DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Over the last decades, there has been significant progress in the studies of the mechanisms of biologically important reactions mediated by radicals. The accumulated knowledge and progress in research methodology allow for accurate monitoring, understanding and prediction of the role of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) in processes in cells, tissues and entire organisms. During the last 20 years two Nobel Prizes (in 1998 and 2002) have beed awarded for the research on mechanisms directly related to participation of radicals as in signaling processes and regul;ation (including regulation of blood vessel tension, apoptosis). However, despite some positive role of radicals, their overproduction and spreading to oxidation-sensitive places leads to the formation of oxidative stress and induces pathological states associated with oxidative degradation of biomolecules (lipids, proteins, enzymes, sugars, DNA) that might trigger 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 diseases, autoimmune disorders, acute lung injury, acute respiratory distress syndrome, and hyperoxia. Some compounds present endogenously or introduced in small amounts, give prophylactic and therapeutic effect. The role of these substances, called antioxidants, is either to remove ROS and RFA in order to prevent the initiation of radical chain of lipid peroxidation, or when the peroxidation is already running, this process can be stopped by another class of antioxidants, called chain-breaking antioxidants.

There are many parameters and factors determining the reaction rate of antioxidants with various types of ROS and RNS, from simple structure-activity relationship considerations, though thermodynamics and reaction kinetics, the influence of co-antioxidants, reaction mechanisms (Hydrogen Atom Transfer, Proton Coupled Electron Transfer, Sequential Proton-Liss Electron-Transfer, and others), however, one of the key elements is the accessibility of the antioxidant to radicals (ROS, RNS) associated with its localisation and possible interactions with microenvironment. We suppose that lack of careful consideration of the interfacial phenomena is a cause of a number of controversies in the literature about antioxidant activity and mechanism of action of even such flagship antioxidants like tocopherols, resveratrol, melanonin, and flavonoids. Therefore, the aim of the project is a comprehensive study of a number of classes of phenolic and non-phenolic antioxidants in terms of their interaction with lipids in dispersed systems, some of them (micelles) are broadly employed as standard model lipid system whereas quite different results can be obtained in self-assembled phospholipid systems being more relevant to biological membranes. The variety of phospholipids is employed in nature to adjust the properties depending on the cell membrane, including surface charge, type of interactions with other molecules (including antioxidant) and tailoring its phase transition parameters. All these factors also determine the localisation of the antioxidants molecule, the mode of antioxidant action (preventive versus chain-breaking) and the rate of reaction with radical. In our research we want to use variety of phospholipid to tailor the mambrane properties as close to some classes of natural membranes as possible, but we also want to get insights into the role of soem structural physico-chemical parameters on the interaction with antioxidant molecules. Understanding the impact of these factors will contribute to a deeper understanding of the antioxidant activity and will result in design and synthesis new substances capable of preventing the oxidative stress or reducing the level of radical reactive oxygen species in cells and tissues.

The proposed novel antioxidants will bring a number of advantages over conventional antioxidants - they should exhibit better ability to penetrate the cell without loss of anti-radical properties. The additional goal is to design antioxidants with features tailored to the specific material being protected and to protect the exact site that is most exposed to oxidative stress. Such antioxidants should have the ability to capture radicals attacking the surface of the biomembranes from the water side as well as lipophilic radicals, located in the double layer of biomembrane.

The integral part of the research (third stage) will be verification of our research hypotheses about mechanisms and our idea of hybrid antioxidant 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 antioxidant response including Superoxide Dismutase, catalase, sirtuins, and hemoxygenase-1. We will also evaluate the action of hybrid antioxidants as a protectors of single and double stranded DNA.

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