THE IMPACT OF RUTHENIUM TERMINATED CARBOSILANE DENDRIMERS ON CELL MEMBRANES

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Nanotechnology is the most developing field of science. The new, hitherto unknown versatile nanomaterials with unique properties have been synthesized [1]. Many of them such as carbon nanotubes, mesoporous silica, dendrimers can be sucesfully used in medicine as drug carriers. In this field the attention of scientists has been focused on dendrimers due to their structure and monodispersity, as well as their controlled synthesis [2]. Dendrimers are branched spherical polymers. They consist of acore, and radial branching. New branches attached to the core form successive generations. At the ends of the branches there are free functional groups. The physical and chemical properties of dendrimers can be modified. It is also possible to precisely determine the shape, size and charge of formed nanoparticles. Many types of dendrimers such as amine-terminated poly (amidoamine) PAMAM, poly- (propylenimine) PPI, phosphorus, carbosilane are known [3]. The size of dendrimers is similar with some biomolecules naturally occurring in animals such as insulin, cytochrome or haemoglobin. Due to dendrimers shape and surface charge various types of substituents can be bound to them. There are many works describing the potential of dendrimers as efficient carriers of gene material or drugs. Recently the new class of dendrimers have been synthesized to improve their biomedical properties. One of the modifications aimed to increase the antitumor characteristics of dendrimers is introducing to their structure the molecules of metals such as gold, silver, titanium or ruthenium exhibiting anticancer properties [4].

In our previous work we have studied the mechanisms of interaction between dendrimers and artificial lipid membranes [5]. Here we are discussing the effect of ruthenium terminated carbosilane dendrimers on human erythrocyte cell membrane. Figure 1 shows the haemolytic activity of metallodendrimers of generations 0, 1 and 2 measured as a hemoglobin release from erythrocytes as a result of red blood cell membrane destruction.

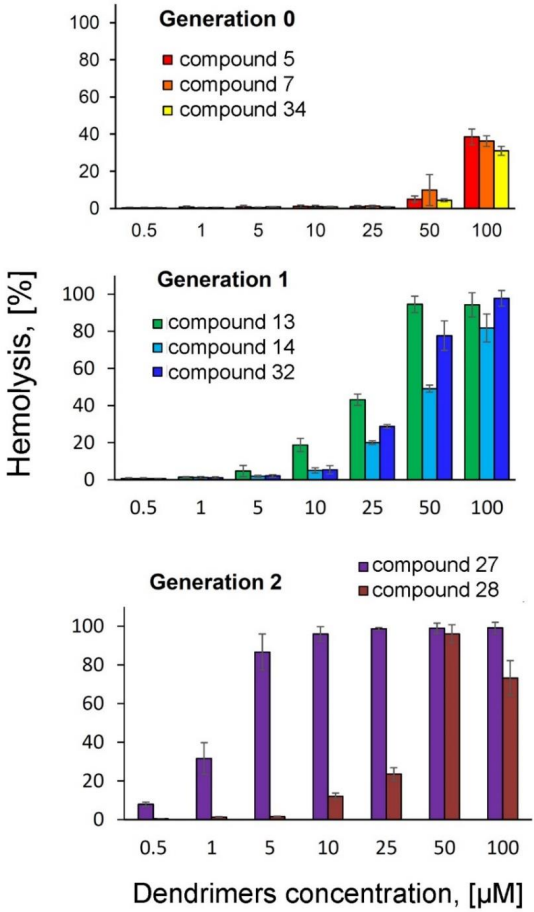

Figure 1 – Haemolysis in human erythrocytes caused by carbosilane metallodendrimers at the concentrations range from 0.5 to 100 μmol/L. A 2 % suspension of freshly isolated human erythrocytes in 10 mmol/L PBS, pH 7.4 was incubated for 24h at 37°C in the presence of dendrimers

Blood of healthy donors were obtained from Central Blood Bank in Lodz. The blood was anticoagulated, centrifuged and washed three times with PBS, pH=7.4. Erythrocytes were used immediately after isolation. Dendrimers at the concentration of 0.5–100 μmol/L were added to red blood cell suspensions (2 % haematocrit) and incubated at 37 °C for 24 h with shaking. The level of hemolysis was calculated as follows: H (%) = (A_{sample}540 nm/A_{water} 540 nm)×100 %, where H (%) is the percentage of haemolysis of the erythrocytes; A_{sample} 540 nm is the absorbance of the erythrocytes incubated with dendrimers; and A_{water} 540 nm is the absorbance of the sample of complete haemolysis in water (100 %). The results were obtained from minimum three independent experiments (n=6) and were shown as mean ± standard error (SE).

Haemolysis assay was performed to test the ability of dendrimers to affect the cell membrane. All analysed dendrimers caused haemolysis. The effect mostly depended on dendrimer generation and concentration. Lowest effect have been shown for the dendrimers of generation -0 (31-38 % of haemolysis at the concentration of 100 μmol/L). This can be explained by the small number of active surface groups of g-0 dendrimers. In contrast, the haemolytic effect of the dendrimers of generations 1 and 2 washigher and caused massive hemolysis in a concentrations of 25–50 μmol/L.Therefore, the g-1 and g-2 dendrimers can be regarded as haemolytic.

In summary we report that carbosilane ruthenium containing dendrimers of generation 1 and 2 are more toxic than dendrimers of generation 0.

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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].