Tables

Table 1 Demographic and biochemical data of the healthy subjects (n=12).

Variable	Median (25th percentile–75th percentile)
Age (years)	29.50 (22.00-41.00)
Weight (Kg)	61.75 (48.70-95.15)
Height (m)	1.66 (1.57-1.97)
BMI (Kg/m^2)	23.58 (19.76-29.20)
Gender (M/F)	4/8
Serum creatinine concentration (mg/dL)	0.84 (0.60-1.30)
Aspartate aminotransferase (U/L)	19.00 (14.00-35.00)
Total Bilirubin (mg/dL)	0.57 (0.43-2.54)
Direct Bilirubin (mg/dL)	0.19 (0.16-0.60)
Indirect Bilirubin (mg/dL)	0.37 (0.27-1.95)
Glucose (mg/dL)	83.50 (73.00-99.00)
Gamma GT (U/L)	19.00 (12.00-84.00)
TSH (U/mL)	1.17 (0.66-4.00)
Total cholesterol	153.50 (124.00-228.00)
HDL (mg/dL)	43.00 (36.00-98.00)
LDL (mg/dL)	97.00 (76.00-162.00)
Triglycerides (mg/dL)	74.00 (45.00-134.00)

M, male; F, female; BW, bodyweight; Gamma GT, gamma-glutamyl transferase; TSH, thyroid-stimulating hormone; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 2 Non-compartmental estimates of oxcarbazepine (OXC) and the 10-hydroxycarbazepine (MHD) enantiomers in plasma of healthy volunteers (n=12) after oxcarbazepine alone treatment (Occasion O) or OXC + verapamil treatment (Occasion O+V).

Parameter	OXC		R-(-)-MHD		S-(+)-MHD	
	Occasion O	**Occasion O+V**	**Occasion O**	**Occasion O+V**	**Occasion O**	**Occasion O+V**
C_{max} (µg/mL)	1.35 (0.45-2.95)	1.77 (1.17-3.20)	2.60 (1.13-3.93)	3.24* (1.52-4.36)	11.05 (6.80-12.03)	11.94* (8.52-15.35)
t_{max} (h)	1.00 (0.50-2.50)	0.75 (0.25-3.00)	3.50 (1.50-5.00)	2.75 (1.00-5.00)	3.50 (1.50-5.00)	2.75 (1.50-5.00)
AUC_{0-12} (µg.h/mL)	3.98 (1.25-5.78)	4.12 (2.43-6.09)	23.36 (10.07-34.35)	29.06* (13.24-35.52)	97.19 (62.73-121.22)	111.37* (78.75-138.61)
$C_{average}$ (µg/mL)	0.33 (0.10-0.48)	0.34 (0.20-0.51)	2.11 (0.84-2.86)	2.42* (1.10-2.96)	8.10 (5.23-10.10)	9.07* (6.56-11.55)
$t_{1/2}$ (h)	2.45 (1.27-3.20)	1.83 (1.18-3.34)	12.13 (7.10-17.67)	10.09 (6.31-24.62)	12.48 (5.21-19.47)	13.31 (6.01-22.91)
Kel (h^{-1})	0.28 (0.22-054)	0.38 (0.21-0.59)	0.06 (0.04-0.10)	0.07 (0.03-0.11)	0.06 (0.04-0.13)	0.06 (0.03-0.11)

Data are expressed as median (25th percentile–75th percentile). Wilcoxon matched pairs test, $p < 0.05$: * Occasion O *vs* Occasion O+V; C_{max}, maximum plasma concentration; t_{max}, time to reach C_{max}; AUC_{0-12}, area under the plasma concentration *versus* time curve; $C_{average}$, mean plasma concentration at steady state; $t_{½}$, elimination half-life; Kel, elimination rate constant.

Table 3 Population pharmacokinetic parameter estimates for oxcarbazepine (OXC) and the 10-hydroxycarbazepine (MHD) enantiomers.

Parameter		**Estimate (RSE)**	**Inter-individual variability, CV% (RSE)**
Oxcarbazepine			
Mean absorption transit time[a]	MTT (h)	0.514 (11.7)	17.1 (269.2)
Clearance	CLtotal/F (L h^{-1})	84.8 (7.4)	18.1 (150.8)
Inter-compartmental clearance	Q/F (L h^{-1})	55.8 (17.1)	-
Central distribution volume	Vc/F(L)	131 (11.5)	23.5 (117.6)
Peripheral distribution volume	Vp/F(L)	456 (21.9)	-
Relative bioavailability after verapamil	F1 (%)	1.12 (7.1)	30 (103.5)
Residual error Oxcarbazepine	$\sigma_{OXC,prop}$	0.097 (10.5)	
MHD[b]			
Clearance R-(-)-MHD and S-(+)-MHD	CL_{MHD}/F (L h^{-1})	2.01 (3.6)	-
Central distribution volume R-(-)-MHD	V_{RMHD}	23.60 (19.8)	22.2 (60.9)
Central distribution volume S-(+)-MHD	V_{SMHD}	31.70 (14.9)	22.2 (60.9)
Fraction metabolized to MHD	F_{MET}	0.79 (FIX)	-
Residual error R-(-)-MHD and S-(+)-MHD	$\sigma_{MHD,prop}$	0.017 (2.2)	

RSE, relative standard error (%); CV, coefficient of variation; CL/F, clearance (CL_{total}/F and CL_{MHD}/F) was allometrically scaled with the equation $\theta_i = \theta_i * (\frac{WT}{68})^{0.75}$ and exponents of 0.75; V/F, distribution volume (Vc/F, Vp/F, V_{RMHD}, V_{SMHD}) was allometrically scaled with the equation $\theta_i = \theta_i * (\frac{WT}{68})^{1}$ and exponents of 1; F_{MET}, fraction metabolized to MHD, which was fixed to a previously published value of 0.79 (Schütz et al., 1986). *Inter-occasion variability 44.7 CV% (RSE 43.4%).

[b]The oxcarbazepine and MHD models were fit sequentially, i.e. parameters for the MHD model were estimated after estimation of the parameters for oxcarbazepine alone.