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Role of KMUP-3 on diabetes-induced cardiomyocytes injury and its improvement effect on cardiac performance

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Diabetes Mellitus (DM)-related cardiomyopathy has been recognized as one of main problem in diabetes patient since it caused heart failure and raised its mortality risk. Currently studies showed that DM leads cardiac ventricle hypertrophy through mechanism of Cardiomyocytes induced apoptosis and cardiac autophagy suppression. Our previous study indicated that KMUP-3 was able to induce autophagy in cardiomyocytes. So that, in this study we investigated whether KMUP-3 promote autophagy activity, prevent high glucose (HG)-induce cardiac injury and also improve cardiac performance in DM rats. We generated diabetes-induced model by treating high glucose (HG) in neonatal rat cardiomyocytes. Cardiomyocytes were incubated in 30 mM glucose in the presence or absence of KMUP-3 (1 to 10 μM). An experimental diabetic rat model was induced by 65mg/kg of Streptozotocin (STZ) combined with high calorie intake on rats. Dose of KMUP-3 intraperitoneally injection was 1 mg/kg. Cardiac performances were evaluated by serial echocardiography. We found KMUP-3 attenuated HG-induced cell death by MTT assay. Furthermore, KMUP-3 inhibited HG-induced apoptosis which was associated with Bax protein decrease, Bcl-2 protein increase, and caspase-3 cleavage decline. Microtubule-associated protein I light chain 3-II (LC3-II) was the key protein associated with autophagy. KMUP-3 significantly enhanced generation of LC3-II and phosphorylation of AMPK in time-dependent manner. As expected, KMUP-3 pre-treatment dose-dependently reduced the HG-induced LC3- II, Atg7, and phosphor-AMPK expression. Fractional shortening (FS) and ejection fraction (EF), the index of left ventricular systolic function were significantly decreased in DM group. Compared with DM group, these changes were attenuated when diabetic rats were treated with KMUP-3 ($p<0.05$). In sum, KMUP-3 attenuates HG-induced cardiomyocytes apoptosis by inducing autophagy. These findings suggest that KMUP-3 may have great therapeutic potential in the treatment of diabetic cardiomyopathy.

Biography

Erna Sulistyowati has been pursuing her PhD program at Kaohsiung Medical University, Taiwan since 2014. She graduated M.D (Doctor of medicine) from University of Brawijaya, Indonesia. She received Master degree in Biomedics from University of Brawijaya. Currently, she is one of the research team on KMUP-treatment in diabetes-related cardiovascular disease in Department of Pharmacology, School of Medicine, Kaohsiung medical University, Taiwan.

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