DESCRIPTION FOR THE GENERAL PUBLIC

The main purpose of the research project is application of a group of silsesquioxane structures as novel nanocarriers for anticancer drugs – anthracyclines: (doxorubicin – DOX and daunorubicin – DAU). Both these antibiotics of wide action spectrum and high efficacy are widely used in contemporary chemiotherapy in the form of hydrochlorides. They intercalate with DNA, inhibit proliferation of cancer cells and lead to their apoptosis. Unfortunately, they are not selective and administration of higher doses can lead to heart failure. Nowadays they are also applied in a more safe form as drugs encapsulated in liposomes (PDLH – Pegylated Liposamal Doxorubicin Hydrochloride). The liposomal sphere leads to slower release of drugs and partly reduces the main side effect but can often result in fertility issues. Important features of POSS type carriers that are currently regarded as the next generation of materials for biomedicine is biocompatibility, biodegrability, small size (0.5- 3 nm) and lack of toxicity as they are metabolized to harmless silicic acid. The search for effective nanocarriers of anthracyclines is currently intensely developed. The reason for that is obvious as in senescent society cancer is the main killer and every four second someone dies form this highly terminal illness. Till now literature has described anchoring anthracyclines on such carriers as graphene oxide, poly(lactide-*co*- glycolide), polyamideamine (PAMAM) dendrimers or fatty acids. Encapsulation or conjugation of a drug with a carrier leads to slow release of an active substance, extending its time of action but also leading to decreased doses. Nanocarriers, such as silsesquioxanes (compounds, where the ratio of silicon to oxygen atoms is $Si_1O_{1..5}$) allow for anchoring and administration of two or more drugs at the same time, both with imaging agents (fluorescein in diagnostics) and targeting moieties that direct the nanoconjugates to cancer cells (folic acid, hialuronic acid or biotin). Till now, though, there is highly growing interest in application of silsesquioxanes in biomedicine, to my best knowledge, there is only one report concerning binding anthracyclines with organosilicon structures. It originates from our laboratory in Centre of Molecular and Macromolecular Studies of Polish Academy of Sciences [K. Piorecka, E. Radzikowska, J. Kurjata, K. Rozga-Wijas, W. A. Stanczyk, E. Wielgus, *Synthesis of the first POSS cage-anthracycline conjugates via amide bonds*, *New J. Chem*., 2016, DOI: 0.1039/c6nj00347h]. Current project is directed on the novel synthetic cycle, allowing for preparation of nanoconjugates of DOX and DAU with a composition of linear, cyclic and cage silsesquioxanes, obtained from hydroxyalkyl trialkoxysilanes. It would lead to increase cost-effectiveness, when compared to the use of octameric T_8 cage. Additionally, due to coupling of some of hydroxyl groups of the carrier with carboxy terminated, methoxylated poly(ethylene glycol) (PEG), apart from succinic anhydride modified anthracyclines with terminal caboxyl groups, would largely improve solubility of such the prodrugs in water. The number of available –OH moieties of the carrier will allow for additional binding of target moiety – biotin. The planned scope of research will lead to preparation of novel nanoconjugate structures (of a carrier size ~2.7 nm), with optimum composition and yield and to determine selectivity and efficacy of the organosilicon based prodrugs towards cell lines [A. Janaszewska, K. Gradzińska, M. Marcinkowska, B. Klajnert-Maculewicz, W. A. Stańczyk, *In vitro studies of polyhedral oligo silsesquioxanes: evidence for their low cytotoxicity*, *Materials*, 2015, 8, 6062-6070]. Structural and rate of release studies will include multinuclear NMR, IR and fluorescence spectroscopy, mass spectrometry (MALDI TOF), and chromatography (TLC. HPLC). *In vitro* toxicity will be determined by calorimetry (MTT) and reactive oxygen species (ROS) tests.