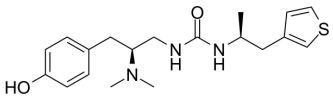
PZM21

Cat. No.:	HY-101386
CAS No.:	1997387-43-5
Molecular Formula:	$C_{19}H_{27}N_3O_2S$
Molecular Weight:	361.5
Target:	Opioid Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (276.63 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7663 mL	13.8313 mL	27.6625 mL
5 mM	0.5533 mL	2.7663 mL	5.5325 mL
10 mM	0.2766 mL	1.3831 mL	2.7663 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.92 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.92 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.92 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PZM21 is a potent and selective μ opioid receptor agonist with an EC_{50} of 1.8 nM[1][2][3].

IC_{50} & Target

EC50: 1.8 nM (μ opioid receptor)[1]

In Vitro

PZM21 has no detectable κOR or nociceptin receptor agonist activity-it is actually an 18 nM κOR antagonist-while it is a 500-fold weaker δOR agonist, making it a selective μOR agonist. At hERG, PZM21 has an IC_{50} of between 2 and 4 μM, 500- to 1,000-fold weaker than its potency as a μOR agonist. Signalling by PZM21 and other μOR 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PZM21 is a potent Gi activator with exceptional selectivity for μOR and minimal β-arrestin-2 recruitment. PZM21 is efficacious for the affective component of analgesia versus the reflexive component and is devoid of respiratory depression 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[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: PZM21 is dissolved in 0.9% sodium chloride. Mice are injected with 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2022 Nov 10;185(23):4361-4375.e19.
- Br J Pharmacol. 2019 Sep;176(17):3110-3125.
- Neuroscience. 2018 Oct 17;394:60-71.
- Patent. US20220276244A1.

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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.

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