

Supplemental Material for

Role of Efficacy as a Determinant of Locomotor Activation

by Mu Opioid Receptor (MOR) Ligands in Female and Male Mice. II.

Effects of Novel MOR-Selective Phenylmorphans with High to Low MOR Efficacy

Edna J. Santos^{*a}, Nima Nassehi^{*a}, Eric W. Bow^b, Dana R. Chambers^b, Eugene S. Gutman^b, Arthur E. Jacobson^b, Joshua A. Lutz^b, Samuel A. Marsh^a, Kenner C. Rice^b, Agnieszka Sulima^b, Dana E. Selley^a, and S. Stevens Negus^a.

*Co-First Authors

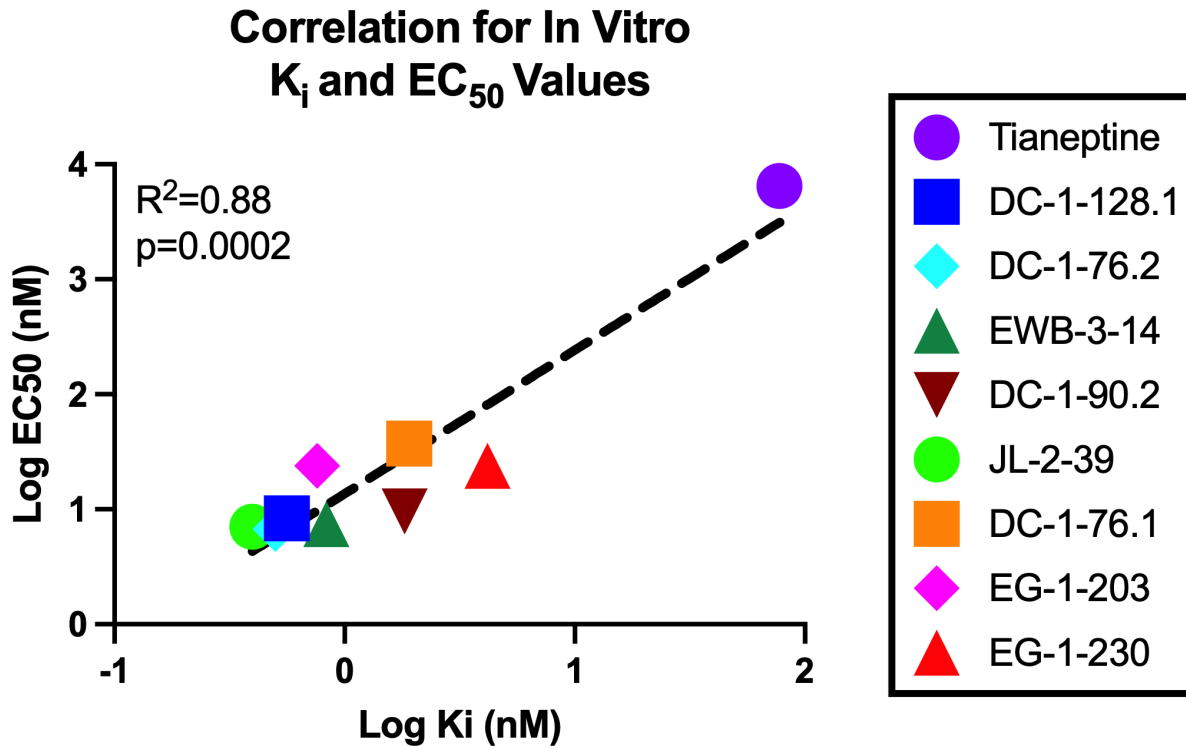
^aDepartment of Pharmacology & Toxicology, Virginia Commonwealth University, Richmond, VA

^bDrug Design and Synthesis Section, Molecular Targets and Medications Discovery Branch, NIDA and NIAAA, Bethesda, MD

Supplemental Table 1: Two-way ANOVA results and post hoc power analyses to assess the role of sex as a determinant of opioid-induced locomotor activation in female and male ICR mice.

Treatment	Dependent measure	Partial eta ²	F statistic, p value	Cohen's Effect Size (Cohen's F)	Current Power	Sample Size: Power≥0.8
Methadone	Dose Main Effect	0.795	F (2.82, 28.20) = 38.74; P<0.0001	1.968	1	3
	Sex Main Effect	0.015	F (1, 10) = 0.42; P=0.5335	0.125	0.123	>100
	Dose x Sex Interaction	0.089	F (4, 40) = 0.98; P=0.4286	0.313	0.739	14
Tianeptine	Dose Main Effect	0.888	F (1.89, 18.85) = 79.10; P<0.0001	2.813	1	3
	Sex Main Effect	0.00007	F (1, 10) = 0.001; P=0.9745	0.009	0.050	>100
	Dose x Sex Interaction	0.003	F (3, 30) = 0.03; P=0.9924	0.056	0.066	>100
DC-01-128.1	Dose Main Effect	0.766	F (2.58, 25.83) = 32.75; P<0.0001	1.809	1	3
	Sex Main Effect	0.061	F (1, 10) = 1.45; P=0.2560	0.254	0.357	34
	Dose x Sex Interaction	0.133	F (4, 40) = 1.54; P=0.2090	0.392	0.919	10
DC-01-76.2	Dose Main Effect	0.683	F (1.90, 19.04) = 21.55; P<0.0001	1.468	1	4
	Sex Main Effect	0.0003	F (1, 10) = 0.001; P=0.9743	0.018	0.052	>100
	Dose x Sex Interaction	0.173	F (4, 40) = 2.09; P=0.0992	0.458	0.979	8
EWB-3-14	Dose Main Effect	0.678	F (2.74, 27.36) = 21.08; P<0.0001	1.452	1	4
	Sex Main Effect	0.004	F (1, 10) = 0.05; P=0.8227	0.059	0.066	>100
	Dose x Sex Interaction	0.0357	F (6, 60) = 0.37; P=0.8952	0.192	0.377	28
JL-02-0039	Dose Main Effect	0.796	F (2.11, 21.07) = 38.95; P<0.0001	1.97	1	3
	Sex Main Effect	0.010	F (1, 10) = 0.05; P=0.8336	0.103	0.099	>100
	Dose x Sex Interaction	0.054	F (4, 40) = 0.57; P=0.6885	0.238	0.474	23
DC-01-0076.1	Dose Main Effect	0.448	F (2.33, 23.28) = 8.11; P=0.0014	0.900	0.999	5
	Sex Main Effect	0.217	F (1, 10) = 2.93; P=0.1179	0.527	0.907	10
	Dose x Sex Interaction	0.132	F (5, 50) = 1.52; P=0.1991	0.390	0.949	9
EG-1-203	Dose Main Effect	0.390	F (1.75, 17.54) = 6.39; P=0.0101	0.800	0.999	6
	Sex Main Effect	0.456	F (1, 10) = 2.30; P=0.1601	0.915	0.999	6
	Dose x Sex Interaction	0.274	F (3, 30) = 3.77; P=0.0208	0.614	0.999	6
EG-1-230	Dose Main Effect	0.031	F (2.43, 21.90) = 0.29; P=0.7949	0.178	0.204	53
	Sex Main Effect	0.012	F (1, 9) = 0.30; P=0.5953	0.108	0.099	>100
	Dose x Sex Interaction	0.012	F (3, 27) = 0.11; P=0.9553	0.109	0.109	>100

Supplemental Figure 1. Relationship between in vitro MOR drug affinities (Log K_i values in nM) determined in receptor binding assays and in vitro MOR-mediated drug potencies (Log EC_{50} values in nM) determined in an assay of ligand-stimulated [35 S]GTP γ S binding. The correlation was statistically significant ($R^2=0.88$, $p=0.0002$).



Supplemental Figure 2. Raw data from studies of locomotor activity in mice. The left panel shows the higher MOR efficacy drugs tested in this study, and the left panel shows effects of the lower MOR efficacy drugs. Abscissae: Drug dose in mg/kg (log scale). Veh=vehicle. Ordinates: total number of locomotor counts (photobeam breaks) during a 60-min test session. Each point shows mean \pm SEM from 12 mice (6 female, 6 male) except EG-1-230, which shows data from 11 mice (6 female, 5 male).

