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BOOK OF ABSTRACTS



P-75 SEPARATION OF NADOLOL STEREOISOMERS BY LIQUID CHROMATOGRAPHY USING C18 COLUMNS

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Nadolol is a nonselective beta-adrenergic receptor antagonist (β -blocker) pharmaceutical drug, widely used in the treatment of cardiovascular diseases, such as hypertension, ischemic heart disease (angina pectoris), congestive heart failure, and certain arrhythmias. Its chemical structure has three stereogenic centers which allows for eight possible stereoisomers. However, the two hydroxyl substituents on the cyclohexane ring are fixed in the cis-configuration, which precludes four stereoisomers; in fact, two pairs of enantiomers. Nadolol is presently marketed as an equal mixture of the four stereoisomers, designated as the diastereomers “racemate A” and “racemate B” [1].

There are still few published works concerning the separation of nadolol stereoisomers. Most of these works refer the resolution at analytical scale and few refer the resolution at preparative scale using the simulated moving bed (SMB) technology. [2] This technology is normally based on the use of chiral adsorbents which must have enough recognition for all the chiral species.

In this work we propose an alternative strategy, implementing a first achiral separation step, which should be followed by two subsequent parallel chiral separation steps. Considering the first achiral step, common C18 columns will be used to perform a reversed-phase separation of the two pairs of nadolol enantiomers, the “racemate A” from the “racemate B”.

Extensive results will be shown considering the choice of the best solvent composition and the potentiality of this alternative strategy, in terms of SMB system performance under reversed-phase conditions and its comparison with a full chiral steps strategy.

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[1] McCarthy J.; *J. Chromatogr. A* **1994**, 685, 349–355.

[2] Ribeiro, A. E.; Rodrigues A. E.; Pais, L. S.; *Chirality* **2013**, 25, 197-205.