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Innovative Enzyme to Treat Ischemia Reperfusion-Induced Heart Injury

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Ischemia is one of the most common causes of myocardial injury, and blood restoration in the form of reperfusion is critical for the ischemic heart to be saved.

However, reperfusion caused myocardial harm in and of itself, hence the phrase ischemia-reperfusion is used to characterize injury that occurs throughout the ischemia-reperfusion process. Even though ischemia-reperfusion-induced myocardial damage is very common, there are no effective medications to prevent it. As a result, new pharmacological agents, and targets for the successful therapy of ischemia reperfusion-induced cardiac injury must be explored and identified. 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase-3 (PFKFB3) is a glycolysis-regulating enzyme that is activated under hypoxic conditions.

Most of the research on this target has been focused on cancer cell proliferation and its significance in various forms of cancer. Furthermore, suppression of PFKFB3 has been found to reduce ischemia-reperfusion-induced brain damage. The role of PFKB3 inhibitors in ischemia-reperfusion-induced myocardial damage, on the other hand, has not been investigated. As a result, the goal of this investigation was to see if pharmacological inhibitors of PFKB3, such as 3-PO and AZ PFKFB3, may be used to treat ischemia reperfusion-induced heart injury.

All the experimental studies were conducted at Lanzhou City's First People's Hospital over three months. The experiments in this study were conducted on male Wistar albino rats weighing 200-250 g. The rats' hearts were extracted after they were sacrificed. The isolated hearts were mounted on the Langendorff System right away and retrogradely perfused with physiological solution (Krebs Solution, 37EC). After 15 min of stability, the intake of the physiological solution was terminated, resulting in 30 min of worldwide ischemia. The physiological solution was collected in the form of coronary effluent after passing through the heart to determine heart-specific biochemicals. The hearts were separated and homogenized in physiological buffer solution after 120 min of reperfusion. The amounts of H2S in the cardiac homogenates were measured using a reverse HPLC technique.

During the reperfusion phase of this investigation, 30 min of global ischemia and 120 min of reperfusion caused considerable myocardial injury, as measured by an increase in the production of heart injury-specific biomarkers such as CK-MB and cTnT in the coronary effluent. The presence of CK-MB and cTnT in coronary effluent is thought to be a sign of myocardial damage. Furthermore, ischemia-reperfusion-exposed rat hearts showed functional deterioration and a substantial drop in the

LVDP (heart contractility measure) in these rat hearts. The current findings, which showed the progression of myocardial damage, were consistent with previous research. Ex vivo cardiac preparation was used in this investigation because it avoids the systemic effects that can occur in vivo preparations.

Additionally, cardiac contractility was greatly preserved, and LVDP values were significantly higher in 3-PO-treated rat hearts. PFKFB3 is an enzyme that is activated under hypoxic environments and plays an important role in glycolysis regulation. It has been demonstrated to be involved in pathological processes in addition to physiological functions. There have been studies that suggest the importance of this enzyme in cancer, pulmonary hypertension, and endotoxemia infections. As a result, PFKFB3 activation may play a vital role in causing ischemia-reperfusion-induced myocardial injury, and that pharmacological inhibitors of PFKFB3 could be used to treat heart injury caused by ischemia-reperfusion.

Pharmacological inhibitors of PFKFB3 could be used as cardio protective drugs to reduce ischemia reperfusion-induced injury, with effects mediated through H2S, Akt, and GSK-3B signalling.

JOURNAL REFERENCE

Han, J. and Y. Zhang, 2021. Exploring the cardioprotective effects of pharmacological inhibitors of 6-phosphofructo-2-kinase/fructose- 2,6-bisphosphatase-3 in ischemia-reperfusion-subjected rats. Int. J. Pharmacol., 18: 346-353.

KEYWORDS

Ischemia, ischemia reperfusion-Induced heart injury, treatment, PFKFB3, cardioprotective drugs, H2S, Akt, and GSK-3B signalling