Peptide crystallization

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Crystallization

Peptide crystallization introduces greater complexity due to molecular flexibility and size. Each peptide requires unique insight to optimize crystallization conditions. There is no substitute for expertise and Cambrex's understanding of crystal formation and thermodynamics allows us to develop custom, scalable crystallization processes for peptides. We leverage the right tools with the best experts to bridge success from the bench to the plant.

Clear advantages

Having a crystalline solid form of a peptide offers clear advantages compared to the amorphous form:

- Significant impurity rejection
- Improved processability
- Enhanced drying properties
- Reduced hygroscopicity
- Increased stability
- Control of aggregation & gelling
- Cost advantage of crystallization when compared to column chromatography methods for purification
- Full structural determination

An in-depth understanding of the thermodynamic and kinetic processes that drive the crystallization for a specific peptide is required before the critical process parameters can be altered to achieve control over nucleation and crystal growth. Typically, crystallization operating ranges for larger peptides are much tighter than for smaller molecules, so the design and assessment of initial screening can make or break scale-up efforts.

Bespoke strategies

Cambrex employs a bespoke stepwise strategy to deliver crystallized peptides:

- **Milestone 1:** Initial high throughput crystallization assessment through solubility evaluation (solvents, pH, temperature, counterion inclusion and excipients), small-scale crystallization trials (free peptide or salt form) and single crystal growth.

There is no substitute for expertise.

Peptide crystallization introduces greater complexity than smaller molecules.

Each peptide requires unique insight to optimize individual conditions.

About Cambrex

Cambrex is a leading global contract development and manufacturing organization (CDMO) that provides drug substance, drug product, and analytical services across the entire drug lifecycle.

With over 40 years of experience and a growing team of over 2,200 experts servicing global clients from North America and Europe, Cambrex is a trusted partner in branded and generic markets for API and finished dosage form development and manufacturing.

- **Milestone 2:** Process development to deliver a controlled, robust and scalable crystallization, through investigation of the scalable elements of the process and assessment of the critical process parameters and conditions to achieve optimized yields, purity and filtration efficiency.
- **Milestone 3:** Technology transfer to ensure a successful crystallization process in the client's facility. Our experts use data from in-house experiments as well as state-of-the-art modeling software and process analytical tools to ensure consistent results in the plant.

Deliverables

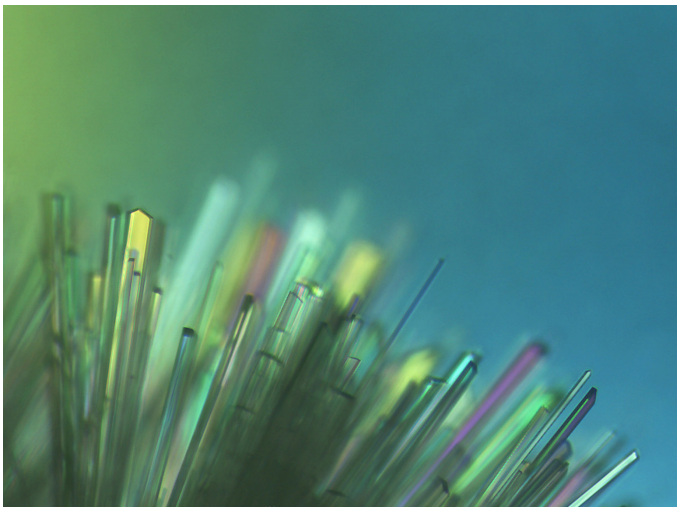
- Isolation of crystalline peptide
- Enhanced chemical purity/impurity profile
- High process yields
- Effective isolation and drying
- Improved downstream processing
- Successful technology transfer

Instrumentation

- Specialized high throughput screening plates
- Controlled reactor systems including Easymax/ automated parallel reactors
- Crystal 16
- Process analytical technology
  - FBRM/ParticleTrack
  - BlazeMetrics
  - Raman
- Isolation and drying
  - Pressure filtration and agitated filter dryer/tray drying
- Single crystal X-ray diffraction analysis
- Full solid form and analytical characterization capability

Process development workflow

- Solubility/identification of appropriate solvent matrix
- High throughput screening for locating initial crystals
- Crystallization trials for scale-up and development of initial promising conditions
- Metastable zone width measurements
- Identification and control of critical crystallization process parameters
  - 50mL to 5L
  - DynoChem scale up/scale down modelling
- Filtration and drying studies
- Design of Experiment (DoE) studies



While crystallization efforts are traditionally associated with smaller molecules, the step-wise approach employed by Cambrex has proven to be a successful strategy to tackle the design of peptide crystallization processes, adding to our command in this space of drug development. The increased understanding provided by these studies is a powerful tool for our clients to assess the potential of their peptide and to reveal its viability as a candidate for crystallization. Knowing whether the properties of a specific crystallized peptide will offer advantages over the amorphous material can prevent wasted scale-up efforts. Speak to Cambrex to find out how we are equipped with the expertise and tools to locate, understand and robustly scale-up crystalline solids of your peptide.