The increased prevalence of cardiovascular disease (CVD) in patients with impaired renal function still remains significantly higher compared with age-matched general population. Recent studies proved that the occurence of oxidative stress (SOX), inflammation and accumulation of toxic products of metabolism have a particular impact on vascular endothelial cell damage and the incidence of thromboembolic events. In the last years there have been evidence that degradation products of tryptophan play a pivotal role in the development of cardiovascular disease. Indoxyl sulphate (IS) is one among the uremic toxins, which is formed during metabolic pathway of tryptophan. Under physiological conditions, the concentration of IS in the body is controlled by glomerular filtration, whereas the decrease in the efficiency of renal excretory function leads to tissue accumulation of this compound. Indoxyl sulfate exerts prooxidative, proinflammatory, and several other biological properties that are directly associated with increased risk of CVD development.

The physiological hemostasis is the result of a dynamic balance between prothrombotic factors and factors associated with inhibition of blood clotting. Among the many anomalies associated with chronic kidney disease, a very important are these manifested by disorders which can increase the risk of thromboembolic events, including myocardial infarction, or stroke. Our initial experiments indicated that IS has an impact on blood clotting system, including modulation of platelets activity. Based on foregoing data we would attempt to evaluate the impact of IS on the process of blood clot creation in an experimental model of arterial thrombosis. We are planning to investigate the mechanism underlying IS-mediated modulation of hemostasis. The research will be carried out in two different models of experimental induced thrombosis with the use of animals. The first part will evaluate the impact of IS on the process of formation a blood clot and stability in intravital model of arterial thrombosis in mice. In order to assess the dynamic of induction and accumulation of intravascular thrombus we will use fluorescent visualization in confocal microscope. The agent that initiates the process of thrombus formation is electromagnetic beam generated using argon laser which damage endothelial cells of cremaster. According to the literature this agent can strongly imitate the cytotoxic effect of proinflammtory factors on endothelial cells. This experimental method is very valuable research tool due to possibility of recording all changes as a function of time during conducting experiment. Moreover it is possible to observe the activation of platelets, plasma coagulation factors and the full range of dynamics of thrombotic properties. In the second experimental task, thrombosis will be induced by constant electric current in the rat’s carotid artery. That model allows us to evaluate the effect of IS on thrombus formation during the exposure of collagen layer and release of von Willebrand factor (vWF), what differentiates the above listed methods. Newly formed thrombus will be dissected and weighted. It is well-known that dysfunctions in hemostasis are strongly related to changes in hemodynamic parameters, therefore these parameters also will be monitored during this part of the study. After complementation of task 2 rat's blood will be collected in order to evaluate a wide spectrum of biochemical and hematological parameters. We deeply hope, that obtained results will allow us to clarify the role of indoxyl sulfate, which increases significantly in patients with chronic kidney disease and influences the process of thrombosis.

The scheduled scheme of the project implementation provides a comprehensive and innovative approach to the problem regarding mechanisms underlying the impact of IS on hemostasis system. Undoubtedly, design of research reveals innovative character, provides outstanding opportunity to find out previously undiscovered properties of indoxyl sulfate, and thus create basics for further studies that will focus on tryptophan degradation products metabolism in the aspect of the circulatory system disorders associated with renal diseases.