Abstract

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Aroylhydrazones are tridentate lipofilic iron chelators with very good entry to cells. In our previous experiments, salicylaldehyde isonicotinoyl hydrazone (SIH), has shown very interesting antioxidant and antiproliferative efficiencies . However, its major disadvantage is low stability caused by a fast hydrolysis of hydrazone bond. Therefore, the series of nine new analogues of SIH derived from aromatic ketones has been synthetized at the Department of Inorganic and Organic Chemistry of our faculty.

Our recent study extends our previous experiments with these substances and examines potential use of these new aroylhydrazones in antitumour treatment. The breast adenocarcinoma cell line MCF-7 and human promyelocytic leukemia cell line HL60 were used. Proliferation tests took 72 hours, when cells were exposed to action of substances or their combinations

Statistically significant antiproliferative activity was noted in all new chelators at the both cell lines. We compared the IC_{50} values of each chelator to cancer cell lines with IC_{50} values of each chelator to non-proliferating H9c2 cells. As compared to SIH, seven substances from nine (in the case of MCF-7 cells) and five substances (in the case of HL60 cells) showed specific increase of selective toxicity to cancer cells compared to non-cancer cells. A significant reductions of the antiproliferative activities of the studied substances were demonstrated following formation of their iron complexes (chelates). This confirms a dependence of their antineoplastic effect on the iron chelation. After an incubation of two of chelators in combination with the estrogen signalisation inhibitor tamoxifen we found significant mutual potentiation of their antiproliferative effects.

Hence, this study demonstrates antiproliferative effects of new SIH analogues and at the same time it suggests further interesting topics for our next research.