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Оценка цитотоксичности гликонаночастиц золота на клетках аденокарциномы ободочной кишки человека

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АННОТАЦИЯ

Введение. Перспективным направлением онкотерапии является использование наночастиц металлов.

Цель. Оценить цитотоксичность наночастиц золота (НЧЗ), модифицированных остатками фукозы, лактозы и галактозы, на клетках *Caco-2*.

Материалы и методы. Клетки культивировали до монослоя с НЧЗ в концентрациях 10–600 мкг/мл для частиц с фукозой, 10–900 мкг/мл для частиц с лактозой и 10–550 мкг/мл для частиц с галактозой. В качестве неопухолевых использовались клетки *Caco-2* после дифференцировки в тонкокишечные энтероциты (инкубация — 21 сут). Цитотоксичность НЧЗ оценивалась МТТ-тестом после инкубации с клетками в течение 2 ч, 8 ч и 24 ч. В качестве препарата сравнения использовался фторурацил в концентрациях 50–2000 мкг/мл. Концентрацию полумаксимального ингибирования (IC_{50}) рассчитывали с помощью программы GraphPad Prizm 8.4.3.

Результаты. IC_{50} для НЧЗ с фукозой по отношению к опухолевым клеткам составила 582 ± 29 и 336 ± 36 мкг/мл после 2 и 8 ч инкубации соответственно; для НЧЗ с лактозой — 769 ± 50 и 515 ± 45 мкг/мл, для НЧЗ с галактозой — 467 ± 299 и 299 ± 28 мкг/мл. В отношении дифференцированных клеток IC_{50} для всех типов НЧЗ была выше, чем для опухолевых клеток при 2 ч и 8 ч инкубации: для частиц с фукозой — 530 ± 3 и 410 ± 15 мкг/мл; для частиц с лактозой — 831 ± 7 и 639 ± 14 мкг/мл; для частиц с галактозой — 511 ± 21 ($p = 0,018$) и 376 ± 36 мкг/мл соответственно. При 24-часовой инкубации клеток *Caco-2* с НЧЗ фукозой IC_{50} по отношению к опухолевой и дифференцированной их разновидностям не отличалась. В случае остальных НЧЗ IC_{50} по отношению к опухолевым клеткам превосходила данный параметр для дифференцированных клеток. Фторурацил проявил цитотоксичность по отношению к опухолевым клеткам с IC_{50} 2108 ± 19 и 1764 ± 193 мкг/мл при 2 ч и 8 ч инкубации соответственно. По отношению к дифференцированным клеткам его IC_{50} составляла 1995 ± 20 мкг/мл после 2 ч инкубации и 1694 ± 102 мкг/мл при 8 ч инкубации. Различий между IC_{50} фторурацила по отношению к дифференцированным и опухолевым клеткам с равной длительностью инкубации не наблюдалось.

Заключение. НЧЗ с фукозой, лактозой и галактозой оказывают цитотоксическое действие на клетки аденокарциномы ободочной кишки человека, превосходя по активности фторурацил.

Ключевые слова: *гликонаночастицы золота; аденокарцинома ободочной кишки человека; Caco-2; фторурацил; МТТ-тест*

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Evaluation of Cytotoxicity of Gold Glyconanoparticles of Human Colon Adenocarcinoma Cells

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ABSTRACT

INTRODUCTION: Use of metal nanoparticles is a promising trend in oncotherapy.

AIM: To evaluate cytotoxicity of gold nanoparticles (GNPs) modified with fucose, lactose and galactose residues, on *Caco-2* cells.

MATERIALS AND METHODS: Cells were cultured to a monolayer with GHPs in concentrations of 10 μg/ml–600 μg/ml for particles with fucose, 10 μg/ml–900 μg/ml for particles with lactose and 10 μg/ml–550 μg/ml for particles with galactose. As non-tumor cells, *Caco-2* cells were used after differentiation into small-intestine enterocytes (incubation time — 21 days). The cytotoxicity of GNPs was evaluated in MTT-test after incubation with cells for 2 hours, 8 hours and 24 hours. A comparison drug was fluorouracil in concentrations of 50 μg/ml–2000 μg/ml. The half-maximal inhibitory concentration (IC_{50}) was calculated in GraphPad Prism 8.4.3 program.

RESULTS: IC_{50} for GNPs with fucose for tumor cells was 582 ± 29 and 336 ± 36 μg/ml after incubation for 2 hours and 8 hours, respectively; for GNPs with lactose — 769 ± 50 and 515 ± 45 μg/ml, for GNPs with galactose — 467 ± 299 and 299 ± 28 μg/ml. For differentiated cells, IC_{50} for all types of GNPs was higher than for tumor cells after incubation for 2 and 8 hours: for particles with fucose — 530 ± 3 and 410 ± 15 μg/ml; for particles with lactose — 831 ± 7 and 639 ± 14 μg/ml; for particles with galactose — 511 ± 21 ($p = 0.018$) and 376 ± 36 μg/ml, respectively. After 24-hour incubation of *Caco-2* cells with fucose, IC50 did not differ for tumor and differentiated varieties. For other GNPs, IC_{50} for tumor cells was higher than for differentiated cells. Fluorouracil showed cytotoxicity for tumor cells with IC_{50} 2108 ± 19 and 1764 ± 193 μg/ml after 2 hours and 8 hours of incubation, respectively. For differentiated cells, IC_{50} of fluorouracil was 1694 ± 102 μg/ml after 2-hour incubation and 1694 ± 102 μg/ml after 8-hour incubation. There were no differences between IC_{50} of fluorouracil for differentiated and tumor cells with equal incubation time.

CONCLUSION: GNPs with fucose, lactose and galactose have a cytotoxic effect on human colon adenocarcinoma cells and in the activity are superior to fluorouracil.

Keywords: *gold glyconanoparticles; human colon adenocarcinoma cells; Caco-2; fluorourcil; MTT-test*

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ECO•VECTOR

LIST OF ABBREVIATIONS

Au-Fuc-MHH — aurum-fucose-mercaptohexanoylhydrazide
Au-Gal-MPH — aurum-galactose-mercaptopropanoylhydrazide
Au-Lac-MPH — aurum-lactose-mercaptopropanoylhydrazide
GGNPs — gold glyconanoparticles
GNPs — gold nanoparticles
IC_{50} — 50% inhibitory concentration
MTT — 3-(4,5-dimethylthiazid-2-yl)-2,5-diphenyl tetrazolium

INTRODUCTION

Oncological diseases are the second most common cause of death in the world after cardiovascular pathology making more than 15% in the structure of total mortality [1]. Currently, National Strategy for combatting oncological diseases in the long-term period (until 2030) is being realized with the priority of providing access to safe, effective, high-quality and affordable basic medical drugs and vaccines for everyone, as well as introduction of modern means and systems with targeted drug delivery [2].

The most common forms of oncological diseases are lung and breast tumors (8.09 million deaths in 2018), colorectal tumors (1.8 million), prostate tumors (1.28 million), tumors of skin (1.04 million) and stomach (1.03 million), each requiring specific methods of treatment: surgical, radio- and pharmacotherapy [2].

One of the promising directions of antitumor drug therapy, as well as of targeted delivery of chemotherapeutic drugs, is the use of noble metal nanoparticles possessing a complex of specific optical and electrical properties, well-developed surface with the possibility of its modification primarily by introducing substituents through a thiol group having a high affinity for metals [3–5].

To use GNPs *in vivo* on experimental tumor models, it is necessary to analyze the cytotoxicity of the tested substances on cultures of normal and tumor cells *in vitro* to establish the concentrations and duration of incubation at which they are more toxic in relation to malformed cells.

The **aim** of this study to evaluate the cytotoxicity of solutions of gold nanoparticles with the surface modified with fucose, lactose and galactose residues, on *Caco-2* human colon adenocarcinoma cell culture.

MATERIALS AND METHODS

In the study, the following aqueous solutions of modified GNPs of 18 nm–21 nm diameter [7] synthesized in the Laboratory of Polymer Nanomaterials and Compositions for Optic Media of the Institute of High Molecular Compounds of the Russian Academy of Sciences, RAS (Saint-Petersburg, Russia) were used:

1) gold-fucose-mercaptohexanoylhydrazide (Au-Fuc-MHH) (1 mg/ml);

2) gold-lactose-mercaptopropanoylhydrazide (Au-Lac-MPH) (2 mg/ml);

3) gold-galactose-mercaptopropanoylhydrazide (Au-Gal-MPX) (1 mg/ml)

The synthesis of gold glyconanoparticles (GGNPs) (III) included two stages: the interaction of natural mono- and disaccharides (I) with hydrazides of 3-mercapto-propionic or 6-mercaptohexane acids and modification of colloidal gold by condensation products (II) obtained in the first stage of the process (Figure 1) [6, 7].

For the preparation of working solutions of GGNPs, the mother liquors were diluted with cell culture medium to final concentrations of 10 μg/ml–600 μg/ml for particles modified with fucose residues (10 μg/ml, 25 μg/ml, 50 μg/ml, 100 μg/ml, 200 μg/ml, 400 μg/ml, 450 μg/ml, 475 μg/ml, 500 μg/ml, 550 μg/ml, 600 μg/ml), 10 μg/ml–900 μg/ml for particles coated with lactose residues (10 μg/ml, 25 μg/ml, 50 μg/ml, 100 μg/ml, 200 μg/ml, 400 μg/ml, 600 μg/ml, 650 μg/ml, 700 μg/ml, 750 μg/ml, 850 μg/ml, 900 μg/ml) and 10 μg/ml–550 μg/ml for particles modified with galactose residues (10 μg/ml, 25 μg/ml, 50 μg/ml, 100 μg/ml, 200 μg/ml, 400 μg/ml, 450 μg/ml, 475 μg/ml, 500 μg/ml, 550 μg/ml). The incubation periods of substances with cells were 2-hour, 8-hour and 24-hours.

As a comparison drug, fluorouracil was used (a standard pharmacopeial sample of Nantong Jinghua Pharmaceutical Co., Ltd.) recommended for adjuvant therapy of colorectal tumors [8], at concentrations of 50 μg/ml–2000 μg/ml (50 μg/ml, 200 μg/ml, 600 μg/ml, 800 μg/ml, 1000 μg/ml, 1500 μg/ml, 2000 μg/ml). The duration of its incubation with cells was 2-hour and 8-hour because in this work, GGNPs demonstrated higher toxicity for tumor cells exactly with these incubation periods.

The cytotoxicity of GGNPs and of fluorouracil was studied on *Caco-2* human colon adenocarcinoma cell line (Center for Collective Use 'Collection of Vertebrate Cell Cultures', Saint-Petersburg, Russia). The cells were cultured at 37°C with 5% CO_2 in WS-189C incubator (WorldScience, Korea) in Dulbecco's modified Eagle's medium with a high glucose content (4,500 mg/L)

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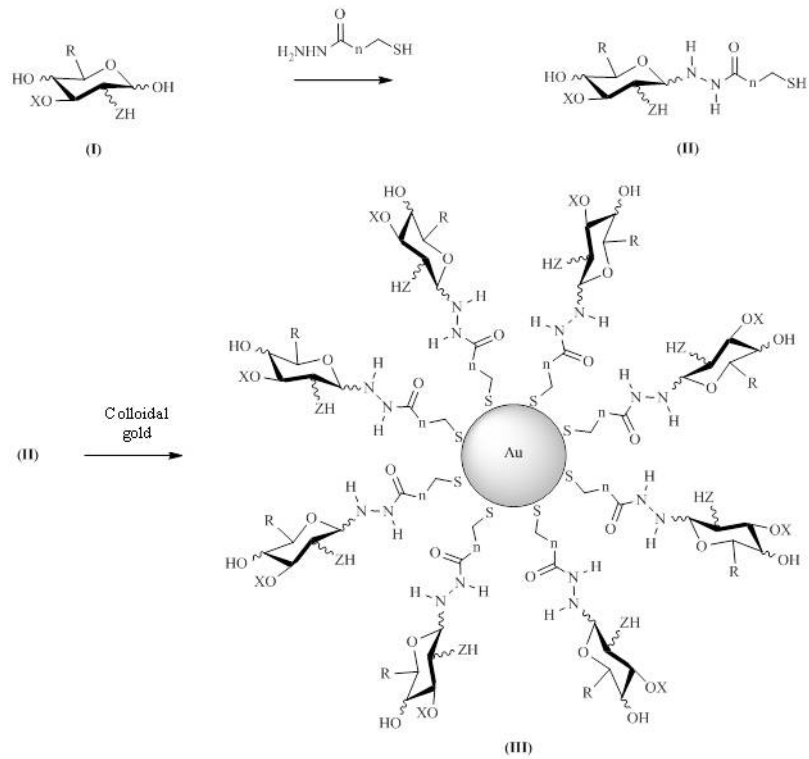

Fig. 1. A scheme of synthesis of gold glyconanoparticles [6, 7].
Notes: X — hydrogen atom or a fragment of D-galactose, Z — oxygen atom, R — methyl or hydroxymethyl group, n — 1-thiopropanoyl group or 4-thiohexanoyl group; I — natural mono- and disaccharides, II — condensation product, III — gold glyconanoparticles.

containing L-glutamine (4 mM), 15% of bovine serum, 100 U/ml and 100 μg/ml of penicillin and streptomycin, respectively (all components of Sigma-Aldrich, Germany). After reaching the 80% monolayer, the cells were removed from the flask by adding trypsin-EDTA solution (0.25% of trypsin and 0.2% of EDTA, Sigma-Aldrich, Germany) and were inoculated into a 96-well plate (Corning, USA) in the amount of 10^4 cells per well. Then the cells were cultured for 48 hours after reaching the monolayer (tumor cell culture — human colon adenocarcinoma — the first series) or for 21 days after the formation of the monolayer (cell culture similar to human small intestine epithelial cells — differentiated cells — the second series [9]). The nutrient medium was changed daily.

Cytotoxicity (influence on the intensity of cell metabolism) of GGNP and fluorouracil solutions was evaluated in MTT-test. Solutions of tested substances of the described concentrations in the incubation medium were added to wells with cells of the first and second series for 2-hour, 8-hour and 24-hours. After the incubation, 0.5% isotonic solution of 3-(4,5-dimethylthiazid-2-yl)-2,5-diphenyl tetrazolium bromide (MTT; Sigma, USA) in the quantity of 20 μl was added to each well followed by incubation for 2 hours, then MTT solution was removed and 100 μl of dimethyl sulfoxide (PanEko, Russia) were added. The optical density of the solution was measured in 10 minutes at 530 nm on StatFax 2100 spectrophotometer for plates (Awareness Technology, USA) with differential filter for 620 nm.

Cytotoxicity was calculated by the formula:

cytotoxicity = (OD of experimental wells — OD blank)/ (OD of control wells — OD blank) × 100%

where OD — optical density, blank — well without cells, control wells — wells with cells incubated with pure nutritional medium.

For each GGNPs and incubation period, 4 repetitions were used.

Then, in GraphPad Prizm 8.4.3 program, 50% inhibitory concentration (IC50) in μg/ml was calculated for each of GGNPs and fluorouracil with all incubation periods, and the obtained data were compared for tumorous and differentiated cells.

To analyze the effect of the studied GGNPs and fluorouracil on the survival of tumor cells at

concentrations corresponding to IC_{50} with incubation periods in which IC_{50} for tumor cells was reliably lower than for differentiated cells, tumor cells were stained with trypan blue (Bio-Rad, USA) by mixing 10 µl of cell suspension with 10 µl of dye and application of the mixture on the cartridge of Countess II FL automatic cell counter (Thermo FS, USA). For analysis, cells were cultured in 96-well plates. For control, cells were used incubated with nutritional medium without addition of the study compounds. For each substance and each incubation period 3 repetitions were used.

Statistical processing of the results was carried out using Statistica 13.0 program (Stat Soft Inc., USA). The data are presented as an arithmetic mean ± standard deviation (M ± SD). The data distribution was analyzed using Shapiro–Wilk test. The intergroup differences of IC_{50} for GGNPs and fluorouracil at different incubation periods with cells, as well as between tumor and differentiated cells, were analyzed using Student's test for unconjugated samples. The differences were considered statistically significant at $p < 0.05$.

RESULTS

In investigation of cytotoxicity of GGNPs and fluorouracil on *Caco-2* cells, the following results were obtained (Figures 2–4).

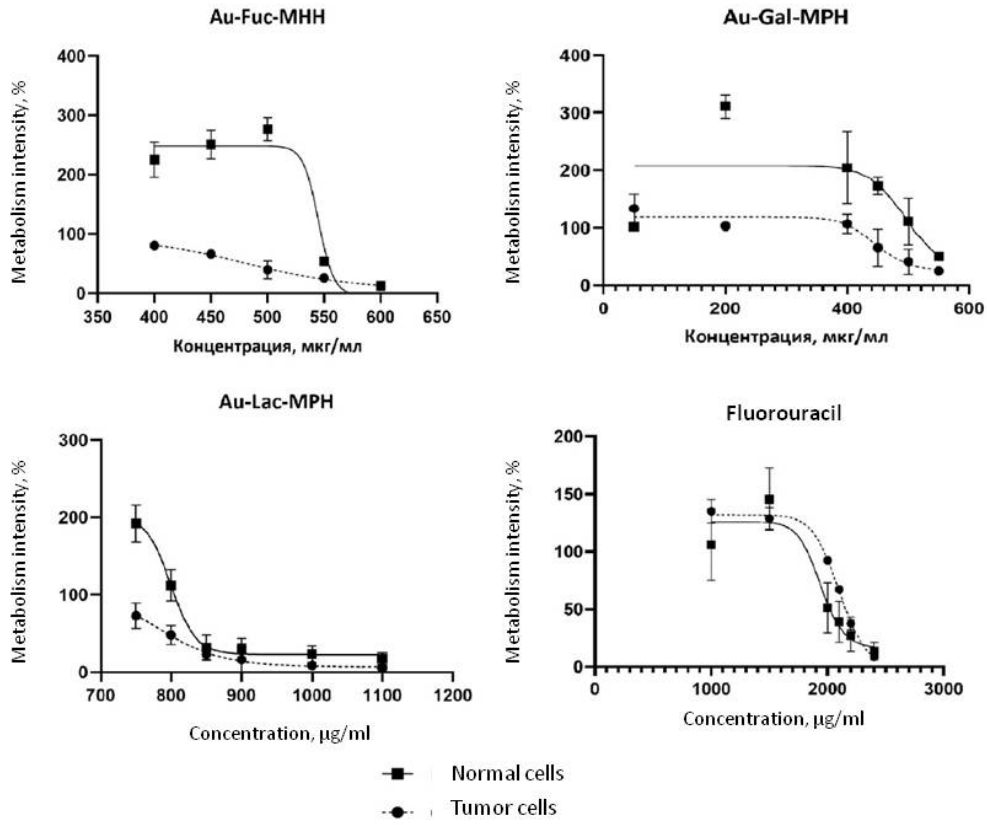

Fig. 2. Graphs of metabolic activity of Caco-2 cells in their incubation with gold glyconanoparticles and fluorouracil for 2 hours..
Notes: Au-Fuc-MHH — aurum-fucose-mercaptohexanoylhydrazide, Au-Gal-MPH — aurum-lactose-mercaptopropanoylhydrazide, Au-Lac-MPH — aurum-galactose-mercaptopropanoylhydrazide. Dots on the graph correspond to the arithmetic meal values, spread of values — to standard deviation.

IC_{50} for nanoparticles with fucose relative to tumor cells (the first series) was 581.5 ± 28.9 and 335.5 ± 35.5 µg/ml after 2-hour and 8-hour incubation, respectively; for nanoparticles with lactose — 768.9 ± 50.3 and 514.5±44.8 µg/ml, for nanoparticles with galactose — 466.9 ± 29.2 and 298.6 ± 27.8 µg/ml. Longer incubation resulted in a reliable decrease in the IC_{50} of the tested nanoparticles by 1.43 ($p = 0.0007$), 1.50 ($p = 0.0003$) and 1.56 times ($p = 0.0003$), respectively, in comparison with incubation for 2 hours.

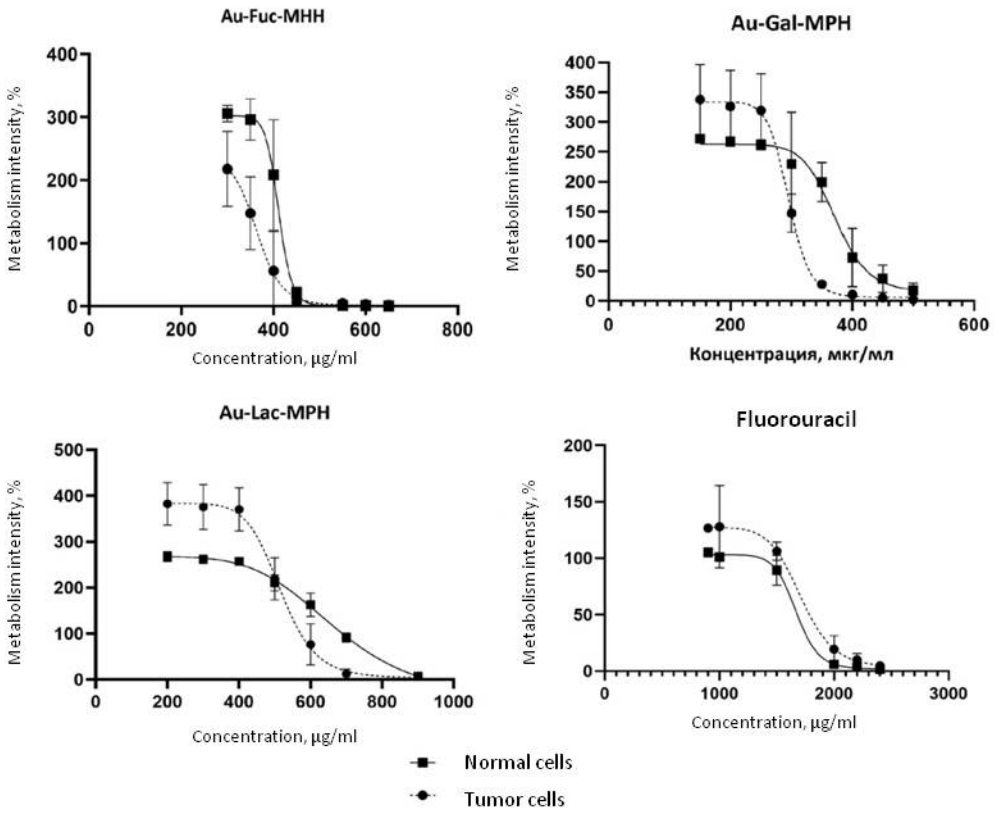

Fig. 3. Graphs of metabolic activity of *Caco-2* cells in their incubation with gold glyconanoparticles and fluorouracil for 8 hours.
Notes: Au-Fuc-MHH — aurum-fucose-mercaptohexanoylhydrazide, Au-Gal-MPH — aurum-lactose-mercaptopropanoylhydrazide, Au-Lac-MPH — aurum-galactose-mercaptopropanoylhydrazide. Dots on the graph correspond to the arithmetic meal value, spread of values — to standard deviation.

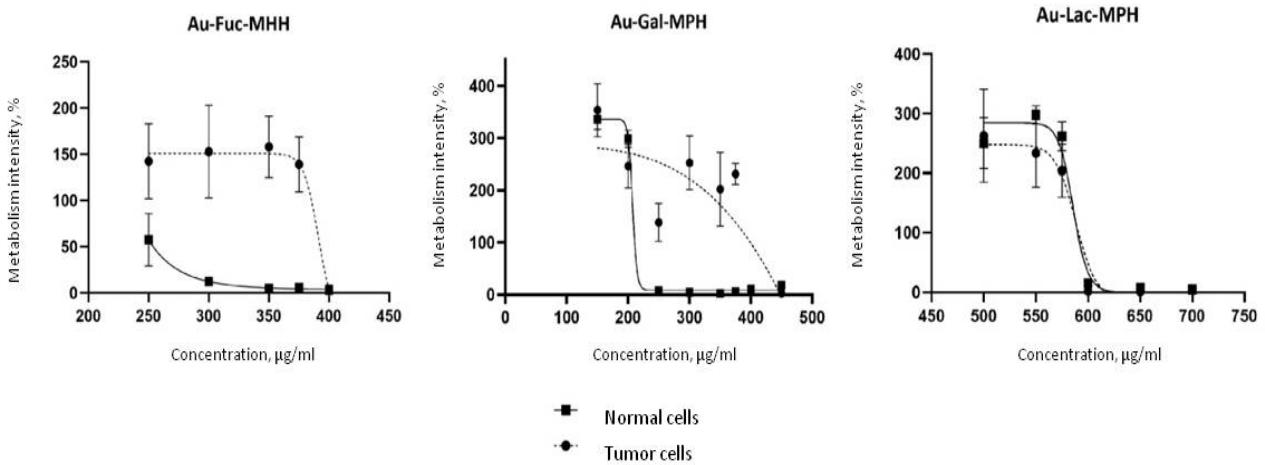

Fig. 4. Graphs of metabolic activity of *Caco-2* cells in their incubation with gold glyconanoparticles and fluorouracil for 24 hours.
Notes: Au-Fuc-MHH — aurum-fucose-mercaptohexanoylhydrazide, Au-Gal-MPH — aurum-lactose-mercaptopropanoylhydrazide, Au-Lac-MPH — aurum-galactose-mercaptopropanoylhydrazide. Dots on the graph correspond to the arithmetic meal value, spread of values — to standard deviation.

For differentiated cells (the second series), the IC_{50} for all types of nanoparticles was reliably higher than for tumor cells: for nanoparticles with fucose — 530.1 ± 2.7 μg/ml with 2-hour incubation (p = 0.037) and 410.0 ± 14.7 μg/ml with 8-hour incubation (p = 0.002); for nanoparticles with lactose — 830.9 ± 6.5 μg/ml with 2-hour incubation (p = 0.019) and 638.9 ± 13.7 μg/ml with 8-hour incubation (p = 0.015); for nanoparticles with galactose — 510.7 ± 20.9 μg/ml with 2-hour incubation (p = 0.018) and 376.1 ± 35.8 μg/ml with 8-hour incubation (p = 0.007).

Increase in duration of incubation of differentiated cells with GGNPs containing residues of fucose, lactose and galactose, from 2-hour to 8-hour led to reliable reduction of IC_{50} by 1.29 (p = 0.000004), 1.30 (p < 0.00001) and 1.36 times (p = 0.0006), respectively.

In 24-hour incubation of *Caco-2* cells with nanoparticles with the surface modified by fucose, IC_{50} did not show any reliable difference for their tumor and differentiated varieties (p > 0.05): 386.2 ± 9.2 μg/ml for the first series and 246.5 ± 1.6 μg/ml for the second series. For the rest of GGNPs, IC_{50} for tumor cells was reliably higher than for differentiated cells: 730.6 ± 139.5 and 591.9 ± 7.8 μg/ml for nanoparticles with lactose (p < 0.0001); 381.4 ± 13.3 and 235.0 ± 7.9 μg/ml for nanoparticles with galactose (p < 0.0001).

In some cases increase in the intensity of cell metabolism of differentiated (predominantly) and tumor cells above 100% was noted in incubation with GGNPs at low doses.

In investigation of survival of tumor cells it was found that in their incubation for 2 hours with GNPs modified by fucose, lactose and galactose, percentage of viable cells did not differ from the values obtained in incubation with a pure nutritional medium (p > 0.05). In 8-hour incubation with nanoparticles these parameters were lower than control values and were 24.17 ± 0.39% (p = 0.041), 30.55 ± 8.56% (p = 0.046), 32.81 ± 3.13%, respectively (p = 0.030, Table 1).

Table 1. Data on Survival of Tumor cells in Incubation with Study Compounds, %

Incubation Period	Au-Fuc-MHH	Au-Lac-MPH	Au-Gal-MPH	Fluorouracil
Control	100	100	100	100
2 hours	36.6 ± 1.78	60.6 ± 15.0	41.8 ± 7.33	28.8 ± 1.25
8 hours	24.17 ± 0.39*	30.55 ± 8.56*	32.81 ± 3.13*	45.37 ± 18.88*

Notes: * — differences compared to control with p < 0.05; Au-Fuc-MHH — aurum-fucose-mercaptohexanoylhydrazide, Au-Lac-MPH — aurum-lactose-mercaptopropanoylhydrazide, Au-Gal-MPH — aurum-galactose-mercaptopropanoylhydrazide

Control drug fluorouracil showed cytotoxicity in relation to tumor cells with IC_{50} 2107.5 ± 19.1 and 1764.0 ± 192.8 μg/ml with 2-hour and 8-hour incubation, respectively. In relation to differentiated cells, IC_{50} of fluorouracil was 1995.0 ± 19.7 μg/ml with 2-hour incubation and 1694.4 ± 101.5 μg/ml with 8-hour incubation (Figures 2, 3). No significant difference was observed between IC_{50} of fluorouracil in relation to differentiated and tumor cells with the same duration of incubation (p > 0.05). Increase in duration of incubation led to reduction of IC_{50} in relation to tumor cells by 1.19 times (p = 0.012); in relation to differentiated cells by 1.18 times (p = 0.0024). IC_{50} of fluorouracil in relation to cells of the first series reliably exceeded this parameter for Au-Fuc-MHH, Au-Lac-MPH and Au-Gal-MPH: with 2-hour incubation by 3.62 times (p = 0.00019), 2.74 times (p = 0.00018) and 4.51 times (p = 0.0002), respectively; with 8-hour incubation by 5.25 times (p = 0.00019), 3.73 times (p = 0.00017) and 5.90 times (p = 0.0002), respectively.

The percentage of viable tumor cells in incubation with fluorouracil at concentrations corresponding to its IC_{50}, was below control only with 8-hour incubation and was 45.37 ± 18.88% (p = 0.035).

In comparison of the percentage of dead tumor cells after 8-hour incubation with tested GGNPs and fluorouracil, no difference was found (p > 0.05). Thus, the effectiveness of the cytostatic effect of substances does not differ from that of fluorouracil.

DISCUSSION

The aim of this study to analysis of cytotoxicity of GNPs modified by fragments of fucose, lactose and galactose through the residue of thiol-containing hydrazides of carboxylic acids in relation to the *Caco-2* cell culture in MMT-test. With this, *Caco-2* line cells were cultured in 96-well plate for 48 hours after reaching the monolayer to obtain tumor cells, or within 21 days after formation of the monolayer, since in this period the cells spontaneously differentiate to physiologically polarized monolayer similar to the epithelium of small intestine [9]. Thus, the work involved cells of different morphology, but *of the common precursor* — human colon adenocarcinoma.

In our work, cytotoxicity of GNPs relative to culture of *Caco-2* cells was demonstrated as early as after

2-hour incubation. Here, higher IC_{50} values of tested substances were shown in relation to cells differentiated to epitheliocytes of small intestine. Similar results were also obtained in 8-hour incubation.

The obtained results may be associated with a different extent of accumulation of GGPNs in differentiated and tumor cells, which is due to the presence of sugar residues on the surface of particles with affinity for surface lectins of tumor cells [10]. Further analysis of the content of nanoparticles in cells after incubation can confirm this assumption. An increase in the incubation period to 24 hours led to the fact that the IC_{50} of nanoparticles in relation to tumor and differentiated cells either did not differ (Au-Fuc-MHH), or became higher for tumor than for normal cells (Au-Lac-MPH and Au-Gal-MPH), which is probably due to the penetration of particles also into normal cells by other than receptor-dependent mechanism [11]. Thus, nanoparticles can also penetrate into tumor tissues passively by the enhanced permeability and retention (EPR) effect associated with accelerated growth of tumor tissues and the appearance of significant cavities between cells and in cell membranes, as well as with defective tumor vascularization and irregular epithelium, reduced number of lymphatic vessels and insignificant absorption of interstitial fluid [5].

One should note the identified increase in the metabolic activity both of cells differentiated to epitheliocytes of the small intestine (predominantly) and tumor cells in incubation with GGNPs within the specified periods. One of the probable causes of this phenomenon is G2/M block of cell cycle accompanied by enhanced mitochondrial activity. This process precedes cell death [12].

Another probable cause of growth of metabolic activity is inhibition of the efflux transporter protein glycoprotein-P (ABCB1-protein) by nanoparticles. MTT is glycoprotein-P substrate, and decrease in its activity can probably be associated with more intensive intracellular accumulation of the substance and its reduction to formazan that absorbs light in the UV spectrum [13]. Attention should be paid to the fact that the preliminary joint incubation of GGNPs and MTT within 8 hours did not lead to a change of the optical absorption of the latter, which theoretically could lead to re-evaluation of metabolic activity of cells in MTT-test.

Predomination of this or that mechanism of intracellular penetration of nanoparticles, and consequently, the results of their use depend on the type of cells. For example, an increased need of colorectal cancer cells for L-fucose monosaccharides was demonstrated, which created prerequisites for the use of liposomes with this substance for targeted delivery of antitumor agents [14]. Specific receptors binding to fucose have also been found on the membranes of pancreatic cancer cells [15], and the *B16F10* melanoma cell culture interacts more intensively with galactose-modified magnetic nanoparticles [16].

In our work, comparison drug was chosen to be fluorouracil approved by FDA due to effectiveness it demonstrated in the treatment of a large number of malignant neoplasms, including colon adenocarcinoma. The drug inhibits thymidilate synthase enzyme, which frustrates intracellular nucleotide balance and causes double-stranded breaks of DNA [17]. There is also information about the stimulation of the transcription factor of p53 by the drug [18].

The results of our work demonstrate a higher selectivity of cytotoxic action of FFNPs compared to the chemical drug of comparison. It is relevant to continue *in vitro* analysis of possible mechanisms of cytotoxicity of GNPs. Here, it is reasonable to use 2-hour and 8-hour incubation duration, which is associated with a higher activity of particles against tumor cells compared to cells differentiated to intestinal epithelium.

CONCLUSION

Thus, gold nanoparticles with surface modified with fucose, lactose and galactose residues, have a cytotoxic effect on human colon adenocarcinoma cells, being superior in the activity to a classic cytostatic fluorouracil.

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