Gastric ulcer is a cyclic occurrence of gastric mucosal defects accompanied by inflammatory infiltration and necrosis. This is the most common gastrointestinal (GI) disorder and can affect up to 10% of population. Gastric ulcer disease is the result of imbalance between irritant and protective factors within GI mucosa. On the other hand, hydrogen sulfide (H_2S) is an essential endogenous signaling molecule involved in many biological regulatory pathways. Therefore, novel H_2S-prodrugs have been developed. It has been shown that H_2S-releasing compounds accelerate gastric ulcers healing. There is an evidence that this molecule plays an important role in the regulation of cellular metabolism and mitochondrial activity. AP39 is a H_2S donor that releases this molecule directly into the mitochondrion. Thus, we hypothesize that the beneficial effects of AP39 may be associated with a reduction of cellular oxidative stress occurring in the mitochondria.

The aim of this project is to assess whether H_2S released directly to mitochondria from AP39 accelerates gastric ulcer healing in translational experimental models. These models reflect clinical course of peptic ulcer disease in human. Additionally, fibroblasts play a major role in tissue formation being important step in tissue regeneration due to the ability of these cells to migrate into the ulcer crater and actively multiply and synthesize extracellular matrix components. Firoblasts are affected by growth factors (GF) and inflammatory cytokines.

The role of mitochondrion and its possible modulation by H_2S in gastric ulcer healing has not been investigated yet. Innovative approach of the project is related to novel synthetic H_2S-releasing donor aiming directly to the energetic center of the cell - the mitochondrion. According to the recent data, the role of H_2S in modulation of mitochondrial activity within GI tract and the effects of AP39 in the mechanism of gastroprotection and ulcer healing has not been examined. It remains unknown whether this potential ulcer healing effect could be accompanied by mitochondrial H_2S-dependent regulation of GBF and interaction with GF and anti-inflammatory pathways. The project will provide complex data to improve current knowledge in the field of GI tract pathophysiology and pharmacology with special emphasis on modulation of mitochondrial activity by H_2S donor in the course of gastric ulcer healing. In addition, the project will provide new complex data on the anti-inflammatory and anti-oxidative properties of AP39 in GI tract. The obtained results may be the starting point for further application tests.