Development of a Therapeutic Drug for Alzheimer's Disease: A Chemical Approach to Cease Amyloidosis

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Alzheimer's disease (AD) is a disease destroying humanity. Researches suggest that the aggregation of misfolded beta-amyloid is responsible for Alzheimer's disease. pi-Stacking, the key force that causes deadly oligomers of amyloid to aggregate, is manipulated to go against the phenomenon itself. Thus, a strategic chemical approach to terminate the aggregation is boldly attempted. Based on previous results, initially, organic compounds were attempted to be synthesized. These potential drugs showed a strong self-aggregation power which boasted the strong pi- stacking ability. However, disappointingly, when the drug was tested for dissemination of aggregation of beta amyloid, the drug caused more severe aggregation compared to the self-aggregation, itself. In order to improve drug's aggregation inhibiting ability, the more polar dipeptide was synthesized through solid phase synthesis. After successful synthesis, self-aggregation tests were carried out and reveal that the strong pi-stacking power was preserved from the previous organic molecules, thus exhibiting high self-aggregation activity. However, again, although somewhat improved, the mediating activity of the dipeptide drug was not strong enough. Once again, the peptide was further modified to improve the efficiency of the role of the mediator. Series of computational research led to the idea of introducing additional hydrogen bonding ability to the short peptide chain, thus aiding in the ability to mediate. A longer peptide drug was synthesized and put in in vitro tests for prevention of the progress of the aggregation of amyloid. Finally, the increasing trend of the turbidity stopped upon the addition of the mediator, showing strong drug activity.

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