The spread of metabolic diseases related to hepatic dysfunction requires an increased investment in treatment around the world. The development of chronic liver diseases is associated with disorders of the immune system and the induction of inflammation. Therefore, it is not surprising that people with liver disease may be more likely to experience side effects from being infected with SARS-CoV-2. Some COVID-19 studies also indicate that infected people show abnormal liver function tests, suggesting a possible direct effect of SARS-CoV-2 on liver damage. The function of the liver, apart from genes, the environment, pathogen infections, what we eat, how much we eat, is also influenced by the quality of the food we eat, including the presence of toxic substances. Therefore, multi-level molecular studies on hepatoprotective bioactive ingredients are of great importance to indicate their appropriate supplementation in order to restore or protect the disturbed metabolism of liver cells caused by food contaminated with AFB_1.

Despite careful quality control of agri-food production, it is not possible to completely avoid eating contaminated food. Food intended for human consumption, and for feeding livestock, can be contaminated naturally with harmful substances. Aflatoxin B_1 (AFB_1) is considered as the most toxic of the aflatoxin family. Pigs receiving feed containing high levels of aflatoxin develop severe aflatoxicosis symptoms associated with liver failure. In the early stages, however, some liver disorders may be alleviated by the addition of bioactive ingredients derived from medicinal herbs to the feed / diet. Some of them show unique hepatoprotective properties, including Andrographis paniculata (AP: Andrographolide), Silybum marianum (SM: Silymarin) or Curcuma longa L (CL: Curcumin). In general, feeding intake of natural of dietary components can significantly change the expression of genes responsible for the course of biological processes and metabolic pathways related to detoxification and protection against oxidative stress in liver cells. Therefore, detailed studies of these dietary compounds based on the simultaneous application of various modern high-throughput molecular methods seem to be of particular interest. Identification of changes in gene activity (transcriptomics), quality and quantity of functional and structural proteins (proteomics) and the quality and quantity of metabolite compounds derived from metabolic changes in a given organ (metabolomics) is the key for explaining and understanding the hepatoprotective mechanism of action of the herbs mentioned above. The obtained knowledge makes it possible to develop their appropriate application in reducing the toxic effect of eating contaminated food by AFB_1.

The planned project assumes to conduct in-vivo animal model studies on porcine liver and in-vitro on human and pig hepatocyte lines. Young piglets, about one month of age, are selected as the animal model to eat feed supplemented by medicinal herbs and moderately contaminated by aflatoxin B_1 for the period of one month. The physiological similarity of the pig's organism to the human organism makes it possible to predict with high probability how the addition of hepatoprotective herbs would affect the human organism, protecting it against one of the most harmful and carcinogenic mycotoxins - AFB_1. The molecular changes that occur in the liver cells in-vivo and in-vitro in response to aflatoxin B1, and the protective effects of the herbal extracts on the activity of genes, qualitative and quantitative changes in structural and enzymatic proteins, and the course of metabolic processes will be evaluated. The obtained results will be subjected to a comprehensive bioinformatic analysis, which will reveal/indicate significantly changed biological processes and metabolic pathways. It will allow profound explanation of interaction among bioactive components of herbs and key genes, proteins and metabolites in the liver and identify new biomarkers of the functional state of the liver. Results of multi-level analyses will also uncover the complexity of regulation of liver functions and disorders. Whereas, simultaneous comparisons of selected three herbs AP, SM, and CL facilitate a better and deeper understanding of their hepatoprotective action, similarities and differences in relation to protective role against the toxic effect of AFB_1. The obtained results can be successfully used in the future in planning clinical trials in both veterinary and human medicine, which may contribute to better prevention and control of liver dysfunction, the development of inflammation, and invert process leading to cirrhosis and the development of liver cancer.