

## **Summary**

In the first part of my work, we have studied the effect of sour cherry seed extract on the ischemic/reperfused myocardium. Based on our results, this natural by-product possesses dose-dependent cardioprotective effects. In line with this, the sour cherry seed extract has the capability to reduce the incidence of VT and VF in a dose-dependent manner. Furthermore, our immunohistochemistry experiments revealed the ability of the sour cherry extract to inhibit the caspase 3.

One of the most significant components of the red wine is resveratrol, which has been recognised to possess many health beneficial effects. We have used this phytochemical to test whether it can cure also the pathologic myocardium. Resveratrol treatment improved the postischemic cardiac functions, reduced the bodyweight and the blood glucose level in comparison with the control animals. Based on our results, we concluded that the enhanced Glut-4 protein level and reduced ET-1 play a major role in the cardioprotective effect of resveratrol.

Furthermore, we investigated the effect of resveratrol in combination with  $\gamma$ -tocotrienol. Based on our results we concluded that resveratrol and  $\gamma$ -tocotrienol to some extent possess synergic effect against I/R injury. We measured the level of the antiapoptotic Bcl-2 and the ratio of the survival p-Akt/Akt. Both of them were significantly induced by resveratrol or  $\gamma$ -tocotrienol compared to the vehicle treated control group. More enhanced level of Bcl-2 and ratio of p-Akt/Akt were observed in samples obtained from the dual treated rats, further supporting the existence of synergetic features between resveratrol and  $\gamma$ -tocotrienol. Beside apoptosis, we studied the autophagy. To check the role of autophagy, first we studied the level of Beclin-1 and the ratio of LC3II/LC3I by Western-blot. In case of both resveratrol and  $\gamma$ -tocotrienol we detected enhanced level of Beclin-1 and ratio of LC3II/LC3I, which were more intense in the dual treated group. The phosphorylation status of mTor was studied to examine the mechanisms of initiation of the autophagy. It appears from our results that  $\gamma$ -tocotrienol-induced autophagy, at least in part, is being mediated through mTOR pathway, and resveratrol-mediated autophagy is less dependent on mTOR.

Ischemia/reperfusion, Arrhythmia, Isolated heart, Sour cherry seed extract, Resveratrol,  $\gamma$ -tocotrienol, Autophagy, Endothelin, Infarct size