DESCRIPTION FOR THE GENERAL PUBLIC

Carbon monoxide (CO) is a gas that in large doses causes serious and harmful effects on the human body. This compound is known as toxin which combined with hemoglobin interferes with its ability to transport oxygen, resulting in anoxia and consequently even death. However, recent research in physiology and medicine have shown that, paradoxically, CO is produced in living animal tissues and is beneficial for the organism functions. Therefore, along with other gaseous molecules such as nitric oxide (NO) and hydrogen sulfide (H_2S) has been included by scientists into the group of endogenous gaseous mediators.

CO is formed next to biliverdin and iron from the heme degradation, which is a component of hemoglobin. CO is produced by the enzyme, heme oxygenase (HO). This protein is present in two isoforms- HO-2, which is present under physiological homeostasis, and HO-1, which appears in pathological conditions such as inflammation with the presence of pro-inflammatory cytokines, oxidative stress, hypoxia etc. There is also HO-3, which seems to be catalytically inactive. However, the role of this protein has not been fully understood.

Produced endogenously CO serves as a protective factor. It has been shown that this gaseous mediator have anti-inflammatory and neromodulating properties, broadly affects vasocontriction and regulates the activity of NO synthesizing enzymes. As we know, the GI tract is a system, which is one of the mostly exposed to exogenous agents. However, naturally occurring protective barrier in the form of gastric mucosa, protects this part of the body against damage. The protective mucosal barrier includes endogenous prostaglandins, gastric blood flow (GBF) which supplies the tissue in oxygen and nutrients and is controlled by the activity of afferent sensory fibers, NO and H_2S. However, the disintegrity of this structure by exposure to chronic stress, drugs (eg. aspirin), chemicals (eg. ethanol), hypoxia and infection with *Helicobacter pylori* causes peptic ulcer disease, which if left untreated leads to serious complications.

Therefore, the question arises whether the CO exerts protective function in gastric mucosa and what are the possible mechanisms involved in this action. This project aims to demonstrate that endogenous CO produced by HO-1 in pathological conditions and released from its exogenous donor, CORM-2 (CO releasing molecule) has a protective effect on the gastric mucosa experimentally compromised by hypoxia (ischemia) followed by a reperfusion, resulting in extensive gastric damage. These studies will prove whether the protective effect of CO involves regulation of gastric blood flow (GBF), activation of afferent sensory nerves, biosynthesis of endogenous prostaglandins and interaction between this molecule and other gaseous mediators such as NO and H_2S. The project will demonstrate if the effect of CO in the GI tract is due to its antioxidant and anti-inflammatory potential and will determine whether this protective mechanism is regulated by molecular cytoprotective mechanisms, activated in pathological states. Experiments will be performed using various techniques including 1) measurement of functional parameters such as GBF, 2) the microscopy to asses the depth of gastric damage 3) genetic and molecular evaluation of genes and proteins expression, 4) biochemical assays.

In conclusion, results of the project will expand the current knowledge regarding the role of CO in the body and mechanisms of its action in the context of the physiology and pathophysiology of the upper GI tract. Therefore, these studies seem to be interesting and useful for the development of general knowledge in the field of experimental gastroenterology and physiology of endogenous gaseous mediators.