ABSTRAKT

Cancer is a significant health problem among people around the world. Conventional chemotherapy involving the administration of cytostatic drugs to the patient's body, in addition to the intended effect related to the apoptosis of cancer cells, has many side effects. The reason is the non-selective action of anticancer drugs and their effect on normal cells. The searching for solutions aimed at improving the effectiveness of chemotherapy and patient comfort is very indicated. One of the solutions that can increase the effectiveness of chemotherapy is the use of drug carriers. The main task of the carrier is to transport drugs to the target site and reduce the toxicity of therapy. Congo red (CR) was used as the drug carrier in this study. CR is a supramolecular compound that creates self- assembled ribbon like structures in aqueous solutions capable of intercalating smaller molecules, e.g. drugs.

The aim of the research was to present CR as a model supramolecular carrier system for drug transport. Studies were carried out to understand the mechanism of its action and to evaluate its effectiveness *in vitro*. The model drug was doxorubicin (DOX). It is presumed that the obtained results will be a universal model of the mechanism of action of supramolecular structures as carrier systems. The research was carried out using computational methods of quantum chemistry, molecular dynamics simulation, Raman spectroscopy together with cell studies and the Langmuir monolayer technique (measurements of π - A isotherms and adsorption kinetics).

As a result of the conducted research, it was proved that supramolecular CR structures are stabilized by van der Waals interactions and hydrogen bonds, which additionally "glue" ribbon like structures into large agglomerates. It was noticed that in the case of a mixed CR/DOX system, the drug molecule easily incorporated into the CR structures. This is because the aromatic part of the drug is easily incorporated into the CR ribbon like structure, while the sugar part of the drug protrudes above the surface. It was confirmed that weak intermolecular interactions are responsible for the complexation of the molecules.

Cell studies conducted on the MCF7 breast cancer cell line and the T24 bladder cancer cell line showed the effectiveness of using CR as a DOX carrier for cancer cells. The presence of CR in the system contributed to increasing the efficiency of drug transport. Increased accumulation of carrier-transported DOX in MCF7 cells was observed already for the lowest

tested concentration (1 nM) and the shortest stimulation time (1 h). It was noted that the higher the concentration of the drug in the system and the longer the stimulation time, the more visible the accumulation of DOX inside the cells. Qualitatively identical results were obtained for both tested cell lines, which suggests that CR is a non-selective carrier for cancer cells.

The model lipid membrane in the study was dipalmitoylphosphatidylcholine (DPPC). Experiments on monolayers showed that DOX in combination with CR showed increased penetration into the lipid monolayer and affect its organization. Based on the performed molecular dynamics simulations, it is concluded that CR contributes to the reduction of the free energy barrier for transport across the membrane. It was noticed that the presence of CR increases the adsorption of the system to the monolayer. Visual observation of the trajectory showed that CR has the ability to "cut" DOX agglomerates formed in water, which contributes to increased incorporation of the drug into the CR ribbon like structures. The performed molecular dynamics simulations gave results qualitatively equivalent to those obtained during the experimental study of monolayers. These results confirm the stability of CR/DOX clusters in the monolayer, which may be the first step of drug transport across the membrane.

The research results presented in this doctoral dissertation confirm the usefulness of using supramolecular CR as a drug carrier in cancer therapy. Due to the key role of weak intermolecular interactions, the presence of which is very characteristic of supramolecular systems, proved as a result of the analyzes carried out, it is presumed that each compound with a structure similar to CR may be a potential drug carrier.