

The first sweeteners used by humans were honey and plant juices. Currently, the most commonly used sweetener in the traditional food industry is sucrose - disaccharide, naturally occurring e.g. in sugarcane and sugar beet. Due to sucrose's omnipresence in food products, the feeling of sweet taste is adapted to its sweetness. Numerous epidemiological studies confirm the link between the consumption of sugared high-calorie products and health disorders. For this reason, low-energy substitutes are being sought, exhibiting physical and chemical properties comparable to sucrose but are low in calories and providing additional health benefits. Dihydrochalcones, which, like other flavonoids, occur naturally in fruits, vegetables, herbs, raise considerable interest in this area. Furthermore, they are an integral part of the human diet. Flavonoids have been proven to be safe for the human body, and their estimated daily intake is up to 1g. These compounds, consumed with food of plant origin, are an essential factor responsible for the prevention of many civilization diseases (including diabetes, heart disease, and even depression). In addition, they are also components of many preparations available in pharmacies (mainly dietary supplements, syrups, or plant extracts), which are used because of their antioxidant, anti-inflammatory, anti-cancer, antiallergic, antiatherosclerotic, anti-diabetic, anti-microbial, and anti-viral properties.

This project aims to obtain a library of dihydrochalcones and their glycoside derivatives with increased bioavailability and activity using biotechnological methods. The obtained compounds can be used in the food industry as potential sweeteners with healthpromoting properties. To obtain these compounds, the synthesis of hydroxy, methoxy, bromochalcones, and compounds containing combinations of these functional groups in their structure will be performed. In contrast, corresponding dihydrochalcones will be obtained due to biotransformation in unconventional yeast cultures and by the use of enzymes – ene-reductases. We also plan to obtain dihydrochalcone glycosides as a result of the use of entomopathogenic strains cultures and glucosyltransferases. Such a variety of derivatives will show the dependence of the number and type of substituents present in the structure of the obtained compounds and the presence of a sugar unit on their biological activity. The high bioactivity of flavonoids shown in *in vitro* tests is often not confirmed by mammalian studies. These compounds are relatively rarely becoming components of pharmaceutical formulations due to the low bioavailability of flavonoid compounds, among other things, due to insufficient water solubility. The microbiological synthesis of dihydrochalcones glycosides is an excellent way to improve the physical properties of compounds relevant to their use in the pharmaceutical industry.

Determining the level of safety of the obtained products is crucial prior to their introduction into the food industry; we will assess this in cytotoxicity studies on normal mammalian cell lines. Compounds that turn out non-cytotoxic will be subjected to an organoleptic evaluation. Subsequently, the obtained compounds will be tested for their biological activities towards cancer cell lines. We will also mimic the digestion process to verify the hypothesis of the higher bioavailability of obtained compounds using an artificial digestive system.

The effect of the obtained compounds on the intestinal microbiome of healthy people and people suffering from various diseases in a simulated *in vitro* digestive system will be assessed and compared. The results obtained in the project will enrich the available database of compounds exhibiting interesting biological properties that (potentially) could be used as sweeteners, and taking into account, the properties of flavonoid compounds, they may have a positive effect on the human intestinal flora, support therapies, including anti-cancer and anti-diabetic treatments.