ABSTRACT

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Title of thesis: Analysis of oxidative stress in the model of isoprenaline carditoxicity after intravenous administration of rutin

Cardiovascular diseases are the leading cause of mortality in the developed countries. Among the most serious acute forms of ischemic heart disease belongs acute myocardial infarction (AMI), which can be caused by high levels of endogenous catecholamines. Isoprenaline (ISO), a synthetic catecholamine, evokes a pathological state similar to that of AIM, which is accompanied by an increase in both of unbound iron and copper and the consequent formation of hydroxyl radical in Fenton chemistry.

Flavonoids are a large group of substances of natural origin, which represent an important component of human diet and are considered to be beneficial for health status. Their effects include free radical scavenging, iron/copper-chelating properties and inhibiting enzymes producing reactive oxygen species. However, several representatives have showed negative pro-oxidative effects as well.

The main aim of this thesis was an analysis of oxidative stress in the model of isoprenaline cardiotoxicity (isoprenaline, ISO, 100 mg/kg s.c.) after intravenous administration of rutin (11.5 mg/kg and 46 mg/kg) in Wistar:Han rats. Oxidized and total glutathione, a ratio of reduced and oxidized glutathione and a free fraction of 8-

isoprostane as variables assessing oxidative stress were determined within 2 h *in vivo* experiment, resp. 4 h experiment, in whole blood, resp. in plasma.

The thesis showed that the intravenous administration of rutin before the subcutaneous application of ISO was associated with increase in mortality within the both experiments. On the other hand, a co-administration of the solvent (aqueous solution 1.26 % w/V of $NaHCO_3$, i.v.) and ISO was associated with lower mortality in general.

In conclusion it can be stated that the free fraction of 8-isoprostane appeared as a more suitable biomarker of oxidative stress particularly due to its more frequent tendencies to increase and the higher variability in percent changes of concentrations after administration of ISO in comparison with glutathion.

KEYWORDS

isoprenaline, cardiotoxicity, oxidative stress, glutathione, 8-isoprostane, rutin