Influence of platinum nanoparticles of different sizes on the activity of selected anticancer drugs

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In 2022, almost 10 million cancer-related deaths were recorded worldwide. Despite significant progress in anticancer therapies, chemotherapy still remains one of the most commonly employed and most effective treatment methods. Unfortunately, administration of cytostatic drugs is associated with the occurrence of serious side effects, including multi-organ toxicity, as well as the development of resistance in cancer cells, which significantly reduces the quality of patients' life and limits treatment options. Therefore, the search for therapy modifications is one of the key challenges of modern medicine. One of the promising areas that can contribute to improving the efficiency of anticancer therapies is nanotechnology, including the use of nanoparticles (NPs). Due to their unique properties, primarily their small size with a high surface-to-volume ratio, NPs can be used as drug delivery systems (DDS) for precise, controlled, and selective penetration into cancer cells, which minimizes the exposure of healthy cells to the chemotherapeutic agent itself. Importantly, the size of nanoparticles may be particularly relevant in the context of cell membrane penetration and toxicity. Platinum nanoparticles (PtNPs), which belong to metallic nanoparticles, due to their specific properties such as antibacterial, antifungal, but also anticancer activity, may be a very promising tool in the field of medicine.

Therefore, the aim of this doctoral thesis was to investigate the occurrence of direct interactions between platinum nanoparticles and selected anticancer drugs such as cisplatin (CDDP), doxorubicin (DOX) and epirubicin (EPI). In addition, it was examined whether these interactions affect the biological activity, including mutagenicity and cytotoxicity, of the tested compounds. The research was conducted in the context of potential differences resulting from the use of nanoparticles of diverse sizes. The project included analysis of PtNPs aggregation under the influence of selected chemotherapeutic agents. A number of physicochemical analyses, including spectroscopic, fluorometric, and calorimetric methods were employed to confirm the occurrence of direct interactions between the tested nanoparticles and the mentioned drugs. In the biological part, the effect of PtNPs on the mutagenic activity of selected anticancer drugs was assessed using *Salmonella enterica* serovar Typhimurium. Additionally, cytotoxicity studies of both the nanoparticles themselves and their effect on the activity of selected cytostatics were performed using human breast cancer cell lines MDA-MB-231 and SKBR-3 (PtNPs - CDDP), melanoma MelJuSo (PtNPs - DOX and PtNPs - EPI), and a non-cancerous keratinocyte cell line HaCaT (PtNPs - DOX and PtNPs - EPI).

The obtained results indicate the considerable potential of using platinum nanoparticles in the future, both to increase the effectiveness of existing and to develop new anticancer chemotherapy regimens. One of the key aspects of their application may be to reduce the side effects of anticancer chemotherapeutics on healthy tissues and cells. Moreover, employing nanoparticles of different sizes may contribute to the modulation of anticancer drugs' activity, which is particularly significant in the case of the therapy of cancers that are either initially resistant to treatment or acquire resistance during therapy.