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BOOK OF ABSTRACTS

OC-44 STRATEGIES FOR MULTICOMPONENT SEPARATION OF NADOLOL STEREOISOMERS BY PREPARATIVE LIQUID CHROMATOGRAPHY

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The Simulated Moving Bed (SMB) technology is receiving an increasing interest as an alternative technique for the production of fine chemicals and pharmaceuticals. However, the classic SMB process is limited to the separation of binary (or pseudo-binary) mixtures or to the recovery of one single component from a multicomponent mixture. Several configurations have been proposed in order to extend the SMB technology to the separation of multicomponent mixtures by using a cascade of SMBs in series or other complex SMB related techniques like multi-zone SMB, intermittent SMB and JO processes. The JO technology allows the separation of ternary mixtures through a cyclic process constituted by two discrete steps. [1,2]

Nadolol is a pharmaceutical drug marketed as a mixture of its four stereoisomers and its prescription is related with some severe risks such as heart failure. The nadolol stereoisomers will be used in this work as a case study for the development of chromatographic strategies for multicomponent separation.

Recently, our research group reported the pseudo-binary separation of nadolol stereoisomers by SMB chromatography [3]. A SMB pilot unit with Chiralpak AD chiral stationary phase (CSP) was used to obtained the more retained stereoisomer 100% pure in the extract and the mixture of the other three stereoisomers being co-eluted in the raffinate.

This work will show how different strategies for multicomponent separation can be implemented, using different CSP, solvent compositions and SMB related techniques, namely:

a) The use of a different CSP, the Chiralpak IA, allowing the use of a wider range of solvents and therefore better separation performances than Chiralpak AD;

b) To achieve a final ternary separation, using the mixture of the three stereoisomers co-eluted in the raffinate, previously referred, as the feed for a subsequent JO process;

c) The separation of the two pairs of nadolol enantiomers using an achiral C18 material, followed by two parallel classic SMB binary enantioseparation processes.

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