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Exploring Phytochemicals in *Glycyrrhiza Glabra* L. Root as Potential Therapeutics for Gastroesophageal Reflux Disease: A Molecular Docking and Dynamics Study

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Phytochemicals offer diverse molecular structures that can target various biological pathways, making them promising candidates as novel therapeutic agents. This study investigates the phytochemicals present in *Glycyrrhiza glabra* L. (Licorice) root as a potential alternative treatment for Gastroesophageal Reflux Disease (GERD) as the conventional therapies still provide limited therapeutic benefits with more side effects. Thirty-four major phytochemicals belonging to three secondary metabolites (flavonoids, tannins, and coumarins) were selected for virtual screening against the histamine H_2 receptor (H_2R), keeping Famotidine as the reference drug. The 3D structures of these compounds were sourced from the PubChem database and docked with H_2R (PDB ID: 7UL3) using the AutoDock Vina 1.2 docking package. Based on the docking results, selected phytochemicals and protein complexes underwent Molecular Dynamics (MD) simulations with GROMACS mimicking physiological conditions and under the CHARMM36 force field to evaluate the stability of the complexes over 100ns. Molecular docking results showed that Isoliquiritigenin 1 and Licochalcone B 80 had binding affinities of -6.0 kcal/mol and -6.4 kcal/mol, respectively, compared to -5.5 kcal/mol for Famotidine. MD simulations confirmed the stability of these complexes, with acceptable Root Mean Square Deviation (RMSD), Root Mean Square Fluctuation (RMSF), Radius of Gyration (RoG), and Solvent Accessible Surface Area (SASA) values. Additionally, the selected phytochemicals displayed favorable pharmacokinetic properties, with no violations of Lipinski's rule and favorable toxicity profiles according to SwissADME and Protox-II results. The study suggests Isoliquiritigenin 1 and Licochalcone B 80 are potential novel therapeutic agents for GERD. Yet, further *in-vitro* and *in-vivo* studies are required to confirm their efficacy and safety.

Keywords: *Glycyrrhiza glabra L., molecular docking, molecular dynamic*