**Carpaine promotes proliferation and repair of H9c2 cardiomyocytes after oxidative insults**

## ABSTRACT

Carpaine has long been identified as the major alkaloid in Carica papaya leaves that possess muscle relaxant properties. Limited study on the molecular signaling properties of carpaine urges us to conduct this study that aims to elucidate the mechanism underlying the cardioprotective effect of carpaine in embryonic cardiomyocytes of the H9c2 cell line. The 50% inhibitory concentration (IC50) of carpaine was first determined using a colorimetric MTT assay to establish the minimum inhibitory concentration for the subsequent test. Using a 1 □ M carpaine treatment, a significant increase in the H9c2 proliferation rate was observed following 24 and 48 h of incubation. A Western blot analysis also revealed that carpaine promotes the upregulation of the cell cycle marker proteins cyclin D1 and PCNA. Carpaine-induced H9c2 cell proliferation is mediated by the activation of the FAK-ERK1/2 and FAK-AKT signaling pathways. In the setting of ischemia-reperfusion injury (IRI), carpaine provided a significant protective role to recover the wounded area affected by the hydrogen peroxide (H2O2) treatment. Furthermore, the oxidative-stress-induced reduction in mitochondrial membrane potential (MMP) and overproduction of reactive oxygen species (ROS) were attenuated by carpaine treatment. The current study revealed a novel therapeutic potential of carpaine in promoting in vitro cardiomyocyte proliferation and repair following injury.