Bioactivation of GPR40 Agonist MK-8666: Formation of Protein Adducts in Vitro from Reactive Acyl Glucuronide and Acyl CoA Thioester

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Table S1. MS Characterization of MK-8666 and its major metabolites.

Metabolite	observed mass (m/z)	formula	calculated mass (m/z)	Δppm	MSMS
MK-8666	522.1970	$C_{29}H_{32}NO_6S^+$	522.1945	4.8	522, 331, 121
M1	538.1903	$C_9H_{32}NO_7S^+$	538.1899	0.7	538, 502, 347, 329, 192, 121
M2	538.1921	$C_9H_{32}NO_7S^+$	538.1899	4.1	538, 520, 331, 121
M3	538.1913	$C_9H_{32}NO_7S^+$	538.1899	2.6	538, 520, 331, 121
M4	698.2275	$C_{35}H_{40}NO_{12}S^+$	698.2271	0.6	698, 522, 331, 121
M5	629.1981	$C_{35}H_{40}NO_{12}S^+$	629.1991	-1.6	629, 504, 331, 121

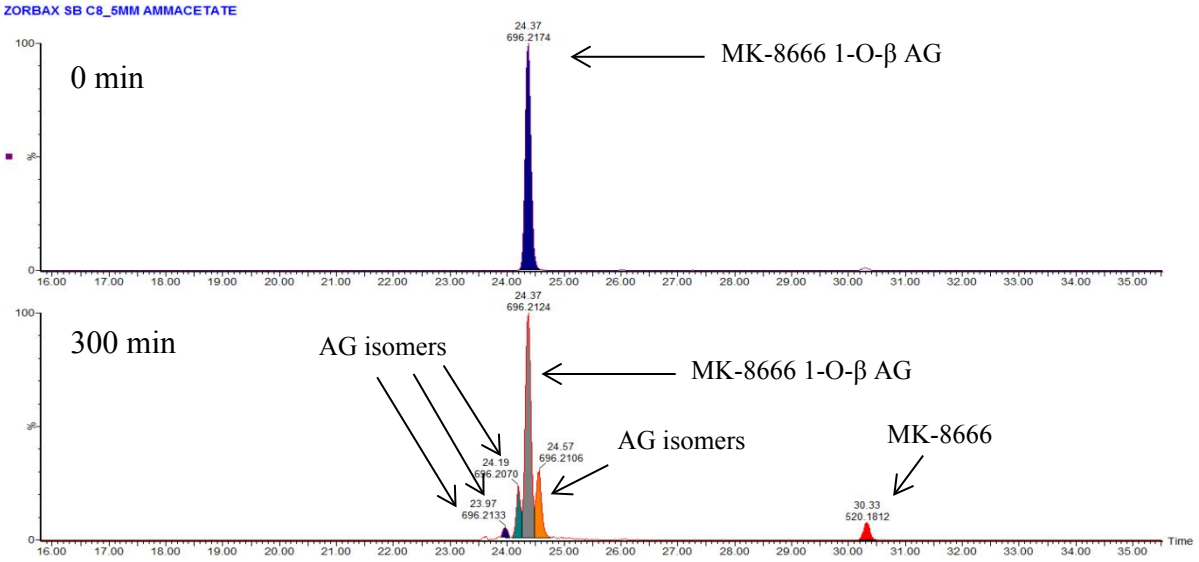

Figure S1. Representative extracted ion chromatograms of MK-8666-1-O-β-acyl glucuronide and its rearranged isomers following incubation of MK-8666-1-O-β-acyl glucuronide (10 µM) in 0.1 M phosphate buffer (pH 7.4) at 0 & 300 min. The detection of mutiple peaks at m/z 696.2120 confirmed that MK-8666-1-O-β-acyl glucuronide formed rearranged isomers.

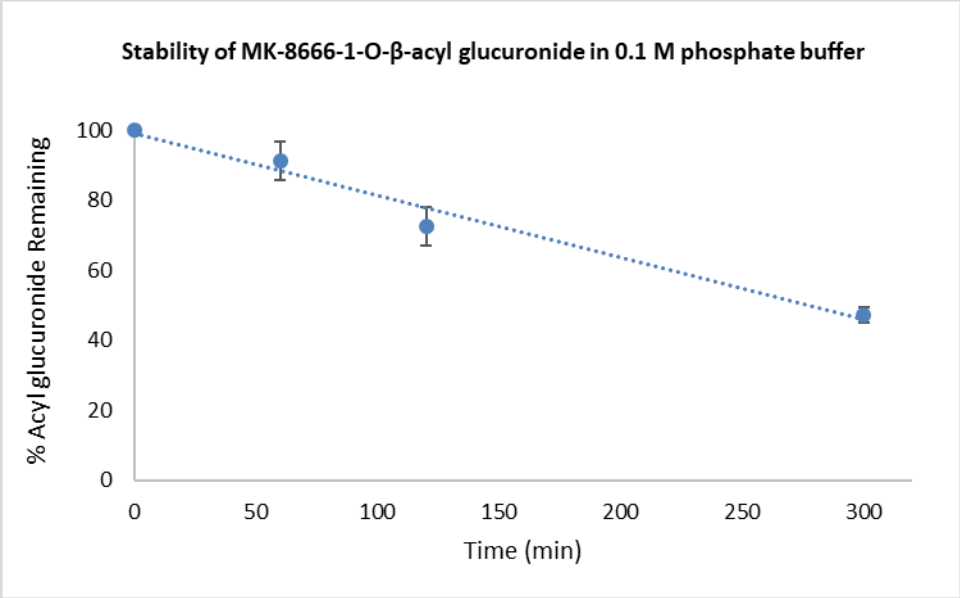

Figure S2. Percentage of MK-8666-1-O-β-acyl glucuronide remaining with the time course following incubation with 0.1 M phosphate buffer (pH 7.4) at 37°C. The degradation half-life of MK-8666-1-O-β-acyl glucuronide was determined from the percentage of AG remaining versus time curve by linear regression of the semilogarithmic plot. The half-life was calculated by the equation ln2/k, where k is the degradation rate constant.