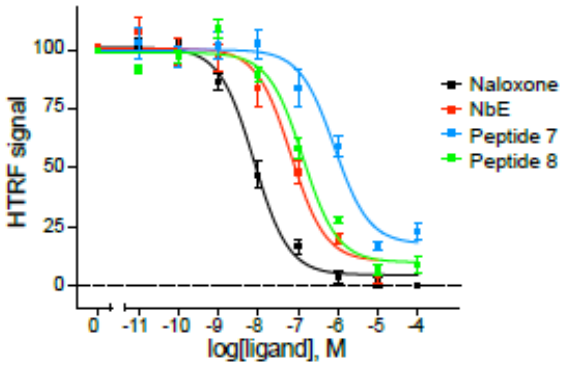
Peptidic μ-opioid receptor antagonists

Invention

The μ-opioid receptor (μOR) is a key target for pain relief, yet existing μOR antagonists like naloxone often have short half-lives and may cross the blood-brain barrier, leading to challenges in maintaining efficacy. This invention introduces peptidic antagonists targeting the μ-opioid receptor (μOR). These peptides are mimetic versions of the CDR3 loop of a single domain antibody (NbE) designed to bind selectively to μORs, blocking their activity. By mimicking the structure of NbE, these peptides achieve high affinity and slow dissociation rates, potentially resulting in prolonged in vivo effects. The peptides can be formulated in both linear and cyclic versions, with the cyclic peptides demonstrating enhanced stability and binding affinity.

Key data



Ligand	IC_{50} (nM)	Ki (nM)
Naloxone	7.89	2.39
NbE	66	20.07
Peptide 7	810	244.83
Peptide-8	132	39.98

Features & Benefits

- **High Selectivity:** Specifically targets μOR, minimizing off-target effects on other opioid receptor subtypes.
- **Prolonged Action:** Slow dissociation rates suggest longer-lasting effects compared to traditional antagonists like naloxone.
- **Reduced Central Nervous System Side Effects:** Potential to limit blood-brain barrier penetration, focusing action peripherally and reducing the impact on CNS-mediated analgesia.
- **Enhanced Stability:** Cyclic versions of the peptides offer improved stability and bioavailability, increasing therapeutic potential.

Applications

- **Opioid Overdose Reversal:** Effective in counteracting opioid effects, potentially offering a longer duration of action than current options.
- **Opioid-Induced Constipation:** Useful in managing gastrointestinal side effects of opioids without affecting central pain relief.
- **Addiction Treatment:** May aid in therapies aimed at reducing opioid cravings and dependency by blocking μOR-mediated reward pathways.

Partnership sought

Exclusive licensing and optionally R&D collaboration.

Intellectual Property

Patent: Cyclic peptides that selectively modulate mu-opioid receptor function
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Earliest priority date: 12.08.2024

Technology Readiness Level

In vitro validation of the binding properties and efficacy of the antagonistic peptides using binding assays, functional assays and structural assays.

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