Supplementary figure 1

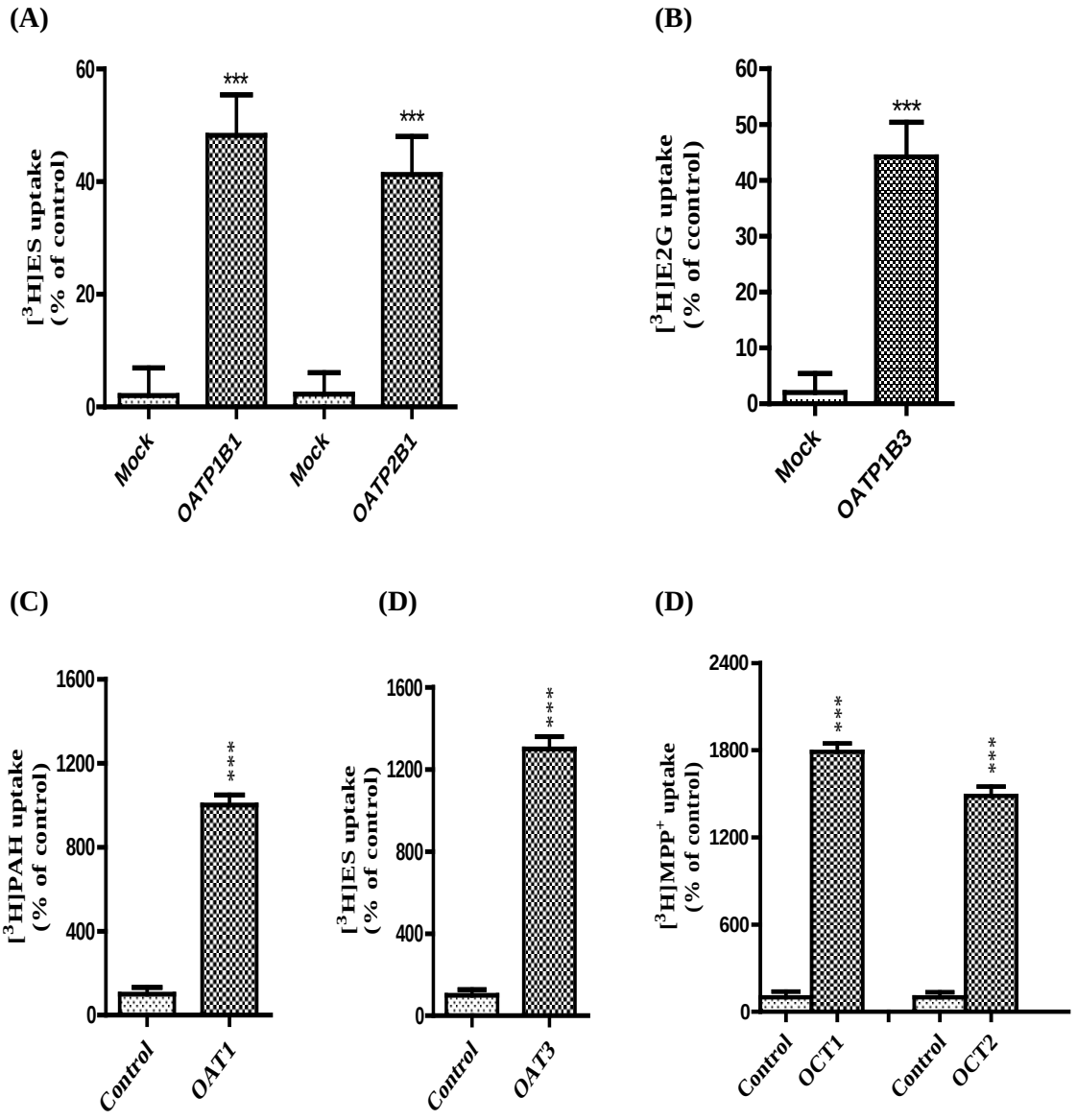

Figure S1. Characterization of HEK cell stably transfected with human transporters. (A) Intracellular uptake of 45nM [^{3}H]ES in HEK-OATP1B1 (A), 45nM [^{3}H]ES in HEK-OATP2B1 (B), [^{3}H]E2G in HEK-OATP1B3 (C), 89nM [^{3}H]P AH in HEK-OAT1 (D), 45nM [^{3}H]ES in HEK-OAT3 (B) and 25nM [^{3}H]MPP+ in HEK-OCT1 and HEK-OCT2 cells. The uptake amount w as determined by subtracting the total amount of uptake in control cells from the uptake in OAT and OCT transporter-expressing cells which was expressed as % of control. Data are presented as the means ±SDs from three or more independent experiments. Significant differences compared with the percent uptake for the control (no inhibitor) are indicated (***, $P > 0.001$).

Supplementary figure 2

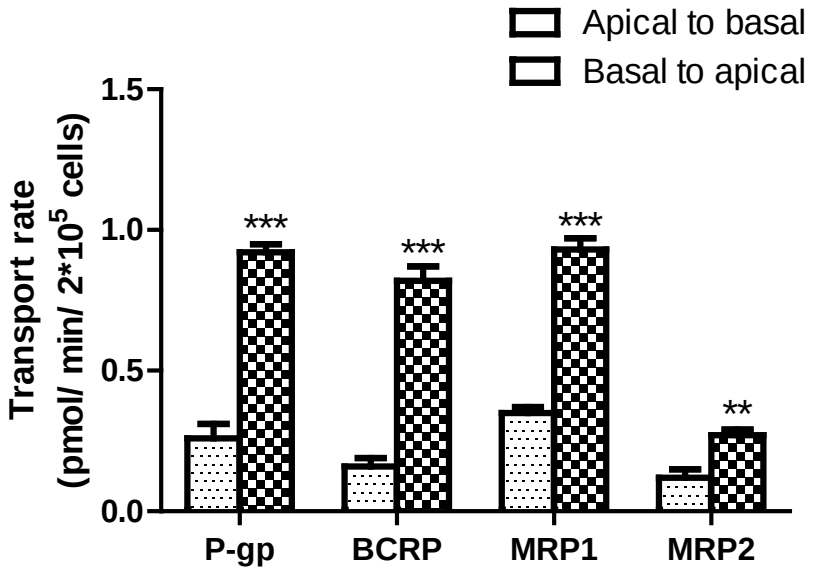

Figure S2. Transepithelial transport of probe substrate for P-gp, BCRP, MRP1 and MRP2-cells. The apical to basal and basal to apical transport of 50nM digoxin (P-gp), 24nM prazosin (BCRP), 45nM estrone sulphate (MRP1), and 24 nM vinblastin (MRP2) across LLCPK-MDR1, LLCPK-BCRP and MDCKII-MRP1, MDCKII-MRP2 cell monolayers. Each data point presents the means ±SDs of three or more independent experiments. Significant differences compared with the percent uptake for the control (no inhibitor) are indicated (**, *P > 0.01; ***, P > 0.001).*

Supplementary figure 3

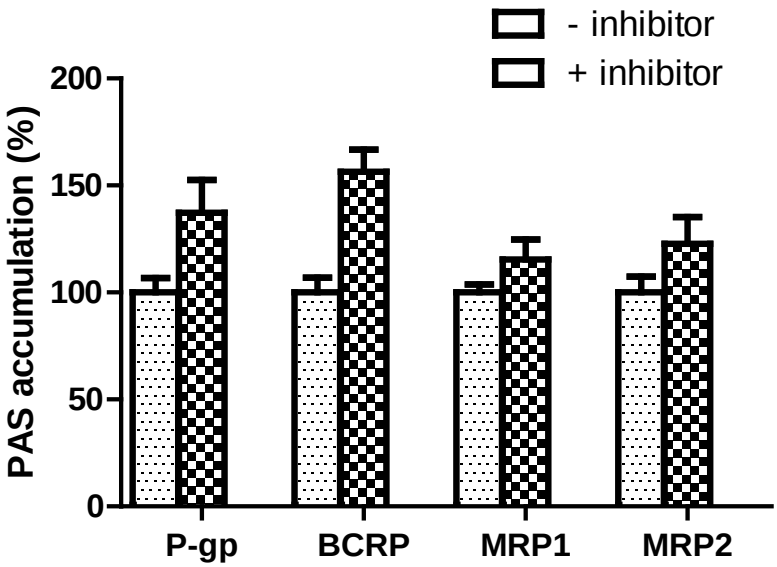

Figure S3. Cellular accumulation of PAS in ABC efflux transporters. The accumulation of 10 µM PAS was measured in presence or absence of 20 µM verapamil for P-gp, 20 µM rosuvastatin for BCRP, 20 µM MK571 for MRP1 and MRP2 across LLCPK-MDR1, LLCPK-BCRP and MDCKII-MRP1, MDCKII-MRP2 cells. Each data point presents the means ±SDs of three or more independent experiments.

Supplementary table 1. Cellular uptake of *in vitro* radiolabeled prototype substrates into stably transfected HEK-OATP1B1, HEK-OATP2B1, HEK-1B3, HEK-OAT1, HEK-OAT3, HEK-OCT1 and HEK-OCT2 cells [a].

Substrate [b]	**Transporter**	K_m **(µM)**	V_{max} **(pmol/min/ mg protein)**	Cl_{int} **(µl/min/mg protein)**	**Reported** K_m **(µM)** [c]
[^{3}H]ES	OATP1B1	2.3	28.0	12.17	2.4(1), 12.5(2)
[^{3}H]ES	OATP2B1	5.8	32.0	6.4	7.1(3), 8.09(4),10.2(5)
[^{3}H]E2G	OATP1B3	8.4	12.0	1.52	15.8(1), 24.6(6)
[^{3}H]PAH	OAT1	23.9	517.8	21.7	28(7), 15.4(8)
[^{3}H]ES	OAT3	7.6	130.6	17.2	6.3(7)
[^{3}H]MPP$^+$	OCT1	17.0	132.6	7.80	14.6(9), 21(10)
[^{3}H]MPP$^+$	OCT2	21.0	515.5	24.5	16 (11), 19.5 (12)

[A] Shown are the intracellular uptake kinetics of the cells derived from *in vitro* experiments: K_m, Michelis-Menten constant; *Vmax*, maximum rate of uptake; CL_{int}, intrinsic clearance per unit of time. Data represent the mean values from triplicate experiments.

[b] [^{3}H]-estrone sulphate for OATP1B1 and OATP2B1, [^{3}H]-estradiol 17β-D-glucuronide, [^{3}H]-para-aminohippurate ([^{3}H]-PAH) for OAT1, [^{3}H]-estrone-3-sulfate ([^{3}H]-ES) for OAT3 and [^{3}H] N-methyl-4-phenylpylidinium ([^{3}H]-MPP$^+$) for OCT1 and OCT2 with the substrate in a concentration range of 0.1-100 µM were normalized to the control and used to determine cell function.

[C] Reported K_m values represent previously published reference data from the references cited in parentheses

Supplementary figure 4

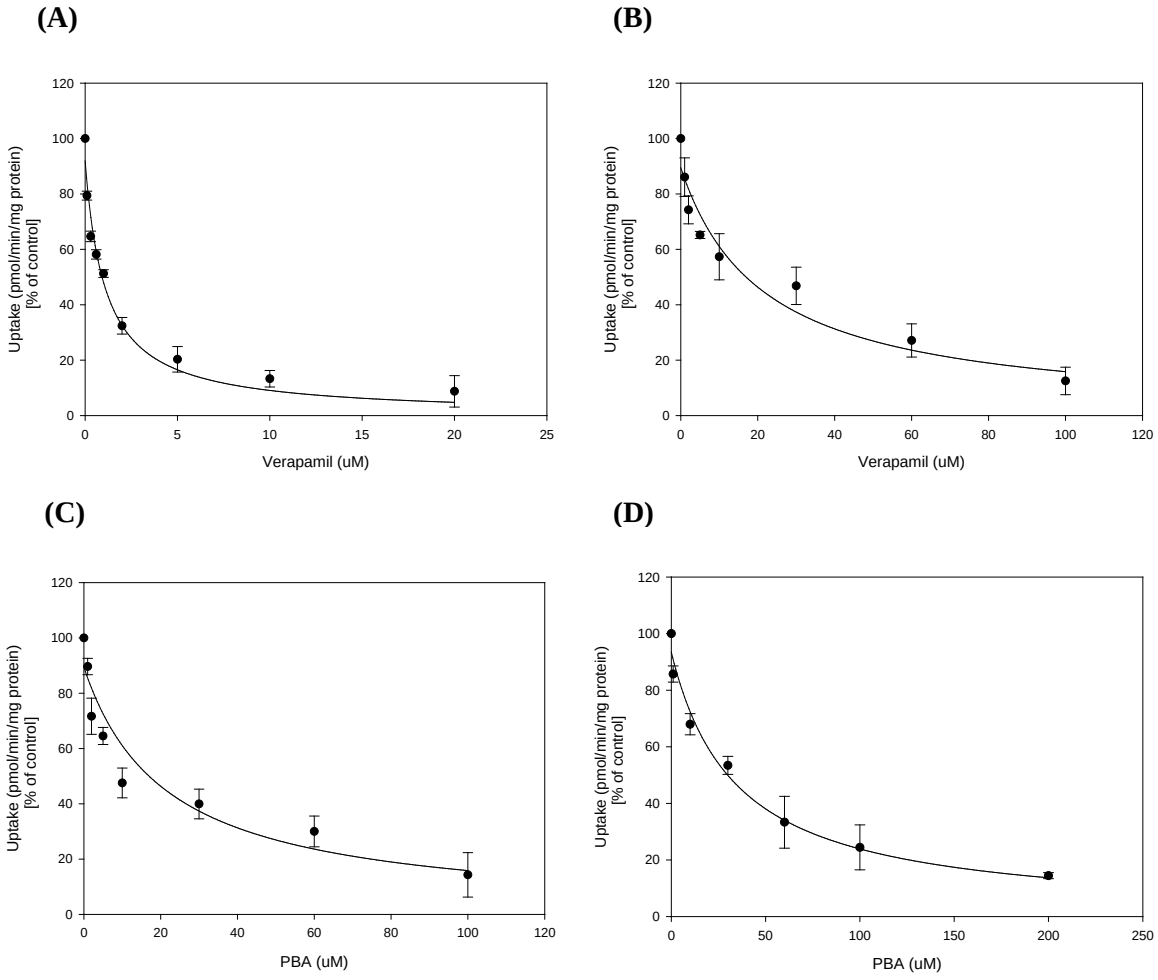

Figure S4. Concentration dependent inhibition of PAS Uptake in (A) hOCT1 overexpressed HEK293 cells by Verapamil (B) hOCT2 by Verapamil, (C) hOAT1 by Probenecid, (D) hOAT3 by Probenecid. All the data showed relative to control (no inhibitor) and mean ±SDs of triplicate of experiment.

Supplementary table 2. Kinetic parameters of inhibitors used for the calculation of R-values

$[I]_{u,inlet,max}$ (estimated maximum unbound inhibitor concentrations at the inlet to the liver) of anti-TB drugs, were calculated by the equation, as described under *Materials and Methods*, in which ka of 0.1 min-1, Fa×Fg of 1, and Qh of 1500mL/min were used. The blood to plasma concentration ratios of the inhibitors were assumed to be unity in the $[I]_{u,inlet,max}$ calculations.

Drugs	Dose	Fu	C_{max}	$C_{max,u}$
	mg		μM	μM
Probenecid	1000	0.15(13)	243.9(13)	36.6
Verapamil	180	0.1(14)	0.55(14)	0.055
Ibuprofen	800	0.01(15)*	266.1(15)	2.66
Indomethacin	75	0.01(16)*	4.05(16)	0.040
Diclofenac	50	0.004(17)	9.42(17)	0.045
Naproxen	250	0.01(18)*	270.1(18)	2.70
Omeprazole	20	0.03(19)	3.12(20)	0.10
Lansoprazole	30	0.03(21)	4.87(22)	0.150
Cimetidine	400	0.8(23)	9352(24)	7481
Metformin	500	1(25)	10.99(26)	10.99
Quinidine	325	0.5(27)	13.56(28)	6.78
Rifampin	600	0.15(29)	23.0(30)	3.45

*Asterisk indicates an arbitrary 1% free fraction was used according to the FDA draft guidance for drug interaction prediction to avoid false prediction.

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