Title: Characterization of protein-excipient interactions for designing formulation

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Abstract (upto 300 words)

Proteins often perform diverse and complex set of functions within the cell, including catalyzing metabolic reactions, transport of specific substances from one location to another, etc. Therefore, proteins are regularly used in protein-based therapies to treat diseases. They have numerous advantages over small molecule drugs, as human body naturally produce many of the therapeutic proteins, also called biologics. Biologics are often characterized by high specificity and potency with low toxicity, and thus have interested many pharmaceutical industries. Several challenges confront pharmaceutical scientists involved in the development of protein therapeutics. For instance, the proper stabilization of biologics is one of the major concerns. To overcome this issue, excipients play a major role in stabilizing biologics to prevent protein-protein interactions and hence aggregation. Currently, a detailed molecular understanding of the effect of different physicochemical formulation conditions on the stability of proteins are sparse as molecular interactions are difficult to investigate experimentally at the molecular level. Thus, computational approaches as applied in the current study can provide insight on the single-molecule level.

The main objectives are to identify potential hotspots for excipient-protein interactions, to determine preferential interaction coefficients of excipients using molecular docking approaches further validated by molecular dynamics (MD) simulations. Using free energy approaches such as implicit solvent molecular mechanics (MM-PBSA) and explicit solvent linear interaction energy (LIE) methods, relative binding affinities of excipients to the proteins are predicted in order to rank excipients and to determine the effect of excipients on protein dynamics and flexibility.
Additionally, independent protein MD simulations were performed and further analyzed for potential protein-excipient interaction hotspots by using a clustering method to find the most representative structures from the simulations and then applying FTMap to locate potential hotspot region for protein-excipient interactions. These results will be further supported by NMR studies.

Biography (upto 150 words)

Sowmya Indrakumar holds a Bachelor of Science (by Research) and Master of Science degree in Biology from Indian Institute of Science, Bangalore, India. Throughout her undergraduate studies, she was a recipient of 'Innovation in Science Pursuit for Inspired Research-Department of Science & Technology (INSPIRE-DST) fellowship. In 2016, she became part of the PIPPI (http://www.pippi.kemi.dtu.dk/) project as a PhD researcher at Technical University of Denmark, Denmark. This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant.

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