SUPERCRITICAL FLUID CHROMATOGRAPHY PROCESS OPTIMISATION OF THE SEPARATION OF TOCOPHEROL HOMOLOGUES

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ABSTRACT

The separation of tocopherol homologues by Supercritical Fluid Chromatography (SFC) has been studied in two different operation modes: Simulated Moving Bed (SMB) and Elution. Both operation modes are compared regarding their optimized specific productivity and solvent consumption. The influence of column configuration of the SFC SMB process on the maximum productivity and the solvent consumption was investigated in parameter studies. A dynamic simulation program based on a plug flow model with axial dispersion and a linear mass transfer resistance was used to predict the effect of operating variables on the process performance. On the basis of these results, experiments were performed. The experimental SMB results were in good agreement with the results of the simulations.

INTRODUCTION

Simulated Moving Bed (SMB) chromatography is a powerful countercurrent process allowing the continuous separation of a feed mixture into two streams of products. The countercurrent flow is simulated by periodically switching the ports of the inlet (feed, desorbent) and outlet (raffinate, extract, recycling) lines in the same direction as the fluid flow. The combination of the SMB technique with supercritical fluid chromatography (SFC) leads to an apparatus with unique features. Besides the advantages of the SMB process, the use of supercritical carbon dioxide as mobile phase offers an easy eluent - solute separation and eluent recycle, low pressure drop and high efficiency. In this work, results of the preparative separation of two tocopherol homologues with supercritical fluid simulated moving bed chromatography are shown.

SFC SMB APPARATUS

The SFC SMB plant consists of eight custom made columns (inner diameter 30 mm) with dynamic axial compression and variable bed length. The columns are designed for pressures up to 40 MPa and temperatures up to 200°C. The five in- and outgoing streams (feed, desorbens, raffinate, extract and recycling) are guided by five 8+1 way valves. Between two columns, shut-off valves are located. From the bottom of an autoclave, liquid CO2 is charged by an air-driven pump into the system up to flow rates of 18 kg/h. Modifier can be added by a HPLC pump. A more detailed description of the system has been published before [1]

PROCEDURE FOR DETERMINING OPERATING CONDITIONS

At low concentration an initial set of operating parameters can be calculated using the 'triangle theory' which has been developed in the frame of the Equilibrium Theory (i.e., neglecting axial dispersion and mass transfer resistance) [2]. By this method the True Moving-Bed process as well as the SMB process can be described with four key parameters, namely the net flow rates m_j. Each zone m_j. is defined as (j=1…4):

$$m_j = \frac{\dot{V}_j^{\mathrm{SMB}} t_{\mathrm{shift}} - Ve}{V\left(1-e\right)} \qquad (1)$$

The actual separation of the components takes place in zones 2 and 3. It is rather useful to consider the projection of the regions of separation onto a (m_2, m_3) plane. Different separation regions can be distinguished by the purity of the outlet streams (Fig. 1).

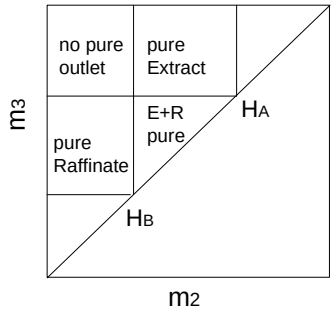

Figure 1: Regions of the (m_2, m_3) plane with different separation regimes in terms of purity of the outlet streams for a system described by a linear adsorption isotherm

However, the 'triangle theory' has a low significance for separations characterized by nonlinear adsorption equilibrium. In that case the shape and location of the complete separation region changes and can be calculated analytically only in special cases (e.g. Langmuir isotherm [3]). For that reason, in this work the region of complete separation in the (m_2, m_3) plane was calculated numerically. The used program simulates the SMB-SFC process dynamically, which means, that the switching of the valves are explicit mentioned. For the dynamic simulation a plug flow model with axial dispersion and linear mass transfer resistance was used. The resulting mass balance equations was solved with a finite difference method first developed by Rouchon [4] and adapted to the conditions of the SMB process by Kniep et al. [5]. The pressure drop in the columns is calculated with the Darcy equation. The equation of state from Span and Wagner [6] is used to calculate the mobile phase density. The density of the mobile phase is considered variable.

Due to the fact, that the pressure drop in the columns leads to a variable volume flow in the different zones of the SMB, a new parameter m_j* (constant for each zone), based on the mass flows in the different SMB zones, were defined [1]:

$$m_j^* = \frac{\dot{V}_j^{\mathrm{SMB}} t_{\mathrm{shift}} r_{\mathrm{mobile\ phase}} - V e r_{\mathrm{ref}}}{V(1-e) r_{\mathrm{ref}}} \qquad (2)$$

The needed parameters of the adsorption isotherms were obtained experimentally using the perturbation method. The single component adsorption were described by using the Hill-isotherm [7]. In Tab. 1 the isotherms and their parameters are shown.

Table 1: Isotherm parameters of α- and δ-tocopherol on Kromasil silica, 10 µm. T = 40 °C; p = 20 MPa; 5 wt.-% 2-propanol

$q = \frac{q_s}{3} \cdot \frac{b_1 \cdot c + 2 \cdot b_2 \cdot c^2 + 3 \cdot b_3 \cdot c^3}{1 + b_1 \cdot c + b_2 \cdot c^2 + b_3 \cdot c^3}$	q_s kg/m^3	b_1 $(kg/m^3)^{-1}$	b_2 $(kg/m^3)^{-2}$	b_3 $(kg/m^3)^{-3}$
α-tocopherol	4314	7.832e-3	2.088e-4	2.579e-5
δ-tocopherol	6860	8.575e-3	3.444e-4	3.547e-5

For describing binary adsorption, an ideal adsorbed solution (IAS) was assumed as described by Seidel and Gelbin [8].

RESULTS AND DISCUSSION

In parameter studies, the influence of column configuration on the reachable productivity of the SFC SMB separation of α- and δ-tocopherol and the consumption of solvent was investigated. The described simulation program was used to calculate the region of complete separation in the (m2*, m3*) plane for a 2/2/2/2, 1/3/2/2, 1/3/3/1 and a 1/2/2/1 configuration (columns per zone). All calculations were performed assuming a constant operating temperature (T=40°C), column length (L=144 mm), content of modifier (5 wt.-% 2-propanol), number of theoretical stages (n_{th} = 1400/m) and the same average operating pressure (p = 20 MPa).

First simulations were done with a feed concentration of 6 mg/ml. Shape and location of the region of complete separation does not differ between the 1/2/2/1 and 2/2/2/2 configuration. That means, that a six column configuration is adequate for the separation of α- and δ-tocopherol. For the cleaning of adsorbens in zone I and the cleaning of desorbens in zone 4 only one column is necessary. The region of complete separation of the 1/3/2/2 and 1/3/3/1 configuration is larger than that of the 1/2/2/1 and 2/2/2/2 configuration, respectively (Fig. 2). However, for all configurations, the same ‘optimal’ operating points were found.

To show the influence of the feed concentration on the separation of the two tocopherol homologues, the region of complete separation (purity > 99%) was calculated for a higher feed concentration (c_{inj} = 15 g/ml). As described before, temperature, average operating pressure, column length and content of modifier were kept constant (T = 40 °C; p = 20 MPa; L_{column} = 144 mm; 5 wt.-% 2-propanol).

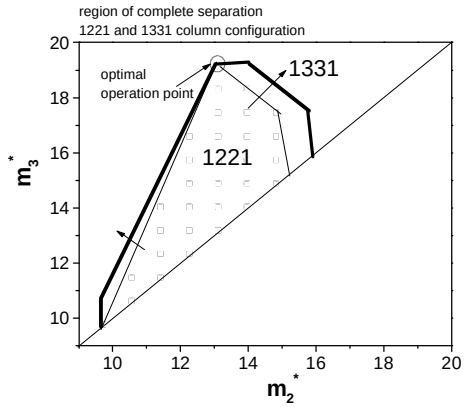

Figure 2: Region of complete separation for 1/2/2/1 and 1/3/3/1 configuration

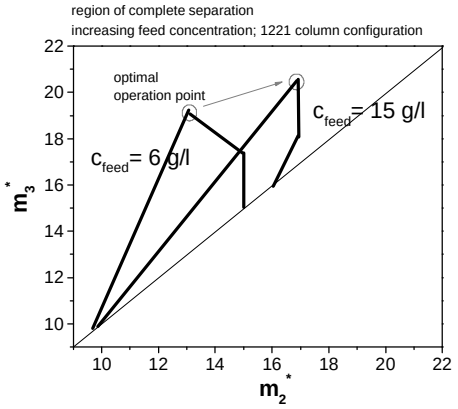

Figure 3: Region of complete separation for different feed concentrations

As shown in Fig. 3 increasing the feed concentration from 6 to 15 mg/ml leads to a smaller region of complete separation. The feed concentration of the components to be separated is a key factor in determining the efficiency of the separation, as well as its robustness. Increasing feed concentration yields larger productivity but lower robustness. The closer the operating point to the boundary of the region of complete separation, the higher the risk, that the operating point would drive out of the complete separation region. Even small fluctuations in operating conditions (flow rate or feed composition) or the effect of non-idealities (mass transfer resistance and axial dispersion) or model uncertainties (in estimation of adsorption isotherm parameters) would lead to a shifting of the operating point out of the region of complete separation region. It could be seen, that with increasing feed, the position of the vertex shifts upwards to the right and the complete separation region becomes smaller i.e., less and less robust. For that reason, a further increase of feed concentration is not useful here. Beside the feed concentration the length of column has a significant influence on the specific productivity of the SMB process. In Tab. 2, the optimized operating parameters for the column length of 144 and 50 mm are shown. For the calculation of maximum of productivity, the linear velocity of mobile phase was restricted to 0.6 cm/s in order to limit the pressure drop across the columns and to get a high number of theoretical stages (the minimum of height of theoretical stage H_s in SFC for packed columns with particle diameters of 10 µm can be reached for linear velocities between 0.2 and 0.6 cm/s [9]).

Table 2: Optimized operating parameters. T = 40 °C; p = 20 MPa; 5 wt-% 2-propanol

	1221 (1331)	**1221 (1331)**	**1221**
column length [mm]	144	144	60
feed concentration [g/l]	6	15	15
optimal operating point (m2*;m3*)	13.1; 19.1	16.8; 20.3	15.1; 16.9
Switching time [min]	2.1	2.2	0.85
feed [g/min]	43.0	24.0	13.3
extract [g/min]	38.0	21.0	30.0
raffinate [g/min]	78.3	82.4	61.3
recycling [g/min]	100.0	96.0	106
solvent [g/min]	73.3	79.5	78.0
tocopherol [mg/min]	310	432	240
productivity [g_{toco} /(l*day)]	730 (548)	1008 (756)	1344
solvent consumption [g_{CO2} /$g_{tocopherol}$]	347	219	343

The productivity could be increased from 1.0 kg/(l*day) to 1.3 kg/(l*day) by reducing the column length from 144 to 60 mm.

The productivities of the SFC SMB process should be compared with possible productivities in elution mode. Therefore the dependence of the productivity from the length of the column was investigated. The investigation was done under the same conditions as described above (T = 40 °C; p = 20 MPa; 5 wt.-% 2-propanol; n_{th} = 14 /cm). The maximum of linear velocity of mobile phase was restricted to 0.6 cm/s. For the investigation of the specific productivity, the maximum of injectable amount of tocopherol was determined. Thereby the purity of both homologues should be higher than 99 %. The entire width of the two eluted peaks is used as the injection interval. The productivity can be calculated on the basis of the injection interval. In case the column length is reduced to a length below 12.5 cm, a separation of the required purity is not feasible any more. In Fig. 4 and Fig. 5 the maximum of injectable amount of feed solution and the productivity, respectively, is shown as a function of the column length.

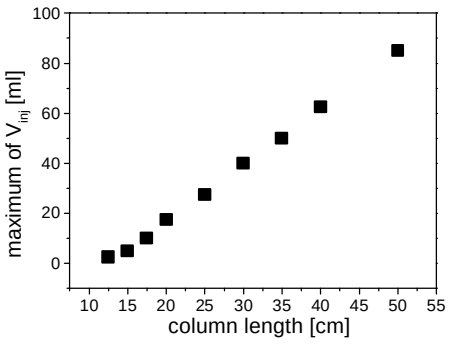

Figure 4: Maximum of V_{inj}. T = 40 °C; p = 20 MPa; c_{inj} = 40 mg/ml ; 5 wt.-% 2-propanol, purity of products > 99.5 %

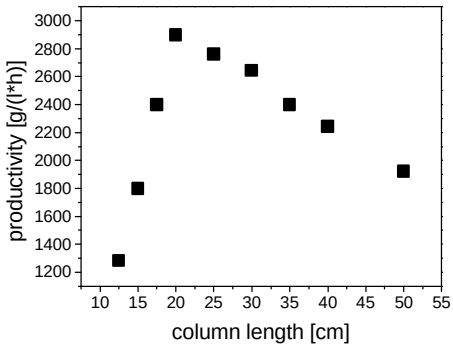

Figure 5: Productivity in terms of column length. T = 40 °C; p = 20 MPa; c_{inj} = 40 mg/ml ; 5 wt.-% 2-propanol, purity of products > 99.5 %

For the investigated system, the elution mode enables a two times higher specific productivity compared with the SFC SMB process (elution mode: 2.9 kg/(l*day); SMB mode: 1.3 kg/(l*day)). On the other hand, the solvent consumption of the separation in elution mode is two times higher than the solvent consumption of the SMB process (620 vs. 343 $g_{CO2}/g_{tocopherol}$).

However, up to now the system is not completely optimized. Operating pressure, operating temperature and content of modifier were kept constant. For example, a change of modifier might positively influence both the adsorption equilibrium and the solubility of the homologues in the mobile phase in terms of the productivity. For further optimization of the process, the influence of all parameter have to be investigated.

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REFERENCES:

[1] DEPTA, A., GIESE, T., JOHANNSEN, M., BRUNNER, G., J.Chromatogr. A, 865, **1999**, p. 175

[2] STORTI, G., MAZZOTTI, M., MORBIDELLI, M., CARRA, S., AIChe J, Vol. 39, **1993**, p. 471

[3] MIGLIORINI, C., MAZZOTTI, M., MORBIDELLI, M., J. Chromatogr. A, 827, **1998**, p. 161

[4] ROUCHON, P., SCHNAUER, M., VALENTIN, P., GUIOCHON, G., Sep. Sci. Technol., Vol. 22, **1987**, p. 1793

[5] KNIEP, H., FALK, T., SEIDEL-MORGENSTERN, A., PREP, Basle, September 1-4, **1996**

[6] SPAN, R., WAGNER, W., J. Phy. Chem. Ref. Data, Vol 25, **1996**, p. 1509

[7] HILL, T.L., An Introduction to statistical Thermodynamics; Dover Publications: New York, 1986.

[8] SEIDEL, A., GELBIN, D., Chem. Eng. Sci., Vol. 43, **1988**, p. 79

[9] GERE, D., BOARD, R., MC MANIGILL, D., Hewlett-Packard Publ 43-5953-1647, Avondale, Pennsylvania, **1982**, p. 7