Agomelatine hydrochloride

Cat. No.: HY-17038A
CAS No.: 1176316-99-6
Molecular Formula: C₁₅H₁₈ClNO₂
Molecular Weight: 279.76
Target: Melatonin Receptor; 5-HT 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 : ≥ 100 mg/mL (357.45 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.5745 mL</td>
<td>17.8725 mL</td>
<td>35.7449 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.7149 mL</td>
<td>3.5745 mL</td>
<td>7.1490 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3574 mL</td>
<td>1.7872 mL</td>
<td>3.5745 mL</td>
</tr>
</tbody>
</table>

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 (8.94 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.94 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Agomelatine hydrochloride (S-20098 hydrochloride) is a specific agonist of MT1 and MT2 receptors with Kᵢs of 0.1, 0.06, 0.12, and 0.27 nM for CHO-hMT1, HEK-hMT1, CHO-hMT2, and HEK-hMT2, respectively[1]. Agomelatine hydrochloride is a selective 5-HT2C receptor antagonist with pKᵢs of 6.4 and 6.2 at native (porcine) and cloned, human 5-HT2C receptors, respectively[2].
<table>
<thead>
<tr>
<th>IC50 &amp; Target</th>
<th>5-HT2C Receptor 6.4 (pKi, native porcine)</th>
<th>5-HT2C Receptor 6.2 (pKi, human)</th>
<th>hMT1 0.1 (Ki, CHO Cells)</th>
<th>hMT1 0.06 (Ki, HEK Cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>hMT2</td>
<td>0.12 (Ki, CHO Cells)</td>
<td>hMT2</td>
<td>0.27 (Ki, HEK Cells)</td>
<td></td>
</tr>
</tbody>
</table>

**In Vitro**

Agomelatine (S 20098) acts as a full agonist of MT1 and MT2 receptors with EC50s of 1.6±0.4, 0.10±0.04 nM for CHO hMT1 CHO-hMT2 (hMT1 and hMT2 receptors expressed in CHO or HEK cell membranes)[1]. Agomelatine (S20098) also interacts with h5-HT2B receptors (6.6), whereas it shows low affinity at native (rat)/cloned, human 5-HT2A (<5.0/5.3) and 5-HT1A (<5.0/5.2) receptors, and negligible (<5.0) affinity for other 5-HT receptors[2].

**In Vivo**

Agomelatine (25, 50, or 75 mg/kg; i.p.) has antioxidant activity in Strychnine (75 mg/kg, i.p.) or Pilocarpine (400 mg/kg, i.p.) induced seizure models in mice. Agomelatine dose not have any antioxidant effects on parameters of oxidative stress produced by Pentylenetetrazole (PTZ) or Picrotoxin (PTX) induced seizure models when compared to controls[3].

**Animal Model:** Female Swiss mice (20-30 g) were administered PTZ (85 mg/kg, i.p.), PTX (7 mg/kg, i.p.), strychnine (75 mg/kg, i.p.), Pilocarpine (400 mg/kg, i.p.), respectively[3].

**Dosage:** 25, 50, or 75 mg/kg

**Administration:** Administered intraperitoneally (i.p.)

**Result:**

- All dosages showed a significant decrease in thiobarbituric acid reactive substances (TBARS) levels and nitrite content in all brain areas when compared to controls in the Pilocarpine induced seizure model.
- All dosages decreased TBARS levels in all brain areas, and at low doses (25 or 50 mg/kg) decreased nitrite contents, but only at 25 or 50 mg/kg showed a significant increase in catalase activity in three brain areas when compared to controls in the Strychnine-induced seizure model.
- Did not have any antioxidant effects on parameters of oxidative stress produced by PTX- or PTZ-induced seizure models when compared to controls.

**REFERENCES**


