

Product Data Sheet

Product Name: PZM21
Cat. No.: GC30771

Chemical Properties

Cas. No. 1997387-43-5

SMILES O=C(N[C@@H](C)CC1=CSC=C1)NC[C@@H](N(C)C)CC2=CC=C(O)C=C2

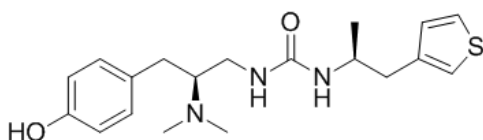
Formula $C_{19}H_{27}N_3O_2S$ M.Wt 361.5

Solubility DMSO : ≥ 72 mg/mL (199.17 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Animal experiment: Mice: PZM21 is dissolved in 0.9% sodium chloride. Mice are injected with either vehicle, morphine (5 mg/kg, or 10 mg/kg), TRV130 (1.2 mg/kg) or PZM21 (10 mg/kg; 20 mg/kg; or 40 mg/kg). After injection of drug, the analgesic effect expressed as percentage maximum possible effect (%MPE) is measured at 15, 30, 60, 90 and 120 min after drug treatment[1].

Caution: Product has not been fully validated for medical applications. For research use only.

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Address: 10292 Central Ave. #205, Montclair, CA, USA

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References:

- [1]. Manglik A, et al. Structure-based discovery of opioid analgesics with reduced side effects. *Nature*. 2016 Sep 8;537(7619):185-190.
- [2]. Kostic M, et al. Biasing Opioid Receptors and Cholesterol as a Player in Developmental Biology.
- [3]. Araldi D, et al. Mu-opioid Receptor (MOR) Biased Agonists Induce Biphasic Dose-dependent Hyperalgesia and Analgesia, and Hyperalgesic Priming in the Rat. *Neuroscience*. 2018 Oct 17;394:60-71.

Background

PZM21 is a potent and selective μ opioid receptor agonist with an EC₅₀ of 1.8 nM.

PZM21 has no detectable κ OR or nociceptin receptor agonist activity-it is actually an 18 nM κ OR antagonist-while it is a 500-fold weaker δ OR agonist, making it a selective μ OR agonist. At hERG, PZM21 has an IC₅₀ of between 2 and 4 μ M, 500- to 1,000-fold weaker than its potency as a μ OR agonist. Signalling by PZM21 and other μ OR agonists appears to be mediated primarily by the heterotrimeric G protein Gi/o, as its effect on cAMP levels is eliminated by pertussis toxin and no activity is observed in a calcium release assay [1].

PZM21 is a potent Gi activator with exceptional selectivity for μ OR and minimal β -arrestin-2 recruitment. Unlike morphine, PZM21 is more efficacious for the affective component of analgesia versus the reflexive component and is devoid of both respiratory depression and morphine-like reinforcing activity in mice at equi-analgesic doses. PZM21 displays dose-dependent analgesia in a mouse hotplate assay, with a per cent maximal possible effect (% MPE) of 87% reached 15 min after administration of the highest dose of drug tested [1]. PZM21 has a long-lasting analgesic effect on CNS mediated-pain responses, but does not cause respiratory depression and constipation, two key side effects of opioid agonists. PZM21 does not exhibit the type of biomarker responses, such as hyperlocomotion or conditioned place preference response, that are observed when morphine and other opioids are used and are associated with reinforcement and addiction[2].

- [1]. Manglik A, et al. Structure-based discovery of opioid analgesics with reduced side effects. *Nature*. 2016 Sep 8;537(7619):185-190. [2]. Kostic M, et al. Biasing Opioid Receptors and Cholesterol as a Player in Developmental Biology. [3]. Araldi D, et al. Mu-opioid Receptor (MOR) Biased Agonists Induce Biphasic Dose-dependent Hyperalgesia and Analgesia, and Hyperalgesic Priming in the Rat.

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