

Abstract

# Novel Copper(II) Complexes with S-Substituted Isothiosemicarbazone as Highly Selective Anticancer Compounds against BxPC-3 Cell Line <sup>†</sup>

Vasilii Graur <sup>1,\*</sup> , Irina Usataia <sup>1</sup>, Olga Garbuz <sup>1,2</sup>  and Aurelian Gulea <sup>1</sup>

<sup>1</sup> Laboratory of Advanced Materials in Biopharmaceutics and Technics, Moldova State University, MD-2009 Chişinău, Moldova

<sup>2</sup> Institute of Zoology, MD-2028 Chişinău, Moldova

\* Correspondence: vgraur@gmail.com

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**Abstract:** Cancer is a major disease worldwide. Therefore, scientists are in a constant search for new, more effective and selective substances, not damaging normal cells, for the treatment of this disease. The use of coordination compounds such as anticancer agents is based on the interaction between DNA and metal-based complexes. It is known that thiosemicarbazones, isothiosemicarbazones, and 3d metal complexes with them often exhibit high anticancer activity. In this work, the S-methyl group in the composition of 2-acetylpyridine 4-allyl-S-methylisothiosemicarbazone (HL<sup>1</sup>) was replaced by an S-allyl group. As a result, 2-acetylpyridine 4,S-diallylisothiosemicarbazone (HL<sup>2</sup>) was obtained. Two novel copper(II) coordination compounds were synthesized with HL<sup>2</sup>: Cu(HL<sup>2</sup>)Cl<sub>2</sub> and Cu(HL<sup>2</sup>)Br<sub>2</sub>. The inhibitory activity of these novel coordination compounds was tested and compared with the corresponding activities of previously described complexes with 2-acetylpyridine 4-allyl-S-methylisothiosemicarbazone. The inhibitory activity toward the normal MDCK cell line decreased. Their IC<sub>50</sub> values are in the range of 1.2–1.4 µM, while the corresponding complexes with HL<sup>1</sup> have IC<sub>50</sub> values of 0.35–1.0 µM. Therefore, the novel complexes have a lower impact on normal cells. At the same time, the inhibitory activity toward the human pancreatic cancer cell line (BxPC-3) increased 2.5–18 times. The IC<sub>50</sub> values of the novel complexes toward BxPC-3 cells are in the range of 5–8 nM. This means that the selectivity indexes (the ratio between IC<sub>50</sub> values of normal cells and cancer cells) of the novel complexes are in the range of 150–280, which is very promising for further study of these complexes as potent selective anticancer drugs.

**Keywords:** coordination compounds; anticancer; selectivity; BxPC-3; isothiosemicarbazones



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