18th National and 3rd International Conference of Iranian Biophysical chemistry

هجدهمین همایش ملی و سومین همایش بین المللی بیوشیمی فیزیک ایران

25-26 Des, 2024, University of Hormozgan

۶-۵ دی ماه ۱۴۰۳، دانشگاه هرمزگان

Inhibition of A53T Alpha-Synuclein Fibrillation by Quercetin and Deep Eutectic Solvents

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Abstract

The aggregation of the alpha-synuclein protein, particularly the A53T mutant, is strongly linked to neurodegenerative diseases like Parkinson's disease. Inhibiting alpha-synuclein fibrillation is a promising therapeutic strategy. Quercetin, a bioactive flavonoid known for its antioxidant and anti-aggregative properties, has limited solubility in aqueous environments, hindering its therapeutic use. Recently, deep eutectic solvents (DES) are eco-friendly solvents that can enhance the solubility of hydrophobic compounds. This study investigates the inhibitory effects of quercetin dissolved in DES on A53T alpha-synuclein fibrillation. Using fluorescence microscopy and fibrillation kinetics, we assess the ability of this combination to reduce protein aggregation, suggesting a potential therapy for neurodegenerative diseases. Fluorescence microscopy results demonstrated that quercetin dissolved in DES significantly curbs the fibrillation of A53T alpha-synuclein, as indicated by the reduced formation of fibrils. Furthermore, kinetic analysis revealed that quercetin dissolved in DES prolonged the lag phase of fibrillation from 7 hours to 12 hours, indicating a marked delay in the aggregation process. These findings suggest that quercetin, when combined with DES, can effectively impede the initial stages of protein fibrillation. Our research highlights the therapeutic potential of quercetin in DES for protein misfolding disorders, offering new avenues for research in treating neurodegenerative diseases such as Parkinson's disease.

Key words: Alpha-synuclein; Parkinson's disease; Fibril; Quercetin; Deep eutectic solvents