NanoInnovation 2024

Copper complexes with biological active molecule amantadine as potential anticancer and antiviral agents

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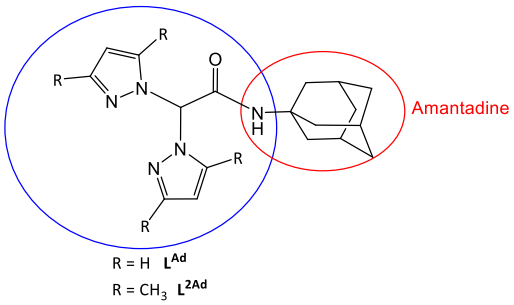
The use of metal compounds in cancer therapy is well known. Platinum-based compounds have demonstrated great effectiveness in this field. Despite this, their clinical use is limited by severe toxicities and drug resistance phenomena. These drawbacks have encouraged researchers to in-depth develop new metal-based anticancer drugs to improve clinical effectiveness, reduce general toxicity and to broaden the spectrum of activity. In this context, copper-based compounds have proven to be effective, modulating cancer cell survival by generating reactive oxygen species, accumulating excess copper, inhibiting proteasome activity and inhibiting angiogenesis [1].

The aim of our work was to design and synthetize new Cu(I) and Cu(II) complexes using as chelators the new ligands L^{Ad} and L^{2Ad} obtained by conjugating the bifunctional species bis(pyrazol-1-yl)- and bis(3,5-dimethylpyrazol-1-yl)-acetate and the drug Amantadine. Phosphane co-ligands were employed for the synthesis of the Cu(I) complexes to stabilize copper in the +1 oxidation state and to vary the solubility properties of the corresponding complexes. All the complexes were fully characterized both in solid state and in solution, and their electronic and molecular structures were investigated by X-ray photoelectron spectroscopy, near-edge X-ray absorption and for $[Cu(L^{2Ad})_2]Br_2$ by X-ray diffraction analysis [2].

The effects of L^{2Ad} copper complexes as potential anticancer agents have been evaluated by MTT assay on three different glioblastoma cell lines, showing a decrease in their viability with IC_{50} values significantly lower than cisplatin, affecting cell growth, proliferation and death. Moreover, these copper complexes demonstrated high selectivity showing a low toxicity toward immortalized BV2 cells, a type of microglial cell line derived from C57/BL6 murine. A relevant property of the most promising antitumoral copper compounds was that their non-toxic doses demonstrated to enhance the ability of temozolomide, key chemotherapeutic agent for treatment of glioblastoma, to induce cell death.

Currently, studies are in progress to investigate the mechanisms of anticancer activity of L^{Ad} and L^{2Ad} copper complexes as well as to assess their potential as antiviral agents.



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