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SAXAGLIPTIN REPAIRS RENAL ISCHEMIA/REPERFUSION INJURY: ROLE OF KIM-1/STAT- 3 SIGNALING

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Saxagliptin, a 2009 FDA-approved dipeptidyl peptidase-4 (DPP-4) inhibitor, is currently used to treat type 2 diabetes mellitus either as monotherapy or in combinations; however, its potential role against the renal ischemia/reperfusion (I/R) insult has not been fully studied. Saxagliptin (10 and 30 mg/kg; p.o) was administered after acute renal ischemia (1 hour)/reperfusion (120 hours) at 1, 24, 48, 72, and 96 hours after reperfusion in male Wistar rats. Assessing the renal tissues revealed that saxaglipitin repaired renal damage caused by I/R via a kidney injury molecule-1 (Kim-1)- dependent mechanism. Kim-1, which is a type-1 membrane protein, was able to activate the signal transducer and activator of transcription 3 (STAT3) by phosphorylation at tyrosine 705, and the latter activated hypoxia inducible factor-1 alpha (HIF-1α), and its downstream vascular endothelial growth factor (VEGF). This led to enhancing the neovascularization repair of renal tissue, as well as improving the histological structure of the I/R-damaged renal glomeruli and tubules. Neovascularization involved the formation of new renal blood vessels, either from already existing vasculature, in a process termed angiogenesis, or the *de novo* formation of new vessels, in a process termed vasculogenesis. This may indicate a possible usefulness of clinical application of saxagliptin in renal transplantation surgeries during which I/R injury commonly occurs

Biography

Nada Mohamed Kamel Mohamed is currently working as a Pharmacology and Toxicology Teaching Assistant at the Faculty of Pharmacy, Cairo University. Her Master's degree is based on a study to decrease mortality rates and organ rejection after transplantation surgeries. For this study, she used Wistar rats and renal ischemia/reperfusion model.

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