ANQUE ICCE 2012

24 - 27 June

SCIENTIFIC Programme

INTERNATIONAL
CONGRESS OF
CHEMICAL
ENGINEERING

www.anqueicce2012.org

ANQUE

EFCE Event No.701

EFCE

ORAL SESSION T1.1 – SEPARATION PROCESSES

Chairperson

J. Coronas, University of Zaragoza, Spain

Keynote

T1-003	LIMITATIONS OF THE CLASSICAL MODELS FOR THE VLE DATA CORRELATION AND PROPOSAL OF A REALLY EFFICIENT CHANGE FOR A SUBSTANTIAL IMPROVEMENT OF THE RESULTS A. Marcilla, M.M Olaya, J.A. Reyes and M.D. Serrano Department of Chemical Engineering, University of Alicante, Spain

Lectures

T1-007	CHIRAL SEPARATION OF NADOLOL STEREOISOMERS BY LIQUID CHROMATOGRAPHY: SCREENING OF MOBILE PHASE COMPOSITION AND SMB SEPARATION A.E. Ribeiro[a], L.S. Pais[a] and A.E. Rodrigues[b] a,Laboratory of Separation and Reaction Engineering, School of Technology and Management, Polytechnic Institute of Bragança, Campus de Santa Apolónia, Bragança, Portugal bLaboratory of Separation and Reaction Engineering, Faculty of Engineering, University of Porto, Porto, Portugal
T1-011	NOVEL ULTRAFILTRATION PES MEMBRANES INCORPORATED WITH METAL OXIDE NANOPARTICLES FOR WASTEWATER FILTRATION L. Yepes[1], J. M. Arsuaga[1], A. Sotto[1], S. Teli[2], S. Molina[2], J. de Abajo[2] 1Department of Chemical and Energy Technology, Rey Juan Carlos University, Madrid, Spain. 2Department of Macromolecular Chemistry, Institut of Polymer Science and Technology, Spanish National Research Council (CSIC). Madrid, Spain
T1-014	ADSORPTION PROCESS FOR BUTANOL RECOVERY FROM AQUEOUS SOLUTIONS WITH SILICALITE PELLETS M. A. Uguina, V. I. Águeda, J. A. Delgado, J. L. Sotelo, A. García Department of Chemical Engineering, Complutense University of Madrid, Madrid, Spain.
T1-015	SELECTIVE ADSORBENTS: A BASIS FOR INNOVATIVE SEPARATION PROCESSES B. Niemeyer, J.F. Fernández Helmut-Schmidt-University / University of the Federal Armed Forces Hamburg Hamburg, Germany

T1-007

CHIRAL SEPARATION OF NADOLOL STEREOISOMERS BY LIQUID CHROMATOGRAPHY:

Screening of mobile phase composition and SMB separation

A.E. Ribeiro[a,*], L.S. Pais[a] and A.E. Rodrigues[b]

[a,*]*Laboratory of Separation and Reaction Engineering, School of Technology and Management, Polytechnic Institute of Bragança, Campus de Santa Apolónia, Apartado 1134, 5301-857 Bragança, Portugal*

[b]*Laboratory of Separation and Reaction Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias s/n, 4200-465 Porto, Portugal*

aribeiro@ipb.pt; Tel: +351 273 303 125; Fax: +351 273 313 051

Separation Processes

Nadolol is a non-selective beta-adrenergic receptor antagonist (β-blocker) pharmaceutical drug, widely used in the treatment of cardiovascular system diseases, such as hypertension, ischemic heart disease (angina pectoris), congestive heart failure and certain arrhythmias (*Brunton el al., 2001*). 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 (*McCarthy, 1994*). Regardless the considerable evidence that it is important to characterize the stereochemical components when describing the pharmacodynamics and pharmokinetics of a racemic drug, the narrow international legislation concerning chiral drugs safety still allows the nadolol commercialization in the form of a racemic mixture of four stereoisomers (see Fig. 1).

Today, preparative chiral chromatography has become an attractive technology, used to obtain single enantiomeric drugs, in the biotechnology, fine chemical products and pharmaceutical industries. The chiral separation process is a complex task, governed by several different interactions between the chiral solutes, the solvent and the chiral stationary phase. In 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 followed at analytical scale. In this choice, a high solubility and low retention time should also be taken into account, in order to improve the preparative process performance (*Ribeiro et al., 2008 and 2009*).

This work describes a systematic approach to rapid development of simulated moving bed (SMB) chiral chromatography separations. The presented methodology involves several pulse experiments using a single-column to screen the "best" mobile phase composition using a Chiralpak® AD stationary phase and equilibrium adsorption data used to specify the initial flow rates of the SMB operation.

Experimental results include a detailed screening of different mobile phase compositions for the nadolol stereoisomers separation (analytical and preparative). Results show that the "best" mobile phase composition is, generally, very different if we consider an analytical or a preparative separation point of view. Finally, after the preliminary selection of the solvent composition we present the main results for the

ISBN: 988-84-695-3536-3

pseudo-binary separation of nadolol stereoisomers by SMB chromatography, using a 6-column FlexSMB-LSRE® unit (*Sá Gomes et al., 2010*).

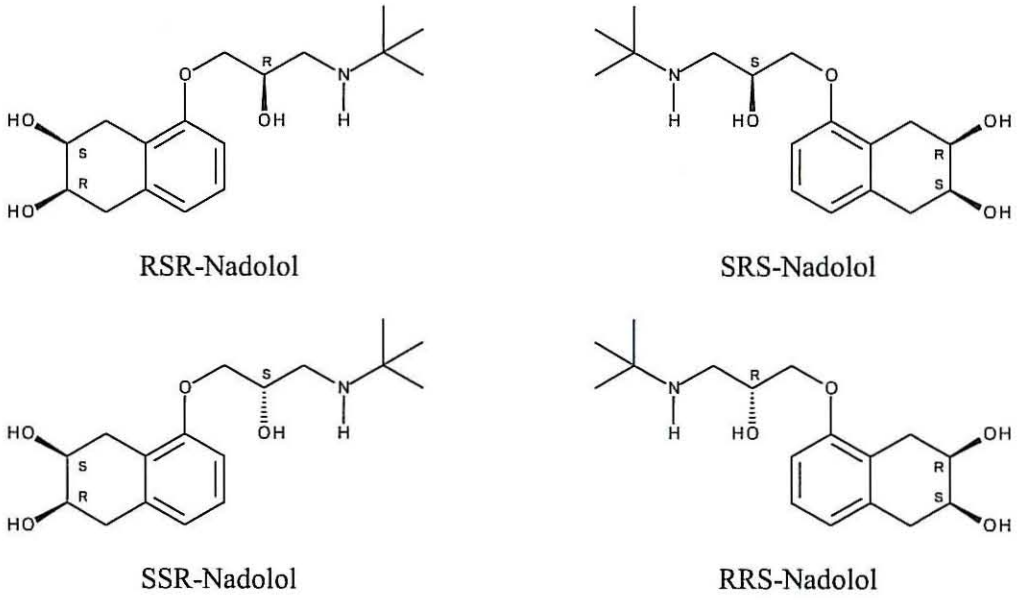

Figure 1. Structural representation of the four stereoisomers of nadolol.

References:
[1] L.L. Brunton, J.S. Lazo, K.L. Parker, Goodman & Gilman's, The Pharmacological Basis of Therapeutics, Mc Graw Hill, New York, 2001.
[2] McCarthy, Direct enantiomeric separation of the four stereoisomers of nadolol using normal-phase and reversed-phase high-performance liquid chromatography with Chiralpak AD, J. Chromatogr. A 685 (1994) 349-355.
[3] A.E. Ribeiro, N.S. Graça, L.S. Pais and A.E. Rodrigues, Preparative separation of ketoprofen enantiomers: Choice of mobile phase composition and measurement of competitive adsorption isotherms, Sep. Pur. Technol. 61 (2008) 375-383.
[4] A.E. Ribeiro, N.S. Graça, L.S. Pais and A.E. Rodrigues, Optimization of the mobile phase composition for preparative chiral separation of flurbiprofen enantiomers, Sep. Pur. Technol. 68 (2009) 9-23.
[5] P. Sá Gomes, M. Minceva, M. Zabka and A.E. Rodrigues, Separation of Chiral Mixtures in Real SMB Units: The FlexSMB-LSRE®, AIChE J. 56 (2010) 125-142.