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Title: Evaluation of central-metal effect on anticancer activity and mechanism of action of isostructural Cu(II) and Ni(II) complexes containing pyridine-2,6-dicarboxylate

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Two Cu(II) (C1) and Ni(II) (C2) complexes were designed through the one-pot reaction of pyridine-2,6-dicarboxylic acid and 2-aminobenzimidazole respectively with copper(II) nitrate hexahydrate and nickel(II) nitrate hexahydrate. Both complexes were characterized by single-crystal X-ray diffraction and the distorted octahedral geometry was recognized for them. The MTT assay indicated that the complexes have a significant antiproliferative effect on BEL-7404 cells. IC_{50} values confirmed that C1 (IC_{50}= 0.56 µM) is several times more potent than C2 (IC_{50}= 5.13 µM). The similar cellular uptake of the complexes in mentioned cells led to this proposal that the production of ROS with different values can be the main reason for different cytotoxicity of the complexes. In this study, C1 and C2 caused BEL-7404 cells arrest at the G2/M and S phases, respectively. The expression of p53, Bax up-regulation, and Bcl-2 down-regulation and also activation of procaspase-9, and 3 indicated that apoptosis through a caspase-dependent mitochondrion pathway is a remarkable pathway in BEL-7404 cells treated by C1 while mechanistic studies proved that C2 induce death of BEL-7404 cells through the activation of RAGE/PI3KC3/Beclin 1 autophagic cell signaling pathway, more specifically. The cytostatic effect of the complexes in the BEL-7404 3D spheroid model was depicted.

Keywords: Cu(II) and Ni(II) complexes, Anticancer effect, Production of ROS, Apoptosis, Autophagy

References

[1] S. Abdolmaleki, M. Ghadermazi, A. Fattahi, S. Sheshmani, Inorg. Chim. Acta **2016**, 443, 284-98.

[2] S. Abdolmaleki, M. Ghadermazi, Inorg. Chim. Acta **2017**, 461, 221-32.

[3] S. Abdolmaleki, M. Ghadermazi, A. Fattahi, S. Shokraii, M. Alimoradi, B. Shahbazi, A. R. Judy Azar, J. Coord. Chem. **2017**, 70, 1406-23.