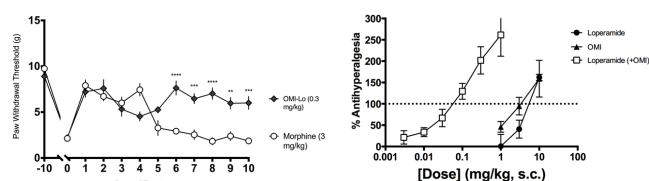




Pain therapy without the risk of respiratory depression, addiction or abuse

An analgesic combination of peripherally restricted opioids that eliminates the risk of respiratory depression, chemical addiction or abuse.



Technology ID

20160199

Category

Life Sciences/Human Health

Life Sciences/Pharmaceuticals

Agriculture &

Veterinary/Veterinary Medicine

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The costly problem of pain

It is estimated that up to 100 million Americans live with moderate to severe pain as a result of disease or injuries. Opioid-based analgesics are the gold standard for pain treatment. However, the long-term use of these analgesics carries significant risk for lethal respiratory depression, tolerance, addiction and diversion. Approximately 25% of patients prescribed opioids for chronic pain misuse them at an estimated economic burden of \$78.5 billion annually. There is a significant unmet need for pain management modalities without this social-economic burden. Opioid receptors reside in both the central and peripheral nervous system and risks associated with opioid analgesics are primarily due to actions within the central nervous system. There have been several strategies employed to avoid these risks, including: (1) slow-release opioid analgesics, (2) combining drugs that activate opioid receptors (agonists) with drugs that block opioid receptors (antagonists), (3) adding abuse-deterrent compounds to the formulation, and (4) using opioid agonists that do not enter the brain. Unfortunately, these approaches have failed to provide effective pain management that truly eliminates the risk of addiction.

Finding relief

University of Minnesota researchers Dr. George Wilcox and Dr. Carolyn Fairbanks have developed a novel method for treating pain by administering a peripherally restricted μ -opioid analgesics in combination with a δ -opioid receptor analgesic. Combining loperamide, a highly efficacious μ -opioid receptor agonist that is excluded from the central nervous system, and oxymorphone, a δ -opioid receptor agonist that was shown to synergize with morphine spinally, elicits an analgesic effect in inflamed animals at doses as much as 150 times less than administration of either compound alone. Restriction of the μ -opioid agonist to the peripheral nervous system eliminates the respiratory depression and abuse/addiction potential associated with opioid-based analgesics that gain access to the CNS. Furthermore, while the compounds behave synergistically in relation to their analgesic properties, their combination does not multiply observed side effects, which results in a therapeutic treatment window that is 5-50 times larger than either compound used alone. Taken together the loperamide-oxymorphone combination is a promising pain intervention with a significantly diminished risk profile.

Phase of Development

TRL: 4-5. In vivo animal data.

Features & Benefits

- **Non-addictive pain management:** Use of μ -opioid compound that is restricted from entering the CNS eliminates the development of chemical dependence.
- **Highly-potent analgesic:** Synergism between μ - and δ -opioid receptor agonists leads full analgesic effects at doses as much as 50 times less than their use alone.
- **Minimal side effects and low dosing:** The greatly increased analgesic potency does not generalize to the side effects, so that the use of both agonists together results in a therapeutic window 5-50 times larger than either alone.
- **No development of opioid tolerance:** The greatly reduced doses of the two analgesics allows repeated dosing without the development of opioid tolerance.

Applications

- Non-addictive post-operative pain management
- Chronic and cancer related pain management
- Prescription or OTC medication
- Long-term dosing for chronic pain without the development of opioid tolerance

Researchers

- [George Wilcox, PhD](#) Professor, Dept. of Neuroscience
- [Carolyn Fairbanks, PhD](#) Associate Dean for Research and Professor, Dept. of Pharmaceutics
- [Philip Portoghese, PhD](#) Distinguished Professor, Dept. of Medicinal Chemistry
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Desired Partnerships

This technology is now available for:

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- Co-development

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References

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