

SUPPORTING INFORMATION

Consideration of nevirapine analogs to reduce metabolically linked hepatotoxicity: a cautionary tale of the deuteration approach

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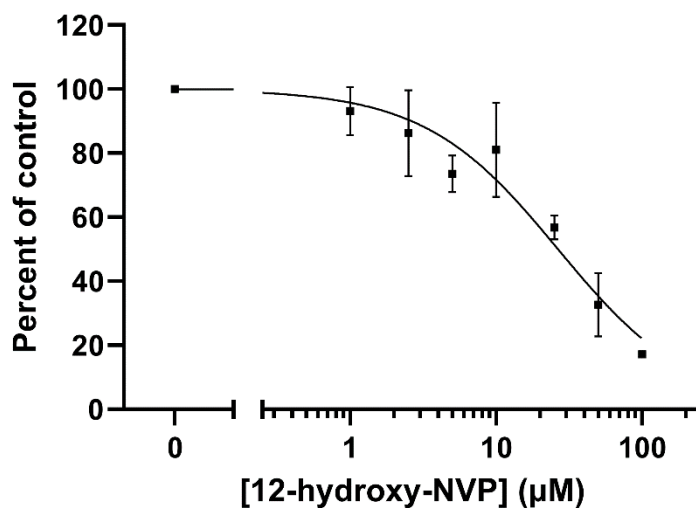


Figure S1. Dose-response curve of 12-hydroxy-NVP against HIV reverse transcriptase. HIV-RT inhibition by 12OH-NVP was characterized by an IC_{50} value \pm standard error of $26.5 \pm 3.3 \mu\text{M}$ ($R^2 = 0.899$). Each data point represents the average of triplicate measurements, with error bars representing standard deviations.

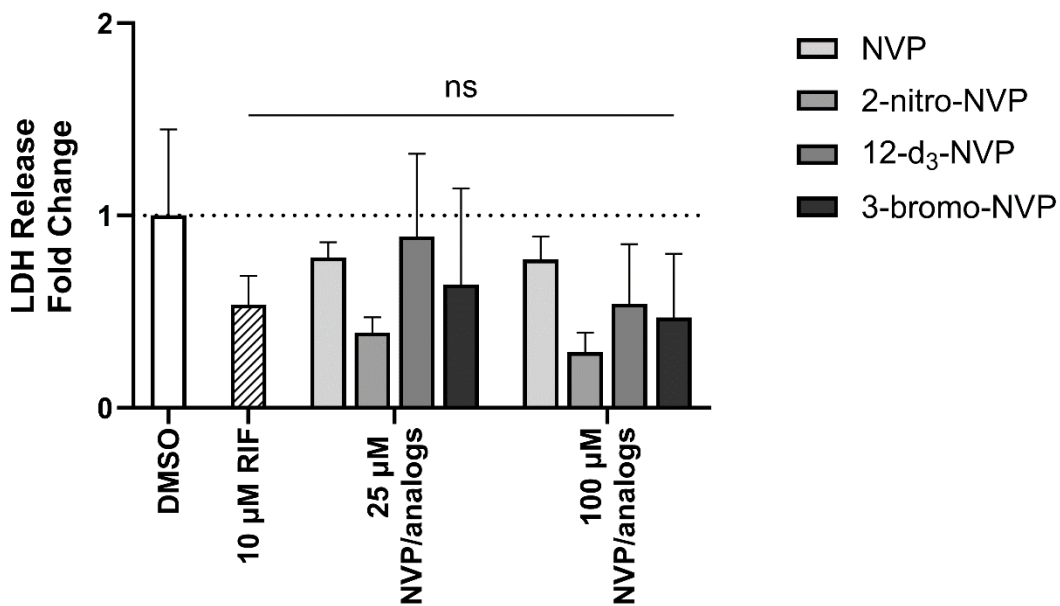


Figure S2. Hepatocyte LDH cytotoxicity. Normalized LDH release at 72 h for primary hepatocytes treated with 25 and 100 μM NVP, 12-d₃-NVP, 2-nitro-NVP, 3-bromo-NVP, and controls 10 μM RIF (rifampicin) and DMSO. The LDH release fold changes were calculated compared to the DMSO control. Bars represent the means of at least three biological replicates ± standard deviation. Data were analyzed by one-way ANOVA against the DMSO control and no statistically significant (ns) differences were observed.

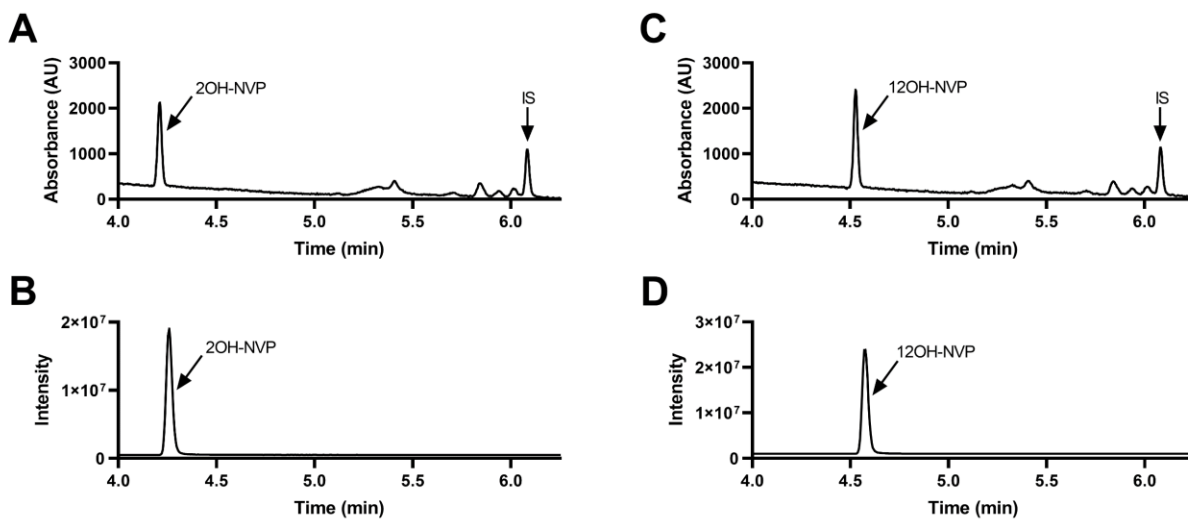


Figure S3. NVP hydroxy metabolite standards. Representative UV (A, C) and MRM (B, D) chromatograms for the 2OH-NVP (A, B) and 12OH-NVP (C, D) standards prepared at 1 μ M in matrix. For the extracted MRM chromatograms, the mass transitions were 283>161 and 283>223 for 2OH-NVP (B) and 12OH-NVP (D), respectively.

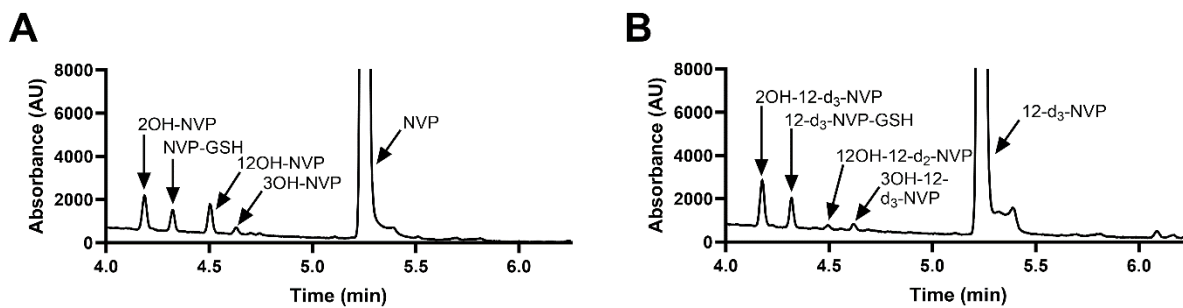


Figure S4. NVP and 12-d₃-NVP metabolism in HLMs. Representative UV chromatograms (280 nm) for NVP (A) and 12-d₃-NVP (B) incubated at 100 μ M for 60 min with adult pooled HLMs (1 mg/mL) in presence of the co-factor NADPH.