Yuri Tsuruya, Koji Kato, Yamato Sano, Yuichiro Imamura, Kazuya Maeda, Yuji Kumagai, Yuichi Sugiyama, and Hiroyuki Kusuhara, Investigation of endogenous compounds applicable to drug–drug interaction studies involving the renal organic anion transporters, OAT1 and OAT3, in humans. Drug Metab Dispos

Supplemental Table 1 Analytical conditions for test compounds

Compound	**Column**	**Mobile phase**		**Gradient condition**	**Flow rate**	***m/z***	**Ion mode**
		A	**B**	**(B concentration %)**	**(mL/min)**		
GCDCA-S	ZORBAX SB-C18 (3.5 μm, 50 mm × 4.6 mm, Agilent Technologies)	Formic acid (0.1%)	Acetonitrile	0 min; 10%	1.2	528.1→448.3	Negative
[D5]GCDCA-S				1.5 min; 98%		533.3→453.1	Negative
Furosemide				1.7 min; 98%		328.9→284.9	Negative
Benzylpenicillin				1.71 min; 10%		335.2→160.0	Negative
Rosuvastatin				2.2 min; 10%		480.1→418.0	Negative

Pravastatin						423.1→320.9	Negative
Probenecid	ZORBAX SB-C18 (3.5 μm, 50 mm × 4.6 mm, Agilent Technologies)	Formic acid (0.1%)	Acetonitrile	0 min; 10% 1.2 min; 98% 1.7 min; 98% 1.71 min; 10% 2.2 min; 10%	1.2	283.9→240.0	Negative
Taurine	XBridge Amide (3.5 μm, 50 mm × 4.6 mm, Waters)	Ammonium acetate (10 mM)	Acetonitrile	0 min; 95% 0.3 min; 95% 3.0 min; 50% 4.0 min; 50% 4.01 min; 95%	1.0	123.9→79.9	Negative
[D5]-Taurine						127.9→79.9	Negative

5.0 min; 95%
4.6 min; 0%
6.5 min; 0%

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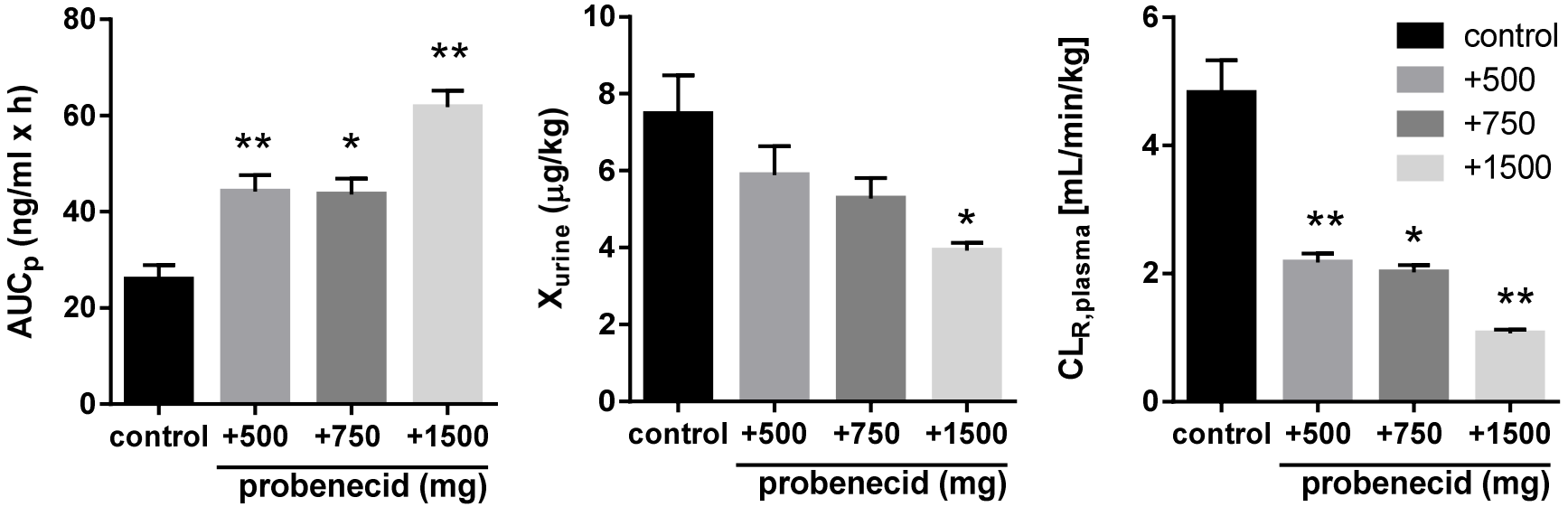

Supplemental Figure 1. Effect of probenecid on the AUC_p, X_{urine} and $CL_{R,plasma}$ of 6β-hydroxycortisol in healthy subjects

6β-Hydroxycortisol concentrations in the plasma and urine specimens from subjects without and with oral doses of probenecid (500, 750 and 1500 mg) were determined using LC-MS/MS. AUC_p was calculated from time zero to 8 hours after benzylpenicillin administration, X_{urine} represents the amount excreted into the urine from time zero to 8 hours. $CL_{R,plasma}$ was calculated by dividing the X_{urine} by AUC_p.
The data for cotnrol and +750 mg were cited from Imamura et al., XX.

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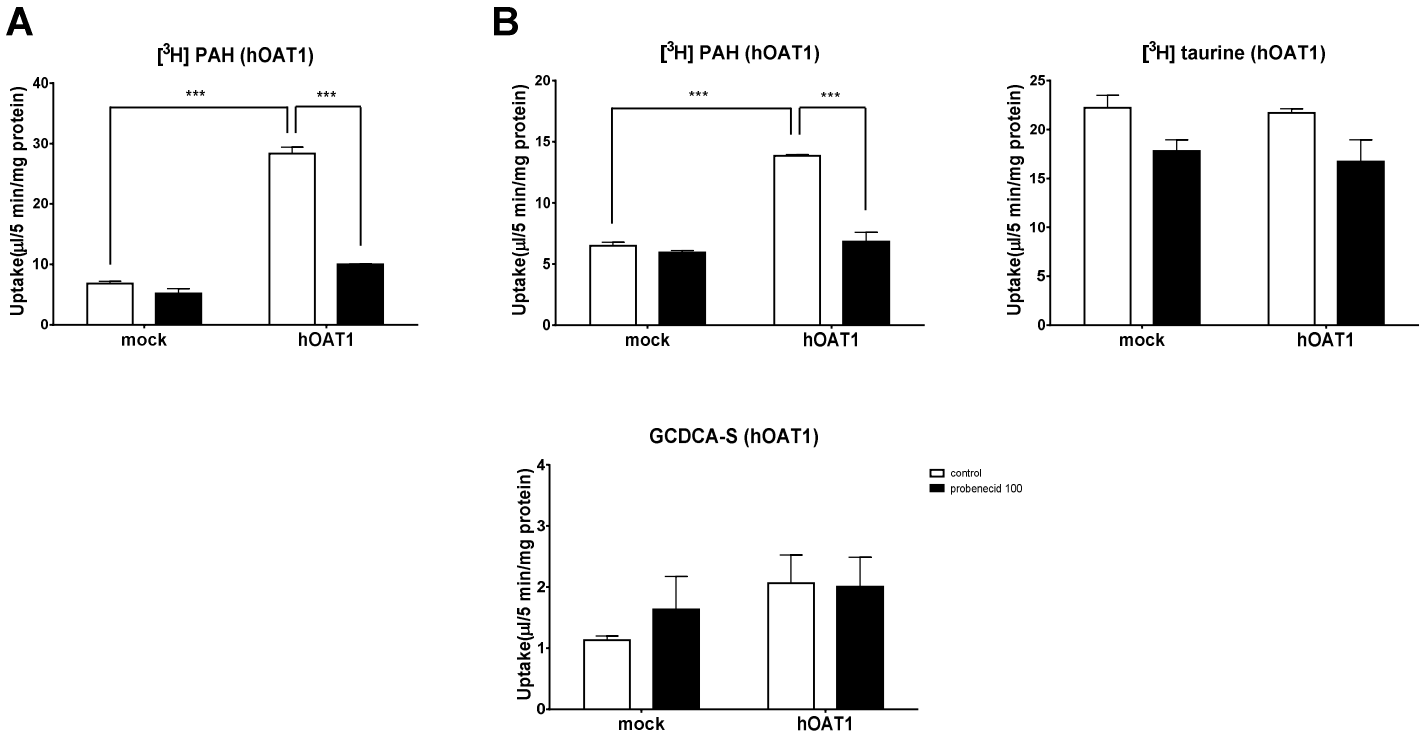

Supplemental Figure 2. Uptake studies of PAH, taurine and GCDCA-S by HEK293 cells stably expressing hOAT1 and HEK293T cells transiently expressing hOAT1.

A The uptake of [^{3}H]PAH was measured by HEK293 cells transiently expressing hOAT1. The uptake of [^{3}H]PAH, [^{3}H]taurine and GCDCA-S were measure in HEK293T cells stably expressing hOAT1. The cellular accumulation of [^{3}H]PAH (20 nM), [^{3}H]taurine (5 nM), and GCDCA-S (1 μM) was determined following 5 min incubation at 37° C in the absence (open bar) or presence of 100 μM probenecid (closed bar). Each bar graph represents the mean with S.E. M (n=3). Significant differences between the groups were denoted by asterisks (***$p<0.001$; one-way analysis of variance with Tukey's test).

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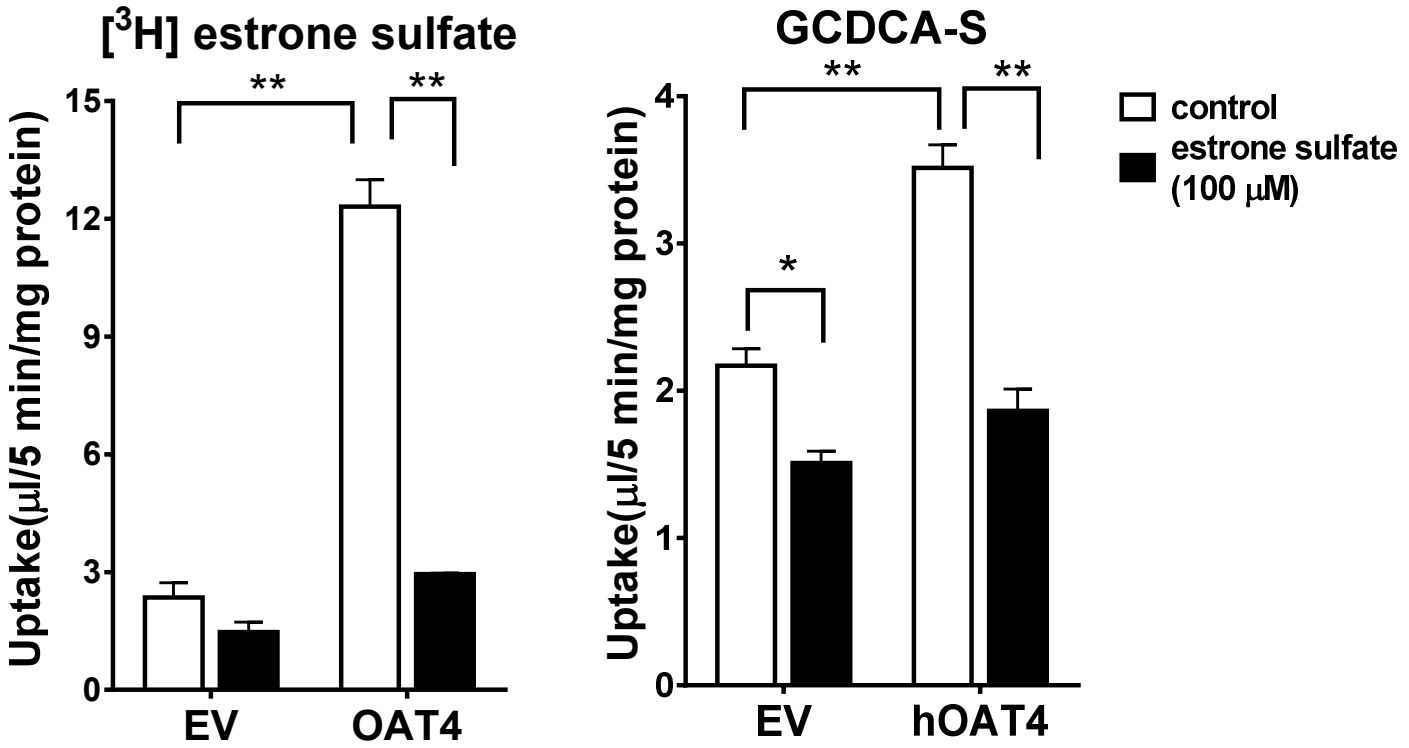

Supplemental Figure 3. Uptake studies of [^{3}H]estrone sulfate and GCDCA-S by HEK293 cells stably expressing hOAT4.

A The uptake of [^{3}H]estrone sulfate and GCDCA-S was measured by empty-vector (EV) transfected HEK293 cells, and those stably expressing hOAT4. The cellular accumulation of [^{3}H]estrone sulfate(10 nM), and GCDCA-S (1 μM) was determined following 5 min incubation at 37° C in the absence (open bar) or presence of 100 μM unlabeled estrone sulfate (closed bar). Each bar graph represents the mean with S.E. M (n=3). Significant differences between the groups were denoted by asterisks (***p<0.001; one-way analysis of variance with Tukey's test).