

Longo et al, Pharmacologic inhibition of ghrelin receptor signaling is insulin sparing and promotes insulin sensitivity. JPET

Supplemental Table 1: Intrinsic and functional properties of five ghrelin receptor antagonists. See text for details on analysis of K_i values. %F was calculated using area under the curve (AUC) values for plasma concentrations of compounds following their iv and oral administration. Analyses were performed by plasma extraction and compound-specific liquid chromatography/mass spectrometry assays.

Compound	MW (Da)	Functional K_i (μ M)	Binding K_i (μ M)	%F
A	474	0.013	0.038	16
B	486	0.015	0.015	63
C	500	0.020	0.025	34
D	550	0.016	0.052	11
E	568	0.051	0.076	5

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Supplemental Table 2: Blood biochemistry parameters evaluated in HFD-fed C57BL/6 mice dosed for 56 days (60mg/Kg, bid, po). The results are suggestive of no overt systemic toxicities.

	56 Days				
	Vehicle		Compound B		<i>p</i> value
	Mean	±Std Dev	Mean	±Std Dev	T-Test
Sodium (MEQ/L)	154.3	1.0	152.3	2.2	ns
Chloride (MEQ/L)	108.1	3.1	107.7	4.4	ns
Phosphorus (mg/dL)	8.5	1.4	7.8	0.8	ns
Bicarbonate (MEQ/L)	24.3	1.9	23.5	2.8	ns
CPK (U/L)	292.1	267.4	203.3	80.8	ns
LDH (U/L)	1495.4	434.7	396.5	76.5	<i>p</i> < 0.0001
AST (U/L)	395.3	83.8	159.7	24.1	<i>p</i> < 0.0001
ALT (U/L)	416.7	74.8	110.7	37.4	<i>p</i> < 0.0001
Amylase (U/L)	2203.9	183.3	1940.60	263.20	ns
Bilirubin, Total (mg/dL)	0.2	0.1	0.4	0.3	ns
Bilirubin, Direct (mg/dL)	0.01	0.04	0.00	0.00	ns
BUN (mg/dL)	24.4	1.7	15.7	2.7	<i>p</i> < 0.0001
Creatinine (mg/dL)	0.4	0.0	0.4	0.1	ns
Uric Acid (mg/dL)	1.7	0.9	2.0	0.7	ns
Albumin (g/dL)	3.6	0.1	3.5	0.1	<i>p</i> = 0.0289
Protein, Total	6.5	0.2	6.4	0.3	ns
Globulin	2.8	0.2	3.0	0.2	ns
SDH	27.9	3.2	20.8	3.1	<i>p</i> = 0.0021

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Main effects	Comparison	n	Median survival (days)	Chi square	<i>p</i> value
Gender	Male	65	747	11.94	0.0005
	Female	78	668		
Diet	LFD	76	755	23.64	<0.0001
	HFD	67	612		
Genotype	WT	68	705	0.43	0.511
	KO	75	719		
Within Diet*Gender groups					
LFD*male	WT	18	821	0.39	0.531
	KO	18	777		
LFD*female	WT	17	732	0.27	0.602
	KO	23	725		
HFD*male	WT	12	652	2.25	0.133
	KO	17	700		
HFD*female	WT	21	560	2.14	0.144
	KO	17	649		

Supplemental Table 3. Statistical analysis of survival for the main effects, and genotype effects with Diet*Gender groups. Fractions of surviving animals were calculated using the Kaplan-Meier method, and significance was evaluated using the chi-square test. Censored animals were not included in the analysis.