

Summary

Cardiac ischemia/reperfusion is among the most common causes of morbidity and mortality. Decreased oxygen supply and perfusion can cause serious injuries. The overall aims of our studies were to investigate pharmacological approaches capable of reducing ischemia/reperfusion induced damage.

In the first part of our experiments, we examined the effects of preconditioning (PC) on the infarct size in isolated rabbit hearts with hypercholesterolemia. The results clearly show that 3XPC and 4XPC significantly increased the infarct size in group with hypercholesterolemia. In conclusion, the PC is only effective on “healthy heart” and the beneficial effects of PC cannot be seen in hearts with hypercholesterolemia.

In the second part of our study, we examined the role of lipid rafts in ceramide and NO signaling in the ischemic and preconditioned hearts. Our results confirm the concept that ceramide can associate with lipid rafts, where eNOS, which is induced by I/R, become associated with caveolin-1 consequently the generated NO become unavailable to the heart tissue. PC can increase the metabolism of ceramide, thus, the generation of the cardioprotective sphingosine-1-phosphate and the release of eNOS from caveolae are also increasing. Furthermore, our results can give an explanation for the dichotomy of NO behaviour in the heart during I/R and PC. I/R decreases the availability of NO for the heart tissue by the association of eNOS with caveolin-1. The process of PC can dissociate this and makes NO available again.

In the third part of our study we focused on the cardioprotective effects of Makhana in acut and chronic model. The results of our study suggest that Makhana has two different cardioprotective properties. First Makhana has potent reactive oxygen scavenging activity. The antibody array test results showed that the expression of TRX1 and TRP32 proteins are increased in chronic model. These points to the fact that Makhana can modulate the redox state of the heart by this way. These results were also confirmed by Western blot analysis.

In the last part of our study, we examined the effect of the treatment of ACTH (4-10). Our results demonstrate that the ACTH (4-10) in 200 µg/kg dose can improve the postischemic cardiac function, decrease the infarct size and reduce the number of apoptotic cardiomyocytes and endothel cells. The lower concentration of ACTH (4-10) (50 µg/kg) could not reduce the cardiac failure significantly. Considerably more experimentation will be needed in the field of ischemia/reperfusion–induced injury in order to establish the most helpful cardioprotective ACTH fragment without any adrenocorticotrophic side-effects.