SIGNIFICANCE STATEMENT

CKD changes the pharmacokinetics of many drugs, both those with renal and nonrenal clearance, leading to reduced effectiveness and an increase in secondary effects. This paper describes effects of indoxyl sulfate, a uremic toxin, on hepatocyte expression and activity of P-glycoprotein operating through an aryl hydrocarbon receptor pathway. Studies show that P-glycoprotein expression is increased in uremic mice. In transplant recipients with CKD, high levels of indoxyl sulfate are associated with increases in the required dose of cyclosporin, a substrate of P-glycoprotein. Thus, indoxyl sulfate increases P-glycoprotein expression and can modify the pharmacokinetics of drugs. Monitoring indoxyl sulfate levels could improve drug management in patients with CKD.