Cytotoxic effects of gold core-shell hybrid nanostructures

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Abstract

Currently, world production of nanomaterials used in medicine and pharmacology is intensively increasing. Hybrid nanomaterials based on metal cores and organic polymer shells seem to be the most promising therapeutic, in particular, theranostic agents. Active developments of new hybrid nanostructures arise a question concerning their interaction with living organisms and biosafety. One of the effective approaches for toxicological studies of nanomaterials is the use of *in vitro* models.

In this study, the *in vitro* effects of gold-based hybrid nanostructures (GHNs) with immunoglobulin coatings were studied.

Introduction

Metal nanoparticles are nowadays one of the most widely used nanomaterials having a number of production and practical applications. Among them, gold hybrid nanostructures (GHNs) can be mentioned as promising materials used for various biomedical purposes including targeted delivery systems, photothermal therapy, bioimaging, cancer treatment, drug development, etc. Using of nanoparticles as therapeutic agents raises the issue regarding their biosafety toward humans. One of the effective approaches for toxicological studies is the use of cell cultures (*in vitro* test systems). Although *in vitro* experiments cannot completely replace *in vivo* studies, they can contribute to assessing the safety of engineered nanoparticles, including hybrid nanostructures. A number of undoubted advantages characterizes *in vitro* test systems based on human and animal cell cultures: the simplicity of cell cultivation by proven methods, the possibility of visual detection of viable cells during the whole experiment using microscopic methods, and a higher reproducibility in comparison to *in vivo* test systems. Cost-effective and not time-consuming *in vitro* models allow decreasing the number of experimental animals or a complete replacing of *in vivo* test systems.

Methods and Materials

GHNs were obtained on the base of gold nanoparticles (GNPs) of a 30 nm diameter synthesized by a reduction of sodium citrate. GNPs were coated by immunoglobulins G by physical adsorption method and characterized by a transmission electron microscopy.

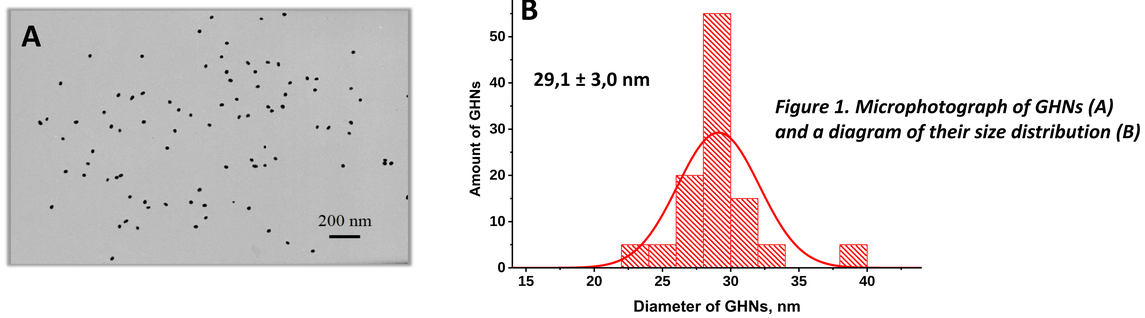


Figure 1. Microphotograph of GHNs (A) and a diagram of their size distribution (B)

Murine embryonal fibroblast (NIH-3T3) and murine monocyte/macrophage (P388-D1) cell lines were used to evaluate the cytotoxicity. Cells were exposed to GHNs in a concentration range of 0.1–250 μg/mL for 24-48-72 h. After exposure to GHNs, the amount of living cells was assessed by MTT assay. Besides, the concentration of glutathione as a key antioxidant parameter was determined.

Results

NIH-3T3 cells viability evaluated by MTT test after exposure to GHNs

Dosage, μg/mL	Relative viability, %		
	24 h of exposure	48 h of exposure	72 h of exposure
250	21,2±0,7	12,6±2,6	28,3±4,5
100	37,1±3,0	24,7±6,7	51,6±5,7
50	67,0±5,2	55,1±4,2	77,7±2,6
25	72,3±2,7	73,3±1,6	78,1±4,8
10	84,7±4,0	85,4±2,9	82,58±3,7
5	80,1±6,3	92,9±2,6	89,8±3,4
1	83,0±4,1	93,9±1,6	85,9±2,1
0.5	86,7±3,8	96,8±4,4	92,3±2,2
0.1	103,6±1,4	102,5±2,9	92,0±4,4

P388-D1 cells viability evaluated by MTT test after exposure to GHNs

Dose, μg/mL	Relative viability, %		
	24 h of exposure	48 h of exposure	72 h of exposure
250	86,8±2,2	86,8±0,3	88,6±1,6
100	90,1±1,8	89,1±0,8	92,3±1,3
50	92,9±3,6	90,8±2,2	94,4±1,5
25	90,0±7,3	89,2±1,0	95,4±0,7
10	93,6±1,0	93,1±4,6	91,7±0,4
5	92,7±5,4	92,9±1,8	94,7±1,3
1	98,8±1,4	97,9±1,5	95,1±1,4
0.5	99,8±0,7	102,0±0,9	109,9±8,1
0.1	106,9±2,0	107,6±3,2	103,5±4,4

Glutathione content in NIH-3T3 cells after exposure to GHNs

Dose, μg/mL	Glutathione content (in % to control values)		
	24 h of exposure	48 h of exposure	72 h of exposure
250	106,6±21,0	165,5±30,1	121,8±12,9
100	105,2±10,96	137,4±6,4	112,5±15,7
10	70,8±1,6	139,8±16,8	139,1±11,7
1	84,3±8,2	161,9±1,8	129,4±20,6

Glutathione content in P388-D1 cells after exposure to GHNs

Dose, μg/mL	Glutathione content (in % to control values)		
	24 h of exposure	48 h of exposure	72 h of exposure
250	62,1±4,1	141,4±13,3	10,9±0,2
100	68,0±2,2	191,3±6,9	1,8±0,5
10	92,2±3,9	96,1±5,4	9,6±1,9
1	82,7±1,6	165,2±1,1	15,8±3,1

Discussion

At all exposure periods studied, a decrease in NIH-3T3 viability was monitored (up to 20%). The percentage of living cells was reduced mainly upon incubation in the 24–48 h interval. For the P388-D1 line, the level of living cells dropped to only 80% after incubation in all doses and periods of exposure. The determination of glutathione demonstrated that GHNs induced oxidative stress in NIH-3T3 cells. The maximum increase in glutathione level was found in cells incubated with GHNs at the highest concentration for 72 h. Changes in glutathione concentrations in P388-D1 cells were also time- and dose-dependent.

Conclusions

Overall, the cytotoxic effect of GHNs on mammalian cells of two cell lines was studied. A dose- and time-dependent effect on cell viability was demonstrated using the MTT test. Changes in glutathione content after exposure to GHNs was observed which was the evidence of oxidative stress caused by GHNs. Difference in the sensitivity of cell lines to the studied GHNs was demonstrated.

Future Directions

Further investigations of cytotoxic effects of different core-shell gold hybrid nanostructures to mammalian cell lines are planned. A series of *in vitro* tests will be used.

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