Cancer treatment assisted by light: TiO_2-based nanoparticles as drug nanocarriers

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1. Introduction

Photodynamic therapy (PDT) involves administration of an inactive form of a medicament, or a carrier/medicament system, that can be activated by light illumination in a target tissue. This therapy results in a sequence of photochemical and photobiological processes that cause irreversible photodamage of a tumor tissues with minimum damage of surrounding, healthy tissue [1]. Various medicaments have been tested as photosensitizers. My previous studies have demonstrated that TiO_2-based nanoparticles (NPs) in a combination with Ru-complex can be used as photo-tunable nanocomposite system (NCS) against A375 human melanoma cell line. The Ru-complex releasing kinetics can be enhanced by illumination with the UV light, and sustained when the system was illuminated with visible light. This was in a correlation with cell cytotoxicity. Other studies have, however, shown that the cellular uptake of nanoparticles depends on their size and shape. Therefore, **the aim of this study was to test the differences in the UV-induced cytotoxicity of TiO_2 nanoparticles of various size and shapes and on three different types of cancer cell lines.**

2. Material and methods

Metallo-drug complex cis-dichlorobis (2,2'-bipyridyl-4,4'-dicarboxylic acid) ruthenium(II) was synthesized, and it was later characterized by FT-IR, UV/VIS spectroscopy and with MALDI TOF mass spectrometry [2]. TiO_2 nanotubes (NT) and prolate nanospheroids (PNS) and colloidal nanoparticles were synthesized using the modified hydrothermal procedure and were characterized by TEM and XRD. The nanocomposite system was prepared, and nanoparticles loaded with complex were separated from free-standing molecules by centrifugation, and bonded supernatant was determined by UV/VIS spectroscopy. *In vitro* complex release test of nanocomposite system was performed. The following human cell cultures were used: A375-melanoma, PANC1-pancreatic cancer and SKBR3-breast cancer, which were obtained from the ATCC. Oxidative stress status was estimated by MDA assay in treated cell lines. Cytotoxicity of cells, after incubation with nanoparticles and nanocomposite system, in the dark, and under UV light illumination, was determined using sulforodamine B assay.

3. Results and discussion

Obtained spectra of desired metallo-drug complex have confirmed that product of synthesis has not isomerized during sensitive synthesis, and photobehavior of complex was evaluated based on maximum spectra. TEM and XRD of nanoparticles showed the structure of wanted nanoparticles and determined size and shape of synthetized particles. Drug entrapment efficiency was estimated to (62±2)%, while the loading efficiency was (18.5±0.5)%, and they were lower compared to those determined for colloidal nanoparticles. Also, when tested on the A375 cell lines, the maximum cytotoxicity is obtained after UV illumination of cells treated with the PNSs loaded with Ru-complex (Figure 1). When the cells are treated with individual components, the cytotoxicity was not much lower in comparison to control. These results are in agreement with the concentration of MDA (data not shown).

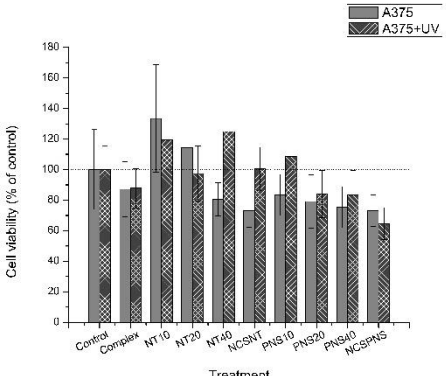

Figure 1. - A375 cell viability after incubation with NTs, PNSs and the nanocomposite system with both nanoparticles. Bars on the left represent the cell viability without UV illumination, whereas on the right, the viability with UV illumination are given

4. Conclusion

These experiments represent an important step for optimization of photodynamic therapy with new photosensitizing agents and medicaments. The results obtained with NTs and PNSs as potential photo-sensitive carriers for metallo-drugs indicate their lower cytotoxicity compared to previous results obtained with colloidal nanoparticles. Also, the results obtained with other SKBR3 and PANC1 cell lines demonstrated stimulating effect in terms of cell growth. Therefore, further studies will be undertaken to determine the localization of the nanocomposite systems, to elucidate the mechanism of action and to unequivocally determine the type of tumors against which the system is the most efficient. So far, based on the results, I can speculate that the nanoparticles are mostly aggregated on the cell surface and the cytotoxic effect is most likely mediated by the reactive oxygen species, i.e. the oxidative stress.

5. References

[1] Dougherty TJ, Gomer CJ, Henderson BW, Jori G, Kessel D, Korbelik M, et al. Photodynamic Therapy. JNCI: Journal of the National Cancer Institute. 1998;90(12):889-905.

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