

# **Pioglitazone, an Insulin Sensitizing Drug, Attenuates the Development of Kidney and Liver Disease in the PCK Rodent Model of Polycystic Kidney Disease.**

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## **Abstract**

Polycystic kidney disease is a genetic disorder characterized by growth of fluid-filled cysts predominately in kidney and liver. The only treatment currently available is the removal/aspiration of the largest cysts or organ transplantation. Promising pharmaceutical agents in clinical trials interfere with the action of hormones that increase cAMP thereby inhibiting secretion of  $\text{Cl}^-$ , and compensatory fluid flux, into the cysts. Other treatments proposed include chemotherapeutic and immunosuppressive drugs that interfere with cellular proliferation as well as with signaling pathways for  $\text{Cl}^-$  secretion. Long-term use of these agents will have multiple side effects. Based on a recent observation that peroxisome proliferator activated receptor  $\gamma$  agonists such as Actos (pioglitazone) and Avandia (rosiglitazone) decrease mRNA levels of a  $\text{Cl}^-$  transport protein and the  $\text{Cl}^-$  secretory response to vasopressin stimulation in cultured renal cells, it is hypothesized that PPAR $\gamma$  agonists will inhibit cyst growth. The current studies show that a 7 or 14 week feeding regimen of 20 mg/Kg BW pioglitazone inhibits renal and hepatic bile duct cyst growth in a rodent model orthologous to human PKD. In addition, the degree of renal cortical fibrosis was diminished in the pioglitazone-treated animals after 14 weeks. These results suggest that PPAR $\gamma$  agonists may be effective in controlling both renal and hepatic cyst growth and renal fibrotic development in polycystic kidney disease.