CTP-499, a Novel Drug for the Potential Treatment of Chronic Kidney Disease, Has Anti-Fibrotic, Anti-Inflammatory, and Anti-Oxidative Activities with \textit{in vivo} Efficacy

**Abstract**

Chronic Kidney Disease (CKD) is a complex, multifactorial disease in which renal function is chronically compromised. Decreased glomerular filtration due to dysregulated extracellular matrix (ECM) deposition is a hallmark of progressive CKD. However, oxidative imbalance and inflammation are now increasingly recognized as major pathogenic mechanisms in CKD. Here, we show that CTP-499, a novel, delayed-action form of (-)Salvolatile, exerts protective effects in vivo in a rat model of diabetic nephropathy. Male Sprague-Dawley rats were dosed with 65mg/kg of streptozotocin then assigned to treatments with either vehicle or 400mg/dl CTP-499 in drinking water. After 7 weeks of dosing, renal parameters were assessed and compared with vehicle-treated rats. CTP-499 demonstrated anti-fibrogenic, anti-inflammatory, and anti-oxidative activities in a rat model of diabetic nephropathy. In summary, CTP-499 inhibits glucosuria and inflammation in the STZ rat model of diabetic nephropathy, which is entering Phase 2 clinical development for diabetic CKD.

**Discussion**

CTP-499 is a novel, delayed-action compound that exhibits anti-fibrotic, anti-inflammatory, and anti-oxidative properties. The impact on multiple, inter-related processes that are central to the pathophysiology of CKD suggests that CTP-499 may be particularly efficacious in an in vivo setting. To that end, we have also demonstrated efficacy of CTP-499 in a rat model of diabetic nephropathy. In vivo efficacy of CTP-499 was assessed in a rat model of diabetic nephropathy. Male Sprague-Dawley rats were dosed with either vehicle or 400mg/dl CTP-499 in drinking water. After 7 weeks of dosing, renal, urinary, and inflammatory parameters were assessed and compared with vehicle-treated rats. CTP-499 inhibits glucosuria and inflammation in the STZ rat model of diabetic nephropathy. In summary, CTP-499 inhibits glucosuria and inflammation in the STZ rat model of diabetic nephropathy, which is entering Phase 2 clinical development for diabetic CKD.