

Diabetic nephropathy is a prevalent complication in both type 1 and type 2 diabetes, which contributes to the progression of end-stage renal disease. Previous research indicates that hyperglycemia leads to renal fibrosis. Extracellular matrix deposits are a key feature of renal fibrosis, and as part of this process, interstitial myofibroblasts produce alpha-smooth muscle actin. This study investigates the role of dapagliflozin – a sodium-glucose cotransporter 2 inhibitor – in mitigating renal damage of rats induced with diabetes. Alpha-smooth muscle actin acts as a surrogate marker in detecting renal fibrosis within this study.

Immunohistochemical techniques were used to assess the area affected by alpha-smooth muscle actin in five experimental groups: healthy control, diabetic control, and three groups of diabetic rats treated with insulin, dapagliflozin, or a combination of both. Kidney sections were stained with antibodies targeting alpha-smooth muscle actin, which functions as the biomarker for detection of renal damage. DAPI and phalloidin stains were also used to assist in visualizing kidney structures including nuclei, glomeruli, and renal tubules. Confocal microscopy and Fiji software were utilized for data collection and analysis, respectively, to quantify the area affected. Preliminary data suggests dapagliflozin reduces alpha-smooth muscle actin, indicating it may reduce renal tubule damage. This supports the findings in previous clinical trials such as the DAPA-CKD trial where patients both with and without diabetes treated with dapagliflozin had a slower rate of eGFR decline than those treated with placebo.

This study showed that dapagliflozin attenuated damage in the renal cortex, but not the renal medulla while dapagliflozin in combination with insulin therapy attenuated damage in both the renal cortex and renal medulla when compared to the untreated diabetic arm. More data points and longer studies are required to draw definitive conclusions when comparing the results of treatment arms with those of the healthy control arm.