After radiolabeling with 177Lu, RCP of the purified radiolabeled conjugates was found to be >98% as determined by both PC and column chromatography. *In vitro* studies in CHO cells showed significant accumulation of nanoconjugates under hypoxic conditions with hypoxic to normoxic ratio of 7.10±0.45 at 2h post incubation, which steadily increased to 9.5±0.29 at 4h post incubation. Flow cytometry studies with FITC-Au-2-NIM-DOTAGA provided supporting evidence for enhanced uptake of nanoparticles under hypoxic condition as compared to normoxic condition.

Conclusion: The present work describes the preparation and *in vitro* evaluation of 177Lu-labeled AuNP's decorated with 2-nitroimidazole

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Multimodal radiobioconjugate - Trastuzumab-PEG-[^{198}Au]AuNPs-PEG-DOX for targeted radionuclide therapy of HER2-positive cancers

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Objectives: Gold nanoparticles (AuNPs) are interesting for scientists, because they can be applied in innovative treatment methods, which can be an alternative or a supplement of chemotherapy. AuNPs are used in medicine due to their unique properties, such as small size, universal biocompatibility, low toxicity, versatility and ease of surface functionalization [1,2]. The aim of this study is the synthesis of novel multimodal radiobioconjugate containing simultaneously in a one structure β^- emitter - ^{198}Au (^{198}AuNPs), a chemotherapeutic – doxorubicin (DOX) and a guiding vector – Trastuzumab (TMAB).

Methods: Based on Turkevich method [3], the synthesis of 30 nm gold nanoparticles using radioactive precursor (^{198}Au) was performed [4]. The size, zeta potential and shape of nanoparticles were determined by TEM (Transmission Electron Microscopy) and DLS (Dynamic Light Scattering) techniques. To stabilize nanoparticles, polyethylene glycol (PEG, 5000 kDa) was used. DOX and TMAB were attached to a bifunctional PEG linker comprising the thiol and carboxylic groups at both ends. To analyze obtained bioconjugates, DLS and UV-Vis methods were applied. Cytotoxicity studies of SKOV-3 (HER 2+) and MDA-MB-231 (HER 2-) cancer cells after treatment with radioactive AuNPs were investigated with the use of the MTS colorimetric assay and cytometry method.

Results: The DLS and TEM measurements confirmed the expected average size (~30 nm) and spherical shape. The zeta potential value showed high stability of ^{198}AuNPs without a tendency to agglomeration. The ^{198}AuNPs were successfully modified with bifunctional hydrophilic polymer PEG due to high chemical affinity of sulphur to gold. Subsequently, doxorubicin and Trastuzumab were attached to activated carboxylic groups of PEG leading to form irreversible peptide bond. The size and zeta potential values of obtained conjugates examined at each stage, confirmed the formation of compounds. The doxorubicin attachment efficiency determined by UV-Vis technique was approximately 70%. Using ^{131}I-labeled TMAB it was calculated that 73±8 Trastuzumab molecules were conjugated with one AuNP. TMAB-PEG-^{198}AuNPs-PEG-DOX exhibited high stability in saline and PBS buffer. The preliminary results of MTS and apoptosis assays showed cytotoxicity of obtained radioconjugates in a time and dose-dependent manner.

Conclusions: The obtained multimodal radiobioconjugate TMAB-PEG-^{198}AuNPs-PEG-DOX shows promising properties for further *in vitro* and *in vivo* studies.

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Development of radiolabeled polymer nano- and micron-sized carriers

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Objectives. The most important aim of modern medicine is the search for new approaches that would significantly increase the effectiveness of treating malignant neoplasms. One of such approaches is the development of transport systems for targeted drugs [1]. Today the use of carriers for targeted delivery of radionuclides is severely limited due to their low encapsulating ability and suboptimal binding activity [2]. This problem can be solved by using hybrid multilayer capsules [3]. The physicochemical properties can be widely varied, creating a multifunctional platform that is sensitive to various types of physical and chemical influences [4]. This investigation is aimed at developing reproducible technologies for encapsulating diagnostic and therapeutic radionuclides in the individual form of micro- and nanoparticles of complex composition with directional ligands.

Methods. The synthesis of 225Ac-doped CaCO3 core-shell particles (225Ac-MPs and 225Ac- SPs) was performed by the next protocol: 100 µL of DOTA-modified human serum albumin (HSA) solution (3 mg/mL in 0.05 M ammonium acetate, pH 7.4) was incubated with 25 µL of [225Ac]Ac(NO3)3 (20-100 µCi, solution in 0.1 M HCl) 37°C for 60 min. Then 1M Na2CO3 and 1M CaCl2 solutions were mixed together with 225Ac-DOTA-HSA to form CaCO3 particles. Then, the particles were coated with HSA and tannic acid 7 times (3.5 bilayers) using the Layer- by-Layer procedure. Finally, 225Ac-doped core-shell particles were resuspended in 1 mL of normal saline.

Results. In this work, the protocols for 225Ac-loaded nano- and micron-sized carriers were developed. The full physicochemical characteristics (size, morphology, surface charge, permeability) were also studied. The biocompatibility and stability of complexes in biological media were confirmed. The radiological activity of the system has been established *in vitro* experiments. The efficiency of incorporation of the 225Ac was ~ 65%, while the efficiency of retaining daughter nuclei (francium-221 and bismuth-213) was > 85%. *In vivo* studies demonstrated the biodistribution of carriers in the organs of Wistar rats using SPECT and computed tomography. Histological analysis was performed on animal tissues of the studied organs for to assess the toxicological effect of carriers with 225Ac.

Conclusions. Thus, a new form of a radiopharmaceutical based on nano- and micro-sized particles of a complex composition was developed. Protocols were developed for modifying the surface of capsules with molecular vectors. The specificity of the developed carriers for tumor cells was demonstrated in comparison with primary cultures of healthy cells *in vitro*, as well as in *in vivo* models of oncological diseases (melanoma).