Co-amorphous polyphenol systems

Plant raw materials are valuable sources of many biologically active compounds for which beneficial pharmacological effects and the possibility of use in the prevention of many civilization diseases have been proven. Polyphenols have a special place among plant-based active compounds, whose absorption is also limited by poor water solubility. The essential proven mechanisms of the pharmacological action of polyphenols include the possibility of neutralizing free radicals that arise in the body as a result of many metabolic and pathological processes. While the excess production of free radicals is the reason for the development of many diseases, the most important are the process of cancer development, cardiovascular, and autoimmune diseases.

As mentioned, the limitation on the use of the medicinal properties of many polyphenols is their low bioavailability, which is the result of poor water solubility. One effective method of increasing solubility is the transformation to amorphous dispersion. Obtaining amorphous dispersion of compounds can significantly increase solubility, and at the same time improve bioavailability for compounds belonging to class II and III of BCS (system of classification of compounds in relation to the relationship between bioavailability and solubility). However, the energy state and mobility of the molecules in conditions of amorphous dispersion, promotes their physical instability. The conversion of amorphous polyphenols to less soluble crystalline forms can be inhibited by combining with other polyphenols or low molecular weight compounds with amorphous dispersion.

The purpose of this project is to obtain co-amorphous systems of flavonoid polyphenols (analogs of phenolic acids, flavanones, curcuminoids, isoflavones) and non-flavonoid (lignans, stilbenes, cannabinoids), which are poorly soluble compounds. The preparation of co-amorphous polyphenol systems using various amorphization techniques and assessment of system identity using appropriate spectroscopic and thermal techniques will constitute the first stage of research. Preparation of complex amorphous polyphenol systems will be carried out by various methods (milling, cryomilling, spray drying, vitrification, holt-melt extrusion), which will be properly selected for the properties of polyphenols and the specificity of inducing intermolecular interactions between them.

The possibility of changes in the physicochemical properties of polyphenols, relevant for their pharmaceutical use, will be defined in relation to the assessment of changes in dissolution rate, chemical and physical stability, and membrane penetration by passive diffusion for polyphenols introduced into co-amorphous systems. With respect to the potential for synergism of the effects of many polyphenols and the impact of their water solubility on biological properties, changes in the biological activity of polyphenols after their introduction into co-amorphous systems will be defined. The evaluation of changes in the biological activity of polyphenols will include studies on the antioxidant potential, studies on the inhibition of the activity of enzymes of metabolic pathways induced by a pathological condition, and studies on microbiological activity. As part of the project, co-amorphous lyophilisates of extracts of selected plant materials, standardized for the presence of polyphenols, will also be obtained. Assessment of changes in the physicochemical and biological properties of polyphenols present in these co-amorphous systems will additionally allow for the assessment of the "*entourage* effect" of the entire plant matrix present in extract lyophilisates on changes in the properties of selected polyphenols.

The obtained results will provide knowledge on the intermolecular interactions responsible for the formation of co-amorphous systems with increased solubility, which may induce better bioavailability. In addition, they will translate into the possibility of better utilization of valuable biological activities of many polyphenols.