COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar

Wednesday, September 16, 2020
https://umich-health.zoom.us/j/5652976039
4:00-5:00 pm

"Forced Degradation in the Development of Biopharmaceutical Products"

Presented by:

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Abstract: Biotherapeutic products are complex molecules ranging from small peptides, such as GLP1, to large proteins, like monoclonal antibodies. Their therapeutic applications span across a wide variety of disease states including autoimmune disorders, cancers and infectious diseases. In the last few years, the pharmaceutical industry has seen a massive spike in the development of biologics - over 2,700 biologics were reported to be in development in 2018 alone. This trend is fueled by an ever-growing understanding of the efficacy and safety of biologics, as well as by recent advancements in applicable analytical characterization technologies. While academia, industry and regulatory bodies have made great strides in progressing biotherapeutics forward, there are still uncertainties surrounding the analytical characterization techniques that need to be conducted in order to ensure their post-market success.

In the first project discussed hereafter, we investigated the long-term stability of exenatide, a 39 amino acid GLP1 receptor agonist peptide used to treat type 2 diabetes. When the peptide, exenatide, was studied at elevated pH levels, we observed rapid chemical degradation, a pH-dependent increase of deamidation impurities, and physical degradation. We attributed these product degradations to aggregation, loss of α-helicity and, subsequently, to an increase of unordered structural content. Such degradations were also observed after the addition of common excipients to the peptide solution, despite some of their presumed protective functions. In fact, trehalose seemed to further destabilize exenatide. In the second project presented here, our goal was to establish a characterization method to detect and quantify disulfide bonds, shuffled disulfide bonds and trisulfide bonds in two monoclonal antibodies, innovator Remicade® and biosimilar Remsima™. We observed a drastic pH-dependence in the presentation of artifacts stemming from trypsin digestion. At the higher of the two pH values studied, pH 8, we noticed that there was greater disparity between the innovator and biosimilar in the number and types of disulfide bonds and artifacts formed during digestion. Our analysis at pH 5, however, showed no differences between Remicade® and Remsima™ in terms of expected and shuffled disulfide bonds.

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