Supplemental Information

Drug Metabolism and Disposition

DMD-AR-2023-001257

Mechanistic Investigation of the Time-Dependent Aldehyde Oxidase Inhibitor Hydralazine

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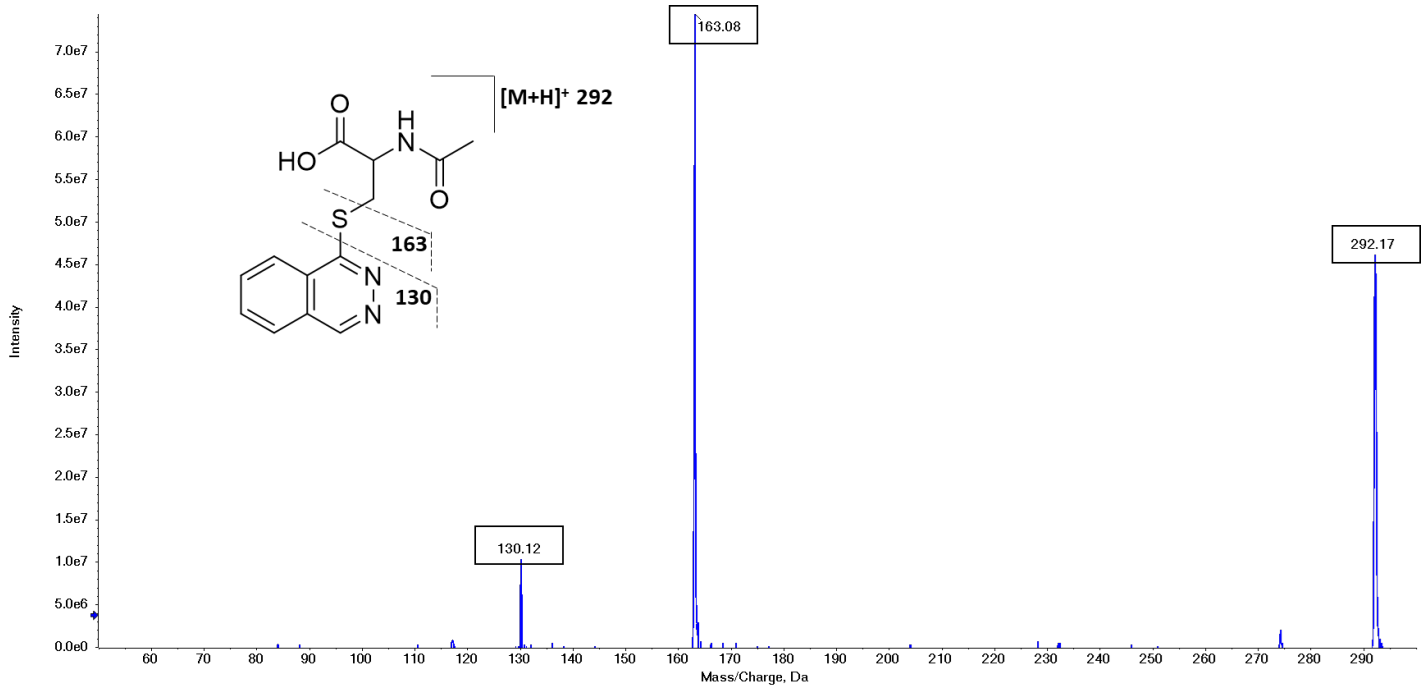
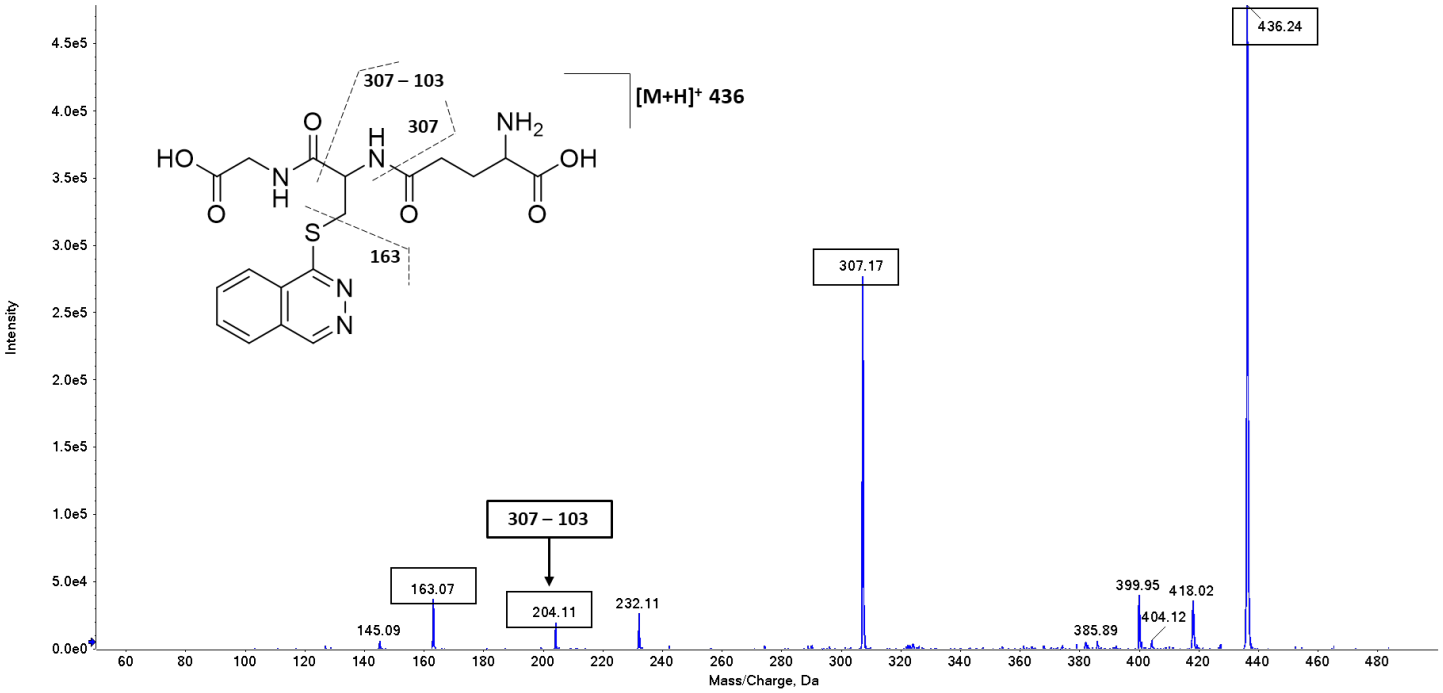
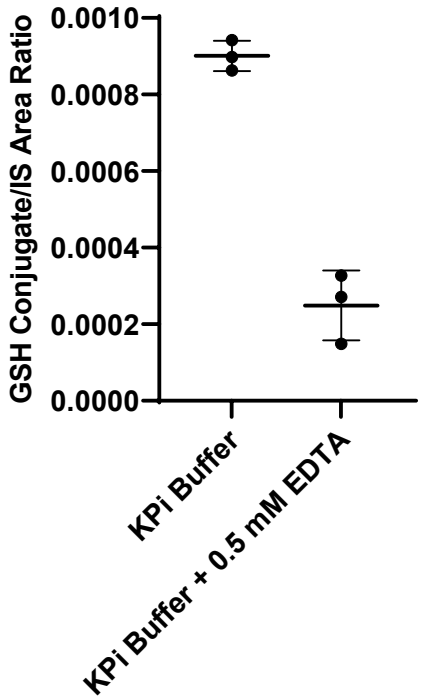


Supplemental Figure 1. MS/MS spectrum and proposed structure of the 1-phthalazyl-N-acetylcysteine conjugate detected in extracts from co-incubation of hydralazine and N-acetylcysteine in potassium phosphate buffer containing human liver cytosol.



Supplemental Figure 2. MS/MS spectrum and proposed structure of the 1-phthalazyl-glutathione conjugate detected in extracts from co-incubation of hydralazine and GSH in potassium phosphate buffer containing human liver cytosol.



Supplemental Figure 3. Formation of the 1-phthalazyl-GSH conjugate in potassium phosphate buffer in the presence and absence of EDTA. Hydralazine (50 μM) was incubated at 37^{O}C for 60 minutes in potassium phosphate buffer (100 mM, pH 7.4) with or without 0.5 mM EDTA. Relative metabolite levels were determined based on the peak area ratio of analyte to internal standard. Data points represent individual replicates from a single experiment performed in triplicate. The bars represent the means ± SD.