In recent years, intensive research on gut homeostasis has underscored the significance of Hippocrates' words spoken almost 2500 years ago, stating that 'all diseases begin in the gut.' Scientific evidence now demonstrates that imbalances in the gut may contribute to the development of seemingly unrelated diseases, such as allergies, atopic dermatitis, cancers, cardiovascular diseases, and even mental disorders.

Our intestines are inhabited by approximately 500-1000 different species of microorganisms, with a combined mass of around 1000 grams. The estimated number of microbial cells in the gut is at least equal to the number of human body cells. For years, the role of gut microbiota was marginalized, considered merely to ensure the proper functioning of the digestive system. However, it is now well-established that the microbial balance in the intestines plays a crucial role in maintaining overall health.

An imbalanced microbiota can produce harmful metabolites, damage the intestinal mucosa, allowing allergens and toxins to enter the body, and may also trigger inflammation in the intestines. Inflammation is a complex set of immunological processes aimed at regenerating and repairing damaged tissue. However, inflammatory processes can sometimes escape control, leading to a state of chronic and systemic inflammation. It has been proven that many diseases may originate from inflammatory processes occurring in the intestines.

The search for molecules that can prevent and treat gut dysbiosis is currently one of the leading topics in dietary supplement and food additive research. Health-conscious consumers prefer food enriched with compounds of natural origin.

Flavonoids, a recognized group of natural compounds found in everyday human dietary sources such as fruits, vegetables, and cocoa, exhibit significant potential in restoring gut microbial balance, alleviating inflammation, and potentially preventing and treating tumors. These compounds largely account for the health-promoting effects of plant-based foods. Pure flavonoids would be ideal candidates for dietary supplements or food additives if not for their low solubility, stability, and bioavailability.

In our project, we plan to functionalize well-known natural flavonoids with proven high biological activity, available in Poland as dietary supplements, with recommended daily doses reaching several hundred milligrams. We will obtain ester derivatives in which the flavonoid compound will be connected to a short-chain fatty acid (SCFA). SCFAs, produced in the intestines by a healthy microbiota, have high health-promoting potential for the digestive system. We expect that through these modifications, we will achieve derivatives with high biological activity, stability, and good solubility, enabling them to become components of future dietary supplements or enrich functional foods.

Due to the poor absorption of flavonoids in the small intestine, where 95% of orally taken flavonoids move along to the large intestine unchanged, our project will explore bidirectional interactions between ingested flavonoids and the gut microbiota. Flavonoids can promote the growth of beneficial microorganisms while undergoing metabolism by microorganisms into biologically active compounds (postbiotics). In this context, our goal is to identify and isolate postbiotics produced by probiotic strains from flavonoids and their esters. Subsequently, we will evaluate the potential of all the flavonoids and their derivatives (esters and postbiotics) used in the project to restore homeostasis in the digestive tract.

We will determine the solubility of compounds using computational tools that allow precise calculations of physicochemical parameters of molecules. We will assess the impact of the tested compounds on beneficial probiotic strains as well as pathogenic microorganisms, such as *Staphylococcus aureus* or the frequently infection-causing yeast *Candida albicans*. These studies will pave the way for the future development of new prebiotic preparations—stimulating the growth of beneficial microorganisms, synbiotics—combining probiotic microorganisms with a prebiotic (flavonoid compound), or agents inhibiting the growth of harmful microorganisms, serving as an alternative to traditionally used antibiotics or food preservatives. Finally, we will evaluate the anti-inflammatory and anti-cancer effects of the tested compounds and determine their mechanism of action. For this purpose, we will use cell lines, focusing primarily on gastrointestinal cancer cell lines and cell lines associated with inflammation.

Through our research, we aim to create and assess new derivatives of natural compounds, which, thanks to improved physicochemical parameters and proven high bioactivity, can be applied as dietary supplements and functional foods, providing comprehensive protection for the digestive system and, consequently, enhancing the well-being of the entire organism.