

## **Estimation of rutin and ascorbic acid cooperation in cytoprotective effect on fibroblasts and keratinocytes exposed to UVA and UVB radiation**

UVA and UVB radiation contained in sunlight penetrates the outer layers of the skin and disturbs the metabolism and function of the cells that build these layers. This radiation in particular affects the level of polyunsaturated fatty acids, which are the basic components of biological membranes. Due to the fact that in the membranes of skin cells in the highest amount occurs linolenic acid – the changes in the level of its metabolism products seem to be the most important in the functioning of the skin. Additionally, UV radiation by increasing production of reactive oxygen species leads to increased generation of endocannabinoids and activation of their membrane receptors, which primarily participate in the inflammatory response. UV radiation modifying the composition of lipid membranes also impairs the permeability of biomembrane, and affects signalling pathways of skin cells by modifying lipid mediators such as lipid cyclization products and reactive aldehydes. Moreover, cells exposure to UV radiation results in oxidative damage to the other cellular components, including hydrocarbons, DNA, and proteins. The interaction of proteins with highly reactive free radicals or lipid peroxidation products leads to changes in the protein structure, which, for example, result in the activity of enzymes. In addition, oxidized proteins by cross-linking formation cannot be degraded, thus accumulating them in cells leading to dysfunction and cells death. Electrophilic molecules can interact with signalling proteins by activating, e.g., transcriptional factors, such as responsible for biosynthesis of antioxidant proteins Nrf2, or NFκB that leads to cells inflammatory responses.

UV radiation by modifying cell signalling, also interferes proliferation and cell death processes. Therefore, there is still constantly looking for effective cytoprotective compounds with antioxidant properties. Moreover, these is increasing the number so-called combined therapies that use the synergistic action of similar-acting compounds that can modify their mutual biological properties. Examples of such compounds are: natural polyphenol - rutin and polyhydroxy alcohol - ascorbic acid, known as vitamin C, which interaction in supporting the body's resistance and strengthening of blood vessel walls has been demonstrated and used in oral pharmaceutical formulations. However, the effect of a mixture of rutin and ascorbic acid on the metabolism of skin cells exposed to UV radiation is still unknown.

The ability to modify the structure and activity of cellular compounds in both rutin and ascorbic acid is dependent on the effective penetration of these compounds by biological membranes. Therefore, the aim of the research project will be to determine the interaction between rutin and ascorbic acid on cell membrane permeability and their reducing and cytoprotective properties in relation to fibroblasts and keratinocytes exposed to UVA or UVB radiation in multilayer culture which creates the most favourable to the body conditions.

During experiment, it is also planned to determine the relationship between proinflammatory factors, redox system components, and lipid mediators that occurs under simultaneous incubation of cells with rutin and ascorbic acid and their treatment with UVA and UVB radiation. The final step in the study will be the assessment using modern omics techniques the changes triggered by rutin and ascorbic acid in the lipidomic and proteomic profile of skin cells subjected to UVA and UVB exposure. Obtained results will allow to assess the synergism degree in rutin and ascorbic acid action on the metabolism of skin cells exposed to UV radiation. In addition, the use of 3D culture - the structure closest to the real skin will determine the effect of rutin and ascorbic acid on the proper condition of the skin, which is a determinant of not only well-groomed and young, but also healthy body.