

SUMMARY

The influence of WPC-80 on the coagulation process in venous thrombosis model in rats.

Whey is a natural product of animal origin obtained during the production of cheese. In the research we used whey protein concentrate (WPC-80) containing about 80% whey proteins, with a specific composition (concentrate composition tests were performed in the laboratory SJ Hamilton Poland LTD (Gdynia, Poland)). It may aspire to the status of functional food. Numerous health-promoting properties of whey proteins have been described, but their impact on the development of venous thrombosis has not yet been determined. Despite advances in prevention and therapy, venous thromboembolic disease is still a serious health problem.

The aim of the study was to assess the effect of WPC-80 supplementation on the development of venous thrombosis and the function of the aorta in the model of venous thrombosis in rats.

The studies were carried out on the Wistar rats, which were divided into unsupplemented (control) groups and respective groups supplemented with WPC-80 at a dose of 0.3 g/kg and 0.5 g/kg for 7, 14 and 21 days. After the completion of supplementation, in half of the animals the inferior vena cava was ligated to induce venous thrombosis (according to Reyers et al. 1989, modified by Chabielska et al. 2005 and Gromotowicz et al. 2011), in others a sham operation was performed. The materials for further tests included: thrombus, fragments of the thoracic segment of aorta and blood. Selected parameters of the clotting system (coagulometer), aortic function (organ baths), aortic wall morphology (H + E) and immunohistochemistry were assessed. The obtained results were subjected to statistical analysis using the GraphPad Prism 5.0 program.

The performed studies have shown that venous thrombosis disturbs the endothelial-dependent relaxation of the aorta. WPC-80 supplementation did not alter the aortic systolic-diastolic function in healthy animals and prevented the development of aortic dysfunction in the venous thrombosis model. The most pronounced effects were obtained in the group receiving WPC-80 at a dose of 0.3 g/kg for 7 days. Further research into the mechanism of the obtained results proved that the effects of whey protein concentrate on aortic relaxation depend on nitric oxide, potassium channels and prostanoids, which indicates the role of

vascular endothelium in the presented process. In addition, neither the 1-hour venous thrombosis nor WPC-80 supplementation significantly changed the morphology of the aortic wall. Reduced immunoreactivity of KCNN4 potassium channels and increased vWF immunoreactivity in aortic endothelial cells in rats with venous thrombosis was demonstrated, which was prevented by WPC-80 supplementation. There was a tendency to limit the development of thrombosis after WPC-80 supplementation in both doses, however, statistical significance was obtained only for the 14 and 21-day treatment period. WPC-80 influenced the blood coagulation parameters, but they were still within the normal range.

Based on the conducted research, the following conclusions were formulated:

1. In short-term, 1-hour venous thrombosis, aortic relaxation dependent on the vascular endothelium is disturbed, which indicates the relationship between venous and arterial dysfunction.
2. WPC-80 effectively prevents aortic systolic and diastolic dysfunction in the course of venous thrombosis, but does not affect aortic systolic and diastolic function or aortic morphology in healthy animals.
3. WPC-80 prevents aortic dysfunction in the course of venous thrombosis in mechanisms dependent on nitric oxide, potassium channels and prostanoids.
4. WPC-80 (in both doses tested, 0.3 and 0.5 g/kg) used for 14 and 21 days limits thrombus formation in the venous thrombosis model in rats.
5. The parameters of the coagulation system after application of WPC-80 remain within the normal range.
6. WPC-80 may be a potential component of prophylaxis of venous thromboembolism and cardiovascular diseases.