Streszczenie w języku angielskim

Drug carriers are substances designed to improve bioactive substances delivery to specific target sites within the body. They can be used to transport both drugs and genetic material across biological barriers. In the search for potential drug carriers, various types of nanoparticles are often considered, among which gold nanoparticles (AuNPs) have attracted significant attention. Gold nanoparticles possess a wide range of biophysical properties that make them suitable for biomedical applications. They exhibit high biocompatibility, low cytotoxicity, and can be readily surface-modified. PEGylation of gold nanoparticles (i.e., their conjugation with polyethylene glycol) is regarded as a promising strategy for the delivery of drugs and nucleic acids, particularly for transporting therapeutic siRNA to tissues and cells protected by the blood-brain barrier.

The aim of this study was to investigate whether PEG-coated gold nanoparticles, AuNP14a and AuNP14b, differing in the ratio of carbosilane dendrons to PEG chains, are capable of forming complexes with siRNA and of being internalized by cells in a blood-brain barrier (BBB) model. The selected siRNA targets the *apoE* gene, specifically the ε4 risk allele, which is associated with the development of Alzheimer's disease. Obtained results confirmed the feasibility of conjugating AuNPs with siRNA (siApoE). It has been shown that AuNP14a formed stable complexes with siRNA at lower concentrations than AuNP14b. The nanoparticles interacted with plasma proteins without significantly disrupting their secondary structure and interacted with lipid membranes. Efficient cellular uptake of the AuNP/siRNA complexes was observed in endothelial cells, along with their intracellular accumulation, primarily in the cytoplasm. The tested nanoparticles exhibited low cytotoxicity toward endothelial cells, astrocytes, and pericytes, and the presence of siRNA further reduced their cytotoxic potential. The genotoxicity of both AuNPs and their siRNA complexes was relatively low. Additionally, observed changes in reactive oxygen species level and mitochondrial membrane potential normalized within 24 hours.

The obtained data indicate that PEGylated gold nanoparticles AuNP14a and AuNP14b meet key criteria for therapeutic siRNA carriers. Among the two considered formulations, AuNP14a appears to be more promising than AuNP14b.

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