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**BOOK OF  
ABSTRACTS**

# SEPARATION OF A QUATERNARY CHIRAL MIXTURE USING DIFFERENT SIMULATED MOVING BED STRATEGIES

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The classic SMB process is a continuous process to separate binary (or pseudo-binary) mixtures or to recover one single component from a multicomponent mixture. Several multicolour chromatography (MCC) processes, such as modified SMB processes have been introduced to separate multicomponent mixtures. Among them, the cascade SMB, the intermittent SMB, the JO processes (also called pseudo-SMB) and other complex multi-zone SMB related techniques, are often applied to the separation of multicomponent mixtures. 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 four stereoisomers, used to treat cardiovascular diseases. However, its prescription is also related with some severe risks such as heart failure. It is well known that pure enantiomer separation is important to control chiral drugs safety. Recently, our research group reported the pseudo-binary separation of nadolol by SMB chromatography using both coated Chiralpak AD and Chiralpak IA immobilized chiral stationary phases (CSP) [3,4]. Using the classic SMB mode of operation, the complete separation of nadolol stereoisomers was achieved using both CSP. The more retained stereoisomer was collected 100% pure in the extract and a mixture of the other three stereoisomers was collected in the raffinate. In this work, we will present different strategies for multicomponent separation, using different solvent compositions, different CSP and SMB related techniques. Namely, (a) The use of Chiralpak IA that, comparing to AD CSP, allows the use of a wider range of solvents and therefore better separation performances; (b) The use of the JO process to achieve a final ternary separation, using the mixture of the three stereoisomers that co-eluted in the raffinate in the separation previously referred; and (c) The separation of the two pairs of nadolol enantiomers using an achiral C18 material, followed by two parallel classic SMB binary chiral enantioseparation processes. The application of these different approaches represents possible SMB strategies for the complete separation of the quaternary nadolol chiral mixture.

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