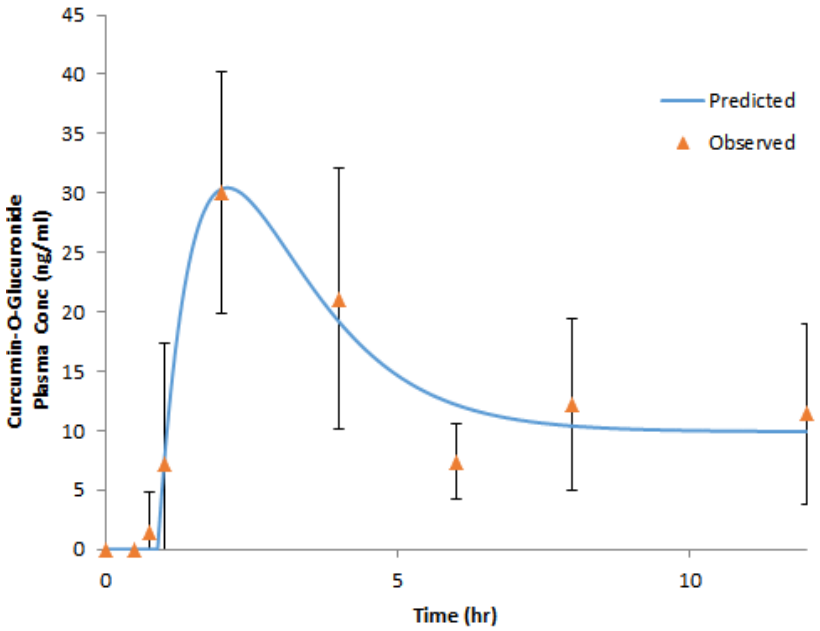
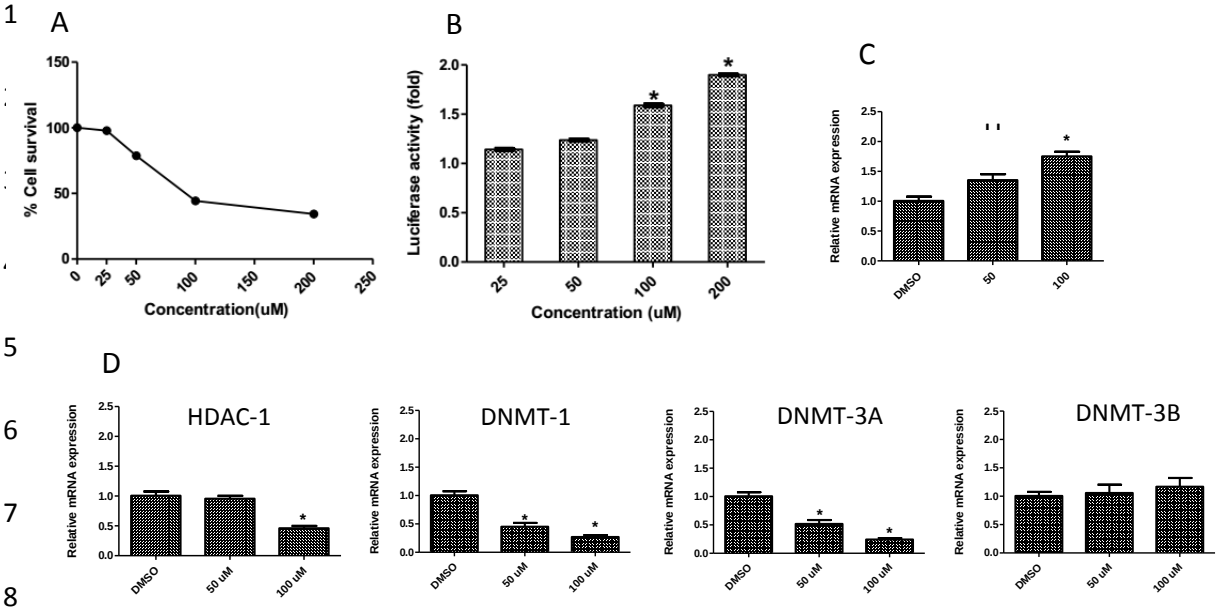


Supplementary Figure 1: Plasma concentration-time profile of curcumin-O-glucuronide. Concentration-time profile of curcumin-O-glucuronide (COG) as described by a two-compartment model. Experimental observation data are shown as the mean +/- SD and the solid line represents the Phoenix WinNonlin model predicted curves after a 4 g oral dose of curcumin to 12 healthy subjects.



Supplementary Figure 2. COG increases NRF2-ARE luciferase activity in HepG2C8 cells. (A) HepG2C8 cells were seeded in 96-well plates and treated with COG for 24 hours. Cytotoxicity of COG was measured by MTS assay (B) Induction of Nrf2-ARE luciferase by COG and results were normalized to protein concentration and DMSO control. (C) Induction of HO-1 mRNA expression compared to control after 24-hour incubation with COG. (D) Decrease in HDAC mRNA expression following treatment with COG. mRNA expression was normalized to GAPDH control. * $P < 0.05$ compared to DMSO control.

Supplementary Table

Supplementary Table 1. Pharmacokinetic (PK) parameters of curcumin-O-glucuronide in human plasma in 2 CM

PK Parameters	Description	**Estimation (CV%)**
kmixed (h^{-1})	First order Intestinal absorption, UGT metabolism and transport rate constant	9.6000(154076)
tlag (h)	Absorption delay	0.8900 (16.11)
Cmax (ng/ml)	Maximum concentration predicted	30.440 (10.20)
tmax (h)	Time to reach maximum concentration	2.0880 (41.5)
AUC0-12h (ng/ml*h)	Area under the curve 0 to 12h	379.87 (237.9)
AUC0-∞ (ng/ml*h)	Area under the curve 0 to infinity	14576 (36900)