

RESEARCH ARTICLE

Anticancer Activity, DFT, Molecular Docking, ADMET, and Molecular Dynamics Simulations Investigations of Schiff Base Derived From 2,3-Diaminophenazine and Its Metal Complexes

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ABSTRACT

In our previous study, Schiff base (1) complexes derived from 2,3-diaminophenazine and metal ions Co(II) (2), Ni(II) (3), Cu(II) (4), and Cd(II) (5) were synthesized and characterized, demonstrating a significant biological activity. This study investigates their anticancer potential, specifically against prostate cancer. The complexes exhibited notable reductions in cancer cell viability, with IC_{50} values of 0.531 μ M Ni(II), 0.630 μ M Cu(II), and 0.655 μ M Co(II), comparable with the standard drug enzalutamide. The Co(II) complex showed the highest efficacy, while Cd(II) displayed the lowest (IC_{50} = 0.648 μ M). The presence of a phenazine ring in these complexes enhances DNA binding, contributing to their anticancer effects. HOMO-LUMO calculations revealed energy gaps ranging from 2.525 to 3.294 eV, indicating varying reactivity and potential for biological interactions. Molecular docking studies revealed that compound (1) exhibited the highest binding affinity (−9.19 kcal/mol) for the prostate cancer-related receptor, with significant hydrogen bond interactions. Molecular dynamics simulations over 100 ns demonstrated stable binding, with RMSD values below 1.5 Å, and RMSF analysis provided insights into protein flexibility. ADMET studies revealed favorable drug-like properties, including good gastrointestinal absorption (> 30%), high blood–brain barrier permeability (LogBBB = 0.64), and high human intestinal absorption (68.47%–88.79%). No inhibition of CYP2D6 was observed, suggesting low risk for drug–drug interactions. These Schiff base-metal complexes show promising anticancer activity and favorable ADMET profiles, indicating their potential as therapeutic agents for prostate cancer treatment.