PZM21

Cat. No.: HY-101386  
CAS No.: 1997387-43-5  
Molecular Formula: C₁₉H₂₇N₃O₂S  
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: 6 months  
-20°C: 1 month

Solvent & Solubility

In Vitro  
DMSO : ≥ 72 mg/mL (199.17 mM)  
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.7663 mL</td>
<td>13.8313 mL</td>
<td>27.6625 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.5533 mL</td>
<td>2.7663 mL</td>
<td>5.5325 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2766 mL</td>
<td>1.3831 mL</td>
<td>2.7663 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

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

IC₅₀ & 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 IC₅₀ 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].

In Vivo  
PZM21 is a potent Gi activator with exceptional selectivity for μOR 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].

**PROTOCOL**

**Animal Administration** [1]

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**
