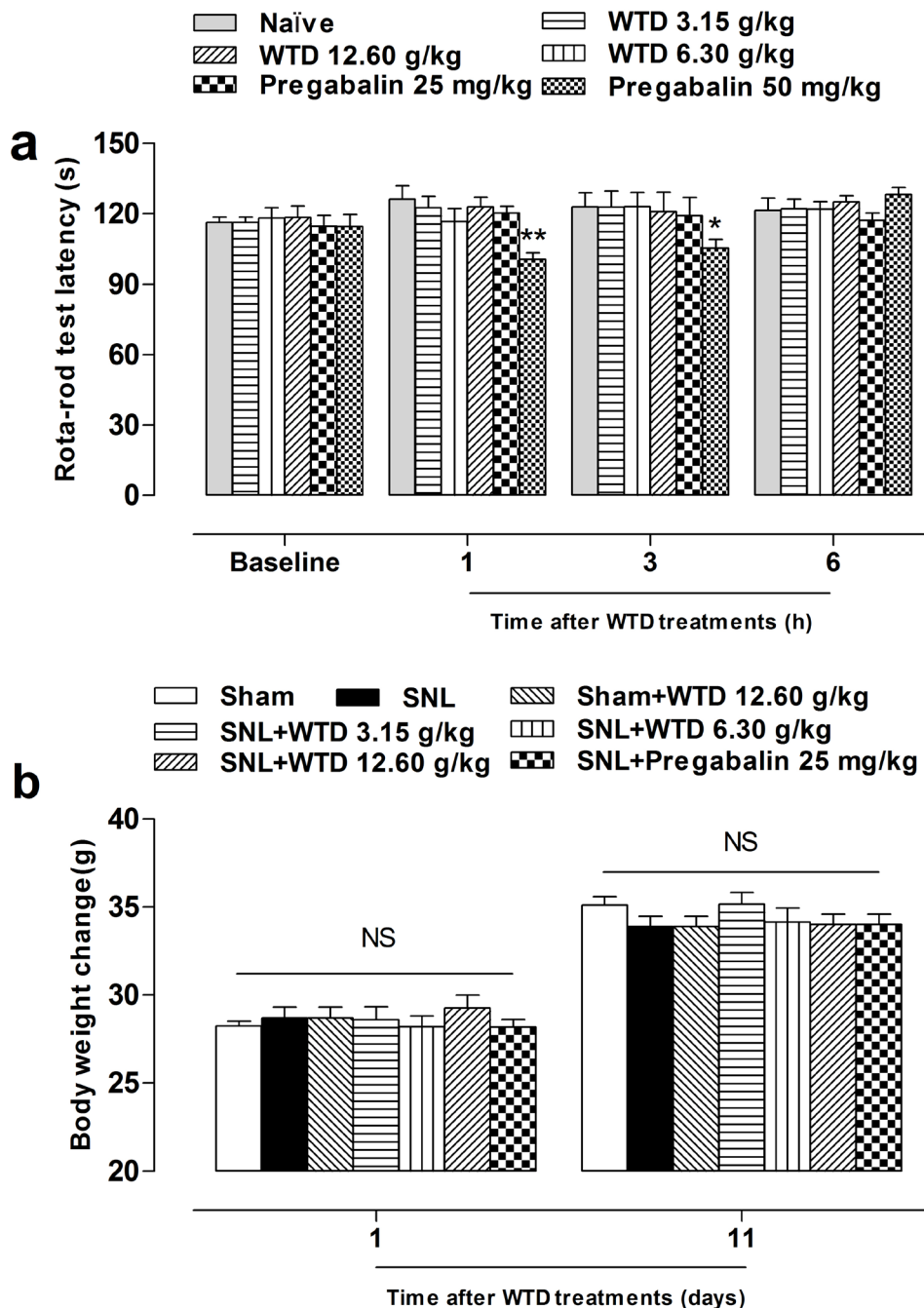
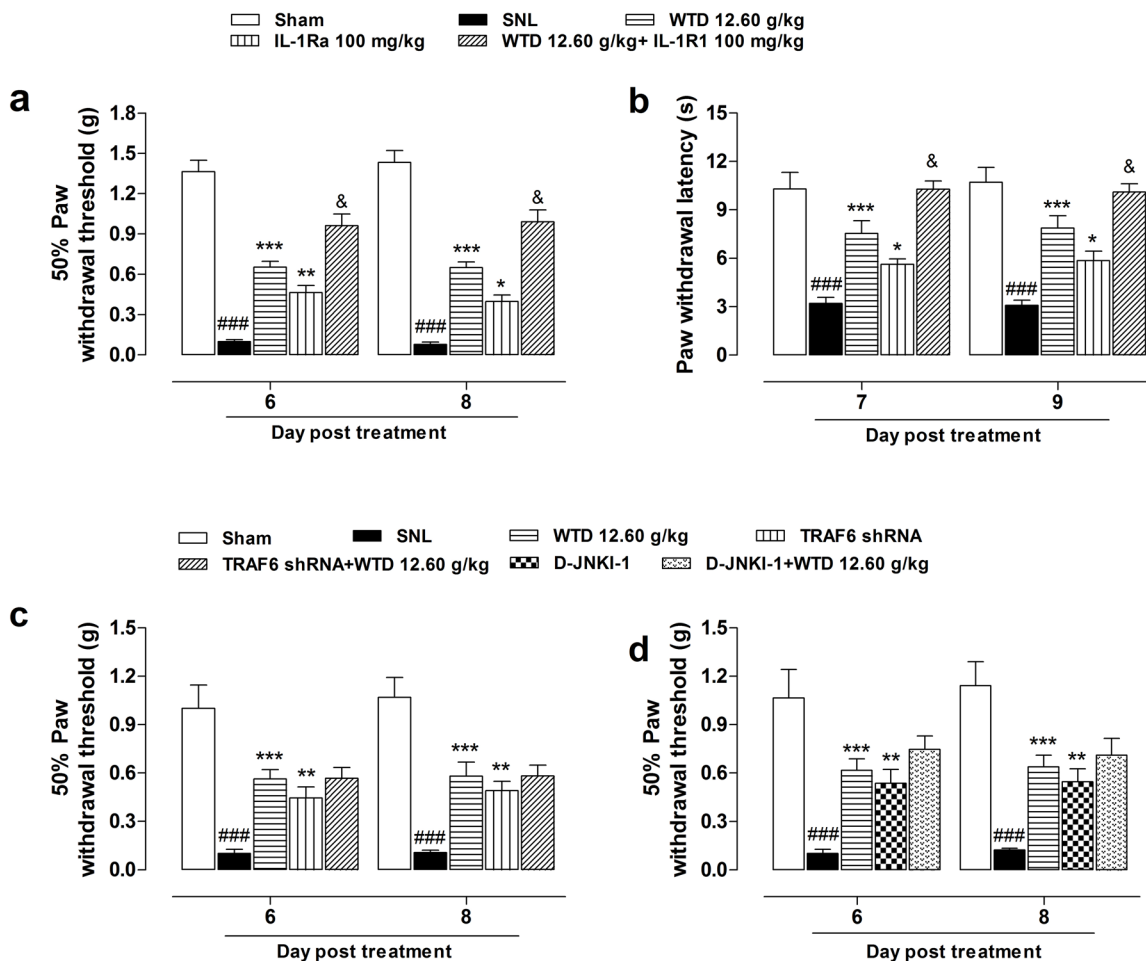


Wu-tou decoction attenuates neuropathic pain via suppressing spinal astrocytic IL-1R1/TRAF6/JNK signaling

SUPPLEMENTARY MATERIALS



Supplementary Figure 1: Side effects assessments of WTD. WTD (3.15-12.60 g/kg, p.o) and pregabalin (25 mg/kg, p.o.) did not impair the locomotor function of naïve mice in the Rota-rod test 1-6 hours after drug administration, while pregabalin (50 mg/kg, p.o.) significantly reduced the latency time of mice 1 and 3 hours post drug treatment (a). WTD did not induce noticeable body weight loss in each group 7 days after drug administration. Data are represented as mean ± SEM. (n=6). * $P < 0.05$, ** $P < 0.01$ in Supplementary Figure 1a vs. naïve mice.



Supplementary Figure 2: Anti-hyperalgesia effects of WTD co-administrated with inhibitors of IL-1R1, TRAF6 or JNK. Pretreatment of IL-Ra (100 mg/kg, i.p., 2 hours before), an specific inhibitor of IL-1R1, with WTD (12.60 g/kg, p.o., 1 hour before) significantly attenuated SNL induced mechanical allodynia, heat hyperalgesia, and increased WTD analgesic effect 5-9 days post drug administration (**a**, **b**). Otherwise, neither co-administration of LV-TRAF6-shRNA (4 μ l, intraspinal injection, 3 days prior to test), the specific inhibitor of TRAF6, nor D-JNKI-1 (0.3 mg/kg, i.p., 30 minutes before), the specific inhibitor of JNK with WTD (12.60 g/kg, p.o., 1 hour before) increased WTD's anti-allodynia effect on 6th and 8th day post drug administration (**c**, **d**). Data are represented as the mean \pm SEM. (n=6). ### P <0.001 vs. Sham group, * P <0.05, ** P <0.01 and *** P <0.001 vs. SNL group. & P <0.01 in Supplementary Figure 2a-2b vs. WTD (12.60 g/kg) group.