Serbian Biochemical Society

Proceedings

Editor: Ivan Spasojević
Technical support: Jovana Trbojević-Ivić, Milena Dimitrijević, Tijana Ćulafić
Cover design: Zoran Beloševac
Publisher: Faculty of Chemistry, Serbian Biochemical Society
Printed by: Colorgrafx, Belgrade
No of printed copies: 130

Serbian Biochemical Society
Twelfth Conference

International scientific meeting

September 21-23, 2023, Belgrade, Serbia

"***Biochemistry in Biotechnology"***

Anticancer potential of diiron thiocarbyne complexes

Ekatarina Mihajlović[1*], Sanja Jelača[1], Lorenzo Biancalana[2], Lorenzo Chiaverini[2] Biljana Dojčinović[3], Sanja Mijatović[1], Stefano Zacchini[4], Fabio Marchetti[2], Danijela Maksimović-Ivanić[1]

[1]Department of Immunology, Institute for Biological Research "Siniša Stanković" – National Institute of Republic of Serbia, University of Belgrade, Serbia
[2]Department of Chemistry and Industrial Chemistry, University of Pisa, Italy
[3]Institute of Chemistry, Technology and Metallurgy – Institute of National Importance for the Republic of Serbia, University of Belgrade
[4]Department of Industrial Chemistry "Toso Montanari", University of Bologna, Italy

[*]e-mail: ekatarina.mihajlovic@ibiss.bg.ac.rs

To improve safety and efficacy of conventional chemotherapeutics, it is important to target cancer cells more selectively. Potential strategies could arise from differences in iron metabolism between healthy and cancer cells, based on cancer cells high demands for iron. Their, so-called, "iron addiction" sets a foundation for new therapeutic approach. In this study, the cytotoxic effect of three diiron carbonyl complexes with a bridging thiocarbyne ligand was evaluated on different human cancer cell lines (HCT116 colorectal carcinoma, MCF-7 breast cancer and A2780 ovarian cancer), as well as on human embryonic lung fibroblasts (MRC-5), which were used for selectivity assessment. The most potent compound (FETPY) decreased viability of all cancer cell lines in dose-dependent manner, while A2780 cells emerged as the most sensitive. Therefore, they were selected for further investigation. On the other hand, the effect of FETPY on lung fibroblasts viability was remarkably less potent, showing its great selectivity towards malignant phenotype. Additionally, it was shown that intracellular iron concentration was much higher in A2780 than in MRC-5 cells after treatment with FETPY. Viability decrease of A2780 cells was a consequence of cell death – ferroptosis, caused by iron-dependent lipid peroxidation and membrane damage. Oxidative stress that caused ferroptosis evolved from intensive production of nitric oxide and superoxide anion. Controversially, it was followed with scavenging of hydrogen peroxide and peroxynitrite. Treatment with FETPY also caused significant decrease of A2780 cells division rate. Overall, these results indicate that the considered diiron derivatives show great potential for further investigation in cancer treatment.

Acknowledgements

This study was supported by the Ministry of Science, Technological Development and Innovation of the Republic of Serbia (Grant No. 451-03-47/2023-01/200007).