CHIRAL SEPARATION OF PROFEN ENANTIOMERS BY PREPARATIVE LIQUID CHROMATOGRAPHY

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Profens are known as a major group of nonsteroidal anti-inflammatory drugs, marketed as racemic mixtures and used in the treatment of arthritis and related diseases. Recently, several pharmacological studies shown that profen enantiomers (such as, ketoprofen and flurbiprofen) can display quite different behaviours and, even more important, new therapeutic actions in the pure enantiomeric form. Preparative chiral liquid chromatography is now a widely accepted alternative separation process to the traditional and too time consuming crystallization or asymmetrical synthesis techniques for the purification of pharmaceuticals intermediates and other added-value products.

At an analytical scale, selectivity is commonly the main parameter to be optimized. However, if the final goal is a preparative separation process development, other parameters must also be considered. In a preparative separation process, such as, in a Simulated Moving Bed (SMB) operation, high productivities are obtained using operating conditions that maximize not only selectivity but also the loading capacity, high feed concentrations and short cycle times. Therefore, a correct selection of the mobile phase composition is advised, since it will affect racemate solubility, selectivity and retention times [1].

In this work, experimental results obtained for the ketoprofen and flurbiprofen enantiomers systems will be shown, including solubility and adsorption measurements, and pulse and breakthrough experiments. Additionally, simulation results, based on the experimental adsorption isotherms measurements, will be presented to compare the performance of fixed-bed and SMB processes. The experimental and simulation results show two different situations. For the separation of ketoprofen enantiomers, pure ethanol is clearly a better mobile phase than the usual high alkane content mobile phases. On the other hand, for the separation of flurbiprofen enantiomers, a 10%ethanol/90%n-hexane is proposed. The results obtained show that an individual study must be carried out for each enantioseparation system, since different profen drugs can show different behaviours.

[1] A.E. Ribeiro, N.S. Graça, L.S. Pais, A.E. Rodrigues. *Sep. Purif. Technol.* 61 (2008) 375.

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