Computational Evaluation of *Hemidesmus indicus* Phytochemicals as Potent HSP90 Inhibitors in Ovarian Cancer Treatment

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Abstract

Ovarian cancer is the most lethal gynaecological malignancy and a significant cause of cancer-related mortality in women, primarily due to its identification at an advanced stage. Present therapies are frequently costly and ineffective, necessitating the urgent exploration of new therapeutic approaches. HSP90, a molecular chaperone, is essential for stabilizing oncogenic proteins that drive cancer growth, making it an attractive target for pharmacological development. Our study utilized receptor-based molecular docking to evaluate bioactive phytochemicals from *Hemidesmus indicus* (L.) R. Br. ex-Schult for their potential to inhibit HSP90. This methodology identified three principal compounds: rutin, isoquercetin, and indicine, which exhibited XP docking scores between −11.73 and −14.99 kcal/mol, advantageous binding conformations, and robust MMGBSA binding free energy estimates ranging from −74.61 to −80.93 kcal/mol. Pharmacokinetic forecasts further corroborated their drug-like characteristics. MD simulations were employed to investigate the structural stability of the HSP90−ligand complexes by analyzing RMSD, RMSF, radius of gyration, and hydrogen bonding. Furthermore, an examination of the free energy landscape based on the main components identified stable, low-energy conformations, whereas MMPBSA computations validated strong interactions with essential residues in the binding pocket. The computational results indicate that the identified phytochemicals may serve as effective HSP90 inhibitors for ovarian cancer treatment; nevertheless, additional *invitro*

investigations are required to validate their efficacy and enhance their potential as anti-cancer medicines.

Keywords: *Ovarian cancer; Bioactive phytochemicals; MD simulation; Principal component analysis; Free energy landscape*