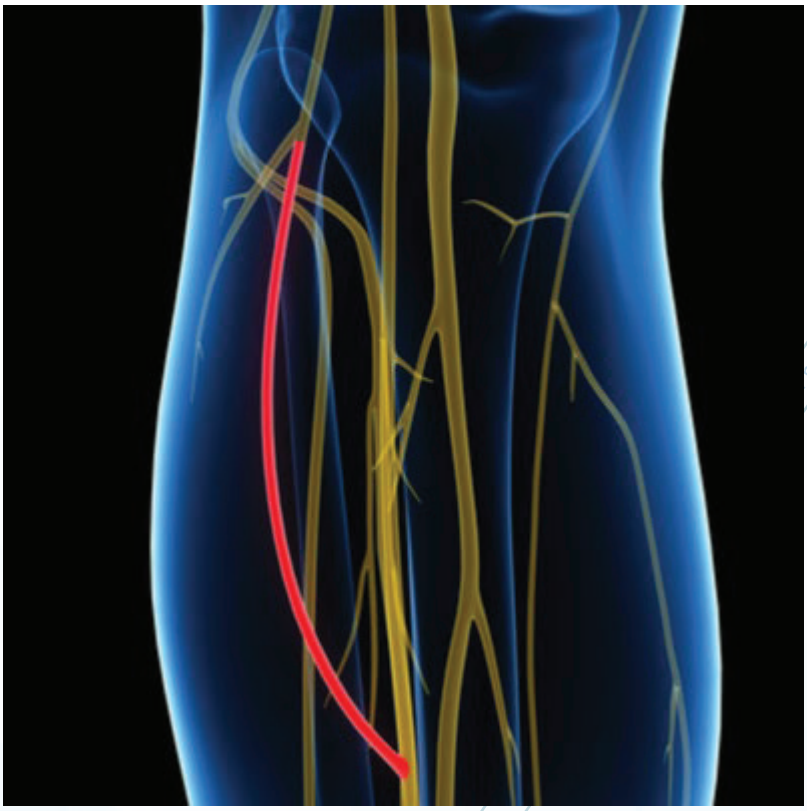


Evaluating Analgesic Efficacy Using the Spared Nerve Injury (SNI) Model with PK–PD–Biomarker Correlation

Overview

The Spared Nerve Injury (SNI) model is a well-established and translationally relevant rodent model that closely replicates key clinical features of human neuropathic pain. It involves ligation and transection of two branches of the sciatic nerve, the tibial and common peroneal while sparing the sural nerve. This selective injury produces robust and long-lasting neuropathic pain behaviours mirroring symptoms commonly observed in patients with partial peripheral nerve damage.

The model effectively recapitulates major pathophysiological mechanisms of neuropathic pain, such as peripheral and central sensitisation and ectopic neuronal activity. Owing to its high reproducibility and clinical relevance, the SNI model serves as a powerful tool to evaluate analgesic candidates and to investigate mechanistic correlates underlying pain modulation.

Study Objective

To assess the pharmacokinetic, pharmacodynamic (PK–PD) and biomarker correlation of a test compound in the SNI model.

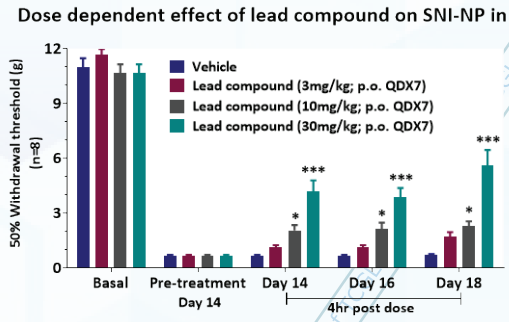
Approach

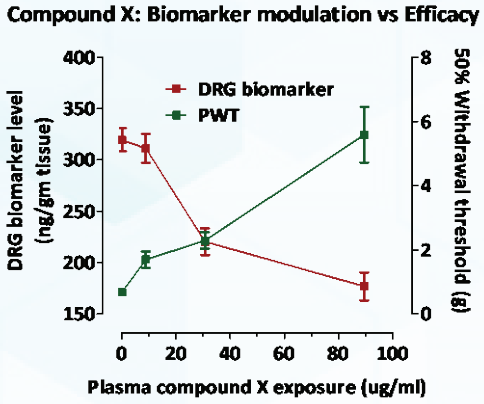
Rodent subjects underwent SNI surgery as per standard protocol, maintaining the sural nerve intact while ligating and transecting the tibial and common peroneal branches of the sciatic nerve. Post-surgical evaluation confirmed the establishment of neuropathic pain phenotypes.

The test compound was administered, and PK–PD assessments were performed with multiple doses to establish systemic exposure and pharmacological activity. Parallel biomarker analyses were conducted to correlate molecular or biochemical markers with behavioural pain responses.

PK–PD–Biomarker Correlation

PK-PD_Biomarker





The integration of pharmacokinetic data with pharmacodynamic outcomes and biomarker expression provided a comprehensive understanding of the compound's mechanism of action. The data demonstrated a clear dose-dependent relationship between systemic exposure and analgesic response, with biomarker trends aligning with the observed behavioural outcomes.

The compound showed to exhibit consistent PK–PD correlation and biomarker modulation in treated groups compared with controls, suggesting effective target engagement and therapeutic potential in neuropathic pain modulation.

Conclusion

The study successfully validated the Spared Nerve Injury (SNI) model as a robust platform for evaluating compounds in neuropathic pain.