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Preparative chromatography with supercritical fluids Comparison of simulated moving bed and batch processes ☆

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Abstract

Preparative chromatography is a key technology for the separation of fine chemicals in production scale. Most of the published studies are carried out using liquid solvents as mobile phase. However, the used organic solvents can often be replaced by supercritical fluids. A reduction or renouncement of organic solvents does not only correspond to the trend of the so-called *green chemistry*—a sustainable, environmentally friendly production of chemical products. But a changeover to chromatography with supercritical fluids can also be reasonable under economic criteria. In this contribution a comparison between the Batch-supercritical fluid chromatography (Batch-SFC) process and the simulated moving bed (SMB)-SFC process is presented. Because of the minor importance of solvent consumption and solvent recovery in SFC, the separation systems were optimized primarily in terms of their specific productivity. For three of the four investigated model systems, the specific productivity of the SMB process is significantly higher than the productivity of the Batch process. Due to the fact, that the process with the higher specific productivity is not inevitably the more economical process, supplementary the costs of the process were considered. Therefore the comparison of the two processes was done from an economic point of view considering the minimum product price that has to be realized to fulfill the defined economic aim. It was found that although the optimized specific productivities of the SMB process were significantly higher than the productivities of the Batch process, the Batch process is the more profitable process for the investigated production rate range between 0.4 and 5 t/a.

Keywords: Simulated moving bed (SMB); Supercritical fluid chromatography (SFC); Tocopherol; Ibuprofen; Process costs

1. Introduction

Nowadays the use of preparative chromatographic techniques for the production of substances with high purities is well established. Beside the classical discontinuous Batch elution process, different concepts for process realization of chromatographic separations have been developed. One important development is, for example, the continuous simulated moving bed (SMB) process. The SMB technique was originally developed in the 1960s by UOP for the separation of hydrocarbons [1]. In the meantime approximately 100 versions of the so-called Sorbex process were patented by UOP. Nowadays the largest plants have product capacities of up to 440×10^6 kg/year and work with columns of up to 6.5 m diameters.

Recently, different strategies for improving the separation performance of the conventional SMB process have been proposed. An advanced mode of the SMB process is for example the so-called VariCol process (variable column length). This principle, which was patented from Novasep (France), implements the same concept as the SMB principle, with the difference that the inlet and outlet ports are switched asynchronously resulting in a more efficient use of the solid and liquid phase [2]. Apart from asynchronous switching of the inlet and outlet ports the modulation of feed parameters offers high potential for the improvement of the separation performance. In this context two operating methods are described in literature: the so-called ModiCon operating mode, where the feed concentration is modified periodically [3,4], and the mode of operation designated as PowerFeed and partial feed, respectively, where the feed flow rate is chanced within a cycle [5–8]. As a further possibility for increasing the productivity, the introduction of gradients in the

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different separation zones of the SMB-process is described in literature. The gradient mode was suggested first for the SMB-SFC process, where the elution strength can be influenced by a pressure gradient [9]. In alternative gradient-variants of the SMB process, the elution strength of the desorbent can be changed by changing the temperature, the pH-value, the content of salt or the modifier concentration [10–12].

Till date, most of the preparative separations are carried out using liquid solvents as mobile phase. However, the used organic solvents can often be replaced by supercritical fluids, which offer many advantages: the gas-like viscosities of supercritical fluids enable high flow rates at low pressure drop and better efficiencies due to the higher diffusion coefficients in comparison to those of liquids. Additionally, the physical properties of the fluid can easily be changed by varying pressure and/or temperature. By depressurizing the fluid, the product can be precipitated and the separated gaseous solvent can be recycled without additional cleaning steps. Up to the early 1980s SFC was developed mainly in analytical scale, instrumental and experimental difficulties prevented a common application of this process. With the patents of Perrut [13–15] a growing interest in SFC in the laboratory-, pilot- and production-scale could be observed. An overview of preparative applications of SFC between 1962 and 1989 is given from Berger and Perrut [16]. Bewan and Mellish [17] and Berger [18] give a detailed description of preparative SFC systems. An overview over preparative enantioseparations with SFC is given by Terfloth [19]. In Jusforgues [20,21] and Johannsen [22] preparative applications are summarized, which are published in the period between 1990 and 2001. Clavier et al. [9] and Mazzotti et al. [23] show the advantages of the use of compressible fluids as mobile phase in connection with SMB technology. With a compressible fluid, the elution strength in the four zones of the SMB process can be varied by changing the density. A skillful manipulation of the elution strength can lead to an increase in productivity. Beside the pressure gradient mode Giovanni et al. [24] analyzed the influence of an increasing feed concentration on the region of complete separation related to the triangle theory [25–27]. However up to now only few experimental results of SMB separation using supercritical carbon dioxide as mobile phase have been published [9,28–31].

In this work the discontinuous Batch process and the continuous SMB process with supercritical carbon dioxide as mobile phase were compared. The basic principles of these two processes are shown in Fig. 1. In Batch chromatography the feed mixture is injected discontinuously as a pulse into the solvent stream at the column inlet. The solvent (mobile phase) carries the mixture components through the adsorbent bed (stationary phase). Because of different adsorption affinities of the feed components, the elution velocities of the components are different. If the distance between the components is large enough at the column outlet, the individual components can be collected in different containers.

A SMB system consists of multiple columns connected to each other in a circle. A counter-current flow between the stationary and mobile phase is simulated by switching the inlet and outlet ports of the columns periodically in the direction of the fluid flow. The four external streams (feed, extract, raffinate and desorbent) divide the system into four sections or zones with different flow rates of the mobile phase. Separation is performed in zones 2 and 3, where the more retained component A has to be adsorbed and carried towards the extract port through simulated movement of the stationary phase, while the less adsorbed component B is transported in the opposite direction with the mobile phase to the raffinate port. In zone 1 the solid phase and in zone 4 the mobile phase is cleaned. If all flow rates and the shifting time of the inlet and outlet ports are determined correctly, raffinate and extract fractions can be withdrawn at high purities. In a SMB process with more than four columns, the relative positions of the four streams are not unique. This creates a large number of possible column configurations in the zones.

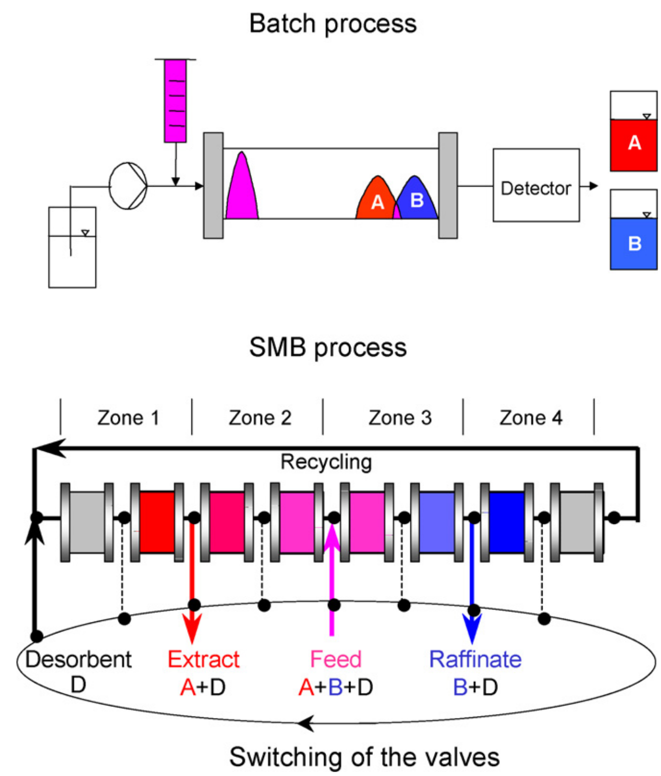

Fig. 1. Functional scheme of the discontinuous Batch process and the continuous SMB process.

For the comparison of the Batch-SFC with the SMB-SFC process the separation of four different model systems (α-/δ-tocopherol, *R*-/*S*-ibuprofen and two further racemic mixtures) was investigated. A process optimization was done by simulation. Therefore, first the adsorption behavior of each model system was investigated experimentally and parameters of the adsorption isotherms were determined. The simulation model was verified by the comparison of experimental results with the results of simulations. Because of the minor importance of solvent consumption and solvent recovery in SFC the primary objective of the optimization was the maximization of the productivity. However, in industrial practice not the technical optimum but the economic optimum is decisive. Therefore the costs of the process have to be considered for the analysis of the economic relevance of the specific productivity. In this work the *net present worth method* was used for the comparison of the profitability of the two processes.