

Speed Up SFC Chiral Method Development with a 8x Parallel System

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Introduction and goal

Racemate separation screening of drug candidates has gained increasing importance for pharmaceutical companies. In order to achieve sufficient separation of racemates several chiral stationary and mobile phases are routinely screened. This time-consuming procedure can be significantly shortened by parallel HPLC (Fig. 1) using the automated Sepmatix System (Fig. 2). This approach has been successfully implemented in the pharmaceutical industry [1,2].

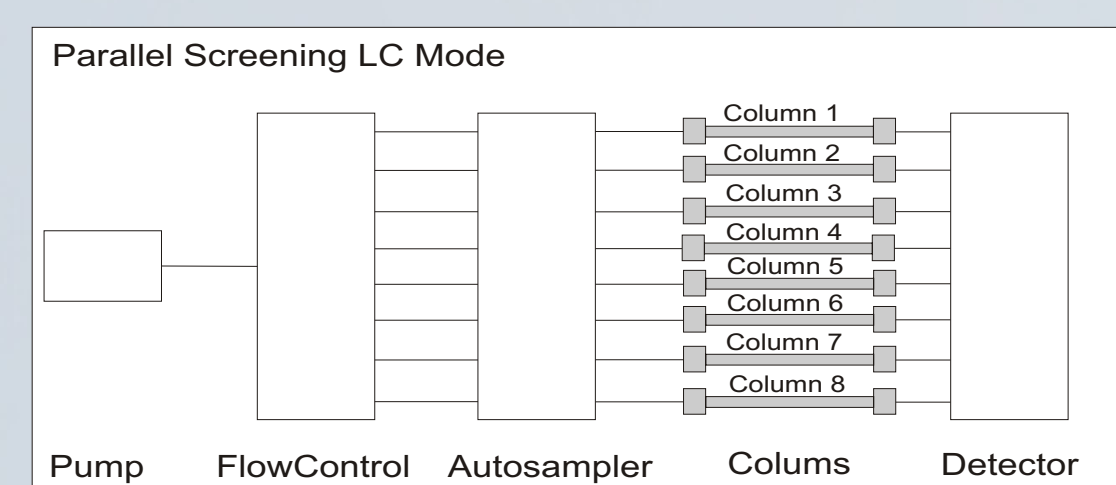


Fig. 1: Schematic 8x parallel HPLC screening

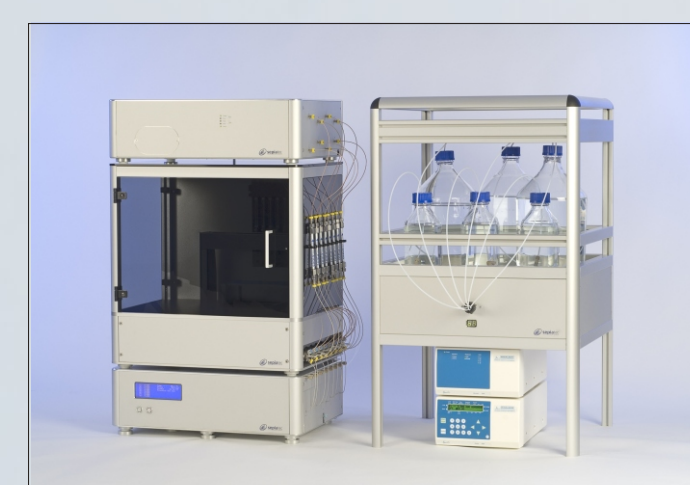


Fig.2: Sepmatix LC System

The demand for shorter runtime and reduction of solvents has rekindled the interest in the use of Supercritical Fluid Chromatography (SFC) for chiral separations. Our goal therefore was to develop a parallel system for SFC screening based on the proven parallel approach of the parallel LC screening system. The Chiral Screening Wizard Software that eases the evaluation of the screening process considerably should also be applicable for the SFC screening results.

Experimental

The following modifications allow the Sepmatix System to be used for SFC applications (Fig. 3 and 4):

- a high pressure gradient system with a CO₂ pump and a modifier pump
- optimization of the sealing material in the FlowControl
- additional heating modul
- additional back pressure regulator (0-250 bar)

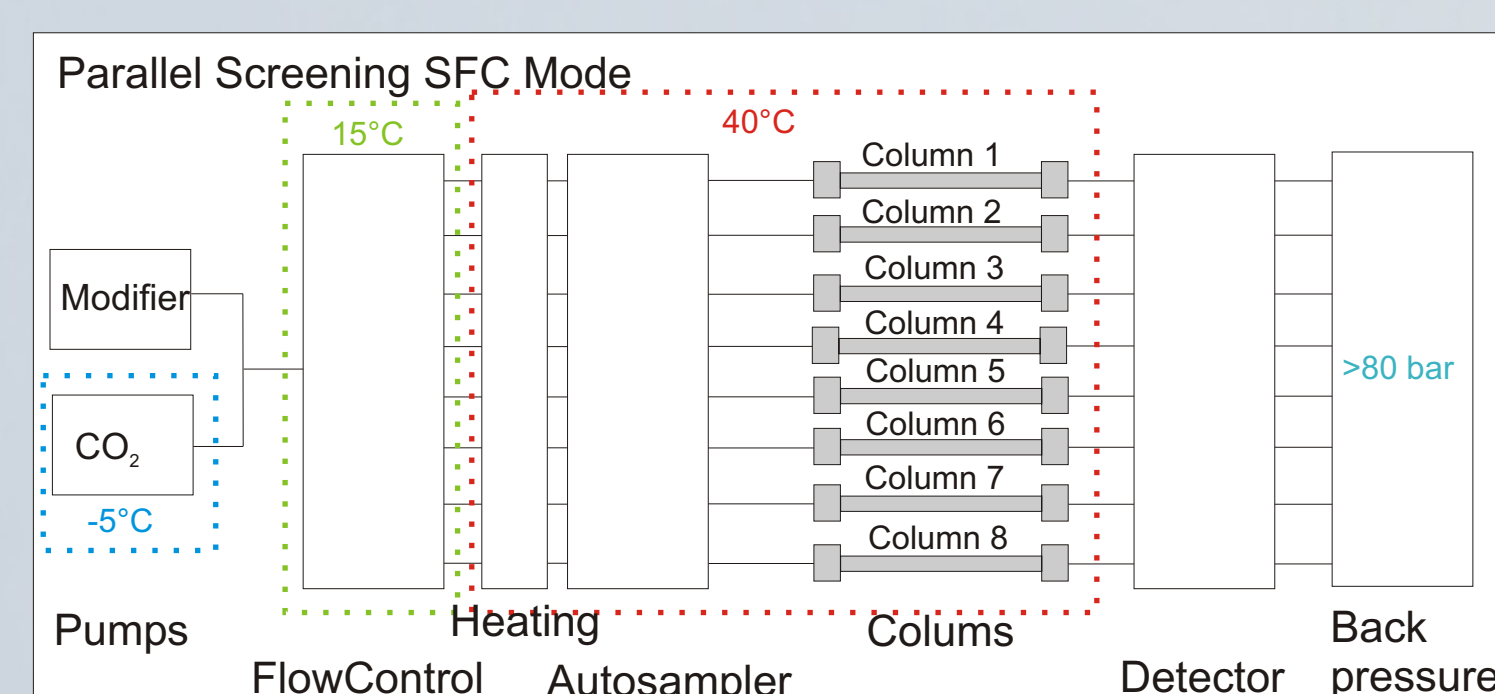


Fig. 3: Schematic 8x parallel SFC screening



Fig. 4: Sepmatix 8x parallel SFC screening system (pre-series)

8x parallel SFC screening

The separation of trans-Stilbene oxide (TSO) has been screened on eight columns (250 x 4.6 mm). Seven polysaccharide based chiral stationary phases (CSP) and one brush-type CSP were used. Particle sizes varied between 3 µm and 20 µm. The first experiment was a screening under 4 different isocratic conditions. With an equilibration time of 5 minutes and a runtime of 10 minutes, these 32 separations were done in one hour in the parallel mode. The flow rate was 4 ml/min per channel, in total 32 ml/min.

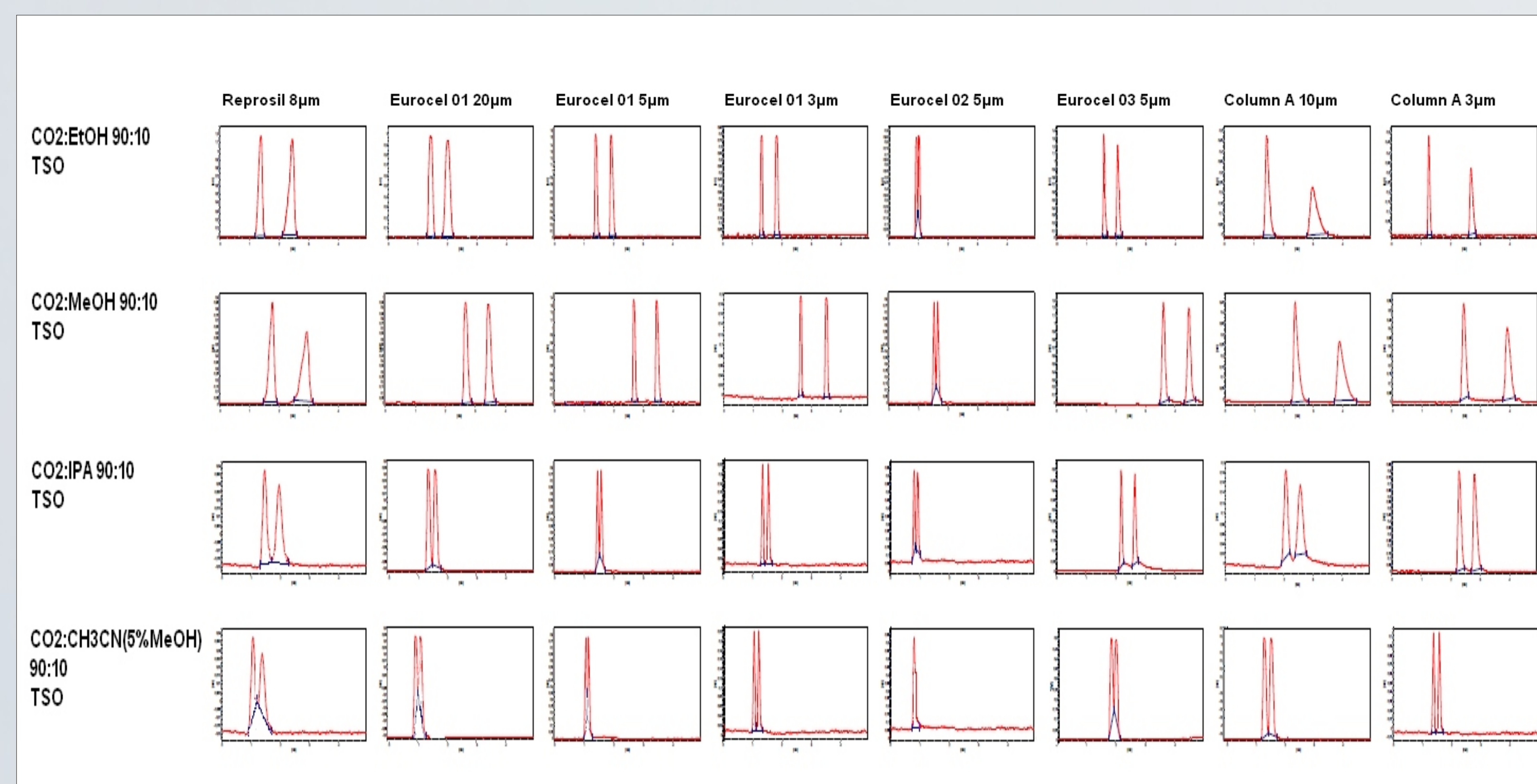


Fig. 5: Chiral Column Screening Software - SFC 8x parallel isocratic screening - 32 chromatograms - 8 columns and 4 solvent combinations

The second setup was a screening under gradient conditions. Starting from 2% modifier up to 50% modifier in 10 min. The flow rate was 3 ml/min per channel, in total 24 ml/min. A four times repeated injection shows the reproducibility of the parallel system (Fig. 6). The 8x FlowControl also works precisely under supercritical fluid conditions.

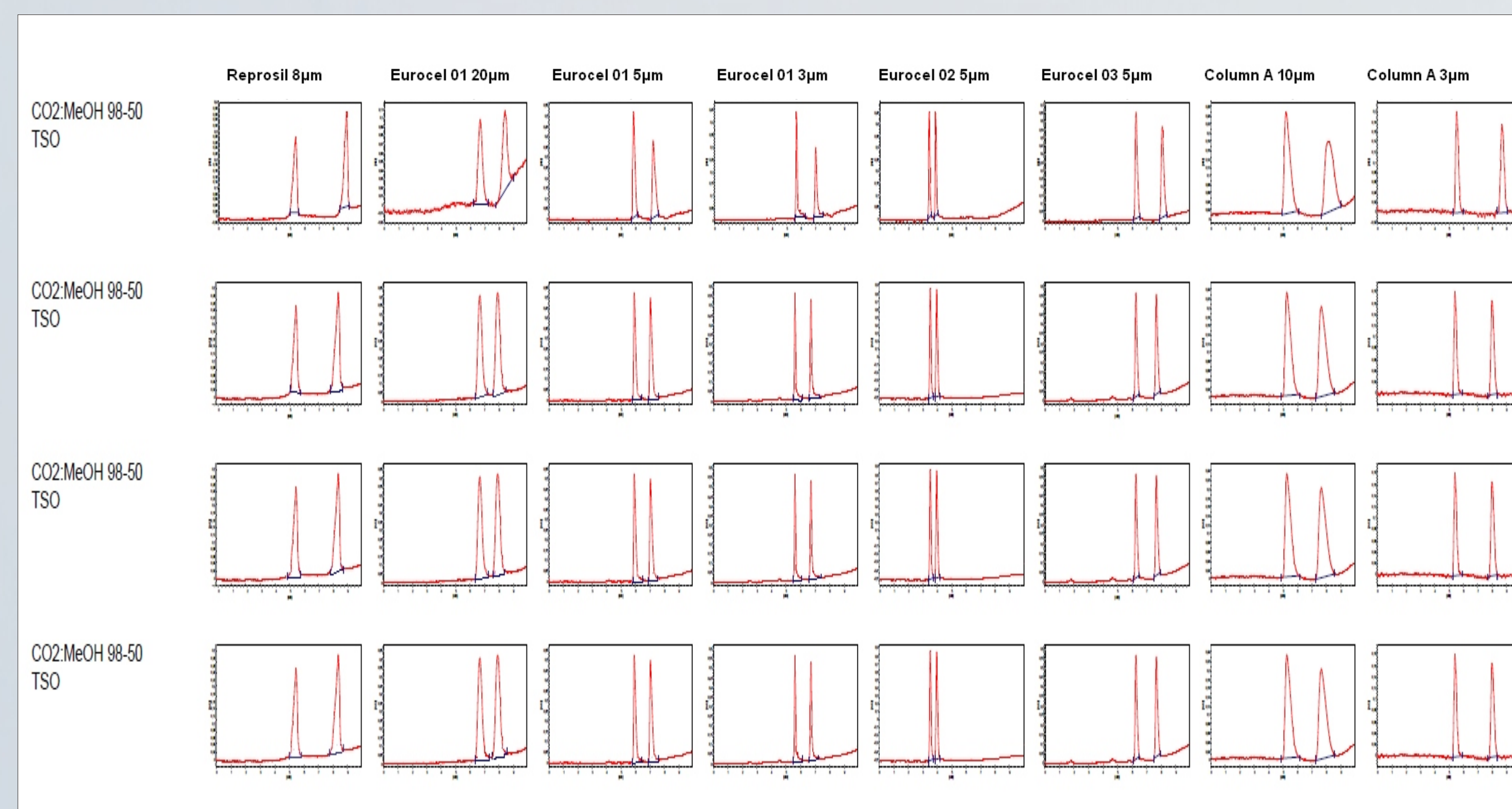


Fig. 6: Chiral Column Screening Software - SFC 8x gradient screening - 32 chromatograms - 8 columns and 4 injections

SFC parameter

System:

Sepmatix 8x FlowControl SFC,
Sepmatix 8x AutoSampler,
Sepmatix 8x ColumnOven,
Sepmatix 8x DAD Analytical,
Preparative pump 1800, 100ml head 2x (Knauer),
Pump head cooling device (Knauer),
Refrigerated circulator (Julabo),
Column dimension: all 250x4.6 mm
Chiral Stationary Phases:
Column A, 3µ and 10µ,
Eurocel 01, 3µ, 5µ and 20µ (Knauer)
Eurocel 02; 5µ (Knauer)
Eurocel 03; 5µ (Knauer),
Reprisil Chiral-NR; 8µ (Dr.Maisch).

Injection volume: 10µl
Flow rate: 3-6 ml/min per channel
Detection: UV 230 nm
Back pressure: 120 bar
Temperature pump head: -5°C
Temperature FlowControl: 15°C
Temperature heating modul: 40°C
Temperature ColumnOven: 40°C
Temperature back pressure regulator: ambient

Conclusions

With a few modifications the 8x parallel Sepmatix LC system can also be used for Supercritical Fluid Chromatography. This new 8x parallel SFC system combines the advantages of SFC such as shorter runtimes and lesser use of solvents with the remarkably time saving of the parallel approach. Using the same detector and data format of the Sepmatix system, the Chiral Screening Wizard Software can be used for evaluation leading to a rapid finding of the optimal separation parameters. By the implementation of the 8x parallel Sepmatix LC system (Sepiatec, 2004) Chiral Column Screening could be carried through 8 times faster compared with conventional HPLC systems. The 8x parallel Sepmatix SFC system shown here increases the speed again considerably.

References

- [1] E.Francotte: Multi-parallel Chiral Screening. G.I.T. Laboratory Journal, 3,46-48 (2006)
- [2] T. Huybrechts et al.: Multimodal HPLC Screening of Polysaccharide- based Chiral Stationary Phases.LCGC Europe, Vol.20, No.6, 320-335 (2007)

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