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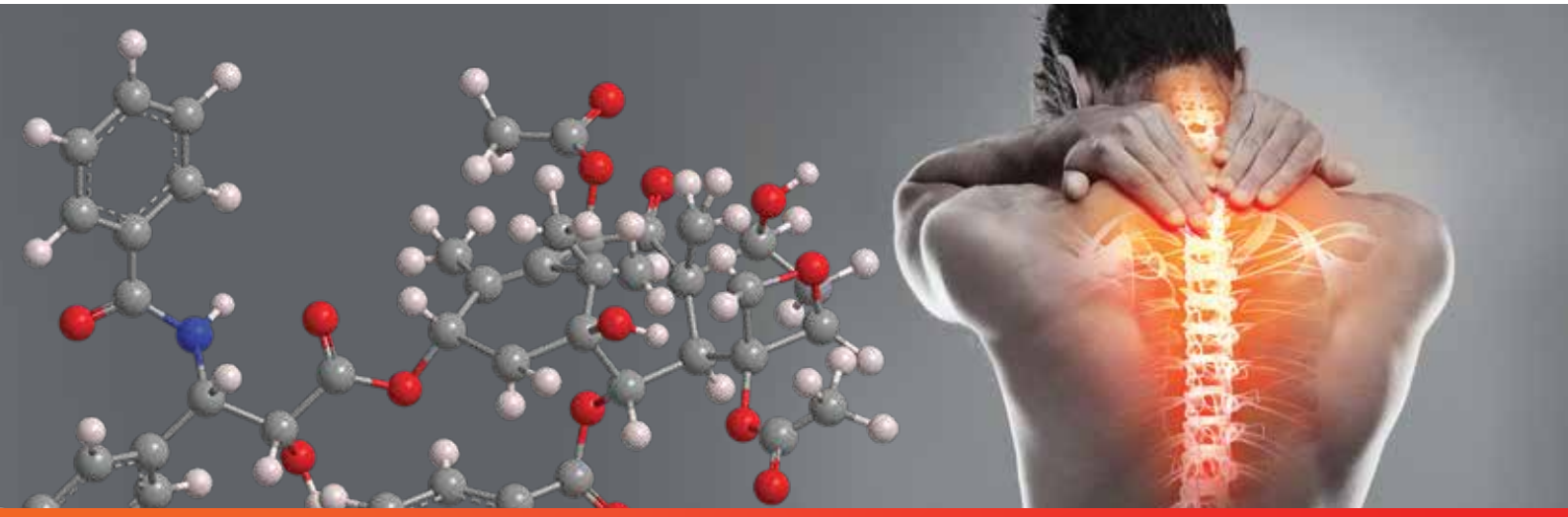


Paclitaxel-induced Peripheral Neuropathic Pain Model Developed at Aragen

Paclitaxel, a widely used anticancer drug in treating ovarian, breast, and prostate cancers, triggers neuropathy in approximately 97% of patients with gynecological and urological cancers. Its primary action involves inducing cell death in cancer cells by stabilizing microtubules, thereby halting cell division. However, paclitaxel also impacts cells in both the central and peripheral nervous systems. Its accumulation in the dorsal root ganglia (DRG) leads to notable symptoms such as pain and tingling sensations in the hands and feet. This accumulation disrupts axonal transport, alters mitochondrial structure and function, and prompts inflammation. Consequently, these pathological alterations result in symmetric damage to axons and the loss of nerve fibers.

Paclitaxel-induced animal models are used in neuropathic pain research because they mimic certain aspects of neuropathic pain observed in humans. Paclitaxel can induce neuropathy in animals, leading to symptoms similar to those experienced by humans with neuropathic pain. These models are essential for various reasons outlined hereafter.

Understanding Pathophysiology:

Models help in comprehending the underlying mechanisms and pathophysiology of neuropathic pain. They aid researchers in studying the processes that lead to nerve damage or malfunction, which in turn cause neuropathic pain.

Drug Development:

These models serve as a basis for testing and developing new drugs or treatments for neuropathic pain. They allow researchers to assess the efficacy and safety of potential medications before clinical trials in humans.

Treatment Evaluation:

Models aid in evaluating the effectiveness of existing treatments or therapeutic interventions for neuropathic pain. This helps researchers and clinicians understand how well current therapies work and if there are any limitations or side effects.

Understanding Pain Pathways:

They provide insights into the pathways and neural circuits involved in transmitting and processing pain signals in neuropathic conditions. This knowledge is essential for devising targeted therapies that can specifically modulate these pathways.

Key features of the model developed at Aragen:

The model is developed using Male SD Rats weighing 230 – 250 g. Neuropathic pain and whole-body hypersensitivity is developed by administrating multiple doses of paclitaxel at 1mg/kg through intraperitoneal route.

Pharmacological validation of Tactile allodynia:

The sensitivity of the hind paw in treated animals to touch and temperature changes was confirmed through tests that measured the 50% paw withdrawal threshold (PWD) following the application of mechanical stimuli with von Frey filaments. Animals treated with paclitaxel exhibited withdrawal responses at ≤ 5g, while those treated with both paclitaxel and gabapentin showed 50% PWD values ≥ 5g. As the concentration of gabapentin increased, there was a gradual rise in PWD values (see Figure 1). Figure 2 displays the post-treatment time for the 50% PWD across different animal groups. Gabapentin, a medication primarily utilized for neuropathic pain (nerve pain), falls under the class of anticonvulsants or antiepileptic drugs. Its mechanism involves influencing specific chemicals and nerves in the body that contribute to seizures and various types of pain.

Figure 1

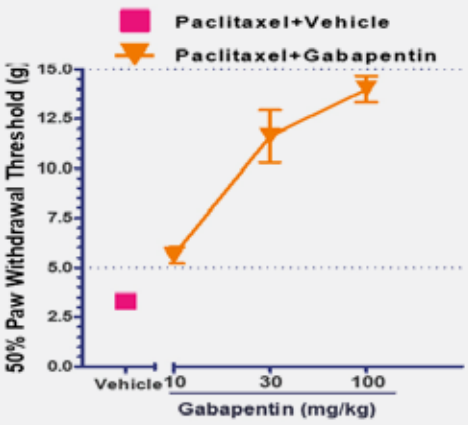
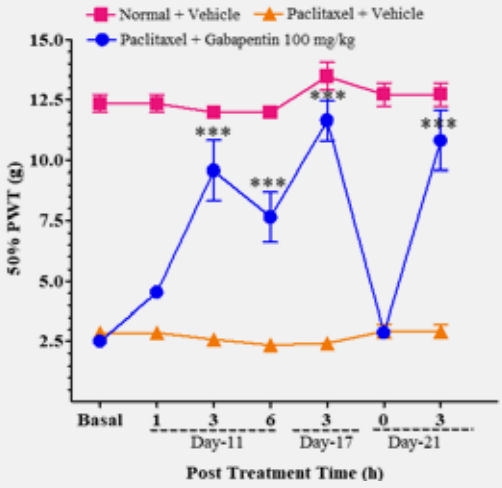


Figure 2



Conclusions:

The experts in vivo pharmacologists at Aragen have successfully developed a robust and reproducible model of paclitaxel-induced poly neuropathic pain. The model is robust and captures the clinical manifestations observed in humans with poly neuropathy. The model is an appropriate tool to screen new analgesics and to study pathophysiological mechanisms of poly neuropathic pain.