**Phytochemicals Based Drug Discovery: An *in-silico* Evaluation of Three Traditional Botanicals in a marketed polyherbal formulation.**

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**Background and aims.** A multi-herbal formulation containing Devil’s Claw, Boswellia serrata, and Rosehip extracts, offered a synergistic approach to target inflammatory pathways, oxidative stress, and cartilage repair. This study aimed to evaluate the binding efficacy, stability, and pharmacokinetic profiles of phytochemicals present in the multi-component herbal preparation against their respective targets using *in-silico* approaches. Specific objectives included analyzing COX-2 inhibition by Devil’s Claw iridoids, 5-LOX suppression by Boswellia’s boswellic acids, and CP4H modulation by Rosehip’s bioactive compounds to determine their anti-inflammatory and chondroprotective mechanisms.

**Methods.** Computational tools from the Schrödinger Suite 2025-1 were employed for molecular docking, molecular dynamics simulations, MM-GBSA calculations, and ADMET profiling. Protein structures (PDB IDs: 5KIR for COX-2, 6NCF for 5-LOX, 6TEC for CP4H) were prepared and docked with phytochemicals present in the polyherbal formulation and reference drugs. Ligand stability, interaction patterns, and pharmacokinetic compliance (Lipinski’s rules) were assessed.

**Results.** Harpagide, pytochemical from Devil’s Claw, exhibited strong COX-2 binding (docking score: -10.26 kcal/mol), forming hydrogen bonds with TYR355 and PHE518, comparable to Celecoxib (-10.29 kcal/mol). MD simulations confirmed stable ligand-protein interactions (RMSD <2.5 Å).

Similarly Acetyl-11-keto-β-boswellic acid present in Boswellia showed moderate 5-LOX inhibition (docking score: -4.58 kcal/mol), though MD revealed ligand instability (RMSD up to 40 Å). Zileuton (-4.88 kcal/mol) demonstrated superior binding.

Vitamin C present in Rosehip displayed robust CP4H interactions (docking score: -9.26 kcal/mol), stabilizing collagen biosynthesis via ionic bonds (LYS89, ASP112) and hydrophobic contacts. ADMET profiles of all phytochemicals aligned with drug-likeness criteria.

**Conclusion/Discussion.** The *in-silico* analyses validated the multi-target therapeutic potential of the polyherbal formulation. Devil’s Claw and Rosehip extracts demonstrated strong, stable interactions with COX-2 and CP4H, respectively, while Boswellia’s 5-LOX inhibition, though less stable, synergized with other components. The phytochemicals of this polyherbal formulation showed good binding with the respective protein targets, thus confirming their use as herbal supplements for treating inflammation, oxidative stress, and cartilage repair simultaneously.

**References:**

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