics and kinetics of the separation process.

The goal of our research was the calculation of thermodynamic parameters of enantioseparation process, that can help to predict the appropriate condition for the given compound on given column and to achieve desired selectivity and enantiomer elution order. Our studied substances are chiral drugs - arylpropionic acids derivatives: Ibuprofen, Ketoprofen, Flurbiprofen and Fenoprofen. HPLC experiments were performed with an Agilent 1200 HPLC instrument. Cellulose-based chiral stationary phases, in particular Cellulose-1 (Cellulose tris (3,5-dimethylphenylcarbamate)), Cellulose-2 (Cellulose tris (3-chloro-4-methylphenylcarbamate)) and Cellulose-4 (Cellulose tris (4-chloro-3-methylphenylcarbamate)) were used in combination with the following mobile phases: n-Hex/EtOH/FA-99/1/0.1 and n-Hex/EtOH/FA-99.5/0.5/0.1.

For the calculation of the thermodynamic quantities, such as standard molar Gibbs' energy (ΔG^0), the standard molar enthalpy (ΔH^0) and the standard molar entropy (ΔS^0) of solute transfer from the mobile to the stationary phase the Van't Hoff's equation can be used:

$$\ln k = -\frac{\Delta H^0}{R} \times \frac{1}{T} + \frac{\Delta S^0}{R} + \ln \varphi$$

On the next step we shall measure thermodynamic parameters (directly) by isothermal titration calorimetry (ITC) and compare with the calculated HPLC-results.