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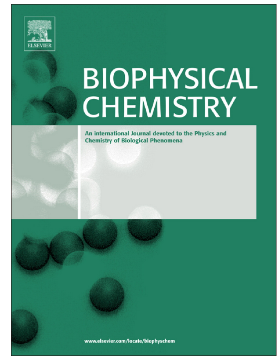

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Capping effects on polymorphic Aβ_{16-21} amyloids depend on their size: a molecular dynamics simulation study

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Abstract

Understanding Aβ amyloid oligomers associated with neuro-degenerative diseases is needed due to their toxic characteristics and mediation of amyloid fibril growth. Depending on various physiological circumstances such as ionic strength, metal ion, and point-residue mutation, oligomeric amyloids exhibit polymorphic behavior and structural stabilities, i.e. showing different conformation and stabilities. Specifically, experimental and computational researchers have found that the capping modulates the physical and chemical properties of amyloids by preserving electrostatic energy interactions, which is one of the dominant factors for amyloid stability. Still, there is no detailed knowledge for the polymorphic amyloids with reflecting the terminal capping effects. In the present study, we investigated the role of terminal capping (i.e. N-terminal acetylation and C-terminal amidation) on polymorphic Aβ_{16-21} amyloid oligomer and protofibrils via molecular dynamics (MD) simulations. We found that the capping effects have differently altered the conformation of polymorphic antiparallel-homo and –hetero Aβ_{16-21} amyloid oligomer, but not Aβ_{16-21} amyloid protofibrils. However, regardless of polymorphic composition of the amyloids, the capping induces the thermodynamic instabilities of Aβ_{16-21} amyloid oligomers, but does not show any distinct affect on Aβ_{16-21} amyloid protofibrils. Specifically, among the molecular mechanic factors, electrostatic energy dominantly contributes the thermodynamic stability of the Aβ_{16-21} amyloids. We hope that our computation study about the role of the capping effects on the polymorphic amyloids will facilitate additional efforts to enhance degradation of amyloids and to design a selective drug in the future.

Keywords: Aβ, Amyloids, Polymorphism, Capping effect, Molecular Dynamics (MD)