發表論文

POSTER COMMUNICATIONS

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Protective Effect of KMUP-1 against ET-1-Induced Cardiac Hypertrophy in H9c2 Cells

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Endothelin-1 (ET-1) has been implicated in cardiac pathology, such as the progression from cardiac hypertrophy to heart failure. KMUP-1 is a unique xanthine and piperazine derivative, combining the sGC stimulation, K^+ channels opening and particularly PDE 5 inhibition activities in one molecule. The purpose of this study was to determine the efficacy and the possible mechanism of action of KMUP-1 on the ET-1-induced cardiac hypertrophy in cardiomyocytes. Hypertrophy was observed as cardiac myoblasts (H9c2 cells) were treated with ET-1 (100 nM) for 4 days, which was assessed by the measurement of cell surface area, and this effect was strongly prevented by KMUP-1. Previous studies have shown that HO-1 can inhibit mitogen-activated protein kinases (MAPKs), calcineurin/NFAT signaling, and hypertrophy in ET-1 induced cardiac myocytes. Our data indicated that KMUP-1 decreased ET-1-induced phosphorylation of ERK1/2, p38, Akt, and calcineurin. Furthermore, KMUP-1 also enhanced HO-1 protein expression. In addition, KMUP-1 also significantly decreased the intracellular peroxide level induced by ET-1, as determined by using DCHF-DA staining. In conclusion, these findings suggest that KMUP-1 attenuates ET-1-induced cardiac hypertrophy by blocking MAPK, Akt and calcineurin activation, enhancing HO-1 protein expression and decreasing ROS generation. Thus, KMUP-1 may be a clinically useful drug for relief of cardiac hypertrophy.