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Computational study of the coordination complex of Cu(II) with 1,10-phenanthroline and chloride ligands with promising antiviral activity: TD-DFT calculations and molecular docking

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The coronavirus (COVID-19) emerged in 2019 and spread rapidly, causing many deaths. Due to the emergence of this new disease, several institutions have been looking for alternative means of antiviral treatment [1]. In an attempt to explore the ability of coordination complexes as potential antiviral agents, researchers have conducted in silico studies, using computational tools [2]. In this work, density functional theory (DFT) and time-dependent density functional theory (TD-DFT) calculations were performed to study several different properties of the Cu(II)(Phen)2Cl complex. A molecular docking was also developed to study the binding of the complex to the main protease of SARS-CoV-2. The DFT and TD-DFT calculations were performed using the Gaussian 16 software, with the DFT functional PBE1PBE. The basis set 6-311++G(d,p) was used for the lighter atoms, while the SDD basis set and pseudopotential was used for the Cu(II). The solvation effects in water were studied with an integral equation formulation of the polarizable continuum model (IEFPCM). Molecular docking was performed based on optimized geometry using AutoDock Vina software and AutoDock Tools (version 1.5.7). The crystal structure of the main protease of SARS-CoV-2 was obtained from the Protein Data Bank (http://www.rcsb.org/) (PDB ID: 7BZ5) [3]. The optimized geometry obtained for the complex is in good agreement with the experimental data [4]. The Gibbs free energy and enthalpy change values associated to the complexation were –343.58 and –369.38 kcal.mol–1, respectively. The calculated HOMO and LUMO energies and the gapHOMO-LUMO are –2.97, –1.90 and 1.07 eV, respectively. TD-DFT results indicated a band at 655 nm attributed to the 2Eg?2T2g transition of the Cu(II), which is close to the experimental value available [4]. Binding energy and an inhibition constant (Ki) of -7.22 kcal.mol?1 and 5.1 ?M were obtained from molecular docking, respectively. The active residues in the interaction of the metal complex with the protein are TYR97, TRP47, ALA60, ASP61, GLY44, PHE99, GLU46, SER62, LEU45, THR98, with electrostatic, cation-?, and anion-? interactions, indicating that the complex has a potential biological application as an antiviral agent. References [1] A. Ali, N. Sepay, M. Afzal, et. al., Bioorgan. Chem., v. 110, p. 104772, 2021. [2] S. V. Rodriguez, D. R. Contreras, L. Noriega, et. al., Front. Chem., v. 11, p.1128859, 2023. [3] Aprajita, M. Choudhary., J Mol Struct, v. 13, n. 3, p. 133114, 2023. [4] P. Sarma, R. M. Gomila, A. Frontera, et. al., Crystals, v. 13, n. 3, p. 517, 2023.