جامعة الفيوم

كلية الطب البشرى

قسم الأمراض الباطنة

ملخص بحث (البحث السادس)

TITLE: E1231/SR647 protects against unilateral renal ischemia-reperfusion injury by modulating SIRT1/FOXO3 interactions with Nrf2 and NFκB pathways

ABSTRACT

Ischemia is a major contributor to acute kidney injury (AKI), for which current treatment options remain limited. One NAD+-dependent deacetylase that can preserve renal cells is SIRT1. To date, no research has directly explored the effects of E1231, a SIRT1 activator, in the context of renal ischemia-reperfusion (IR) injury. Enhancing NAD+ levels is essential for sustaining SIRT1 activity. Hence, the combined use of E1231 and SR647, a NAD+ precursor, could potentially amplify protective effects by supporting prolonged SIRT1 activation. This study is the first to investigate the therapeutic potential of combining E1231 and SR647 in mitigating unilateral renal IR injury. Rats treated with E1231/SR647 effectively demonstrated reduced tubular damage, inflammation, and necrosis. These improvements correlated with reduced kidney-to-body weight ratio and increased urine output and flow rate. Additionally, E1231/SR647 treatment upregulated SIRT1 levels and activity, enhanced FOXO3 activation, boosted Nrf2 levels, and reduced NFκB activity. These findings suggest that E1231/SR647 is a promising therapy for protecting renal function during ischemic events through the modulation of SIRT1/FOXO3 interactions with Nrf2 and NFκB pathways.

Keywords: Unilateral renal ischemia-reperfusion injury, SIRT1, FOXO3, Nrf2, NFκB, E1231, SR647

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