High Throughput Formulation of Biopharmaceuticals

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The formulation of protein drugs is a difficult and time-consuming process, mainly due to the complexity of protein structure and the very specific physical and chemical properties involved. This project concerns the application of high throughput screening techniques in protein formulation development.

A protein high throughput formulation (HTF) platform was developed. Basically, the HTF platform consists of two parts: (i) sample preparation and (ii) sample analysis. Sample preparation involves automated systems for dispensing the drug and the formulation ingredients in both liquid and powder form. The sample analysis involves specific methods developed for each protein to investigate physical and chemical properties of the formulations in microplates.

The use of multi-well plates has the advantage of screening in a short time many parameters using limited amount of sample. A thorough formulation screening will lead to a more complete understanding of the physical and chemical properties of the protein drug, which is needed for the development of safe and active protein drugs. The proof-of-concept of the HTF platform was tested with salmon calcitonin (sCT) as a model protein drug. The sCT physical stability was screened in a 100 formulations composed of 20 different buffer types on: i) protein concentration, ii) volume control by measuring pathlength, iii) turbidity (absorbance at 350 nm), iv) intrinsic tyrosine fluorescence, v) 1,8-ANS fluorescence and vi) Nile Red fluorescence (both are hydrophobic dyes).

Aggregation of sCT was observed independent of pH and buffer type. The screening of 100 sCT formulations resulted in several leads for further optimization. The best found candidate was the commercially used sodium acetate buffer which formed the proof-of-concept of the HTF platform.

References:

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