# Supplementary Materials: Mitochondrial Liver Toxicity of Valproic Acid and Its Acid Derivatives is Related to Inhibition of $\alpha$-Lipoamide Dehydrogenase

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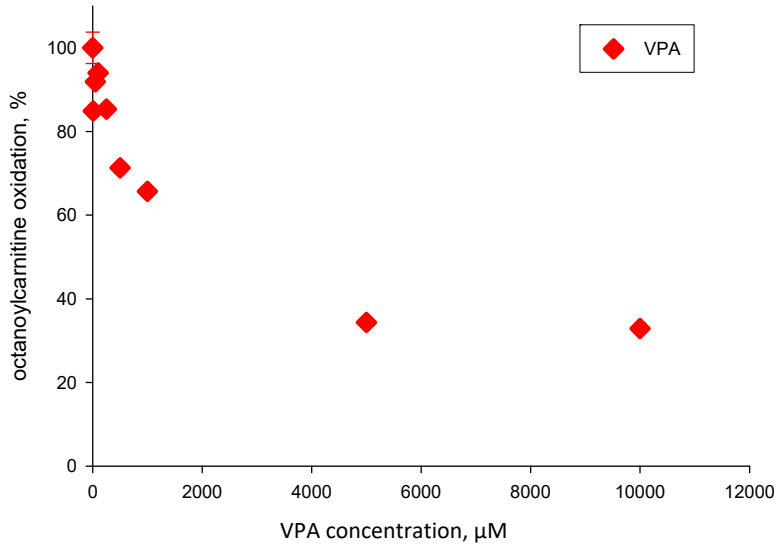
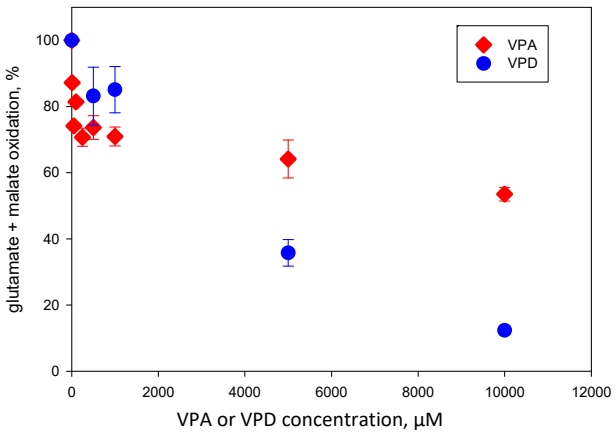
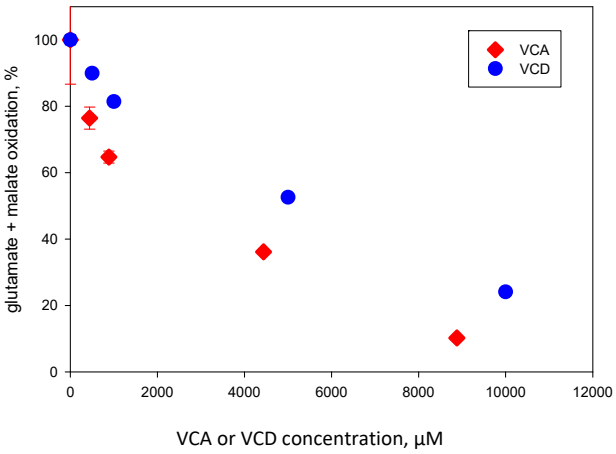


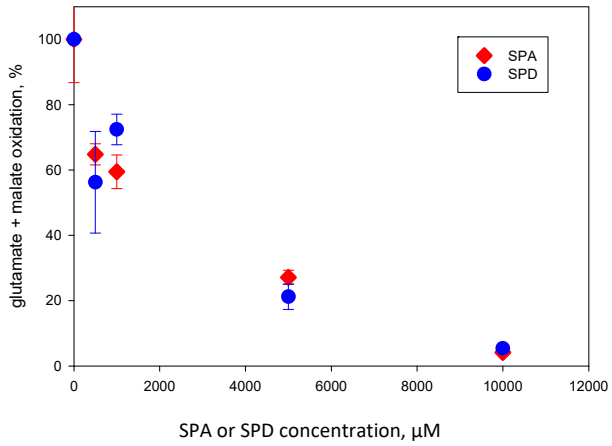

**Figure S1.** Inhibition of ADP-stimulated octanoylcarnitine (+malate) oxidation rate of rat liver mitochondria by valproic acid (VPA). Mitochondria (0.2 mg/mL protein/mL) were preincubated for 3 min in presence of 1 mM ATP, 5 mM $MgCl_2$ with the indicated amount of VPA. The maximal rate of respiration was determined in presence of 1 mM octanoylcarnitine, 5 mM malate, and 1 mM ADP.




(**a**)

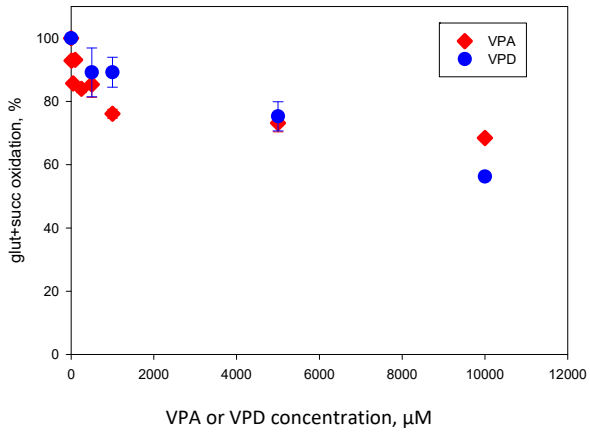



(**b**)

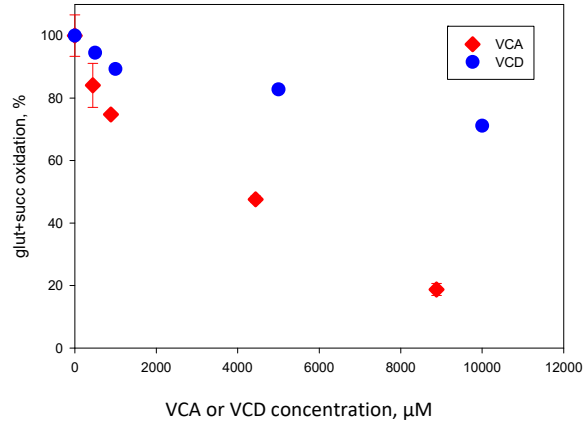



(**c**)

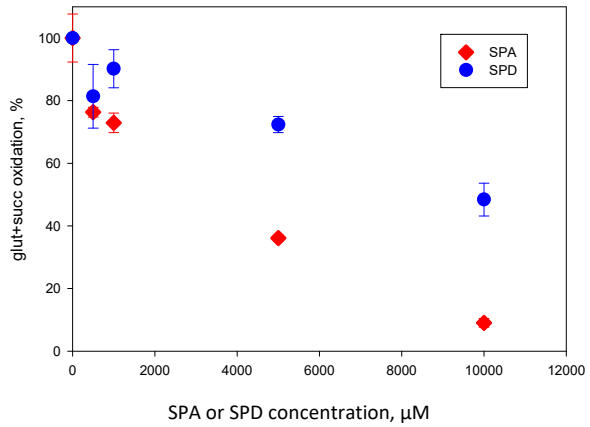
**Figure S2.** Inhibition of ADP-stimulated glutamate + malate oxidation rate of rat liver mitochondria by VPA, valpromide (VPD) (**A**), valnoctic acid (VCA), valnoctamide (VCD) (**B**) and *sec*-butylpropylacetic acid (SPA), *sec*-butylpropylacetamide (SPD) (**C**). Mitochondria (0.2 mg/mL protein/mL) were preincubated for 3 min in presence of 1 mM ATP, 5 mM $MgCl_2$ with the indicated amount of the drugs. The maximal rate of respiration was determined in presence of 10 mM glutamate, 5 mM malate, and 1 mM ADP. The plotted rates are averages of three independent experiments.




(**a**)




(**b**)




(**c**)

**Figure S3:** Inhibition of ADP-stimulated glutamate + succinate oxidation rate of rat liver mitochondria by VPA, VPD (**A**); VCA, VCD (**B**) and SPA, SPD (**C**). Mitochondria (0.2 mg/mL protein/mL) were preincubated for 3 min in presence of 1 mM ATP, 5 mM $MgCl_2$ with the indicated amount of the drugs. The maximal rate of respiration was determined in presence of 10 mM succinate, 10 mM glutamate, 5 mM malate, and 1 mM ADP. The plotted rates are averages of three independent experiments.

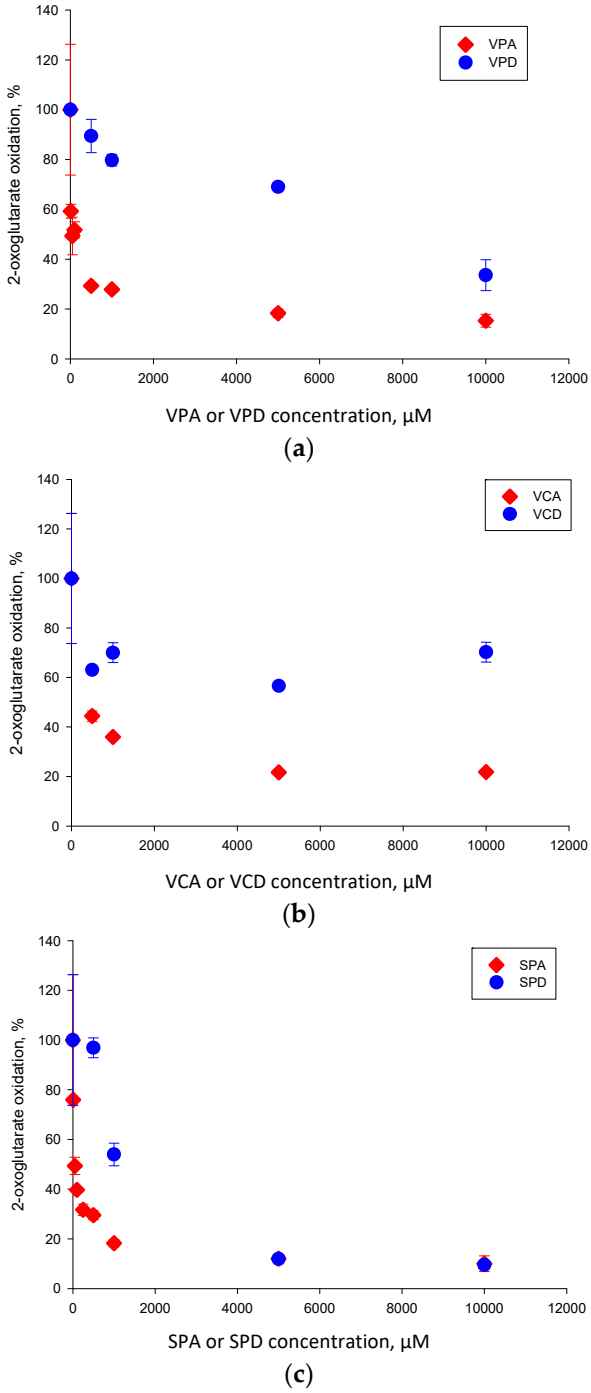



**Figure S4.** Inhibition of ADP-stimulated 2-oxoglutarate oxidation rate of rat liver mitochondria by VPA, VPD (**A**), VCA, VCD (**B**) and and SPA, SPD (**C**). Mitochondria (0.2 mg/mL protein/mL) were preincubated for 3 min in presence of 1 mM ATP, 5 mM $MgCl_2$ with the indicated amount of the drugs. The maximal rate of respiration was determined in presence of 10 mM 2-oxoglutarate and 1 mM ADP. The plotted rates are averages of 3 independent experiments.