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Synthesis, Characterization, Reduction, and Cytotoxicity of Anticancer Platinum (IV) Prodrugs Containing Amine as an axial ligand

Maryam Sadeghi, Mahboube Eslami Moghadam*

Chemistry and Chemical Engineering Research Center of Iran, Tehran, Iran.

E-mail addresses: eslami_moghadam@yahoo.com & M.sadeqhi89@gmail.com

Abstract

Platinum (II)-based drugs are widely used for tumor treatment; however, severe side effects and the emergence of resistance limit their clinical effectiveness [1,2]. Pt(IV) derivatives have been developed to address these issues, offering enhanced stability and solubility [3]. In this study, we designed and synthesized Pt(IV) complexes incorporating carboplatin with an amine axial ligand. The proposed structures of these complexes were confirmed using ^{1}H NMR, ^{13}C NMR, ^{195}Pt NMR, FT-IR, CV, and LC-MS methods. We employed density functional theory (DFT) to examine the geometries of the complexes. The reduction of Pt(IV) complexes by ascorbic acid in phosphate-buffered saline at room temperature was analyzed using UV-Vis monitoring. We also investigated the interactions between Pt(IV) complexes and ct-DNA through UV-Vis spectroscopy and molecular docking simulations. Compared to carboplatin, the synthesized compound exhibited improved water solubility due to the increased polarity of the carboxylate ligands. Additionally, the biological properties of these complexes were analyzed, revealing that those containing succinic acid and amine groups exhibit cytotoxicity comparable to oxaliplatin, likely due to higher cellular accumulation attributed to increased lipophilicity. Our findings suggest that the newly synthesized Pt(IV) complexes represent a promising class of potential anticancer agents that could be explored as clinical drugs soon [4].

Keywords: Pt(IV) complex, Axial ligands, Amine, Anticancer drug, Cytotoxicity.

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