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Research for Repositioning the Quinolone Molecules from Antibiotics to Anticancer Agents †

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Abstract: "Drug repositioning" is a modern strategy to find new applications for out-of-use drugs. In the case of quinolone antibiotics, chemical modifications on the quinolone nucleus and coupling with various metal ions represent the main strategies to repurpose these molecules as anticancer agents. In this context, nalidixic acid, the first member of the quinolone class, which has limited applications nowadays, has been used to obtain nine new metal complexes with lanthanide cations (La^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}, Tb^{3+}). Various modern physicochemical techniques were used to characterize the obtained complexes, experimental data suggesting that the quinolone acts as a bidentate ligand, binding to the metal ion *via* the keto and carboxylate oxygen atoms, findings which are supported by DFT calculations. The affinity towards DNA and manner of binding have been tested using UV-Vis spectroscopy and competitive binding studies, with results indicating that major and minor groove-binding play a significant role in these interactions. The affinity towards serum proteins has also been evaluated, the complexes displaying a higher affinity towards albumin than apo-transferrin. The cytotoxic activity of the complexes has been studied using two tumoral cell lines, MDA-MB 231 and LoVo, and a normal cell line, HUVEC. Overall, the complexes displayed good anticancer activity, with IC_{50} values similar to or lower than cisplatin in some cases and minimum toxicity towards the normal cell line.

Keywords: quinolone; drug repositioning; metal complex; anticancer agent.

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Conflicts of Interest

The authors declare no conflict of interest.