Application of the algal model to determine the non-steroidal anti-inflammatory drugs mitotoxicity – diclofenac as a case study

Thinking about the quality of our life, we often pay attention to two aspects that are particularly important from a personal point of view: a clean natural environment that helps maintain good body condition and the medical care and the pharmaceutical industry that help to regain balance and fitness after illness. Sometimes we do not realize how much these two issues affect each other and how difficult it is to maintain a balance between them.

The pharmaceutical industry has been one of the best-growing sectors of the economy for years. Statistics show that a 25% of the current pharmaceutical market has been generated over the last 5 years only. Every year new medicines and diet supplements are introduced to the market. But are we really aware of the amount of these drugs getting into the environment? Meanwhile, scientific data indicate that the natural environment is degraded due to the contamination with anthropogenic substances, among which pharmaceuticals are common. In recent years, popular medicines, including analgesics and anti-inflammatory drugs, became serious ecotoxicological problem. The concentrations of these substances recorded in the environment are not very high, however due to the widespread use they are continuously introduced into the environment in the form of post-production sewage, medical and municipal wastewater.

Non-steroidal anti-inflammatory drugs (NSAIDs) belong to the most commonly used drugs due to its analgesic, antipyretic and anti-inflammatory effects. An example of such a substance is diclofenac (DF), which is on the list of priority environmental hazards. The detection of this drug in some drinking water intakes caused that in 2013 DF was placed by the European Commission on the list of substances that need to be monitored in the environment (*EU Water Framework Directive 2013/39/EU*). DF was introduced for use in the 1960s and the mechanisms of its therapeutic effect on animal organisms have been described in detail. Unfortunately, this substance is now becoming a common contamination of water reservoirs, and living water organisms, including higher plants and algae, are not the direct "target" of its action. Despite the fact that DF has been used for a long time for medical purposes, there are no detailed data about its effect on non-target plant organisms. It is known, however, that this substance is phytotoxic and that it can be accumulated in plant cells.

The need to monitor the amount and effects of NSAIDs in ecosystems is related to many aspects of environmental research. An indispensable element of such research is bioindication - a method that allows to determine the state of environment on the basis of reactions of organisms called indicators. It should be noted, however, that individual indicators differ significantly in their sensitivity to the tested substances. Comparison of the sensitivity of different systematic groups has shown that planktonic green algae are more sensitive to NSAIDs than other aquatic organisms. From this point of view, promising research object is *Chlamydomonas reinhardtii*, which can be a model organism in toxicological analysis at the population, cellular, biochemical and molecular level. At the same time, it is similar to plant cells in both structure and function, so the results obtained with its use can be extrapolated to higher plants.

The main aim of this project is to assess the physiological and biochemical effects of DF on *C. reinhardtii*. Based on data obtained for animal cells, I hypothesize that one of the reasons of DF phytotoxicity is the adverse effect on the functioning of mitochondria, and consequently the disturbance of cell bioenergetics. To verify this hypothesis, analyses of both *C. reinhardtii* whole cells and the isolated mitochondrial fraction are planned.

I believe, that the deepening knowledge of mechanisms of toxic action of pharmaceuticals on "non-target" organisms will lead drug manufacturers and users to use these substances more sensibly and to follow the rules for their disposal. In this way, the results obtained during the project will be a part of the implementation of the "Sustainable development " concept, aimed at maintaining a balance between meeting society's needs and protecting the natural environment to save it for future generations.