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OPTIMIZATION AND VALIDATION OF PROFILING EFFORTS WITHIN THE NINDS PRECLINICAL SCREENING PLATFORM FOR PAIN (PSPP) TO ACCELERATE THE DEVELOPMENT OF NOVEL NON-OPIOID, NON-ADDICTIVE PAIN THERAPEUTICS

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Main Category: T (translational)
Main Topic: Pharmacological therapies

Background and aims: The NINDS PSPP program of NIH HEAL Initiative facilitates the identification and development of new non-opioid, non-addictive pain therapeutics from academic, industry, and government institutions worldwide, to accelerate development of novel small molecule, biologic, natural product, and device treatments for pain using extensively validated models and endpoints. *E*ffects of clinically used drug, duloxetine will be highlighted as an example.
Methods: Male and female SD rats (Envigo, Indianapolis, IN, 180-250 g), were acclimated for a week, maintained on a 12/12 light/dark cycles (20-23°C) and Chow and water provided *ad libitum*. Tests were performed during the animal's light cycle phase between 8 am – 4 pm. All experiments were conducted in a blinded manner in both sexes.
PK studies guided experiments. The modified Irwin (n=4) and rotarod tests (n=10) evaluated potential neurologic, physiologic, and fine motor effects. Efficacy was evaluated in the plantar incisional (n=10) and L5/L6 spinal nerve ligation (SNL; n=10) models. Data are presented as mean +/- s.e.m.
Results: Duloxetine levels were maintained through 8 hours post-administration in plasma and brain, in both sexes after 60 mg/kg, PO. Duloxetine (10, 30, 60, 100 mg/kg PO) did not affect rotarod performance Duloxetine, 60 mg/kg PO, robustly reduced mechanical allodynia and guarding behaviors in the plantar incision model and reduced mechanical allodynia and acetone cold sensitivity in the SNL model.
Conclusions: In summary, results demonstrated the comprehensive evaluation of a clinically used drug, duloxetine, in the PSPP program. The NINDS PSPP program strives to accelerate the development of novel non-opioid, non-addictive therapeutics for pain.

Do you have any conflict of interest to declare (industry support) for the past 3 years related to this work? No

Has this study been approved by an ethics committee?: Yes

In case of patient case presentations: Do you have approval from the patient/patients? No
Explain why: Preclinical studies, Patients not applicable.

I am interested in participating in a poster walk: No
My abstract has an industry perspective: Yes
I wish to be eligible for a poster prize: No
If selected, I would like to give an oral presentation in addition to the poster presentation: Yes