Title	**Co(II), Ni(II), and Cu(II) complexes of Schiff base derived from 1, 2, 4-triazine: synthesis, spectroscopic characterization, anti-cancer activity, DFT and molecular docking studies with a COVID-19 protein receptor**

Abstract

Three innovative cobalt(II), nickel(II), and copper(II) Schiff base complexes derived from 1,2,4-triazine were synthesized and fully characterized via physicochemical and spectral tools. The elemental analysis and spectroscopic data proved that the ligand behaves as a bidentate ligand and coordinates to the metal ion through the nitrogen of azomethine group and N2-triazine ring in a 1:2 (metal: ligand) ratio. The molar conductance data of the complexes confirmed the electrolytic nature of the complexes. To confirm the molecular geometry of the complexes, DFT calculations were applied that confirmed the octahedral structure of the complexes. The geometry optimization results agree with the experimental observations. The stability of the complexes has been confirmed by TG-DTG measurements. The in vitro antimicrobial potency of the free Schiff base ligand and the reported complexes was tested against different types of bacterial strains. It was found that the complexes have higher antibacterial activities than those of the free ligand, especially the Cu(II) complex which displayed the highest activity compared to the other complexes. These results have shed light on using these complexes in the bioinorganic chemistry field. The antitumor potency of the free ligand and its complexes was inspected against human breast cellular carcinoma (Mcf7 cell line) and referenced to the standard drug, Doxorubicin. The order of the IC_{50} for the Mcf7 can be arranged as follows: Cu(II) < Ni(II) < Co(II) < L. It has been observed that the copper complex has a more powerful anticancer effect with an IC_{50} value of 23mg mL^{-1} against breast cellular carcinoma than other complexes. The molecular docking studies of the ligand and its complexes have been achieved. The binding free energy of the ligand and the metal complexes with the active sites of the receptors of COVID-19 main protease viral protein (PDB ID: 6LU7), breast cancer oxidoreductase (PDB ID: 3HB5), Gram +ve bacteria S. aureus (PDB ID: 3q8u), and E. coli (Gram –ve bacteria) (PDB ID: 1fj4) were also studied. The results confirmed that metal complexes displayed better binding at the active sites compared to the ligand, following the order of Cu(II) > Ni(II) > Co(II) > L. It is suggested from the investigation of antibacterial, cytotoxicity activities, and docking studies that the Cu(II) complex can be utilized as a powerful antimicrobial and anticancer agent.