**Multi-Target Drug Therapeutics for Chronic Obstructive Pulmonary Disease: In Silico Study of Ergosterol and Apigenin 7-β-D-glucoside**

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**Background and aims.** Chronic obstructive pulmonary disease (COPD) is a complex disease requiring multi-target therapeutic approaches. This study investigated the potential of two natural compounds - ergosterol and apigenin 7-β-D-glucoside, both used in traditional medicine - as multi-target drugs for COPD treatment through computational analysis.

**Methods.** Molecular docking was performed using AutoDock Vina to evaluate interactions between the compounds and nine COPD-related proteins including phosphodiesterases (PDE3A, PDE3B, PDE4A, PDE4B, PDE4D), receptors (adenosine A2a, muscarinic M5, substance-P), and NAD-dependent deacetylase sirtuin-1. Best-docked poses underwent 100ns molecular dynamics simulations using GROMACS with amber99sb-ildn forcefield. Binding free energies were calculated using MM/GBSA method. Stability was assessed through RMSD, RMSF, and radius of gyration analyses.

**Results.** Ergosterol demonstrated stable interactions with all nine proteins (RMSD < 0.8nm, Rgyr < 3.5nm) with binding free energies ranging from -33.48 to -59.22 kcal/mol. Apigenin 7-β-D-glucoside showed stable interactions with eight proteins (excluding substance-P receptor 6HLL) with binding free energies from -34.38 to -59.20 kcal/mol. Both compounds exhibited particularly strong binding to adenosine A2a receptor (3PWH).

**Conclusion/Discussion.** Both ergosterol and apigenin 7-β-D-glucoside demonstrated potential multi-target interactions with phosphodiesterases, bronchodilator receptors, and anti-inflammatory targets. These findings suggest both compounds could serve as promising candidates for COPD treatment, acting simultaneously as anti-inflammatory agents and bronchodilators.