Supplemental Tables and Figures

A long-standing mystery solved: The formation of 3-hydroxydesloratadine is catalyzed by CYP2C8 but prior glucuronidation of desloratadine by UGT2B10 is an obligatory requirement

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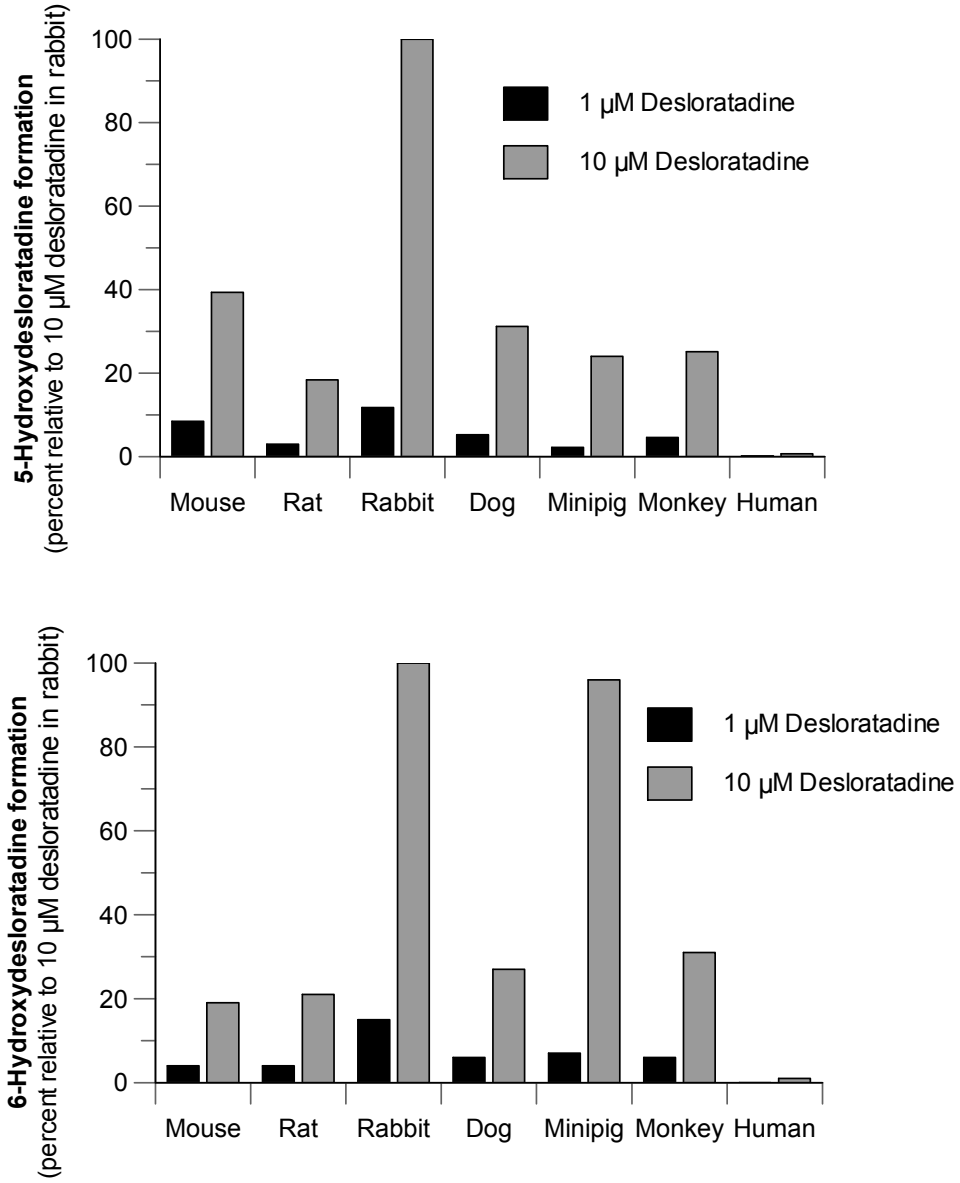
Drug Metabolism and Disposition

Supplemental Table 1: **Individual human donor information for CYP2C8 correlation analysis.**

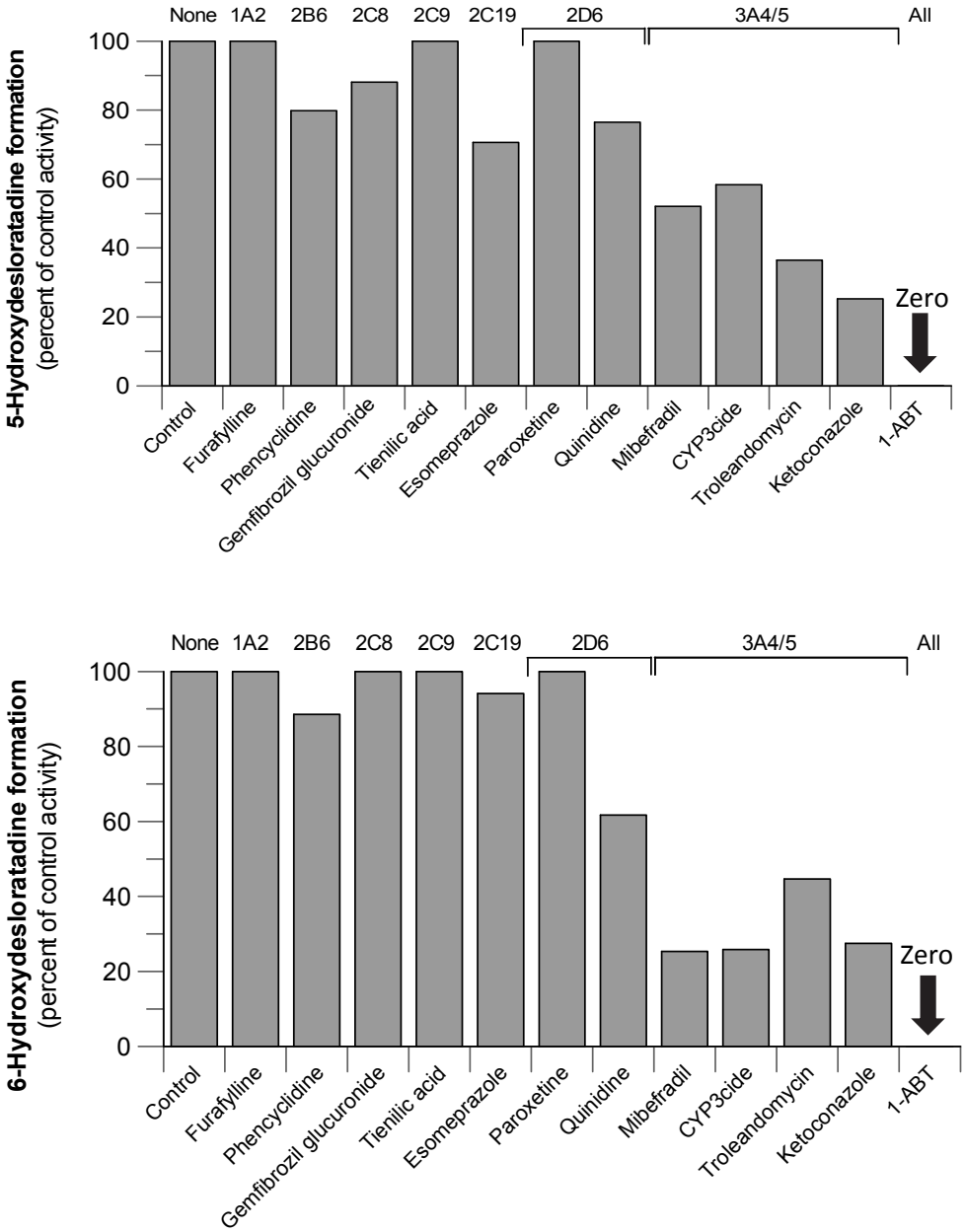
Xenotech Liver Number	Gender	Age (years)	Ethnicity
H924	M	40	Caucasian
H954	M	55	Caucasian
H1008	M	36	Hispanic
H1039	M	61	African American
H1042	M	51	Caucasian
H1059	F	21	Caucasian
H1086	M	63	Caucasian
H1135	F	54	African American
H1141	F	20	Asian

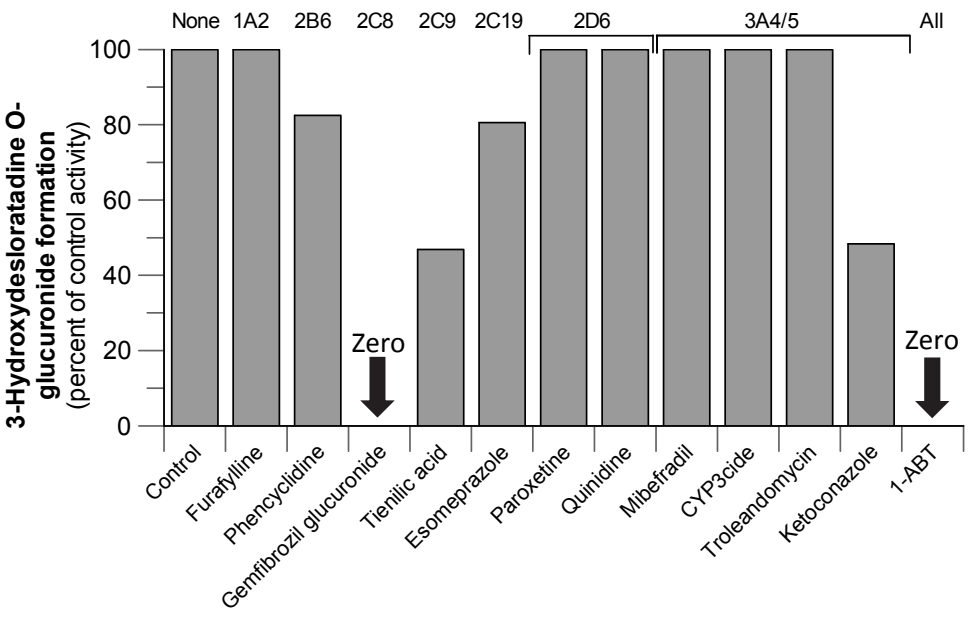
Supplemental Figure 1: **Formation of 5- and 6-hydroxydesloratadine in hepatocytes from mouse, rat, rabbit, dog, minipig, monkey and human.**



Pooled hepatocytes from mouse, rat, rabbit, dog, minipig, monkey and human were incubated at 1 million cells/mL with 1 or 10 µM desloratadine for 2 h. Analysis of 5- and 6-hydroxydesloratadine was conducted as described in *Materials and Methods*.

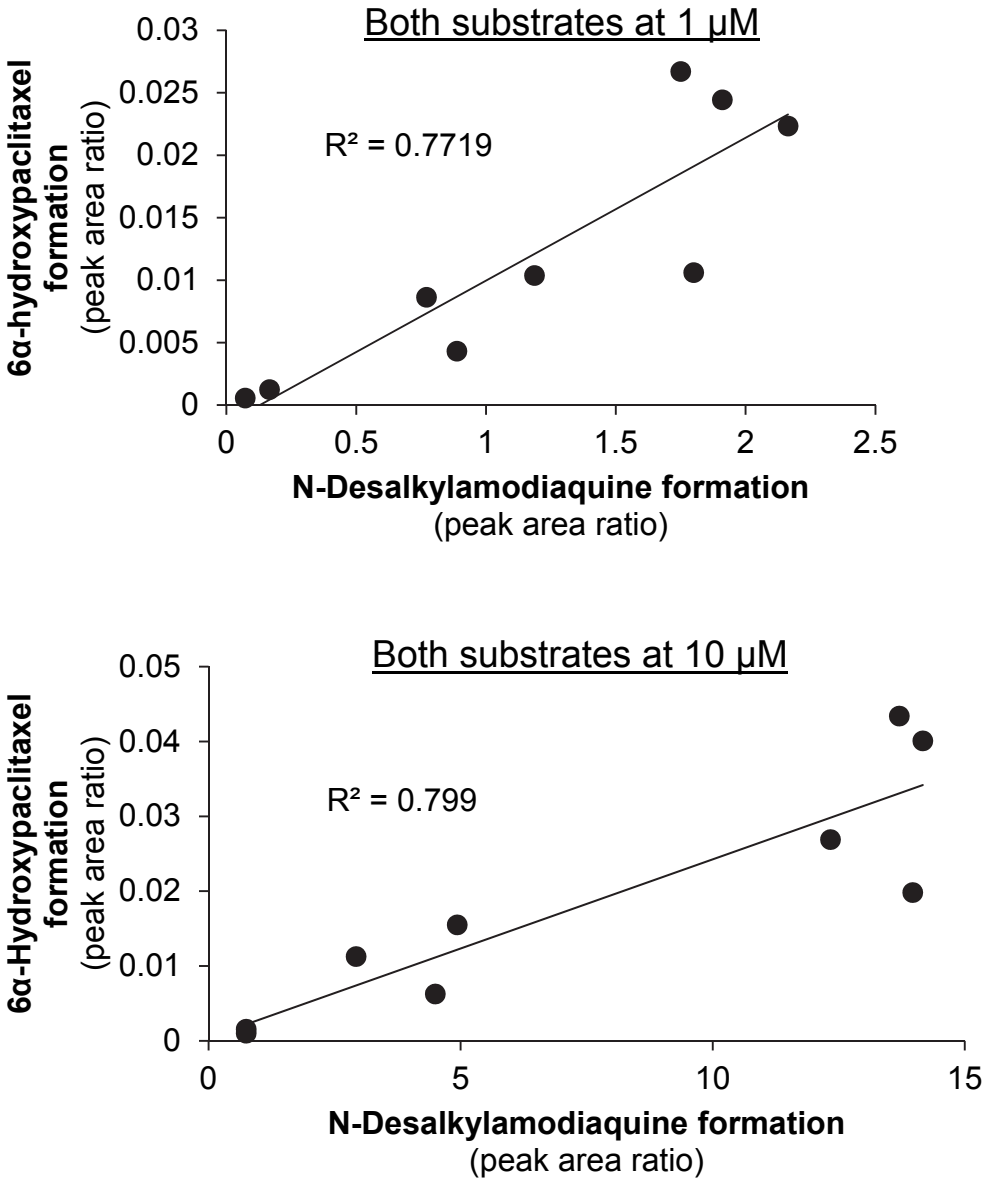
Supplemental Figure 2: **The effect of various P450 chemical inhibitors on 5-hydroxydesloratadine, 6-hydroxydesloratadine and 3-hydroxydesloratadine *O*-glucuronide formation in cryopreserved human hepatocytes (CHHs).**





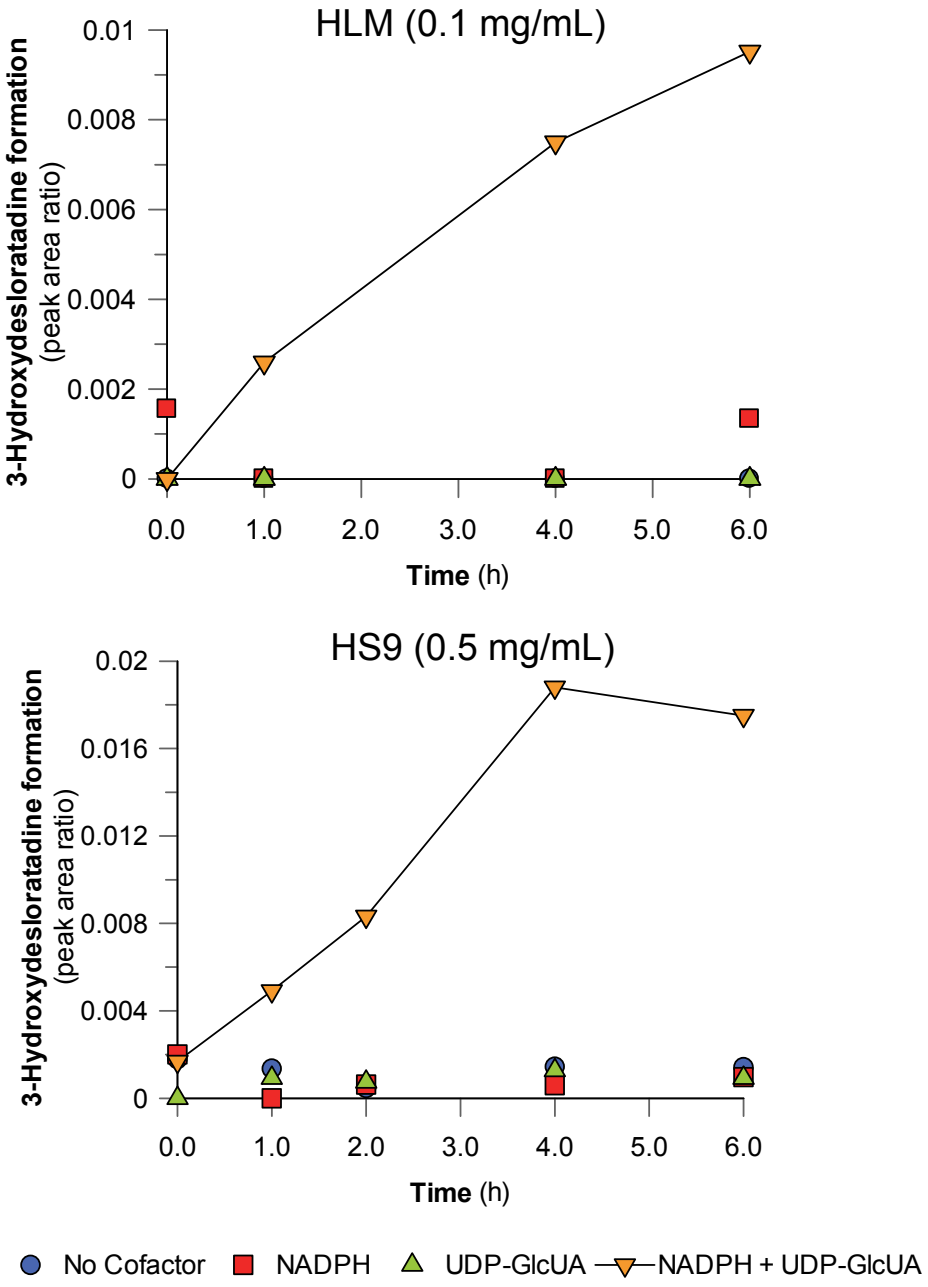
Various P450 chemical inhibitors were incubated with CHHs (1 million cells/mL) for 30 min prior to the addition of 10 μM desloratadine followed by incubation for 2 h and analysis of 5-, 6-hydroxydesloratadine, and 3-hydroxydesloratadine O-glucuronide was conducted as described in *Materials and Methods*.

Supplemental Figure 3: **Correlation of N-desalkylamodiaquine formation with 6α-hydroxypaclitaxel formation in a panel of individual donor cryopreserved human hepatocytes (CHHs).**



Individual donor CHHs were assessed for CYP2C8 activity with 1 and 10 µM paclitaxel and amodiaquine as described in *Materials and Methods*.

Supplemental Figure 4: **Time course of 3-hydroxydesloratadine formation in HLM (0.1 mg/mL) and HS9 (1 mg/mL) with or without NADPH and/or UDP-GlcUA.**



HLM (0.1 mg/mL) and HS9 (0.5 mg/mL) were incubated with 10 μM in a time course up to 6 h with and without the addition of NADPH and/or UDP-GlcUA, as described in *Materials and Methods*.