Master thesis (Abstract)

Development of a Cyclic Peptide as a Therapeutic Tool against Alzheimer's Disease

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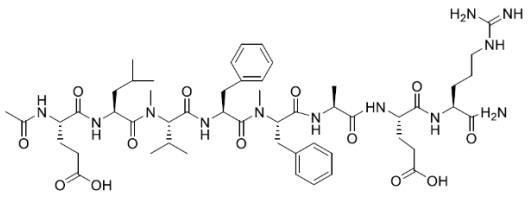
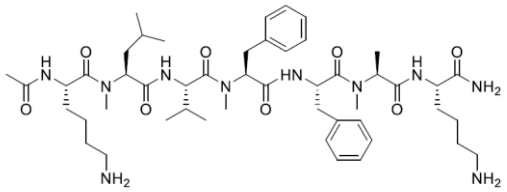
Alzheimer's disease, the leading cause of dementia, is a progressive neurodegenerative disorder. It is the most significant risk factor for aged people. It actually destroys the neuronal connection (synapse), which can result neuronal death. After several research studies regarding Alzheimer's disease, it can be concluded that aggregation of Amyloid-β, which results plaques in between neurones, is mainly responsible for this. So, various types of researches have been done to find out new strategies for preventing aggregation or disrupting the amyloid fibrils.

In this project, we have designed and synthesised a cyclic peptide that intends to disrupt amyloid aggregation under physiological conditions, and so it can be used as a therapeutic tool against AD. We chose cyclic peptide as it has some special advantages over the linear peptide for its conformational rigidity.

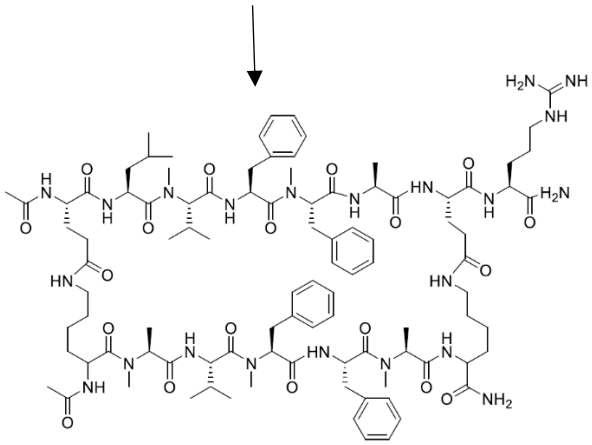
After isolating pure peptide, we are going to use this to industrially available Aβ in PBS buffer at the physiological condition. Then, by using Fluorescence Spectroscopy, IR spectroscopy, TEM, CD, etc. we are going to study the disruption process in a time-dependent manner. Aβ peptide mainly exists in β-sheet conformation. The cyclic peptide was designed in such a way that it can bind from both faces of the β-sheet conformation via mostly hydrophobic interaction, leaving zero possibility of further hydrogen bonding with another β-sheet structure (by N-Methylation). So, aggregation can be disrupted.

$CH_3CO\text{-}EL(^{Me}N)VF(^{Me}N)FAER\text{-}CONH2$ $CH_3CO\text{-}K(^{Me}N)LV(^{Me}N)FF(^{Me}N)AK\text{-}CONH_2$





P1 (Intermolecular side chain cyclisation) P2



P1 +P2 (Cyclic Peptide)

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