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Aspirin Re-Modification as a Multitarget Candidate for Broad-Spectrum Neurodegenerative Diseases: An *In Silico* Study

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Neurodegenerative diseases, including Alzheimer's, Parkinson's, Huntington's, and amyotrophic lateral sclerosis, share overlapping mechanisms such as oxidative stress, neuroinflammation, protein aggregation, and kinase dysregulation. Existing therapies mainly provide symptomatic relief, with limited disease-modifying effects, highlighting the need for multitarget drug approaches. In this study, we explored an aspirin modification with a 4-fluorobenzoyl group and apocynin, aimed at improving antioxidant and anti-inflammatory capacity while broadening activity against neurodegenerative pathways. Target prediction identified glycogen synthase kinase-3β, phosphodiesterase- 4B, cyclooxygenases, and transthyretin as relevant proteins. Docking analysis demonstrated favorable binding affinities across these targets, supporting the potential to modulate tau phosphorylation, amyloid stabilization, synaptic signaling, and inflammatory cascades. In silico ADMET profiling predicted blood–brain barrier penetration, oral bioavailability, and compliance with drug-likeness rules, while toxicity models indicated an acceptable safety margin without major mutagenic or carcinogenic liabilities. Compared with classical aspirin, this modification showed stronger multitarget interactions, positioning it as a promising candidate for broad-spectrum neurodegenerative therapy. Further experimental validation in cellular and animal models is required to establish clinical potential.

Keywords: Aspirin derivative, Drug repurposing, In silico, Multitarget therapy, Neurodegeneration

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