NOVEL GLYCOFULLERENES FOR ANTI-CANCER THERAPIES

Fullerenes were discovered in 1985 as a novel carbon allotrope by American chemists Curl and Smalley, and British astronomer Kroto. Numerous practical applications of these nanoparticles have since been described, including solar cells, drug carriers, photosensitizers in photodynamic therapy and contrast agents used for imaging the tumor tissues. This project refers to previous research, discovering the potential of [60]fullerenes in multitargeted and combination therapies.

Cancer is now the second cause of all deaths in Poland. Therefore, there is urgent need to design and synthesize novel compounds with anti-cancer properties. Moreover, better understanding of the mechanisms of action of such nanoparticles will enable their continuous improvement. An interesting group of potential drugs in this field are sugar derivatives of [60]fullerene. This research project focuses in particular on the medicinal chemistry of fullerenes, including cancer therapy and imaging of sugar derivatives. The main goal of this project is the synthesis and study of anti-cancer properties of sugar derivatives of fullerenes used in photodynamic therapy and combination therapies with clinical anti-cancer drugs. Photodynamic therapy is the method of fighting with tumors and microbial infections in which the corresponding compound called the photosensitizer is excited with the light of a suitable wavelength in the presence of oxygen. The generated in that process reactive oxygen species (ROS) are selectively destroying cancer cells.

The resulting compounds will be visualized in tumor cells by attaching to them fluorescent tags followed by observation using confocal microscopy or flow cytometry. In the synthetic part of the project it is planned to synthesize sugar derivatives of fullerenes and conjugate them with 5-aminolevulinic acid (precursor of endogenous photosensitizer) and gemcitabine (anti-cancer drug Gemzar®). For selected compounds, biophysical measurements will be performed including assessment of the generation of free radicals followed by advanced molecular biology techniques.

The following project is carried out in the interdisciplinary team consisting of specialists in the field of synthetic chemistry, biophysics and molecular biology, in collaboration with University of Silesia, Jagiellonian University and Baylor College of Medicine, USA. Preliminary results of the experiments are very promising, indicating a lack of dark cytotoxicity in normal and neoplastic cells, for selected sugar derivatives of fullerenes. This is an extremely important aspect of photodynamic therapy, necessary for the success of the project.