

Hypertension is one of the most common cardiovascular diseases. Epidemiological data indicate that in Poland it occurs in about 29.5% of the population. A particular medical problem, in this aspect, is the hypertension in pregnant women (about 5-10%). This results in the need for new strategies for effective prevention and treatment of this disease, especially in the female population in the physiologically abnormal state like pregnancy. Methyldopa is currently one of the most commonly used drugs in pregnant women, but its usage leads to the occurrence of several side effects. The above facts justify the search for new, safe antihypertensive drugs.

One of the sources of new drugs are flavonoid compounds present in medicinal plants, vegetables and fruits, such as: apigenin, chrysin, quercetin, scutellarin, baicalein exerting cardiovascular effects on the cardiovascular system.

The purpose of this project will be the investigation of above mentioned flavonoids activities on selected cell lines (human endothelic- and trophoblastic - origin) and the effect of these compounds in pregnant rats with induced hypertension, at the molecular and biochemical level. Studies on three human cell lines will serve as a model for the study of biochemical and molecular changes in placental trophoblast and changes in vascular endothelial cells in the placenta.

In the pharmacological part of the study, pregnant rats with established hypertension (SHR) and their analogues without hypertension (WKY) will receive daily pre-selected flavonoid compounds and methyldopa throughout the gestation period (20-23 days) Circulation studies and evaluation of their mechanism of action at the molecular level (protein and gene expression) for inflammatory factors and markers of oxidative stress and hypoxia in selected organs (heart, aorta, placenta) and in the blood (lymphocytes) of animals. During the experiment, the systolic blood pressure and heart rate in animals before pregnancy (for comparative purposes) and during pregnancy will be controlled. Then, from the decapitated animals, ethically, their heart, aorta, placenta and blood will be collected. The level of oxidative stress in rats' blood will be analyzed by determining the concentration of markers and enzymes activities (eg. superoxide dismutase, glutathione peroxidase). Biochemical parameters of cardiac damage in rats will be also evaluated. Molecular analyzes as mentioned above will be also conducted.

Results from this project will also determine the safety level of selected flavonoid compounds during pregnancy. Despite a number of studies, the molecular mechanism and points of the pharmacological action of these selected flavonoids in the model of gestational hypertension (SHR) and in proposed *in vitro* model have not been investigated and explained yet. Many aspects of this project are aimed at clarifying the expected pharmacological effect of flavonoids as potential drugs or components of food supplements being used during pregnancy. Hence, the relevance of proposed experimental steps in the project in proposed research models.

The results of the project may largely contribute to increasing of knowledge based on scientific evidence.