





ChromaCon



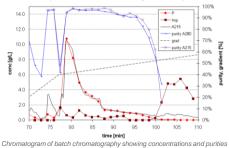
Purification of a synthetic peptide using multi-column chromatography (Contichrom® & MCSGP)

Guido Ströhlein¹, Thomas Müller-Späth¹, Olav Lyngberg², Derek Maclean³

- ¹ ChromaCon AG, Technoparkstr. 1, 8005 Zurich, Switzerland
- ² Bristol-Myers Squibb, Process R&D, 1 Squibb Drive, New Brunswick, NJ 08903, USA
- ³ KAI Pharmaceuticals, 270 Littlefield Avenue, South San Francisco, CA 94080, USA

Purification challenge

- Develop single-step purification for a synthetic polypeptide (20-30) amino acids, feed purity ca. 60%) using reversed-phase chromatography (C18)
- Improve COG (yield, productivity, solvent consumption) and purity by using MCSGP instead of conventional batch chromatography
- Batch reference process was already developed



MCSGP process development

In MCSGP, the same stationary phase and eluent as in batch chromatography was used, but instead of a single column with

25cm bed height, two columns with each 5 (or 10) cm bed height were employed

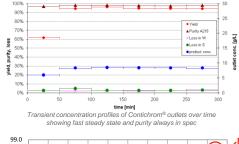
Using the interactive Contichrom® software wizard, the batch process was automatically converted to the MCSGP process

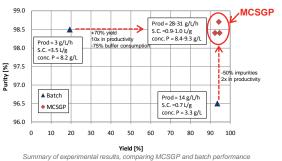


Optional: Process optimization by fine-tuning of process parameters



Experimental results MCSGP

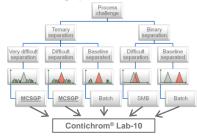




Introduction to Contichrom® & MCSGP

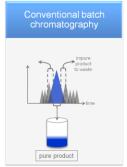
Contichrom® Lab-10 is

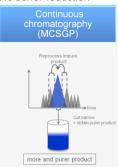
- · a preparative 2-column liquid chromatography system
- designed for discovery, process development and scale-up
- offering flexibility for all process choices (batch, SMB, MCSGP, multi-column) using a single equipment and control software
- · All standard resin and column formats (e.g. RP, IEX, MM, SEC) can be used from low-high pressure with full solvent compatibility



The MCSGP process principle

- · uses twin columns instead of one
- · whereby the impure side fractions containing product are recycled internally extracting all product
- thereby in average increasing both yield and purity by 50% at a 10-fold throughput increase and 70% buffer reduction





Schematic principle of MCSGP. Find detailed animations at <u>www.chromacon.ch</u> in the download section

Conclusions

With Contichrom® Lab-10 and the MCSGP process principle

- yield can be increased by 75% simultaneous with 10x increase in productivity and 75% reduction of buffer requirement
- purity can be increased by 50% simultaneous with 2x increase in productivity
- Contichrom[®] Lab-10/ Prep-100 could produce up to 40g/400g of purified product per day, although having only the foot-print of an HPLC

References:

- L. Aumann, M. Morbidelli, A continuous multicolumn countercurrent solvent gradient purification (MCSGP) process, Biotechnology and Bioengineering, 98 (5), pp. 1043-1055, Dec 2007