DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

The title of our proposal quotes the Italian movie (*Brutti, sporchi e cattivi*, released in 1976), and we hope there is a good match between the subject of our research and the plot of the movie, as the organic compounds with sulfur and nitrogen atoms are on the periphery of the current research on the antioxidants. During the long time N- and S- containing antioxidants were considered as not clean and not as elegant as the family of phenolic antioxidants, thus, there is a huge disproportion between current knowledge on phenolic antioxidants and nonphenolic antioxidants.

During the last 25 years two Nobel Prizes (in 1998 and 2002) were awarded for research on the mechanisms directly related to participation of radicals in signaling processes and regulation (including regulation of blood vessel tension, apoptosis). Progress in research on the role of free radicals in biologically important processes and rapid development of methodology allow for accurate monitoring, understanding, and prediction of the role of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) in metabolic processes in cells, tissues, and entire organisms. However, despite some positive role of radicals, their overproduction and spreading to oxidation-sensitive places leads to oxidative stress and induces pathological states associated with oxidative degradation of biomolecules (lipids, proteins, enzymes, sugars, and DNA) that might result in unfavorable events like cell necrosis, inflammation, and can cause diseases. Examples of diseases with etiology associated with oxidative stress are atherosclerosis. myocardial infarction, hypertension, diabetes, ageing, cancer, Parkinson's and Alzheimer's disease, autoimmune disorders, acute lung injury, acute respiratory distress syndrome, and hyperoxia. The role of antioxidants is either to remove ROS / RNS in order to prevent the initiation of radical chain of lipid peroxidation (thsese compounds are named preventive antioxidants, the examples are Vitamin C or glutathion), or, when the peroxidation is already running, this process can be stopped by another class of antioxidants, called chain-breaking (or radical trapping) antioxidants. The commonly known radical trapping antioxidants are phenols (such as vitamin E, flavonoids, alkylated phenols, resveratrol), some hydrocarbons (carotenoids, terpenes). Aromatic amines are also used in industrial applications. However, there is little knowledge about the mechanisms of antioxidant action of nonphenolic, pharmacologically and biologically active compounds bearing structural motifs of indole, quinoline, benzothiazole, alkysulfinyl and alkylsulfanyl groups, allicin and alliin, hydropersulfides, derivatives of thioureas. Many of those compounds are constituents of our diet (organic sulfur compounds can be found in garlic, onion, broccoli, and cauliflower), while other N- and S- compounds are the building blocks or core structures for hundreds of pharmaceuticals (derivatives of indole, quinoline, and benzothiazole). Some of those compounds are described in the literature as potential antioxidants confirmed by simple tests with model (artificial) radicals, but the mechanisms of action have not yet been detailed.

The purpose of the project is to comprehensively study the above-mentioned N- and S- compounds to check their ability to trap peroxyl and superoxyl radicals, to study the kinetics of such reactions and the role of localisation of the molecule on the mechanism of reaction with radicals and the efficiency of antioxidant action. Knowledge about the impact of these factors will contribute to a deeper understanding of the antioxidant activity of N- and S- antioxidants and will result in the design and synthesis of new substances capable of trapping peroxyl radicals, thus minimizing the oxidative stress in cells and tissues. Moreover, we are going to study the synergistic interactions of N- and S- antioxidants with common phenolic antioxidants.

The integral part of the research will be a verification of our hypotheses about mechanisms of antioxidant action not only in model systems, but also in cellular systems. We will test the cellular response at ROS level and also test the action of enzymes involved in the antioxidant response, including superoxide dismutase, catalase, sirtuins, and hemoxygenase-1.

The presented project is innovative; our intention is to extend current knowledge in order to build a coherent picture of antioxidant activity of various classes of antioxidants. The presented research hypotheses are the result of long-term research on the mechanisms of antioxidant action and antioxidant activity. The implementation of the project will strengthen the existing cooperation with at least two foreign partners and with a team of biologists. Moreover, it will give young researchers the opportunity to gain experience in work in an interdisciplinary scientific environment.