Protein Degradation Evaluation for Product Changeover

Degradation Study

Confidential Client

STUDY OVERVIEW

The laboratory conducted small-scale studies to investigate cleaning cycle induced protein degradation of multiple products.

The results aided the identification of a full-scale cycle capable of protein degradation, as well as the determination of an appropriate strategy for setting carryover limits for patient and product safety.

PROJECT DESCRIPTION

Cleaning cycle conditions of extreme pH and temperature (60°C - 80°C) are known to result in protein degradation [1]. Traditional maximum allowable carryover (MAC) assessments based on acceptable or permissible daily exposure (ADE or PDE) assume intact protein.

Thus, demonstrating the degree of degradation of the product can aid in setting more meaningful acceptance limits for carryover into the subsequent product.

The Hyde Analytical Laboratory was contracted to assess the effectiveness of the client's current full-scale batch cleaning and/or sterilization cycles in protein degradation for multiple products. Additionally, feasible cleaning conditions that could be implemented at full-scale were evaluated to determine a cycle capable of complete degradation of the products.

Degradation of the product at small scale was studied by exposing the process soil to simulated cleaning and/or steaming conditions. The degree of degradation was then assessed by subjecting the treated process soil to sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), which allowed for visualization and quantification of the protein degradation, as applicable.

SCOPE AND DELIVERABLES

Degradation Evaluation:

Determine the effectiveness of the current batch cleaning cycles in degrading the protein of interest. The current cleaning cycle parameters included 1M NaOH at ambient temperature and various concentrations and temperatures of CIP-100.

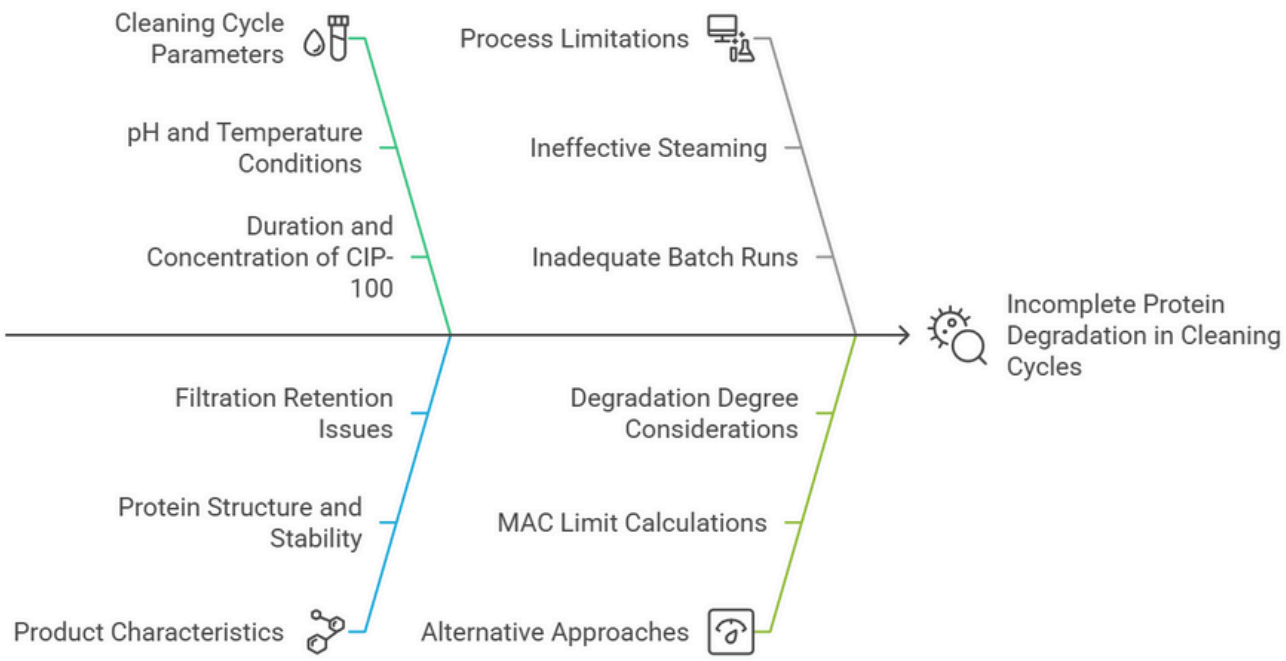
Cycle Parameter Comparison:

Evaluate multiple cycle parameters to identify the set of inputs that is capable of effective degradation of the protein. This included additional concentrations, temperatures, and durations of CIP-100 exposure that were feasible for implementation at full-scale.

Full-Scale Recommendation:

Provide a recommendation for cleaning cycle parameters that effectively degrade the proteins either via routine cleaning or a changeover cycle. Additionally, provide recommendations for an alternative approach to calculating MAC limits based on degraded protein.

ANALYZING PROTEIN DEGRADATION CHALLENGES IN CLEANING CYCLES



SOLUTIONS, RESULTS AND ACCOMPLISHMENTS

- **The current full-scale batch cycles do not achieve complete degradation of the products.** The current cleaning cycle achieves partial degradation of the proteins, but not full degradation of the intact protein. Additionally, all degradants were above the UFDF membrane cut-off size and would be retained with the product during filtration.

- **Steaming does not aid the degradation of the proteins.** Simulation of the current sterilization (steam) cycle did not result in effective degradation.

- **To achieve full degradation, the current batch cycle must be run in triplicate, or a changeover cycle is required.** The changeover cycle consisted of a higher concentration and temperature of CIP-100 as compared to the current batch cycle, as well as a longer duration.

- **If the recommended cleaning cycles cannot be implemented, an alternative approach to calculating MAC limits should be used.** The alternative approach accounts for the degree of degradation achieved during the current batch cleaning cycles.

lab@hyde-ec.com
www.hyde-ec.com
Louisville, Colorado, USA

Hyde ENGINEERING +CONSULTING