Fast and easy method development for large scale processes

Before implementing large scale processes, the most straightforward approach is to develop and refine separation methods on a laboratory scale. Only then, risks and resource consumption can be kept on a bare minimum. Also, it allows fast process modifications.
First, the ideal combination of stationary phase and elution conditions needs to be determined. Ideally a quick phase screening is carried out. In this early stage, the course is set for a successful purification!

A perfect match ensures high productivity: maximum loading capacity and yield in the shortest cycle time.
Self-packed glass columns are “the” lab tool for quick screenings due to two reasons. First, any stationary phase available already in the lab can be chosen. This means the screening kit is completely flexible. Second, the packing is fast so that results are quickly obtained. With glass columns which are compatible with aqueous buffers and organic solvents any separation mode is addressable.

Example: 5 mm ID ECO^{PLUS} columns as the perfect tool in method development

The approach has been successfully used in a recent study by Stefan Schmidt et al. They developed a brand-new method to purify mAb in large-scale production. Their approach was based on self-packed ECO^{PLUS} glass columns.

The advantages are:

- Low sample, resin and solvent consumption
- High reproducibility
- Easy column packing
- Full biocompatibility for BioLC applications

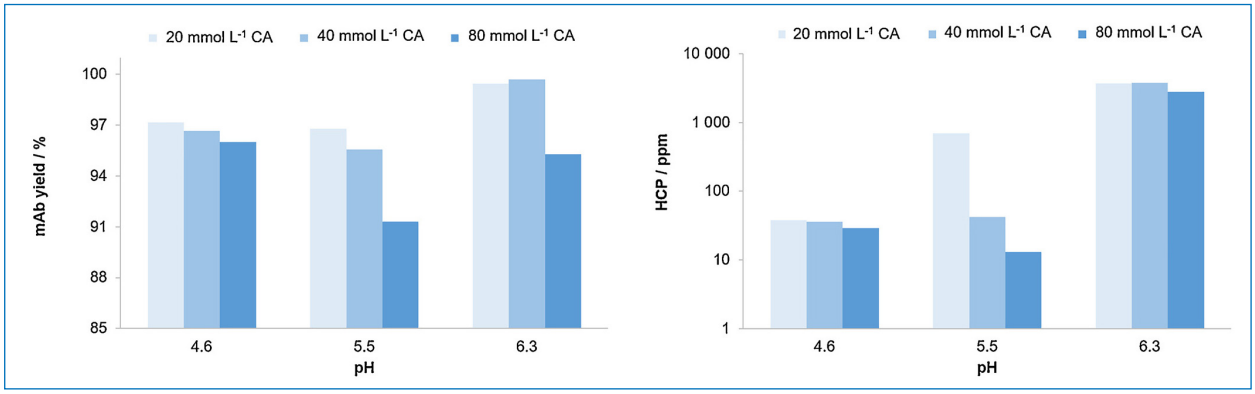

Fig. 1: Effect of caprylic acid (CA) concentration and pH on mAb yield (left) and HCP content (right). Figure was taken from Schmidt et al. [1].

Results of precipitation and virus inactivity with caprylic acid

- Excellent Host Cell Protein (HCP) clearance of up to 2 LRV at pH 4.5–5.5 (80 mmol/L CA)
- High yields of 86% to 98% of entire mAbs remaining in solution
- Complete virus inactivation after 15 min at pH 5.1 (6.2 mmol/L CA)
- Moderate conditions and easy removal of CA in DSP

[1] Stefan R Schmidt et al., Multiple functions of caprylic acid-induced impurity precipitation for process intensification in monoclonal antibody purification

After successful method development, the next step is to perform overloading studies. Again, small column IDs are best suited. In most cases the last method optimisation will be carried out at this stage. The final step is scaling up. The most comprehensive approach in preparative LC is the so-called linear scale-up. Thereby, the integrity of the separation throughout the entire process is maintained by only increasing the column diameter. The column length and particle size stay the same. The benefit: A doubled diameter results in four times the loadability! For smooth operation it is advisable to employ self-packed glass columns which are available with different inner diameters. This facilitates the scale-up studies.

Technical Note

It is essential to purify and isolate target compounds with high purity in the shortest cycle time. The following routine has proven to be very helpful and successful in various projects:

1. fast screening of different stationary and mobile phases in analytical scale,
2. applicable loadability studies at an analytical scale,
3. transfer of the developed process to the required larger scale.

Column hardware plays an important role in simplifying the process of efficient method development. A multi-purpose column line for self-packing such as ECO^{PLUS} is an ideal lab resource. It is compatible with all types of liquid chromatography. A great asset is the high pressure tolerance for maximum sample throughput.

Your advantages at a glance:

- Low sample and resin consumption with small ID columns
- Increased throughput due to higher pressure limits for fast screenings
- Compatible with all common separation modes
- Full scalability: reliable packing results
- Easy handling for fast column packing

YMC Europe GmbH · Schöttmannshof 19 · 46539 Dinslaken · Phone +49 (0)2064 427-0 · Fax +49 (0) 2064 427-222 · Email info@ymc.eu · www.ymc.eu