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## ACCEPTED MANUSCRIPT

The role of Fenton reaction in ROS-induced toxicity underlying atherosclerosis – modeled and analyzed using a Petri net-based approach

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#### Abstract

The superoxide-driven Fenton reaction plays an important role in the transformation of poorly reactive radicals into highly reactive ones. These highly reactive species (ROS), especially hydroxyl radicals can lead to many disturbances contributing to the endothelial dysfunction being a starting point for atherosclerosis. Although, iron has been identified as a possible culprit influencing formation of ROS, its significance in this process is still debatable. To better understand this phenomenon, the influence of blockade of Fenton reaction in a proposed Petri net-based model of the selected aspects of the iron ROS-induced toxicity in atherosclerosis has been evaluated. As a result of the blockade of iron ions formation in the model, even up to 70% of the paths leading to the progression of atherosclerosis in this model has been blocked. In addition, after adding to the model, the blockade of the lipids peroxidation paths, progression of atherosclerotic plaque has been not observed. This allowed to conclude that the superoxide-driven Fenton reaction plays a significant role in the atherosclerosis.

Keywords: iron, atherosclerosis, oxidative stress, Petri nets, t-invariants

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