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Loss of α-helical structure of β-amyloid monomer: A computational study

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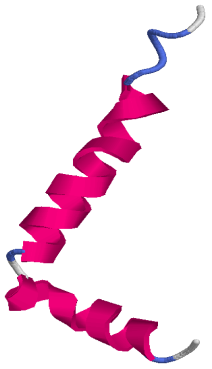
Alzheimer's disease (AD) is a progressive neurodegenerative disease. It is a common form of dementia among the elderly (mainly above 64 years of age). AD brains are characterized by the deposition of proteinaceous aggregates. The major component of amyloid plaques are the β-amyloid peptides with a length from 1 – 39 to 1 – 42 amino acids. The peptide with a length of 1 – 42 amino acids is observed to have the highest percentage in plaques. The mechanism by which the β-amyloid protein misfolds is not completely understood.

A 100 ns long molecular dynamics simulation study was carried out on β-amyloid, a polypeptide with 42 amino acids, in aqueous medium to understand the mechanism of the change in a-helical structure of β-amyloid protein to an aggregation prone conformation. The β-amyloid 1-42 monomer was placed in a cubical box containing SPC/E water. The simulation was conducted using GROMOS 53a6 force field on a LINUX operating system.



β-amyloid

From the simulation results, it was observed that the backbone torsion angles; ϕ and ψ, were concentrated at; ϕ around -120° and ψ around +135° region in the Ramachandram plot for valine and isoleucine, the amino acids which are known to favor β-sheet formation. These observations are in agreement with one of the aggregation mechanisms suggested from NMR experiment and theoretical studies.

Keywords: Alzheimer's disease, aggregation, β-amyloid, molecular dynamics, protein unfolding

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