Type 2 diabetes with concomitant cardiovascular disease is a major health problem. The number of people diagnosed with type 2 diabetes is increasing, and is estimated to reach 500 million patients worldwide in 2035. In type 2 diabetes is characterized by abnormal degradation of the vessel clot (fibrinolysis). Reduced efficiency of fibrinolysis is one of the causes of increased risk of heart and vessel diseases observed in type 2 diabetes. These abnormalities may result from modification of fibrinolytic components associated with elevated blood glucose levels in patients suffering from type 2 diabetes e.g. the attachment of sugar residues (glycation). Previous studies have demonstrated that fibrinogen and plasminogen, two proteins involved in clot degradation, are glycated. α2-antiplasmin is a protein responsible for inhibition of fibrinolysis. Wheter α2-antiplasmin glycation can cause the lower efficiency of fibrinolysis observed in type 2 diabetes, still has to be investigated. Another process that can affect the efficiency of fibrinolysis could be the modification caused by reactive oxygen species (carbonylation). The potential role of fibrinogen and plasminogen carbonylation and their activity in type 2 diabetes is unclear. According to the clinical data, type 2 diabetes is associated with reduced efficacy of aspirin in preventing heart and vascular disease. The reasons for this has to be elucidated. Aspirin, also known as acetylsalicylic acid (ASA), decrease platelet aggregation and inhibit thrombus formation. It is proven that aspirin causes a modification of certain proteins responsible for the clot degradation. For some people, aspirin does not have as strong an effect as for others, an effect known as aspirin resistance. To my knowledge, there are no reports on the effects of aspirin on α2-antiplasmin.

I will investigate whether type 2 diabetes affects the selected proteins responsible for complex processes of fibrin clot degradation and to what extent it is affected by aspirin.

The main hypothesis of this project assumes that the altered properties α2-antiplasmin, fibrinogen and plasminogen due to type 2 diabetes are responsible for the prolonged fibrinolysis and that adverse effects are not as effectively reversed by aspirin as in patients without type 2 diabetes.

The experiments will be conducted in the plasma obtained from 150 patients on admission to hospital due to cardiovascular disease. The efficiency of the fibrinolysis in patients with type 2 diabetes will be compared to patients with normal blood glucose. The experiments will be carried out with a plasma as well as with isolated proteins such as as α2-antiplasmin, fibrinogen and plasminogen. The potential mechanisms that may explain the changes through which the type 2 diabetes affects the efficiency of clot lysis will be assessed (glycation, carbonylation). Eventually, the relationship between aspirin therapy and clot degradation will be investigated. If the prolonged clot degradation corresponds to the above-described processes such as α2-antiplasmin glycation and fibrinogen carbonylation, it may lead to the development of new targeted therapies. Novel future therapies aimed at improving fibrin clot degradation may be an attractive option in the prevention and treatment of such common diseases as diabetes or coronary heart disease.