

Developing peptide drugs faster with the Peptide Easy Clean (PEC) technology

Dominik Sarma

Belyntic GmbH, Richard-Willstätter-Str. 11, 12489 Berlin, Germany, dominik.sarma@belyntic.com

Powerful discovery platforms, including display technologies, venom peptides, and in-silico discovery tools based on artificial intelligence, enable a plethora of peptide therapeutics. However, transforming peptide hits into potent therapeutic leads comes with major manufacturing obstacles. For example, during the early phases of development, the developer requires many pure peptides to confirm the initial hit selection (usually over 100 hits) and screen for optimal amino acid substitutions (e.g., Alanine scanning, D-amino acid substitution, etc.). Moreover, a time-consuming part of selected lead manufacturing is the precipitation step between SPPS and purification. Finally, elaborate chemical peptide modification steps in solution such as disulfide formation are required to turn the peptide hits into a decisive pharmacological lead.

These stages towards a clinical drug lead consume a lot of time and resources when relying on conventional purification with chromatography, especially high-pressure liquid chromatography (HPLC). For example, peptide precipitation is mandatory after SPPS and before loading onto an HPLC column. Then, HPLC can only purify peptides one by one, and modifications typically complicate the purification step resulting in tedious optimization cycles, loss in yield, and enormous solvent consumption.

The Peptide Easy Clean (PEC) technology is a universal peptide manufacturing tool that significantly improves the speed and efficiency of the entire operation. The catch-and-release approach allows for the purification of peptides in automated liquid handling devices. PEC results in high-quality peptide libraries because the chemo-selective method removes most peptidic contaminants that might generate false-positive results, enhancing subsequent screening and validation test reliability. Using a new generation of PEC beads, a direct TFA cocktail immobilization strategy makes the precipitation step after SPPS redundant. This new feature accelerates the workflow significantly while at the same time dispensing solubilization issues for complex peptides. Furthermore, oxidation of the unprotected peptide attached to the purification resin allows for the efficient and quick late-stage formation of disulfide peptides in a combined purification and modification method.

We highlight these PEC features in therapeutically relevant case studies. For example, automated PEC helped manufacture hundreds of SARS-CoV-2 epitopes for vaccine research and development (e.g., T-cell activation assays). Also, we used PEC for the rapid manufacturing of Solnatide, a COVID-19 therapeutic, via on-resin disulfide formation. In a third example, we demonstrate the direct TFA cocktail immobilization strategy to synthesize and purify Bivalirudin in a green and fast peptide manufacturing workflow.