

Pais, L.S., and Rodrigues, A.E.

Simulated Moving Bed and Varicol Processes for Large-Scale Chiral Separations

in *PREPTECH 2002 - Preparative and Process Scale Technology in the Manufacturing of Chemicals and Pharmaceuticals*, Gothenburg, Sweden, May 13-15, 2002.
(*comunicação oral*)

ORAL PROGRAMME

17.00 - 17.30 Latest development in aseptic processing techniques for filtration.
Keith Wickert, Pall Lifesciences

20.00 Boat trip & Dinner
Sponsor Eka Chemicals

Wednesday 15th May.

Chair: Christopher J. Welch

08.30 - 09.00 Scale-up and application of ion-exchange processes with adsorptive membranes.
Wolfgang Demmer, Sartorius, AG., Germany.

09.00 - 09.30 A new integrated membrane process for process scale plasmid purification.
Iggý Gyepi-Garbrah, Pall Lifesciences.

09.30 - 10.00 Affinity membranes: possible application and preliminary results.
Wolfgang Demmer, Sartorius AG, Germany.

10.00 - 10.30 Development, optimisation and documentation of mimetic affinity matrix for purification of coagulation factor VIIa.
Jesper Christensen. Novo Nordisk A/S, Denmark.

10.30 - 11.00 Refreshment

Chair: G. Subramanian

11.00 - 11.30 Preparative production of Proteins.
Lothar Jacob. Merck KGaA Darmstadt, Germany.

11.30 - 12.00 Aspects of purification of peptides by preparative chromatography.
Lars Andersson. Polypeptide Laboratories AB. Sweden.

12.00 - 12.30 High quality Plasmid DNA from Preclinical to Clinical studies.
Urban Olsson. Amersham Biosciences, Sweden.

12.30 - 13.00 Purification of synthetic peptide by reversed-phase chromatography. From Development to industrial scale.

PREPTECH 2002

Preparative and Process Scale
Technology in the Manufacturing of
Chemicals and Pharmaceuticals
MAY 13th - 15th 2002



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ROME MAY 23rd - 25th 2002

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ORGANISER: Dr. G. SUBRAMANIAN

REGISTRATION FORM

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REGISTRATION FEE

The fee of £750 (VAT not applicable) includes full documentation, entry to exhibition/poster presentation, all meals and refreshments, and single room accommodation. For non-residents, the fee will be £600 which includes lunches and refreshments only, full documentation and visits to the exhibition/ poster presentation.

PAYMENT

Registration fees together with the completed registration and cheques should be made payable in Pounds Sterling and drawn on a UK Based Bank payable to Dr. G. SUBRAMANIAN. Your registration will be acknowledged in writing. If paying by bank transfer the fee will be £770. Please forward a copy of your bank transfer to the conference secretariat. It is essential to include the delegate's name and organisation's name on all by bank transfer documentation.

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CANCELLATIONS

Substitutions may be made at any time, but please inform about the names. In the event of written cancellation, a fee of £250 will be charged. If notification is received after 10th April - no refund will be made.

POSTER PRESENTATION & EXHIBITION

Those interested in participating in this event should call the conference secretariat at the address above.

ORAL PROGRAMME

Chairman: G. Subramanian

Monday 13th May
13.00 - 14.00 Registration/Welcome
Chair: Shalini Andersson
14.00 - 14.30 The role of preparative chromatography in the drug process.
Derek van Langen, Merck & co, Inc. USA.
14.30 - 15.00 Chromatography scale-up of pharmaceutical compounds.
Ronald Bates, Pfizer Inc, USA.
15.00 - 15.30 Optimisation of Production scale Chromatography.
Jules Dingenen, Janssen Research Foundation, Belgium.
15.30 - 16.00 Refreshment
Chair: Berni Larsson.
16.00 - 16.30 Preparative Chiral Chromatography in drug discovery.
Shalini Andersson, Astrazeneca, Sweden
16.30 - 17.00 Chiral LC resolution followed by crystallisation, optimisation algorithm for pilot and production.
Evgeny Aronov, Schering Plough, USA.
17.00 - 17.30 Molecular recognition technology in chiral Separation.
Donald Wellings, Avecia, UK
17.30 - 18.00 New tools for high throughput process research: Strategies for rapid adsorbent selection.
Christopher J. Welch, Merck & co., Inc, USA.
19.00 Sherry reception - Merck KGaA
20.00 Dinner sponsored by Astrazeneca
Chair: G. Subramanian
Tuesday 14th May
08.30 - 09.00 CALTRES: New HPLC-phases useful for preparative chromatography.
Ulf Menyes, SYNAPTEC GmbH, Germany.
09.00 - 09.30 Generic Method for phase selection and method optimisation of biochromatographic processes
Martin Lohrmann, Bayer AG., Germany
09.30 - 10.00 Downstream Processing: Alternative approach for optimisation and integration.
Duncan Low, Millipore, USA.
10.00 - 10.30 SMB and Vertical processes for large scale chiral separation. Luis Pais. Instituto Politecnico Bragan, Portugal.

ORAL PROGRAMME

Tuesday 14th May Continued

10.00 - 11.00 Refreshment
Chair: Charles Christy
11.00 - 11.30 Large scale SMB processes: An industrial perspective.
Tobias Reichert, Bayer AG, Germany.
11.30 - 12.00 Novel application of SMB in pharmaceutical industry. Markus Juza, Carbogen Laboratories, Ltd, Switzerland.
12.00 - 12.30 The successful use of SFC-SMB technology for preparative scale chiral separation.
Monike Johanssen, Technical University Hamburg-Harburg, Germany.
12.30 - 13.00 Ternary separation by Pseudo-SMB (Jo Processes) and eventually cyclojet.
Alirio Rodrigues, University of Porto, Portugal.
13.00 - 14.00 Lunch
Chair: Wolfgang Demmer
14.00 - 14.30 New particulate and Monolithic silica sorbents for the separation of Diastereomers and Natural products. Michael Sculte, Merck Darmstadt, Germany.
14.30 - 15.00 Pure compounds "CRUDE 2 PURE" in lesstime at medicinal chemistry.
Mickael Sellin, Astrazeneca, Sweden.
15.00 - 15.30 PSI Port - Interactive data review.
Neil Loftus, Shimadzu Biotech, UK.
15.30 - 16.00 Refreshment
Chair: Michael Schulte.
16.30 - 16.30 Zwitterion chromatography, a novel technique with unique selectivity suitable for preparative scale separation.
Camilla Viklund, SeQuant AB, Sweden.
16.30 - 17.00 From R&D to production: scale-up and optimisation of Downstream Processing techniques and filtration.
Charles Christy, Millipore, France.

Simulated Moving Bed and Varicol Processes for Large-Scale Chromatographic Separations

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Simulated Moving Bed (SMB) is a continuous chromatographic process that overcomes the usual limitations of standard preparative chromatographic methods, namely the high inventories of solvent and adsorbent needed and the high dilution of products. SMB technology, which has been used for decades in large-scale separations in the petrochemical and carbohydrate industries, has recently found new successful applications in the areas of biotechnology, pharmaceuticals and fine chemistry.

The design of SMB units requires the use of modeling and simulation tools. The problem of modeling a SMB separation process can be analyzed by two different strategies: one, by simulating the system directly, taking into account its intermittent behavior, other by representing its operation in terms of a true countercurrent system. The first model represents the real SMB and considers the periodic switch of the injection and collection points. The second, is developed by assuming the equivalence with the true moving bed (TMB), where solid and fluid phases flow in opposite directions.

Recent applications in the pharmaceutical industry uses SMB systems containing a low total number of columns, usually four to eight. *Novasep*, a leading supplier of SMB industrial units, has announced the installation of the largest unit for chiral separations with only six columns. In these cases, the evaluation of the SMB operating conditions shall avoid the use of the countercurrent TMB model, and a more realistic SMB model, which takes into account the periodic switch of the injection and collection points, is needed. For an effective comparison between the predictions given by the two strategies of modeling, two-dimension separation regions can be evaluated using the TMB and SMB models. The differences obtained by the two models depend particularly on the number of columns used and its configuration.

Recently, *Novasep* proposed a new continuous chromatographic process, called *Varicol*. The principle of the *Varicol* process is based on a non-synchronous shift of the inlet and outlet valves in a multicolumn system, in contrast to the SMB operation where this shift is synchronous. This new process makes possible the operation with a number of columns per section that is not constant in time, and can show advantages over the classical SMB operation, particularly when using a low number of columns.

The objective of this work is to evaluate and compare the performance of SMB and *Varicol* systems with a low number of columns. Simulation results will be shown for units with 4, 5, and 6 columns. A special attention will be put on the choice of the better operating conditions for these units, particularly with the objective of solvent consumption minimization. The concept of separation volume, developed by the authors, will be used to analyze this optimization problem.