Purification of anti-hyperlipidemic agents using Four-Zone SMB process

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The simulated moving bed (SMB) technology was developed in the early 1960s by UOP and has been used in petrochemical and sugar industries for large scale separation. Recently, SMB system is extensively applied to pharmaceutical and fine chemical industries; fractionation of enantiomers [1], amino acids and protein, protein desalting and many other separation tasks.
Compactin is an important intermediate and as well as a core structure of anti-hyperlipidemic agents which is 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors. Pravastatin, a bioconversion product of compactin [2], is more effective than compactin in lowering serum cholesterol in most animal species including humans and became a highly successful drug.

In this study, the separation of compactin and pravastatin is carried out using Licosep micro SMB (Novasep, France). The SMB consists of four zones and each zone has two columns (2-2-2-2). The column(10 cm x 1.0 cm I.D) is packed with Kromasil(ODS, 25 m). The mobile phase acetonitrile/deionized water (45/55, v/v), which has high saturation capacity and appropriate selectivity, was found by changing compositions of solvents.Total porosity was estimated by pulse test of NaNO3. The adsorption isotherms of compactin and pravastatinwere obtained by multiple frontal analysis. Mass transfer parameters were estimated by correlations. The optimum operating conditions for the SMB process were obtained from the triangle theory. The simulation results shows over 98 % of purity and yield at the raffinate and extract port respectively.

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2. Y. Peng, A. L. (2000), Demain, Bioconversion of compactin to pravastatin by *Actinomadura* sp. ATCC 55678, *J. Mol. Catal. B: Enzym.* **10**, 151.