TECHNOLOGY

Novel Opioid Analgesics With Reduced Tolerance

OVERVIEW

UMB 425 is a novel opioid with bi-functional activity that combines a delta-opioid antagonist and a mu-opioid agonist in a single compound with antinociceptive effects comparable to morphine. With reduced tolerance liabilities, UMB 425 provides a novel therapeutic approach in the treatment of patients who suffer from chronic pain with reduced risk for the development of tolerance and addiction.

Researchers at UMB have developed a novel opioid analgesic compound (named UMB 425) that combines the activities of both a delta-opioid antagonist and a mu-opioid agonist in a single compound. UMB 425 reduces the development of tolerance to analgesia with substantially fewer side effects than current opioids (such as morphine or oxycodone). In vivo studies performed where Swiss Webster mice (male) were treated with UMB 425 demonstrated a significant reduction in pain sensitivity in the hot plate and tail-flick assays over morphine during a six-day tolerance paradigm. UMB 425 has nanomolar affinity and efficacy for mu-opioid receptors similar to morphine and moderate affinity for delta-opioid receptors for which it exhibits antagonistic effects. The bi-functional activity of UMB 425 has the potential to be an effective treatment for patients who suffer from chronic pain with reduced risk for the development of tolerance and addiction. UMB 425 minimizes tolerance development with no corresponding increase in dosage required, obviating most undesirable side effects associated with opioid use.
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APPLICATIONS

Opioids such as codeine, morphine and oxycodone have long been used to treat moderate to severe pain. Opioid effects are mediated through activity on the delta- and mu- opioid receptors found in the Central Nervous System. Although invaluable in alleviating pain, opioids have the potential for tolerance, wherein the body becomes less responsive to their effects. Tolerance occurs when opioids exert a synergistic analgesic effect that activates both delta- and mu-opioid receptors. Tolerance leads to increased dose requirements to keep the patient in a pain free state. However, increasing doses result in undesired effects such as respiratory depression, tolerance, physical/psychological dependence, constipation, sedation, nausea/vomiting and dizziness. Current therapeutic approaches circumvent tolerance by co-administering a delta-opioid antagonist with a mu-opioid agonist.

ADVANTAGES

A novel opioid compound (UMB 425) with reduced potential for development of opioid tolerance compared to traditional opioids Fewer negative side effects compared to traditional opioids Lower treatment costs and reduced potential for development of tolerance and opioid addiction

STAGE OF DEVELOPMENT

- UMB 425 is a novel, patent protected, opioid compound.
- In vivo studies performed where Swiss Webster mice (male) were treated with UMB 425 demonstrated a significant reduction in pain sensitivity in the hot plate and tail-flick assays over morphine during a six-day tolerance paradigm.
- UMB 425 has nanomolar affinity and efficacy for mu-opioid receptors similar to morphine and moderate affinity for delta-opioid receptors for which it exhibits antagonistic effects.

R&D REQUIRED

Pharmacokinetic and toxicity studies required prior to filing an IND.

LICENSING POTENTIAL

UM seeks to develop and commercialize by an exclusive or non-exclusive license agreement and/or sponsored research with a company active in the area.

CONTACT INFO

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Additional Information

INSTITUTION

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PATENT STATUS

US Patent 9,422,302 EU 2964228 (validated Germany, UK, France)

CATEGORIES

- Therapeutics
- Small molecules

INVESTIGATOR(S)

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ATTACHMENTS

- Download AC-2013-055 Technology Summary.pdf

EXTERNAL RESOURCES

- Deconstructing 14-phenylpropyloxymetopon: minimal requirements for binding to mu opioid receptors.
- Consensus 3D model of ?-opioid receptor ligand efficacy based on a quantitative Conformationally Sampled Pharmacophore.
- Opioid analgesics and P-glycoprotein efflux transporters: a potential systems-level contribution to...

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