Chemico-Biol. Interact. 139, 135-140 (2002)

Sex hormone-regulated renal transport of perfluorooctanoic acid

Naomi Kudo（工藤なをみ）, Masanori Katakura （片倉賢紀）,
Yasunori Sato（佐藤靖典）and Yoichi Kawashima（川嶋洋一）

Faculty of Pharmaceutical Sciences, Josai University, 1-1, Keyakidai,
Sakado, Saitama 350-0295, Japan

The biological half-life of perfluorooctanoic acid (PFOA) in male rats is 70 times longer than that in female rats. The difference is mainly due to the difference in renal clearance (CL_R), which was significantly reduced by probenecid, suggesting that PFOA is excreted by organic anion transporter(s). Castration of male rats caused a 14-fold increase in the $CL_R$of PFOA, which made it comparable with that of female rats. The elevated PFOA CL_Rin castrated males was reduced by treating them with testosterone. Treatment of male rats with estradiol increased the $CL_R$of PFOA. In female rats, ovariectomy caused a significant increase in $CL_R$of PFOA, which was reduced by estradiol treatment. Treatments of female rats with testosterone reduced the $CL_R$of PFOA as observed in castrated male rats. To identify the transporter molecules that are responsible for PFOA transport in rat kidney, renal mRNA levels of OAT1, OAT2, OAT3, oatp1, oatp2 and OAT-K were determined in male and female rats under various hormonal states and compared with the $CL_R$of PFOA. The level of OAT2 mRNA in male rats was only 13% that in female rats. Castration or estradiol treatment increased the level of OAT2 mRNA whereas treatment of castrated male rats with testosterone reduced it. In contrast to OAT2, mRNA levels of both oatp1 and OAT-K were significantly higher in male rats compared with female rats. Castration or estradiol treatment caused a reduction in the levels of mRNA of oatp1 and OAT-K in male rats. Ovariectomy of female rats significantly increased the level of OAT3 mRNA. Multiple regression analysis suggests that the change in the $CL_R$of PFOA is, at least in part, due to altered expression of OAT2 and OAT3.