# ABSTRACT

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Title of Thesis **Effect of Sunitinib on the expression of eNOS in normotensive and hypertensive rats**

**OBJECTIVE:** We monitored the expression of eNOS in the aorta of spontaneously hypertensive rats (SHR) and normotensive rats (WKY) regarding the application of cytostatic sunitinib, i.e. whether the application of sunitinib results in vascular endothelial dysfunction.

**INTRODUCTION:** The application of sunitinib has considerable toxic effects on the human organism. In many cases it can deteriorate the disease itself, which leads either to reducing the doses of the applied medicine, or to interrupting treatment, the most frequent and most important adverse effect being arterial hypertension.

**METHODS:** While working on this thesis we compared two groups of animals: hypertensive SHR inbred males and normotensive WKY inbred males. Both these groups were further divided into two subgroups. While the first group of animals was given sunitinib from the start, the second group served as a control group and was given only water. The scheme of applying sunitinib to the SHR group of rats was as follows: 8 weeks of application, 5 weeks break, and then another 8 weeks of application. In case of the WKY rats, due to discovering symptoms of toxicity, the last stage of the scheme was shortened: 8 weeks of application, 5 weeks break, and 2 weeks of application. We used En Vision methods to detect eNOS expression. To assess the differences between the monitored groups we used stereological assessment.

**RESULTS:** Using imunohistochemical analysis, expression of eNOS was proven in both types of animals, but only in endothelium cells. eNOS expression was detected in all the animals in both groups, however, it was more distinctively expressed in hypertensive SHR rats, which had been given sunitinib. Compared to the control group which had only been given water, stereological analysis has shown a statistically considerably increased expression of eNOS in rats which had been given sunitinib the whole time.

**CONCLUSION:** An imunohistochemical and a subsequent stereological analysis have proven a significant increase in eNOS expression only in spontaneously hypertensive rats which had been given sunitinib. This increased eNOS expression may be related to the development of a potentially protective reaction of vascular endothelium to the application of sunitinib. Thus we can say that sunitinib effects vascular endothelium, however, its potential vascular toxicity must be verified by testing other markers of endothelial dysfunction.

**KEY WORDS:** sunitinib, arterial hypertension, vascular endothelial dysfunction.