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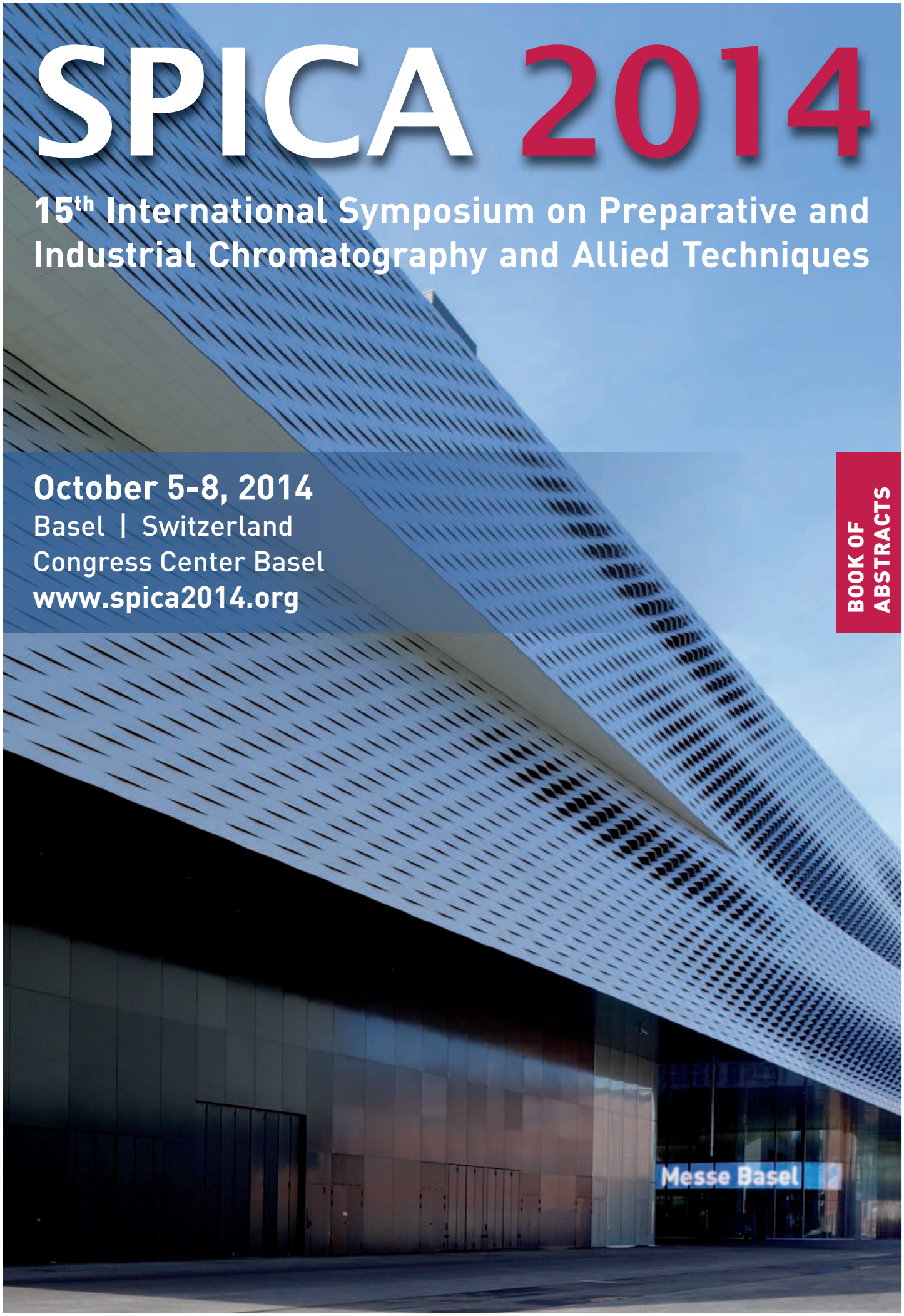
BOOK OF ABSTRACTS



COMPLETE DESIGN AND OPTIMIZATION OF MULTICOMPONENT SEPARATION PROCESSES: THE CASE STUDY OF THE QUATERNARY SEPARATION OF NADOLOL STEREOISEMERS

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The direct chromatographic resolution of enantiomers using chiral stationary phases (CSPs) is actually a very well established separation technique. Several reasons were responsible for the growing success of this technique. The continuous technical development of new chiral stationary phases (CSPs) combined with their commercial availability has been, probably, the most relevant leverage issue.

Chiral liquid chromatography is based on different mutual interactions between the molecules that elute with the liquid (solvent and solutes) and the molecules that are present in the stationary phase. Therefore, optimization of a chiral separation is based on the selection of a proper combination between a CSP and a mobile phase (solvent) composition by promoting, in a favourable way, all possible mutual interactions. The optimization will be a much more challenging task if we are leading not with a traditional binary racemic mixture separation problem but if we are interested in the separation of a quaternary chiral mixture. The complexity degree will be significantly increased if we consider a preparative separation, using a technique such as the simulated moving bed technology, were high feed concentrations are normally used in order to improve the process performance. In these situations, the wanted high concentrations of the different chiral solutes inside the chromatographic columns will enhance significantly the mutual competition between solutes for adsorption with the stationary phase. From a preparative point of view, and when considering the choice of the mobile phase ("solvent") composition, a high selectivity of the enantiomers should not be the only goal to be aimed, as it is frequently the case at analytical scale. Besides the choice of a CSP with high loading capacity, a high solubility of the solutes in the solvent and low retention times should also be taken into account, in order to improve the preparative process performance, as it was extensively explained for the separation of chiral non-steroidal anti-inflammatory drugs[1-4].

Nadolol (1-(tert-butyamino)-3-[(5,6,7,8-tetrahydro-cis-6,7-dihydroxy-1-naphthyl)oxy]-2-propanol) is a non-selective beta-adrenergic antagonist pharmaceutical drug. This class of pharmaceutical drugs is prescribed, mainly, to treat arrhythmias, angina pectoris, hypertension, migraine disorders and for tremor. Today, and in spite of the more and more restricted international legislation towards the commercialization of pharmaceutical drugs based on active principles that are made of single enantiomers, nadolol is still only commercially available as an equal mixture of four stereoisomers. This is even more serious due to the considerable evidence, recently made both by the academic community and pharmaceutical industry, that it is important to characterize the single stereochemical components when describing the pharmacodynamics and pharmacokinetics of a racemic drug.

The separation of nadolol stereoisomers on CHIRALPAK® AD at both analytical and preparative scales was recently reportedby Ribeiro et al[5]. However, nowadays no further work was developed to better understand and exploit the capabilities of Chiralpak® IA both for the analytical and preparative chiral separations of nadolol stereoisomers. This work will present a complete methodology concerning experimental, modelling and simulation results. Both the CHIRALPAK® AD and CHIRALPAK® IA CSP will be evaluated. The selection of the proper CSP/solvent combination for preparative operation will be fully study taking into account the screening strategy proposed by Zhang et al[6]. Additional results include the measurement of nadolol stereoisomers solubilities, equilibrium adsorption data and fixed bed (breakthroughs) experiments. The complete screening of CSP/solvent combination will lead to the choice of the better solutions for the separation of nadolol stereoisomers, considering the target component or components to be obtained. Simulation and experimental results will be presented for the multicomponent separation of nadolol stereoisomers by Simulated Moving Bed adsorption process.

References

1) A.E. Ribeiro, N.S. Graça, L.S. Pais, A.E. Rodrigues, Sep. Pur. Technol., 61, 375 (2008).
2) A.E. Ribeiro, N.S. Graça, L.S. Pais, A.E. Rodrigues, Sep. Pur. Technol., 68, 9 (2009).
3) A.E. Ribeiro, P. Sá Gomes, L.S. Pais, A.E. Rodrigues, Sep. Sci. Technol., 46 1726 (2011).
4) A.E. Ribeiro, P. Sá Gomes, L.S. Pais, A.E. Rodrigues, Chirality, 23, 602 (2011).
5) A.E. Ribeiro, A. E. Rodrigues, L.S. Pais, Chirality, 25, 197 (2013).
6) T. Zhang, D. Nguyen, P. Franco, J. Chromatogr. A, 214, 1191 (2008).