

Revolutionizing pain medication: Preventing addiction and side effects

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Stephen Vanner, president of pHarm Therapeutics Inc., and Christoph Stein, inventor and co-founder, discuss a new class of analgesics for pain caused by tissue injury and inflammation

Severe pain resulting from major tissue injury and inflammation, such as arthritis, trauma, surgery, cancer, migraines, sickle cell crisis, and inflammatory bowel disease, can often only be treated effectively with conventional opioid medication. However, the risks of addiction and serious side effects, such as life-threatening respiratory arrest, have led to an opioid crisis in North America and worldwide.

The 2018 USA Federal Drug Administration roadmap to combat this crisis states that 'transitioning from the current market, dominated by conventional opioids, to one in which opioids have abuse-deterrent properties, holds significant promise for a meaningful public health benefit.' However, so far, competitive approaches, including biased opioid agonists, have failed.

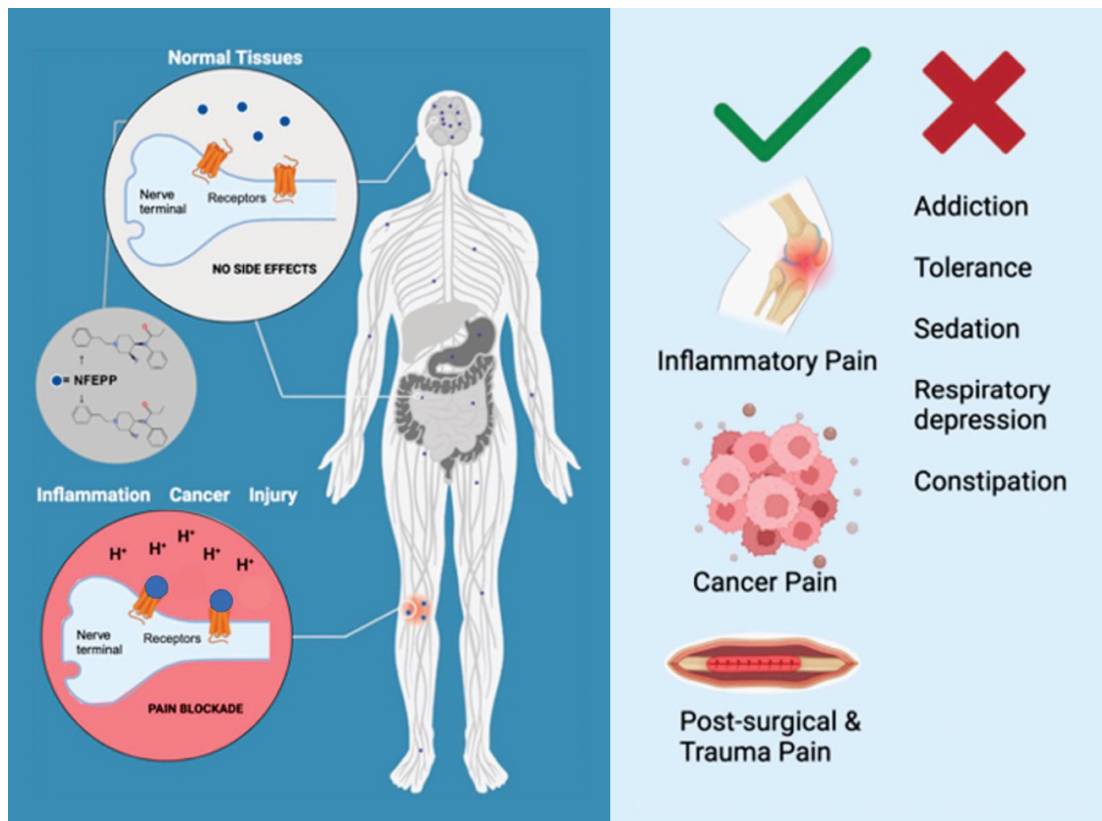


Figure 1: NFEPP's targeted pain treatment is highly effective and lacks the risk of addiction and adverse side effects

How NFEPP targets pain originating from injury and inflammation

We have developed an entirely new approach that circumvents the risks of conventional opioids. Our prototype pH-sensitive drug, **NFEPP**, short for (\pm)-N-(3-fluoro-1-phenethylpiperidine-4-yl)-N-phenyl propionamide, is only active in injured and inflamed tissues where pH is low but not in healthy tissues elsewhere in the body, such as the brain and GI tract, where pH is normal (i.e., pH 7.4) (Figure 1).

Our preclinical studies, conducted in models of arthritis, colitis, post-operative pain, and cancer, have been externally validated in multiple independent laboratories. These studies have consistently shown that NFEPP has comparable analgesic potency to conventional opioids.

However, NFEPP lacks the addiction potential and central effects on the brain (see videos), as well as the tolerance, constipation, respiratory depression, or locomotor impairment commonly associated with opioids.

These findings are supported by our experiments in human tissue and ongoing studies in non-human primates.

Video Player

VIDEO 1 (above): Vehicle

Video Player

VIDEO 2 (above): NFEPP

Video Player

VIDEO 3 (above): FENTANYL

Videos: Similar to control (vehicle) mice, NFEPP-treated mice are relaxed and exhibit normal exploratory and grooming behavior. In contrast, fentanyl-treated mice appear agitated, moving rapidly and clinging to the sides of their enclosure, with their tails unnaturally arched over their backs – signs of centrally-induced anxiety.

Bringing NFEPP to market

We aim to conduct Phase 1-2 clinical trials in the next three years, with an initial focus on managing post-operative pain in orthopaedic surgery. We will collaborate closely with industry partners and regulatory bodies to achieve this goal.

The global pain market is projected to grow from \$71bn to \$91bn by 2027. Our innovative compounds have the potential to provide tremendous societal and healthcare benefits by offering a valuable alternative to conventional opioids and NSAIDs for painful inflammatory disorders.

What experts are saying about this new class of analgesics

‘A particularly exciting and promising strategy’; ‘A revolutionary way of thinking in pharmacology’
(*Behav Pharmacol* 2020; 31:136-158)

‘A key advance’; ‘a pioneering approach to produce safer opioids’
(*Expert Opin Ther Targets* 2019; 23:315-326)

‘NFEPP is a promising candidate for patients with peripheral tissue damage across the spectrum of chronic pain syndromes’
(*Curr Pain Headache Rep* 2021; 25:46)

'...Extremely interesting peripheral visceral antinociceptive agent'
(*Gut* 2022; 71:1-2)

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Seminal study revealing that the activation of opioid receptors in peripheral injured tissue produces clinical pain relief

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