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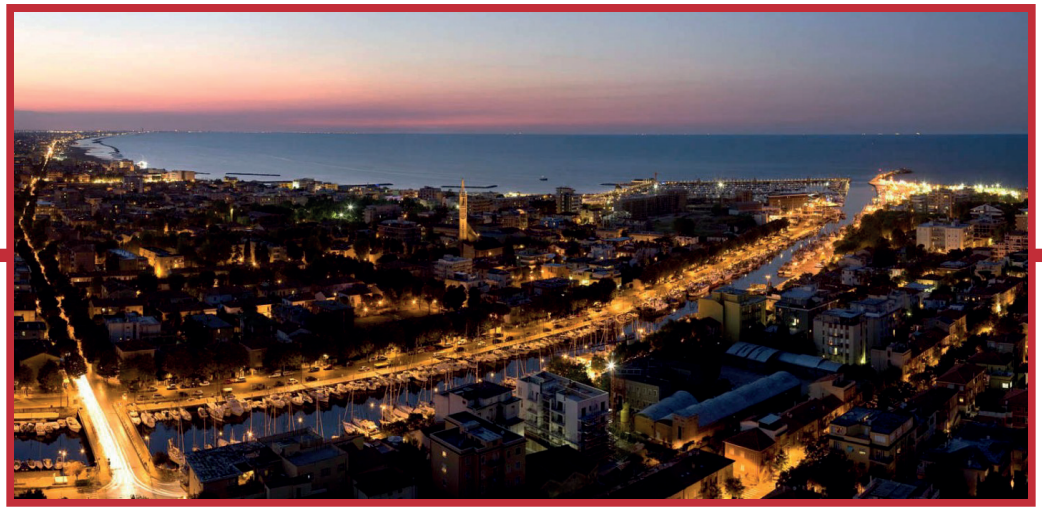

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From preparative batch chromatography to a 2-column Multicolumn Countercurrent Solvent Gradient Purification process for a peptide purification

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Many peptides used for pharmaceutical applications are synthesized through Solid Phase Synthesis. The crude peptide mixture usually contains many impurities chemically very similar to the peptide. Reversed phase preparative chromatography is the preferred choice for downstream purification. However, the separation can be very difficult, resulting in peak overlapping regions not fulfilling the strict purity constraints. To obtain a pool with higher purity, the product collection window must be narrowed, causing a reduction in the product yield [1,2]. This works investigates the possibility of overcoming the purity-yield trade-off through 2-column MCSGP process (a semi-continuous chromatography process) where the columns work alternatively in interconnected or batch mode. While in the first column the gradient method is performed, the overlapping fractions eluting are recycled in the second column, which is also filled with fresh feed. These operations permit to increase the recovery of the peptide, keeping a very high purity. After these tasks are accomplished in the first column, columns exchange position, and half a cycle is completed. Usually, during an MCSGP run, 4 to 6 cycles are carried out [2].

The work started with the determination of batch conditions where the region of the main peak with a purity fulfilling the imposed specifications is as large as possible. From the Pareto (recovery vs purity) curve related to this batch method, a first group of trial values has been established to set-up the MCSGP switching times. The results obtained for the pools collected during the MCSGP run have been compared with those of the batch. By adjusting the times of recycling and collection windows the purity and recovery of the pools as well as the productivity of the method have been significantly modified.

[1] T. Mueller-Spaeth, G. Stroelhein, O. Lyngberg, and D. Maclean, *Chemistry Today* **31** (2013) 56-60.
[2] F. Steinebach, N. Ulmer, L. Decker, L. Aumann, and M. Morbidelli, *J. Chrom. A*, **1492** (2017) 19-26.

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