

Research over the last years has clearly confirmed that the intensive generation of reactive oxygen species (ROS) in cells is a response to external stimuli such as stress, environmental pollution, infections and improper diet. They constitute risk factors associated with the occurrence of chronic civilization diseases - cancers, allergies, diabetes, obesity, cardiovascular diseases and neurodegenerative disorders. Numerous analyzes have proved that there is a negative correlation between a diet rich in plant ingredients (vegetables, fruits, herbs) and the incidence of various types of cancer as well as other diseases of the immunological, cardiological and metabolic systems. It is known that the health-promoting effect of phenolic compounds results from both their direct antioxidant activity per se and also the intermediate one in which they modulate the expression of certain genes and the activity of signal proteins related to the risk of disease. In addition, the natural antimicrobial function of this class of structures present in plants is used in the synthesis of antibiotics, fungicides and antivirals. Among phytochemicals, the narrower class is phenolic acids. Their biological activity (including antioxidant) is strongly determined by the molecular structure i.e. the type, number and position of functional groups. Unfortunately, the human body metabolizes and assimilates phenolic compounds only to a small extent - their bioavailability, permeability through tissue and cell barriers, and therefore therapeutic activity is significantly reduced. There are many strategies to improve bioavailability. One of them is the formation of salts and complexes with non-toxic metals, which influencing changes in the structure of the molecule and the distribution of electron density can improve its lipophilicity, solubility, stability in the cellular environment and strengthen the interactions with cell membranes. Thanks to such a solution it is possible (i) to improve the natural properties of phenolic acid (antioxidant), (ii) to give new (cytotoxic, antimicrobial) traits, and (iii) to improve absorption and metabolism with low toxicity without harmful effects on the natural environment. Our project selected: (a) metals based on their known antimicrobial activity or acting as a macro and microelements in the human body: Ca, K, Na, Mg, Zn(II), Co(II), Fe(III), Mn(II), Ag(I), Cu(II) and (b) ligands classified in three groups: 1) mandelic acid and its derivatives, 2) tartaric acid and its conjugates with caffeic acid, and 3) aromatic and alicyclic trihydroxycarboxylic acids. Some of these acids are used in medicine and cosmetology and have proven antibacterial properties (also against antibiotic resistant strains) and fungicides. The first stage of the research will be to synthesize salts / complexes of selected metals with ligands and to examine their composition and physicochemical properties using spectroscopic methods and computational chemistry. Compounds with the most promising properties will then be subjected to cytotoxicity tests on human cell lines (fibroblasts, keratinocytes and melanocytes). The last stage of the project will be to check whether the substances so obtained show any negative impact on the natural environment (tests of biodegradation and environmental toxicity). The superior goal of our studies will be to find a correlation between molecular structure, physicochemical properties and biological activity of ligands, complexes and salts. A systematic and multi-faceted approach using different research techniques will increase the complexity of analyzes and will allow to determine the structures responsible for the desired biological effect. The key to understanding the mechanisms of biological compounds is to recognize the role of modification of their electronic structures. These paths open (a) the implementation of innovative research, (b) based on an innovative methodology of (c) an effective nature, rejecting the "trial and error" approach for pragmatic planning of research works. It will help to employ specialists in various fields in the project: chemistry, biology, physics, pharmacy, food technology, medical chemistry and microbiology. The interdisciplinary nature of the project and the development of young research staff are guaranteed by a list of consolidators (Bialystok University of Technology and the Institute of Agricultural and Food Industry Biotechnology) and invited partners: (a) MD Anderson Cancer Center, University of Texas, USA; (b) National Medical Institute, Warsaw; (c) Medical University of Warsaw; (d) University of Bialystok, (e) Hebrew University of Jerusalem, Israel. Consequently, this will enable finding new, non-toxic antimicrobial, antioxidant or cytotoxic compounds safe for humans and the natural environment as well as future conduct of targeted modifications of natural compounds that improve their bioavailability.