INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: **Shear and thermal induced aggregation of amyloidogenic and non-amyloidogenic proteins and the effect of a neuroprotective plant, *Centella asiatica* on protein aggregation**

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SHORT ABSTRACT

Shear-induced protein aggregation contributes to aberrant folding, impacting conditions like Alzheimer's disease and thrombosis, with shear forces arising from cerebrospinal fluid flow and vascular abnormalities. In pharmaceutical industries, proteins undergo shear stress from processes like stirring, filling, pumping and freeze-thawing, introducing thermomechanical energy. Understanding shear and thermomechanical aggregation is crucial for both physiological and therapeutic contexts. With this account, two amyloidogenic proteins i.e. Amyloid beta 1-40 [Aβ (1-40)] and Hen egg white lysozyme (HEWL) and two non-amyloidogenic proteins i.e. Bovine serum albumin (BSA) and Bovine fibrinogen (BFG) were selected for study pertaining to the thermomechanical induced aggregation in this doctoral work. To address the aggregation issue, crude extract of neuroprotective plant *Centella asiatica* (*C.asiatica*) was checked for its impact on the aggregation of protein from one of each type studied. The entire thesis has been divided into four main sections. In the first section, shear and thermally induced aggregation of the above two amyloidogenic proteins, Aβ (1-40) and HEWL, were studied. The impact of varying shear as well as constant shearing on Aβ (1-40) was performed, and the impact of pre-shearing on HEWL was determined. In the second part, the impact of the thermomechanical treatment on two non-amyloidogenic proteins, BSA and BFG, were performed. In the first study, the energetics of the thermomechanical treatment of BSA, along with its related impact on the unfolding and aggregation behaviour, have been explored to decipher the roles of the thermal as well as the dissipation energy. Similarly, thermomechanical and thermal induced aggregation were compared and studied in BFG. In the next section, a neuroprotective plant, *C.asiatica* was extracted and characterised. In the last (fourth) section, the extracts of *C.asiatica* were checked for their inhibitory properties against the shear and thermally induced aggregation of BSA, and on the thermally induced aggregation of HEWL. The binding energetics of the extract with these two proteins were also determined through various fluorescence as well as calorimetric techniques. Further, the impact of the aggregates in the presence and absence of the extract was also determined on a neuroblast cell line IMR32 as ultimately, the impact of the extract as well as the aggregates needs to be comprehended on a cellular level. To sum up, the various macro and microanalysis of thermomechanical impact on amyloidogenic as well as non-amyloidogenic proteins was determined and could reveal crucial elements mainly in terms of their secondary structure. The *C.asiatica* extract, through interaction with the monomeric protein, significantly inhibits

thermomechanical as well as thermal induced aggregation. The toxicity of aggregates, mainly the amyloidogenic HEWL, could be protected to an extent by the presence of *C.asiatica* extract. This doctoral work explores the mechanistic insights related to the thermomechanical-induced protein aggregation and its potential prevention using natural sources like *C.asiatica*, offering valuable insights for innovative therapeutic strategies.

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