Popular Science Abstract

Some factors, such as environmental pollution, smoking, intense physical effort, drug abuse, or stressful lifestyle contribute to overproduction of free radicals in the organisms, generally from the Reactive Oxygen Species (ROS) group. The imbalance between the production of ROS and the ability of their deactivation by an organism is called oxidative stress. This process is undesired because it leads to DNA damage and peroxidation of lipids contained in cellular membranes, causing their disintegration. The consequence of long-term oxidative stress is premature ageing or development of certain diseases (mostly neurodegenerative, coronary artery or cancer). One of the defence mechanisms against oxidative stress caused by the overproduction of the ROS is antioxidants. Antioxidants are compounds that even in small concentration are able to stop the oxidation of lipids or other biomolecules, usually by the elimination of free radicals or their precursors. Antioxidants are an essential element of the diet, supporting natural defence mechanisms that neutralize free radicals in the organism. The commonly known antioxidants are vitamins (E, C, A), beta-carotene and polyphenolic compounds, i.e. resveratrol. Presumably, the presence of these substances in the Mediterranean diet (vegetables, wines) is responsible for the “French Paradox”, that consists of a relatively low incidence of coronary heart disease and a relatively long lifespan in France and Italy, despite the consumption of a diet in high saturated fat.

Conventional antioxidants are not always effective, due to problems with: (i) limited bioavailability due to unfavourable pharmacokinetic profile or diet restrictions (age, diseases), (ii) regeneration of the antioxidants, (iii) transport and localization. Our research project is focused on search and development of a new class of compounds that could be used as effective antioxidants and indirectly preventing the development of several diseases. We also believe that our compounds will act as a molecular probes of oxidative stress in cells.

The proposed research is aimed to study the antioxidant properties of the selected nitroxyl radicals (TEMPO, 4-hydroxy-TEMPO, 4-oxo-TEMPO) and their synergistic effects with polyphenols (resveratrol). The research work includes comprehensive studies about antiradical and antioxidant activity of selected groups of compounds that give us information about the influence of several factors (polarity of solvents, types of model systems) to antioxidant ability of nitroxyl radicals. Obtained results allow us to determine the structure-activity relationship and design a novel class of hybrid antioxidants that will contain nitroxyl and phenolic functional groups. We hope the novel hybrid compounds should be effective antioxidants in a wide range of pH and will act as molecular probes for cellular oxidative stress. Polyphenols have been chosen due to their documented pro-health properties, whereas nitroxyl radicals as compounds that are non-toxic (to normal cells) and non-immunogenic. Understanding of the molecular mechanisms of action of the nitroxyl radicals can open the new possibilities of use of this group of compounds, for example, for diagnostic purposes.

The research project connects physical organic chemistry, chemistry of radicals, chemical kinetics (Faculty of Chemistry, University of Warsaw) with cell and molecular biology (Nencki Institute of Experimental Biology, Polish Academy of Science). The results will be significant and pioneering and will extend knowledge in the field of antioxidant and free radical chemistry. We also believe that the results will help us to design a new class of hybrid antioxidants and molecular probe of oxidative stress.