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A Novel Indole-Triazole Derivative with Antioxidant Properties Reduces the Myocardial Infarct Size in Rabbits

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AIM

It is well documented that reactive oxygen species contribute to ischemia-reperfusion injury of the heart. The aim of the present study was: a) to determine the antioxidant properties of the compound 3-[(1H)-indolylmethyl-4-amino 4,5-dihydro-H,1,2,4 triazolo thione] in vitro and b) to investigate the efficacy of the compound on the reduction of the myocardial infarct size as well as the protective ability against the oxidative damage of the myocardium after ischemia-reperfusion.

MATERIALS-METHODS

The antioxidant activity of the tested compound was first established on in vitro non-enzymatic rat hepatic microsomal lipid peroxidation. For a further study of the mechanism of the antioxidant activity, we investigated the interaction of the tested compound with the 1,1-diphenyl-2-picrylhydarzyl (DPPH) stable free radical, and its competition with DMSO for ·OH. The next step was to examine the antioxidant ability of the tested compound on the oxidative damage of the myocardium after ischemia –reperfusion in vivo. For this purose rabbits were subjected in 30 min regional ischemia followed by 120 min of reperfusion. The tested compound was administered by continuous infusion for 30 min starting at 10^{th} min of ischemia and lasted at 10^{th} min of reperfusion at 2 doses (100 μM and 200 μM). The antioxidant activity was detected spectrophotometrically by the measurement of malondialdehyde (MDA). Finally we investigated the efficacy of the tested compound to reduce the myocardial infarct size. Infarct (I) and risk areas R were delineated with Zn-Cd particles and triphenyl tetrazolium chloride (TTC). The infarcted, the risk and the normal areas were quantified by planimetry with the aid of a digitizer. Infarcted and risk area volumes were expressed as cm^3 and the percent of infarct to risk area (I/R) calculated.

RESULTS

The tested compound showed significant antioxidant properties in all the above assays in vitro, by inhibiting lipid peroxidation by 100% even at a concentration of 0.05 mM. It also exerts significant antioxidant activity in vivo and possesses protective effect against free radicals during ischemia –reperfusion in both doses tested. At the dose of 200 μM /Kg BW the tested compound reduced statistically significantly the myocardial infarct size.

CONCLUSION

A novel antioxidant agent was found to possess protective effect against the oxidative damage of the myocardium after ischemia-reperfusion and to reduce myocardial infarct size in rabbits. This beneficial effect may be correlated to its antioxidant and free radical scavenging activity.