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Dissertation Outline

Dissertation Title: Development of Oligo(ethylene glycol) derivatives for suppression of protein aggregation

This dissertation focuses on the suppression of amyloid fibrillation and amorphous protein aggregation using both cyclic and acyclic oligo(ethylene glycol) (OEG) derivatives. It is organized into five chapters:

1. **General Introduction**: This chapter provides an introductory background to protein aggregation research, as well as an overview of existing inhibitors and their limitations.
2. **Establishing a new protocol to study protein fibrillation**: Chapter 2 presents a novel approach for studying protein fibrillation using UPLC chromatography. This technique addresses the limitations of traditional Thioflavin T (ThT) assays, such as competitive binding and false negatives. UPLC effectively detects the disappearance of soluble protein components in the presence of additives that shows mature fibril formation, offering more accurate insights into fibrillation. The chapter also emphasizes the advantages of UPLC in identifying deamidated protein species.
3. **Effect of Oligo(ethylene glycol) derivatives on protein fibrillation**: Chapter 3 explores the suppression of protein fibrillation. The results demonstrate that acyclic OEG derivatives containing naphthalene exhibit better inhibitory effects on insulin fibrillation and moderate effects on lysozyme fibrillation. Conversely, COEGOCH3 slightly accelerates fibrillation, showing the importance of balancing hydrophobic and hydrophilic moieties in designing effective inhibitors.
4. **Effect of Oligo(ethylene glycol) derivatives on protein aggregation**: Chapter 4 focuses on amorphous aggregation. It reveals that cyclic COEGOCH3 molecules and naphthalene derivatives significantly suppress lysozyme aggregation, while COEGNH derivatives show no inhibitory effects. Interestingly, acyclic molecules are more effective than cyclic derivatives in preventing protein aggregation, further highlighting the importance of molecular structure in inhibiting protein aggregation.
5. **Conclusion and perspectives**: The final chapter summarizes the findings and discusses the broader implications of the research. Although the mechanism of aggregation inhibition remains unclear, this work provides a foundation for further studies on inhibition mechanisms. It also opens up the possibility of developing new therapeutic strategies for neurodegenerative diseases, such as Alzheimer's, in the future.