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MOLECULAR DOCKING OF FLAVONOIDS ISORHAMNETIN AND MYRICETIN WITH PARKINSON'S-RELATED TARGETS

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Abstract

The present *in silico* investigation highlights the potential of two naturally occurring flavonoids, Isorhamnetin and Myricetin, as biologically relevant ligands interacting with target proteins associated with cellular stress regulation and neurodegenerative processes in Parkinson's disease (PD). Using molecular docking approaches, their affinity toward cyclin-dependent kinase 2 (CDK2; PDB ID: 3LFN) and DJ-1 (PDB ID: 1P5F) was systematically explored.

This study provides computational evidence that the flavonoids Isorhamnetin and Myricetin demonstrate favorable binding affinities with two proteins implicated in oxidative stress regulation and neurodegenerative pathways relevant to Parkinson's disease: cyclin-dependent kinase 2 (CDK2; PDB ID: 3LFN) and DJ-1 (PDB ID: 1P5F). Molecular docking analyses conducted in 5 independent sessions revealed that both ligands form stable complexes with these targets.

The 3D crystal structures of DJ-1 (PDB ID: 1P5F) and CDK2 (PDB ID: 3LFN) were retrieved from the RCSB Protein Data Bank. Ligand structures of Isorhamnetin and Myricetin were obtained from PubChem. Molecular docking with optimized proteins was performed in UCSF Chimera (www.cgl.ucsf.edu/chimera) using AutoDock Vina. Results were analyzed with BIOVIA Discovery Studio Visualizer 4.5.

Both Isorhamnetin and Myricetin exhibited stronger interactions with CDK2, achieving docking scores of −8.1 (fig. 1), indicative of energetically stable and potentially functionally relevant binding.

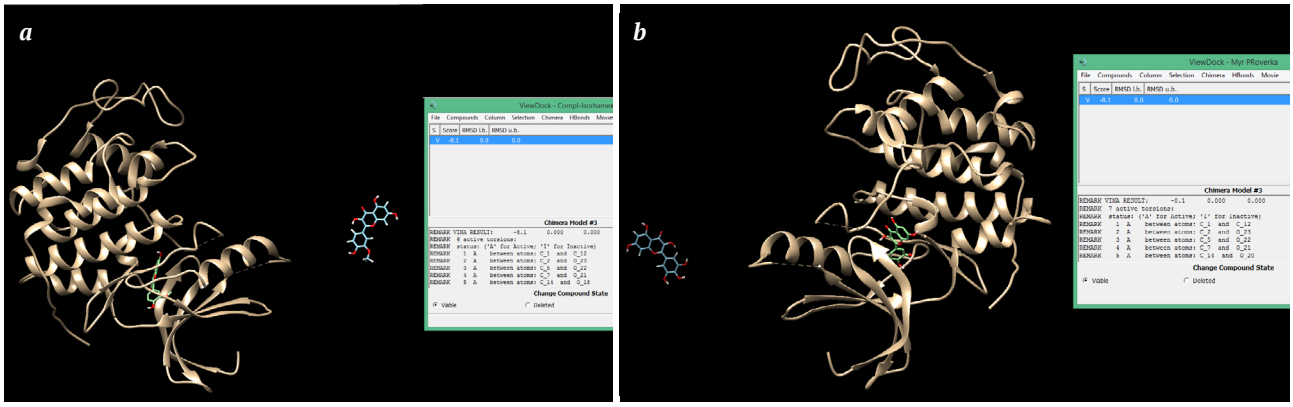

Fig. 1. Isorhamnetin (*a*) and Myricetin (*b*) achieving docking scores of −8.1 with CDK2 (PDB ID: 3LFN)

The interactions with DJ-1 were also notable (fig. 2), yielding docking scores of −6.6 for Isorhamnetin and −6.5 for Myricetin, suggesting a moderate but potentially biologically meaningful binding capacity that could influence DJ-1's redox-regulatory functions under oxidative stress conditions.

Regarding DJ-1 (ID:1P5F), a protein well-characterized for its neuroprotective functions under oxidative stress, both ligands exhibited moderate but notable binding affinities. Isorhamnetin docked with a score of −6.6, and Myricetin with −6.5. Given DJ-1's role as a multifunctional oxidative stress sensor and chaperone protein, these interactions may contribute to enhanced structural stability or functional modulation of the protein under pathological conditions.

The dual-target affinity of these compounds supports a multi-target therapeutic hypothesis in the context of PD. By simultaneously engaging proteins involved in oxidative stress regulation (DJ-1) and cell cycle/apoptotic pathways (CDK2), Isorhamnetin and Myricetin may offer a synergistic mechanism of neuroprotection. This is particularly rele-

vant for the development of disease-modifying strategies that go beyond symptomatic relief to address core pathogenic mechanisms.

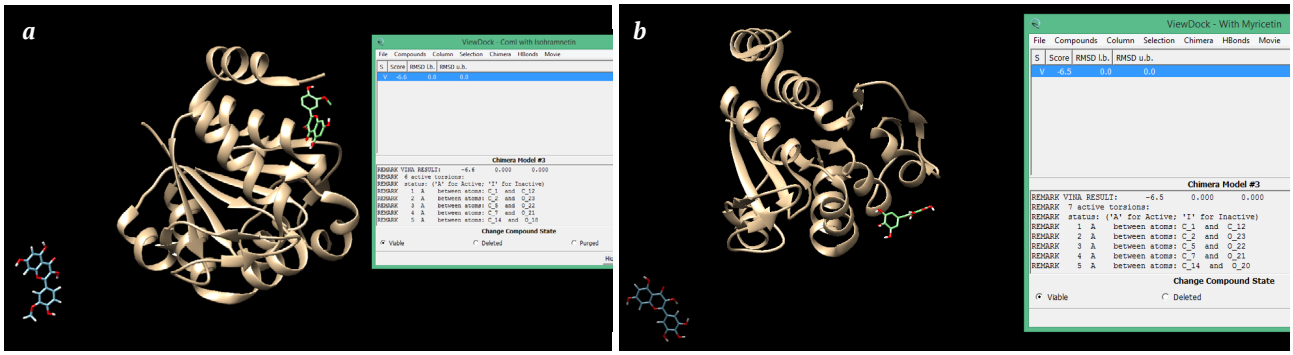

Fig. 2. Isorhamnetin (*a*) and Myricetin (*b*) achieving docking scores of –6.6 and –6.5 with DJ-1 (PDB ID: 1P5F)

Furthermore, both flavonoids are known for their antioxidant, anti-inflammatory, and neuroprotective properties in various experimental models. Their plant-derived origin and documented bioactivity strengthen the rationale for repurposing them as lead compounds in neurodegenerative research pipelines. Taken together, this study reinforces the value of *in silico* docking as a preliminary screening tool to identify phytochemicals with therapeutic potential against PD.

In conclusion, the docking profiles of Isorhamnetin and Myricetin suggest that they are promising candidates for further research as potential multi-target therapeutic agents for the prevention or attenuation of Parkinson's disease progression.

References

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