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Evaluation of the Effect of an Alpha-Adrenergic Blocker, a PPAR-gamma Receptor Agonist, and a Glycemic Regulator on Chronic Kidney Disease in Diabetic Rats

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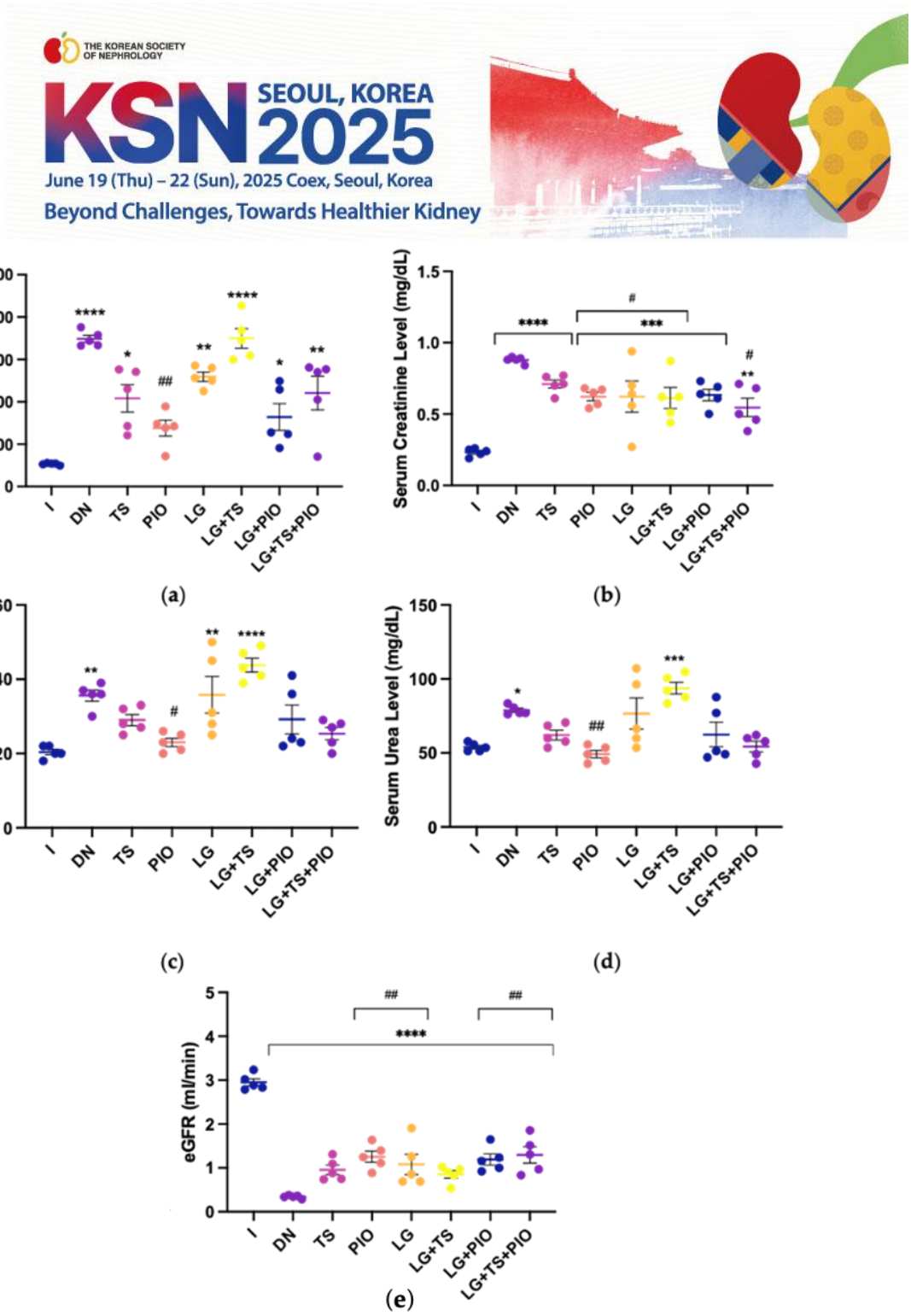
Objectives : Diabetic Nephropathy (DN) is a major complication of Diabetes Mellitus (DM) and a leading cause of end-stage renal disease. Given its high prevalence, rapid progression, and severity, there is a need for new treatment strategies. While pioglitazone and linagliptin show promise in reducing DN risk, the therapeutic role of tamsulosin remains underexplored. This study aims to investigate the effects of pioglitazone, linagliptin, and tamsulosin, individually and in combination, in a Wistar rat model of DN to identify potential new treatments.
Methods : Diabetes was induced in rats with a high dose of streptozotocin. The rats were treated with tamsulosin, pioglitazone, and linagliptin for six weeks. Food and water intake were monitored, and renal function was assessed using the estimated glomerular filtration rate (eGFR). Histological analysis was performed to evaluate tissue morphology, while biochemical parameters were also measured. The expression of key inflammatory and fibrotic markers (NF-κB, IL-1β, IL-10, TGF-β, and collagen IV) were analyzed using immunofluorescence and RT-qPCR.
Results : The DN group exhibited hyperglycemia, reduced eGFR, tissue damage, and increased the expression of NF-κB, TGF-β, along with decreased levels of IL-10 and NRF2. Tamsulosin and linagliptin improved eGFR, reduced urinary glucose, promoted tissue repair, and lowered the expression of IL-1β and TGF-β markers. Additionally, both treatments led to increased levels of IL-10 and NRF2. Pioglitazone, both alone and in combination with other drugs restored serum and urinary parameters, reduced tissue damage, and decreased the NF-κB, IL-1β, Col-IV, and TGF-β, while simultaneously boosting IL-10 and NRF2. Furthermore, linagliptin alone, reduced serum creatinine and tissue injury, decreasing the IL-1β, Col-IV, and TGF-β while increasing IL-10 and NRF2.
Conclusions : The administration of tamsulosin, pioglitazone, linagliptin, and their combinations showed a significant renoprotective effect, improving renal function and reducing fibrosis. These benefits were attributed to the antifibrotic, anti-inflammatory, and antioxidant properties of the treatments.

image1.png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Beyond Challenges, Towards Healthier Kidney
Serum FBG Level (mg/dL)
Serum Creatinine Level (mg/dL)
Serum BUN Level (mg/dL)
Serum Urea Level (mg/dL)
eGFR (ml/min)
I
DN
TS
PIO
LG
LG+TS
LG+PIO
LG+TS+PIO
(a)
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image1.png