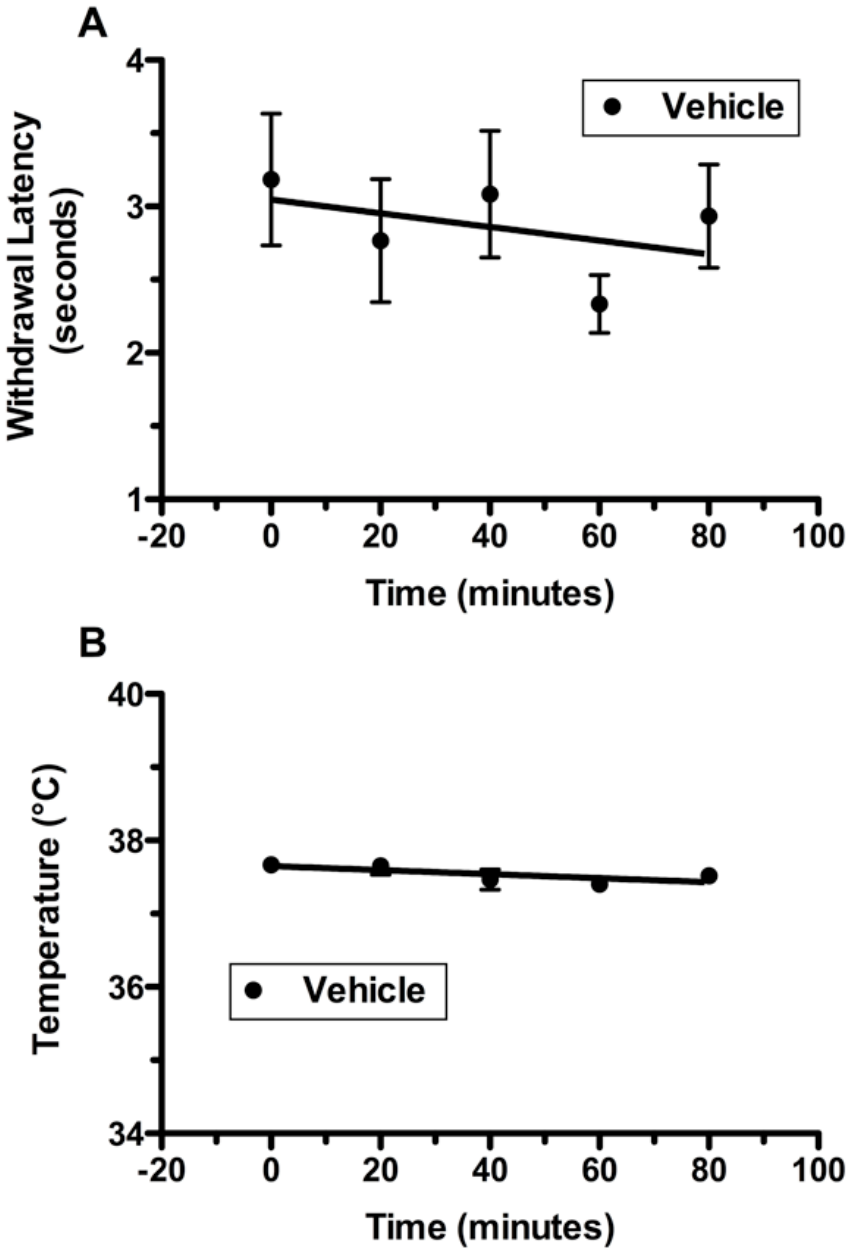
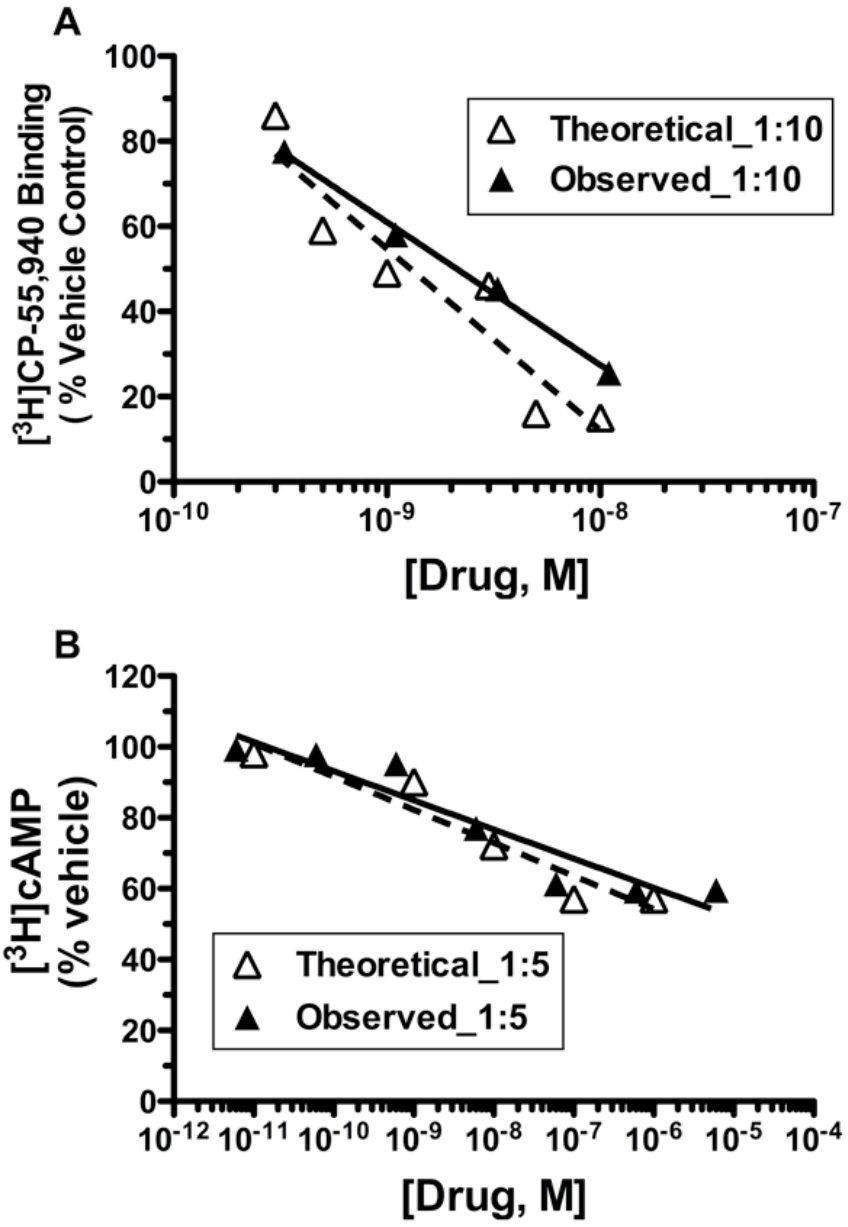
Differential Drug-Drug Interactions of the Synthetic Cannabinoids JWH-018 and JWH-073: Implications for Drug Abuse Liability and Pain Therapy. Lisa K. Brents, Sarah M. Zimmerman, Amanda R. Saffell, Paul L. Prather, William E. Fantegrossi, Journal of Pharmacology and Experimental Therapeutics

Supplemental Figure 1



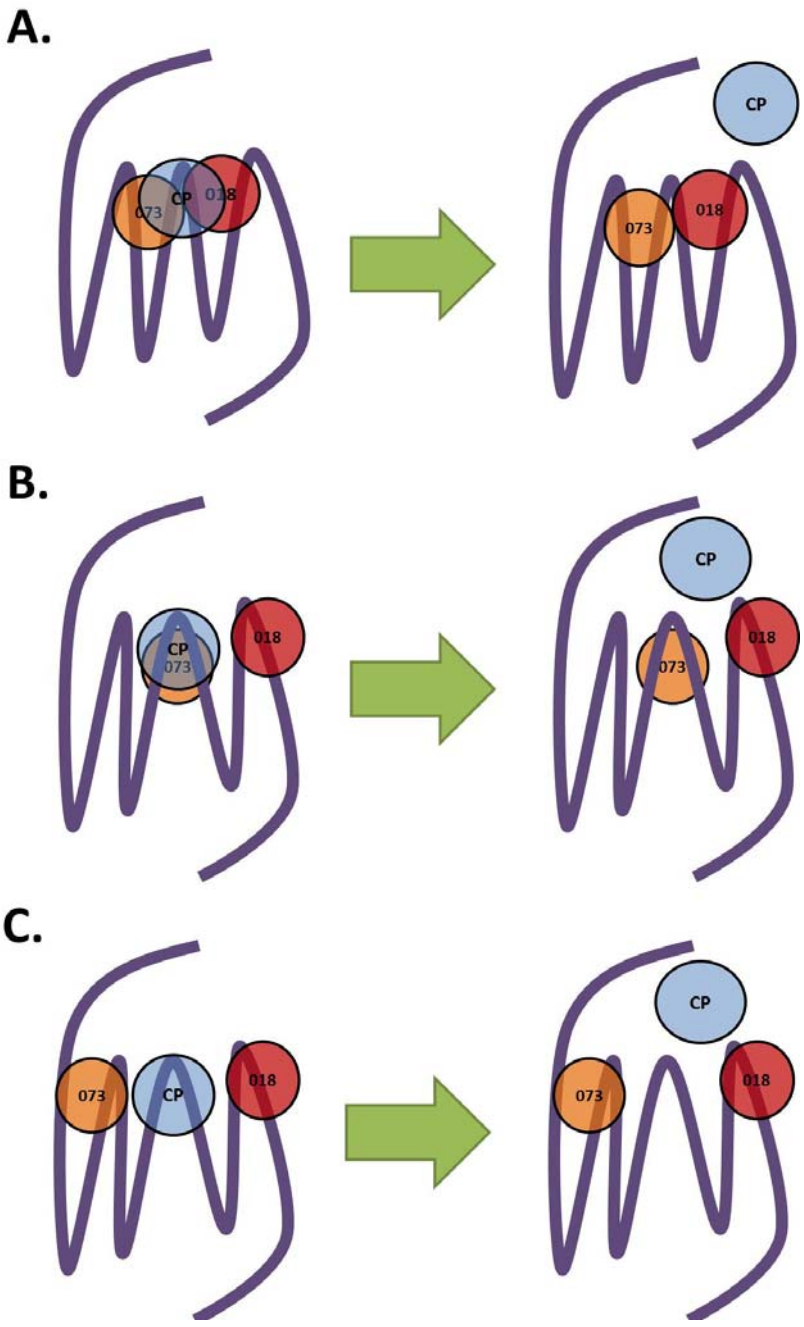
Supplemental Figure 1. Tail withdrawal latency **[A]** and rectal temperature **[B]** remain constant over multiple measurements throughout an experimental session (Slopes do not differ significantly from zero, F-ratio test, n=6).

Supplemental Figure 2



Supplemental Figure 2. JWH-018 combined with JWH-018 produces additive effects on competition receptor binding **[A]** and inhibition of adenylyl cyclase activity **[B]** (*F*-ratio test $P \geq 0.05$, n=3-5).

Supplemental Figure 3



Supplemental Figure 3. Proposed mechanisms of synergistic displacement of [^{3}H]CP-55,940 from CB1Rs by JWH-018 and JWH-073. The concurrent binding of JWH-018 (018) and JWH-073 (073) to CB1R may occupy a greater surface area of the binding site of [^{3}H]CP-55,940 (CP) than either drug alone, enhancing its displacement **[A]**. Alternatively, one JWH-xxx compound may bind to an allosteric site (018) and alter the conformation of CB1R such that the other compound (073) occupies more of the orthosteric site and consequently displaces CP-55,940 (CP) more readily **[B]**. Both JWH-xxx compounds (018 and 073) may bind to allosteric regions in such a way that enhances the displacement of CP-55,940 (CP) **[C]**.