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Preventing Neurodegenerative Diseases by Stabilization of Superoxide Dismutase by Natural Polyphenolic Compounds

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Abstract : Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease caused by misfolding and aggregation of Cu, Zn superoxide dismutase (SOD1). The use of small molecules has been shown to stabilize the SOD1 dimer and preventing its dissociation and aggregation. In this study, we employed molecular docking, molecular dynamics simulation and surface plasmon resonance (SPR) to study the interactions between SOD1 and natural polyphenolic compounds. In order to explore the noncovalent interaction between SOD1 and natural polyphenolic compounds, molecular docking and molecular dynamic (MD) simulations were employed to gain insights into the binding modes and free energies of SOD1-polyphenolic compounds. MM/PBSA methods were used to calculate free energies from obtained MD trajectories. The compounds, Hesperidin, Ergosterol, and Rutin showed the excellent binding affinity in micromolar range with SOD1. Ergosterol and Hesperidin have the strongest binding affinity to SOD1 and was subjected to further characterization. Biophysical experiments using Circular Dichroism and Thioflavin T fluorescence spectroscopy results show that the binding of these two compounds can stabilize SOD1 dimer and inhibit the aggregation of SOD1. Molecular simulation results also suggest that these compounds reduce the dissociation of SOD1 dimers through direct interaction with the dimer interface. This study will be helpful to develop other drug-like molecules which may have the effect to reduce the aggregation of SOD1.

Keywords : amyotrophic lateral sclerosis, molecular dynamics simulation, surface plasmon resonance, superoxide dismutase
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