

Continuous exposure to numerous negative factors related to the changing lifestyle of developed societies, such as an unbalanced diet, low in fruit and vegetables and rich in highly processed food, as well as drug abuse, cause prolonged oxidative and inflammatory stress in human organisms, leading to the development of many disorders. Apart from the cardiovascular diseases, most frequently mentioned in this context, a drastically increasing number of digestive tract inflammations is observed in all age groups, including their chronic types, especially inflammatory bowel diseases (IBDs). The IBD-associated damage and pathological changes to the intestinal epithelium cause abdominal pain, persistent diarrhea, and malabsorption, which significantly reduce the life quality of patients; moreover, they may promote carcinogenesis. Unfortunately, the pharmacological treatment of IBDs is complex, often ineffective, or associated with numerous side effects that require further medical interventions.

In the face of a growing problem, more and more attention is paid to the role of diet and the search for food products that could be used to prevent or treat this group of diseases. A particular interest is aroused by plant foods rich in polyphenols – compounds with the documented ability to normalize and regulate oxidative-inflammatory processes *in vivo*. Moreover, epidemiological studies show a close link between a diet rich in polyphenols and a lower risk of developing IBDs. The relevant activity of polyphenols is also suggested by the centuries-old ethnomedicinal tradition of using polyphenol-rich herbal medicines to treat gastrointestinal inflammation. Therefore, when looking for an effective functional solution, it is worth reaching for products that combine the features of food and traditional medicinal substances, which allow a good pro-health effect to be expected.

One example of such products is the fruit of *Prunus spinosa* L. (blackthorn, sloe), used both as food (tinctures, juices, wines, jams) and as a traditional herbal medicine, recommended by European phytotherapy in the treatment of intestinal inflammation. The available research has reported fresh sloes as a rich source of structurally diverse polyphenols, able to modify the pro-inflammatory functions of human immune cells *in vitro*. However, these data are incomplete and lack a deeper analysis and confirmation of activity in appropriate biological models, taking into account the specificity of the digestive system environment, which limits the wider use of blackthorn fruits as health-promoting agents. In particular, special attention should be paid to the influence of the digestive processes and intestinal microbiota fermentation on the composition and activity of the polyphenolic fraction of the fruit. It is assumed that after oral administration polyphenols reach the small and large intestines in relatively high levels. This fact is potentially beneficial for their activity within the gastrointestinal tract. However, they are also largely converted into low-molecular-weight metabolites that may significantly affect the final effects of the native compounds and food products. Therefore, without insight into the structure and activity parameters of metabolites, it is not possible to meaningfully assess the health potential of polyphenol-rich foods within the intestines.

Given the above, this project aims to thoroughly evaluate the value of blackthorn fruits as a potential source of functional products designed to prevent or treat chronic gastrointestinal inflammatory disorders. In the first stage, the pressurized extraction process of the plant material with high recovery of polyphenols will be optimized, and the active fruit extracts will be isolated. The extracts will be then subjected to four-stage *in vitro* digestion, simulating the critical steps of *in vivo* processes, including fermentation with the human colon microbiota. The phytochemical profile of native extracts, the dynamics of their changes during the digestion process, and the structure of polyphenolic metabolites will also be analyzed. In the next stage, the activity of native extracts and their fractions recovered after digestion will be assessed *in vitro* in biological models using three types of cells involved in intestinal inflammation, i.e., neutrophils, peripheral blood mononuclear cells, and Caco-2 (intestinal epithelial model). The effect of the native and digested extracts on cell viability, production of reactive oxygen species, secretion of a wide range of inflammatory mediators (cytokines, chemokines), pro-inflammatory and pro-oxidant enzymes, elements of the endogenous defense system (anti-inflammatory and anti-oxidant), protein markers of the intestinal epithelial integrity and key transcription factors controlling the inflammatory process will be tested.

The implementation of the project will significantly expand the knowledge of the molecular mechanisms of the biological activity of blackthorn fruits. It will also provide the basis for their wider use as a food and functional product. After eventual *in vivo* verification, it will allow for the future inclusion of the appropriate products in the prophylaxis and supportive treatment of IBDs, which are among the growing health problems of modern societies.