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CYTOTOXICITY OF ANTICANCER CARBOSILANE METALLODENDRIMERS IN HUMAN LEUKEMIA (HL-60) CELLS

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Cancers are now one of the biggest problems of civilization. Researchers around the world are looking for effective methods to fight tumours without damaging healthy tissues. Many of these attempts concentrate on metals such as silver, gold, platinum or ruthenium [1, 2]. Metal compounds are usually insoluble in aqueous solutions. Therefore, in order to increase their solubility in water metal molecules can be bound to carrier nanoparticles such as dendrimers. Dendrimers can be synthesized by a controlled manner and they demonstrate monodispersity. Moreover they have determined shape, size and charge. Dendrimers consist of a core and attached repetitive units (called branches) in the form of successive layers forming increasingly higher generations [3]. At the ends of branches there are free functional groups to which molecules of different metals can be attached [4].

The main objective of the present study was to determine the cytotoxicity of new synthetized ruthenium terminated metallodendrimers of generation 0 (compound 34) and generation 1 (compound 32) to the human leukemia HL-60 cells. The cytotoxicity effect of dendrimers against cancer cells was compared with their effect against normal cells (Chinese hamster B-14 cell line). HL-60 cells were grown in RPMI-1640 (Gibco) with 10 % heat-inactivated FBS (HyClone). B14 cells were grown in DMEM-Glutamax (Gibco) with 10 % heat-inactivated FBS (HyClone). Cells were routinely maintained on plastic tissue culture flasks and plates (Falcon) at 37 °C in a humidified atmosphere containing 5 % CO_2, 95 % air. The cytotoxicity of dendrimers was assessed with the use of Alamar Blue assay (HL-60 cell line) and MTT assay (B14 cell line). Cells viability was calculated from formula:

$$\% \text{ viability} = (A/A_c) \times 100\ \%$$

where A represents the absorbance/fluorescence of the sample, A_c is the absorbance/fluorescence of control cells. The results were obtained in three independent experiments and were shown as mean ± standard deviation (SD).

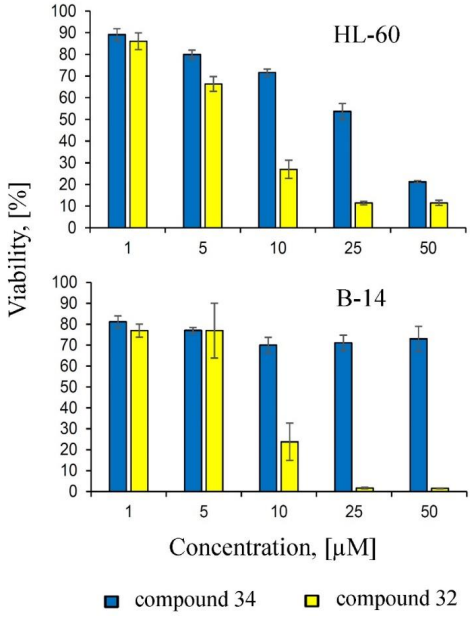

Figure 1 – Top panel – viability of HL-60 cells after 24 h incubation in the presence of metallodendrimers. Bottom panel – viability of B-14 cells after 24 h incubation in the presence of metallodendrimers

The viability of cells decreased with increasing concentrations of dendrimers. Results show that higher generation was more cytotoxic. There were no changes in viability of B14 cells in the presence of the compound 34 (g-0) in a concentration range from 1 to 50 μmol/L, while the same dendrimer significantly decreased the viability of HL-60 cells up to 53.7 % (25 μmol/L) and 21.2 % (50 μmol/L) vs control cells (Fig. 1). Compound 32 (g-1) at the concentrations from1 to 5 μmol/L was not cytotoxic to both HL-60 and B14 cells, while the concentration of 10 μmol/L drastically decreased the number of living cells up to 27 % (HL-60) and 23.7 % (B-14). The presence of this dendrimer in the cell suspension in the concentrations from 25 μmol/L and higher reduced cell viability to 11.5 % for HL-60 and 1-2 % for B-14 cells.

In conclusion, the viability of cells depended mostly on the metallodendrimers generation: generation1 was more cytotoxic than generation 0. Moreover, dendrimers of generation 1 equallyreduced both normal and cancer cell viability, whereas dendrimers of generation 0 were more cytotoxic to the cancer cells.

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