

Figure S1. ¹H-NMR spectrum of NAC conjugate.

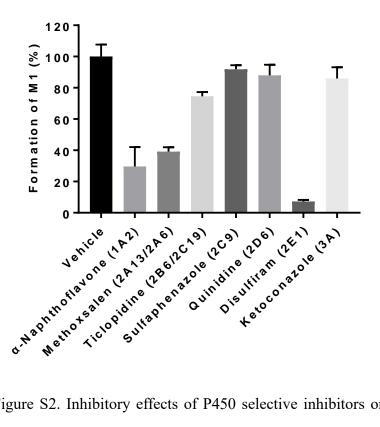


Figure S2. Inhibitory effects of P450 selective inhibitors on the formation of M1 in HLMs. Formation of M1 in 2-MN-fortified human liver microsomal incubations in the presence of individual P450 inhibitors was measured by LC-MS/MS. The most abundant M1 detected was normalized to 100%.

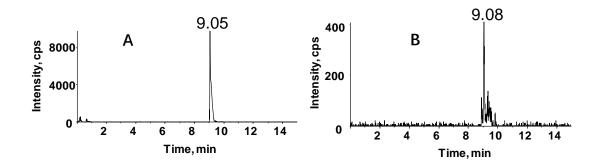


Figure S3. LC-MS/MS analysis of mouse liver microsomal incubations containing 2-MN and GSH in the presence (A) or absence (B) of NADPH.

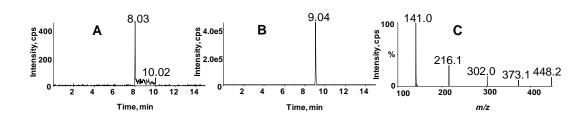


Figure S4. Characterization of 2-NM-derived GSH conjugates. Extracted ions (*m/z* 448/302.2) chromatograms obtained from LC-MS/MS analysis of lysates of cultured primary hepatocytes after exposure to vehicle (A) or 2-NM (B); (C) MS/MS spectrum of 2-NM-derived GSH conjugate produced in (B).

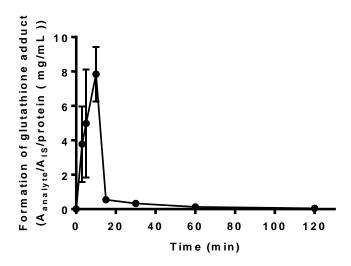


Figure S5. Time-course changes in the formation of 2-NM-derived GSH conjugate in mice given 2-NM. Mice were administered 2-NM at 200 mg/kg, and levels of serum GSH conjugate were determined at designed time points after administration.