Popular science abstract

Oxidative stress, caused by an excessive amount of Radical Oxygen Species (ROS) and its molecular consequences in the form of destructive oxidation of biomolecules, significantly impacts human health, and they are widely studied. The aetiology of several diseases such as atherosclerosis, diabetes, kidney diseases, tumours, as well as neurodegenerative (Alzheimer and Parkinson) diseases, is connected to oxidative stress, namely, to peroxidation of unsaturated lipids as the main component of cell membranes, where peroxyl radicals are the primary mediators of this chain reaction.

Biological systems are very complicated pieces of bio-machinery. Thus, the results of studies of oxidative stress conducted in laboratories not always correspond to studies performed in vivo. For this reason, a lot of work is directed to designing and obtaining such markers of oxidative stress that, thanks to their composition, localisation, sensitivity, and intensity of the analytical signal, will not affect the homeostasis of cell or tissue but will be able to monitor the level of ROS and their interactions with bio components of the cells. Fluorescence is an emission of light by the excited atom, molecule, or other chemical species. Thus, fluorescence could be applied for monitoring and studying oxidative stress in biomembranes. The idea of a fluorescent marker (fluorescent probe, FP) for radicals is based on increasing or decreasing the fluorescence intensity depending on the progress of the reaction of FP with peroxyl radicals. In this way, the monitoring of oxidative stress in real-time would be possible. The building block of some FPs is the 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene, also called BODIPY. Due to excellent fluorescent properties, derivatives of BODIPY are increasingly used in medical sciences, biology, and biochemistry and analytical chemistry. BODIPY-based sensors contain chemical entity sensitive to the analysed factor (“receptor part”) covalently bonded to a functionalised BODIPY called “reporter part”. A change in the oxidation status of the receptor is indicated by the change of fluorescence of the BODIPY “reporter” part. Our idea is that sensitive and responsive markers of oxidative stress can be obtained by functionalising the BODIPY by attaching the molecular fragments containing chemical groups that can react with peroxyl radicals (e.g. polyphenols ). The literature review shows a great demand for new markers of oxidative stress, and our proposal offers such FP for monitoring peroxidation processes of non-polar biomolecules in the systems exposed to high levels of oxidative stress. This kind of FP could contribute to expanding the knowledge about diseases with probable radical aetiology, such as neurodegenerative diseases.

The primary purpose of this project will be the synthesis and characteristics of FPs containing BODIPY as a reporter part with phenol or polyphenol moiety covalently attached as a receptor part. Phenol moiety as a receptor was chosen because of its high reactivity towards the radicals. Furthermore, polyphenols, such as catechols, are analogues of catecholamines (some of them are biologically essential compounds – neurotransmitters and hormones such as adrenaline, noradrenaline, or dopamine). Catechol, as well as catecholamines, are sensitive to oxidative stress induced by peroxyl radicals, and uptake of catecholamines may lead to disturbances in the central nervous system and hormonal economics. Using catechol as a receptor in FP sensitive to peroxyl radicals would allow real-time monitoring of oxidative stress causing oxidation of catecholamines.

In the proposal, the series of FP will be prepared, and their stability and optical properties (change of fluorescent intensity during reaction with radicals) will be examined in homogenous (solvents of various polarity) and heterogeneous systems (analogues of biomembranes).