Case Study

How to reduce the costs for preparative LC processes

Abstract

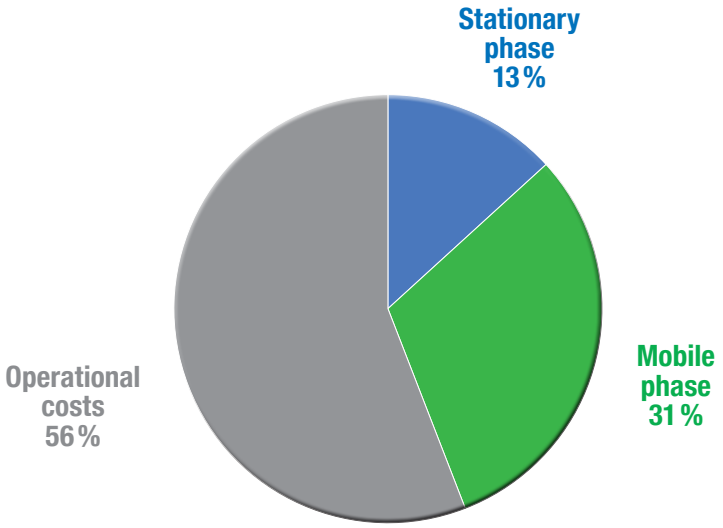
The use of preparative chromatography for the isolation of compounds such as active pharmaceutical ingredients will ensure the highest possible purities. While the costs for the purification of target compounds in high purity via preparative chromatography are frequently considered to be very high, these costs are mainly driven by the costs of the solvents and the running costs of the operation itself. There are huge opportunities for cost savings for virtually all existing and new preparative processes.

The potential to reduce the costs and increase the lifetime of the stationary phase is the most obvious area for cost reductions.

In this case study, all relevant method parameters were evaluated for the isolation of insulin. A comprehensive screening was performed for different stationary phases. Based on the actual results obtained, cost calculations showed that savings of up 40% in the overall product costs were possible!

Typical cost structure for preparative LC processes

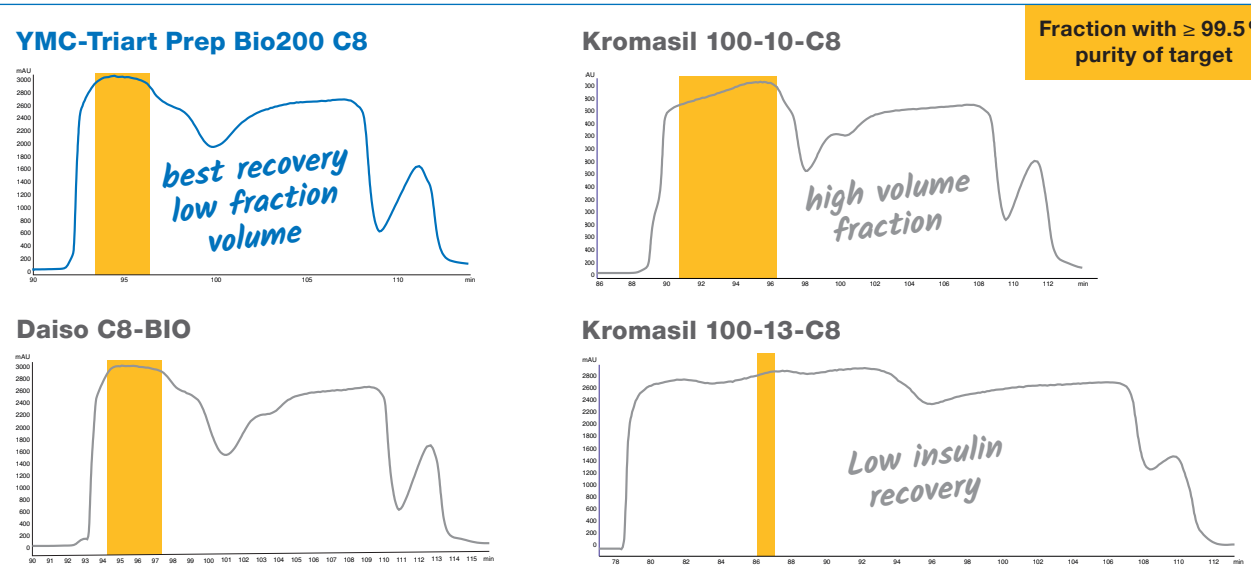
The main cost drivers are the operational costs such as work force and the solvents used as mobile phase. The stationary phase dictates the cost efficiency of a process and defines the required amounts of solvents and operational parameters such as runtimes and the lifetime of the process. Therefore, the choice of the stationary phase is the most important step during the process development. However, the actual cost of the preparative stationary phase itself represents only a small proportion of the overall costs of preparative processes. Based on the cost calculation of this case study, the cost for the stationary phase represents only 13% of the overall costs.



Purification of insulin

For the purification of insulin, a detailed cost calculation and an analysis of possible savings was carried out by YMC. In co-operation with an insulin manufacturer, real insulin samples were used to perform a comprehensive screening and process optimisation study. Different stationary phases were used for the screening.

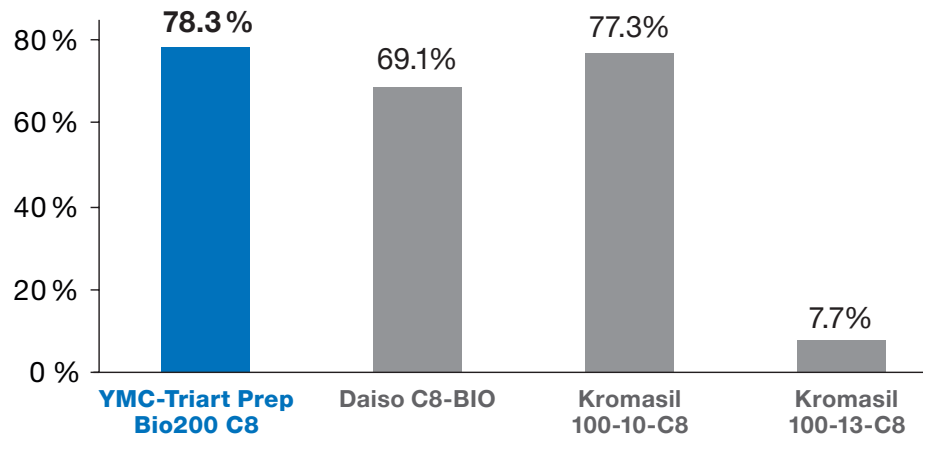
Screening results for a loading of 50 mg insulin



Column Size:	250 x 4.6 mm ID	Flow:	1.0 mL/min
Eluent:	A) buffer/acetonitrile (90/10) B) buffer/acetonitrile (10/90)	Temperature: Sample:	ambient 1 mg/mL Insulin in 0.1 % CH_3COOH (Insulin purity about 75 %)
Gradient:	0%B (0–5 min), 0–20%B (5–10 min), 20–25%B (10–55 min)	Buffer:	20 mM CH_3COONH_4-CH_3COOH (pH 4.3)
Detection:	UV at 214 nm		

It was obvious that the Kromasil 100-13-C8 is not suitable for the purification. The separation is insufficient to recover insulin with the purity of 99.5 % in reasonable quantities. The fraction volume of the Kromasil 100-10-C8 is larger compared to the YMC-Triart Prep Bio200 C8 phase. The smaller fraction volume with the YMC phase simplifies the post-chromatography steps. The chromatograms obtained with YMC and Daiso seem to deliver similar results. Both phases are able to purify in small fraction volumes although the actual recovery amounts show the outstanding performance of YMC-Triart Prep Bio200 C8.

Recovery of insulin at 99.5% purity



Cost estimation for the isolation of 100 kg purified insulin

Based on the obtained data, a cost estimation was carried out for the isolation of 100 kg purified insulin. A linear scale up to a 60 cm ID column was chosen as a realistic scenario. The target for the process is to produce insulin with a purity of 99.5%. The following conditions were set for the calculation.

	Common conditions
Target	100 kg of purified insulin
Target purity	> 99.5%
Material	**1) YMC-Triart Prep Bio200 C8** 2) Daiso C8-BIO 3) Kromasil 100-10-C8
Column	600 mm ID x 250 mm length
Sample	Crude insulin (75 % purity)
Loading per run	850 g of crude insulin
Purification cycle time	120 min/run
Operation	24 hours / 10 cycles per day (20 hours operation + 4 hours CIP)
Condensation capacity	500 L/day
Lyophilisation	10 days

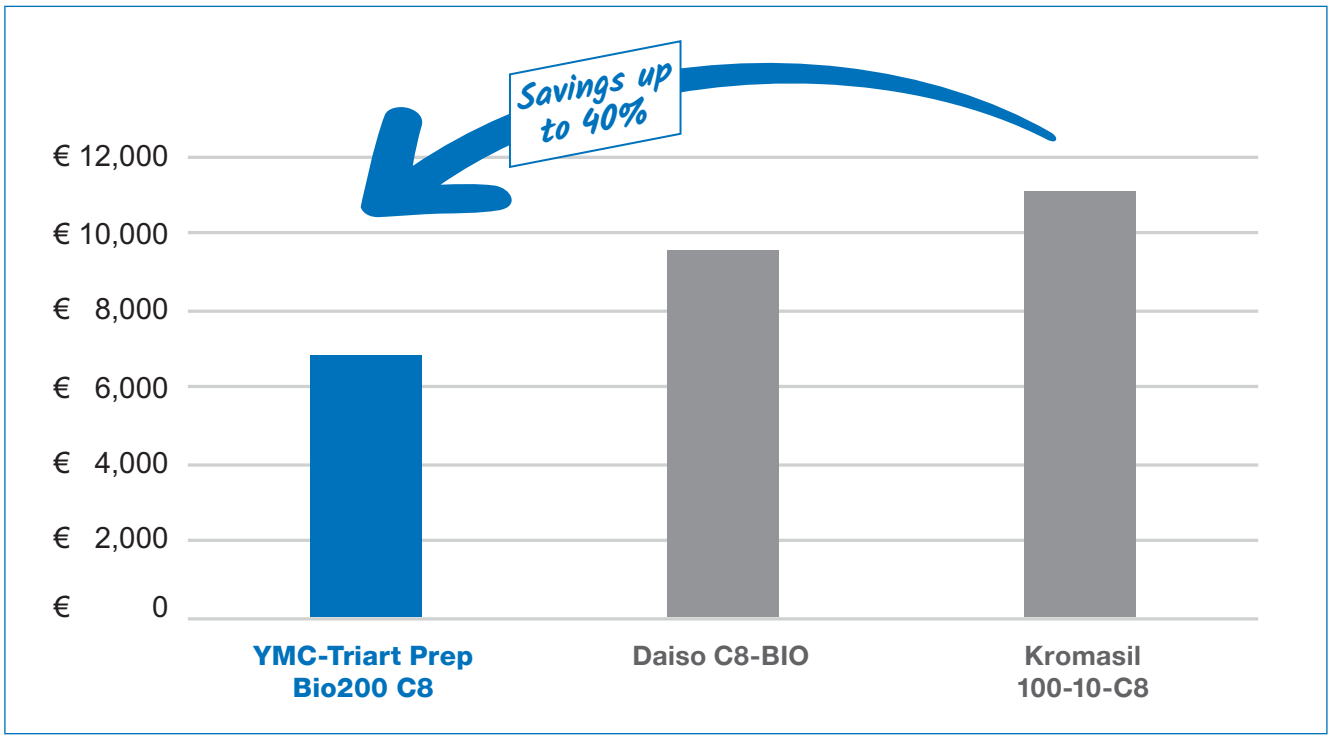
Item	Unit cost in €
Packing material / kg	**3,000**
Mobile phase / 1000 L	**3,000**
Operational costs (incl. work force, equipment) **/ day**	**10,000**

Potential for savings up to 40 %

In summary, the YMC-Triart Prep Bio200 C8 phase shows the highest performance, resulting in the greatest cost efficiency and productivity. The isolation of 100 kg insulin with a purity of 99.5 % is achieved after 35 days with the lowest number of injections. Moreover, the smallest amount of crude is needed with the YMC material which additionally improves the cost efficiency of the overall process.

	YMC-Triart Prep Bio200 C8	Daiso C8-BIO	Kromasil 100-10-C8
Packing material amount (bulk density)	**35.3 kg (0.5 kg/L)**	35.3 kg (0.5 kg/L)	42.2 kg (0.6 kg/L)
Lifetime of packing material	**> 200 runs**	80 runs	100 runs
Recovery	**78 %**	69%	77 %
Required crude	**170 kg**	192 kg	172 kg
Required purification cycle	**200 runs**	225 runs	202 runs
Fraction volume per run	**60 L**	60 L	95 L
Campaign period	**35 days**	38 days	50 days
Total solvent required	**75,600 L**	85,100 L	76,400 L

Purification costs per kg insulin



Conclusions

This case study proves that the YMC-Triart Prep Bio200 C8 phase allows savings up to 40 % to be achieved for the isolation of insulin. High loadability combined with the perfectly matched selectivity and long lifetimes result in a substantial reduction in operational costs. With YMC-Triart Prep Bio200 C8 the best possible process is possible. This phase outperforms all other phases screened in all disciplines: it is the fastest, the most economic, the most ecologic as well as the most efficient phase.

Contact YMC for your free sample today and discover the qualities of YMC-Triart Prep!