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INTERACTION BETWEEN *P*-CRESYL SULFATE AND INDOXYL SULFATE DURING BODY DISPOSITION CAN INFLUENCE THEIR SERUM FREE CONCENTRATIONS IN CHRONIC KIDNEY DISEASE

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ABSTRACT

The serum concentrations of sulfate conjugated uremic toxins (UTs) such as *p*-cresyl sulfate (PCS) and indoxyl sulfate (IS), especially those free concentrations, are associated with chronic kidney disease (CKD) progression, cardiovascular outcomes and the efficacy of hemodialysis. However, the mechanism of changes in their free concentration has been little understood. The purpose of this study is to reveal whether PCS interacts with IS and vice versa during body disposition, especially in the binding to human serum albumin (HSA) and the renal excretion processes. Protein binding of UTs was examined using ultrafiltration and spectroscopic techniques. The renal uptake process of UTs was investigated using rat renal cortical slices. Based on the binding data, it was obvious that PCS bound specifically to Site II of HSA. The binding of PCS to HSA was competitively inhibited by IS. In renal cortical slice experiments, active transport was involved in the basolateral uptake of PCS and it was significantly suppressed by the inhibitors of OATs and IS. Together, competitive interactions between PCS and IS in HSA binding and the renal tubular secretion process via OATs could contribute to the changes in their serum free concentrations in CKD patients.