

BENEFICIAL EFFECTS OF ASTRINGININ, A RESVERATROL ANALOGUE, ON THE ISCHEMIA AND REPERFUSION DAMAGE IN RAT HEART

LI-MAN HUNG,* JAN-KAN CHEN,[†] REN-SHEN LEE,[‡] HSIU-CHUAN LIANG,* and MING-JAI SU*

*Institute of Pharmacology, College of Medicine, National Taiwan University, Taipei, Taiwan; [†]Department of Physiology, College of Medicine, Chang Gung University, Taoyuan, Taiwan; and [‡]Center of General Studies, Chang Gung University, Taoyuan, Taiwan

(Received 14 July 2000; Revised 9 January 2001; Accepted 12 January 2001)

Abstract—Oxidative stress plays an important role in the pathogenesis of myocardial ischemia and infarction. Antioxidants might then be beneficial in the prevention of these diseases. Astringinin (3,3',4',5-tetrahydroxystilbene), a resveratrol (3,4',5-trihydroxystilbene) analogue with considerably higher antioxidative activity and free radical scavenging capacity, was introduced to examine its cardioprotective effects in ischemia or ischemia-reperfusion (I/R) rats. In the present study, the left main coronary artery was occluded by the following procedures: (i) 30 min occlusion, (ii) 5 min occlusion followed by 30 min reperfusion, and (iii) 4 h occlusion. Animals were infused with and without astringinin before coronary artery occlusion. Mortality, and the severity of ischemia- and I/R-induced arrhythmias were compared. Pretreatment of astringinin dramatically reduced the incidence and duration of ventricular tachycardia (VT) and ventricular fibrillation (VF) during either ischemia or I/R period. Astringinin at 2.5×10^{-5} and 2.5×10^{-4} g/kg completely prevented the mortality of animals during ischemia or I/R. During the same period, astringinin pretreatment also increased nitric oxide (NO) and decreased lactate dehydrogenase (LDH) levels in the carotid blood. In animals subjected to 4 h coronary occlusion, the cardiac infarct size (expressed as a percentage of occluded zone) was reduced from $44.4 \pm 4.1\%$ to $19.1 \pm 2.4\%$ by astringinin (2.5×10^{-4} g/kg). We conclude that, astringinin is a potent antiarrhythmic agent with cardioprotective activity in ischemic and ischemic-reperfused rat heart. The beneficial effects of astringinin in the ischemic and ischemic-reperfused hearts may be correlated with its antioxidant activity and upregulation of NO production. © 2001 Elsevier Science Inc.

Keywords—Astringinin, Ischemia-reperfusion, Antiarrhythmia, Myocardial infarction, Antioxidants, Nitric oxide, Free radicals