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ABSTRACT BOOK

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P-052 SEPARATION OF NADOLOL STEREOISOMERS BY FIXED-BED AND CONTINUOUS PREPARATIVE LIQUID CHROMATOGRAPHY USING C18 COLUMNS

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Continuous preparative liquid chromatography is nowadays a well-established technology used for the separation of a wide range of chemical mixtures. Among these techniques, the simulated moving bed (SMB) technology has gained an increasing interest to the industry in the production of fine chemicals and pharmaceuticals. This growing is due to the development of new and more versatile stationary phases, as well as new operating schemes for SMB and other continuous chromatographic processes.

In recent years, the authors have focused in the preparative separation of chemical drugs by chiral SMB chromatography. Different case studies have been considered, including the separation of non-steroidal anti-inflammatory drugs (ketoprofen and flurbiprofen enantiomers) [1-4], and the pseudo-binary separation of nadolol stereoisomers, a beta-blocker pharmaceutical drug [5]. While the first two case studies are typical examples of binary chiral mixtures (a pair of enantiomers), the last is an example of a quaternary mixture, composed by two pairs of enantiomers. This considerably increases the complexity and the difficulty of the separation process, asking for new strategies for the complete resolution of all the four components.

Experimental and simulation results have been recently presented considering a first step of a pseudo-binary separation by SMB (the more retained component being obtained pure in the extract and the other three co-eluting in the raffinate), followed by a ternary separation through a JO process [6]. This work introduces a different strategy

using an achiral C18 stationary phase under reversed-phase mode to perform a first SMB separation step. The C18 achiral adsorbent allows the separation of the two pairs of nadolol diastereomers, i.e., the first racemate (composed by the nadolol compounds 2 and 3) co-eluting in the raffinate, and the second racemate (composed by the nadolol compounds 1 and 4) to be obtained in the extract SMB stream. After this preliminary achiral separation step, two parallel SMB runs must be carried out using a chiral stationary phase to achieve the complete separation of all the four nadolol stereoisomers.

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