JNJ16259685

Cat. No.: HY-100407
CAS No.: 409345-29-5
Molecular Formula: C₂₀H₂₃NO₃
Molecular Weight: 325.4
Target: mGluR
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 (307.31 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass Concentration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mM</td>
<td>3.0731 mL</td>
<td>15.3657 mL</td>
<td>30.7314 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.6146 mL</td>
<td>3.0731 mL</td>
<td>6.1463 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3073 mL</td>
<td>1.5366 mL</td>
<td>3.0731 mL</td>
</tr>
</tbody>
</table>

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.75 mg/mL (8.45 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (8.45 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (8.45 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
JNJ16259685 is a selective antagonist of mGlu1 receptor, and inhibits the synaptic activation of mGlu1 in a concentration-dependent manner with IC₅₀ of 19 nM.

IC₅₀ & Target
mGluR1
19 nM (IC₅₀)
In Vitro

JNJ16259685 potently and completely inhibits the glutamate (30 μM)-induced increase in intracellular Ca^{2+} concentrations at the rat mGlu1a receptor with an IC_{50} value of 3.24±1.00 nM. IC_{50} values for CPCCOEt and BAY 36-7620 are 17.8±10.3 μM and 161±38 nM, respectively. The potency of JNJ16259685 in blocking glutamate (30 μM)-induced Ca^{2+} mobilization at the human mGlu1a receptor is 1.21±0.53 nM (IC_{50} n=3). JNJ16259685 inhibits the glutamate (3 μM)-induced rise in intracellular Ca^{2+} concentrations at the rat mGlu5a receptor with an IC_{50} value of 1.31±0.39 μM (n=4). JNJ16259685 blocks glutamate (3 μM)-induced Ca^{2+} mobilization at the human mGlu5 receptor with an IC_{50} of 28.3±11.7 μM (n=4). JNJ16259685 does not exhibit agonist activity at any of the group I mGlu receptors[3].

In Vivo

JNJ16259685 (0.125, 0.25, 0.5, 1, 2, 4 and 8 mg/kg, i.p) significantly reduces the time spent in digging behaviours (0.25-8 mg/kg), threat (all doses) and attack, in comparison with vehicle group[1]. JNJ16259685 (30 mg/kg) produces very minimal effects on locomotor activity. JNJ16259685 dramatically reduces rearing behavior, exploration of a novel environment and lever pressing for a food reward (rat: 0.3 mg/kg; mouse:1 mg/kg). Subcutaneously administered JNJ16259685 (30 mg/kg) has no effect on reflexive startle responses to loud auditory stimuli or foot shock in mice[2]. JNJ16259685 exhibits high potencies in occupying central mGlu1 receptors in the rat cerebellum and thalamus (ED_{50} =0.040 and 0.014 mg/kg, respectively)[3].

PROTOCOL

Animal Administration[1][2]

Mice[1]

Nine groups of mice are used. Animals are randomly allocated to two control groups (n=15 each) receiving only saline or saline (90%) plus DMSO (10%), and seven experimental groups (N=14-16 each) receiving JNJ16259685 injections. JNJ16259685 is diluted in saline (90%) plus DMSO (10%) to provide appropriate doses for injections and administered in seven doses: 0.125, 0.25, 0.5, 1, 2, 4 and 8 mg/kg. The doses are chosen on the basis of recent behavioural studies using this compound. Drug or vehicle is injected intraperitoneally in a volume of 10 mL/kg.

Rats[2]

This procedure is used to measure overt behavioral, neurological and autonomic responses to the drug challenge. Briefly, rats are randomly separated into four groups (n=6), each of which receives a different dose (0, 3, 10, or 30 mg/kg) of JNJ16259685. An expert observer, blind to the drug treatment of the animals, assesses and scores the animals at 30, 60, 120, and 240 min post-injection. The animals are assessed for passivity, body elevation, limb position, limb tone, body tone, gait, and pupil size. For each of these behaviors, a score of 0 is assigned to animals that appeared “normal”, whereas scores of ±1, ±2, or ±3 indicated mild, moderate, or severe increases (+) or decreases (−) from normality. Individual animals that receive a score of ±2, or greater, are considered to be significantly effected on the measure. A dose is considered to have a significant effect if 3 or more of the animals receive a score of greater than±2.

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

REFERENCES


[4]. I Fukunaga, et al. Potent and Specific Action of the mGlu1 Antagonists YM-298198 and JNJ16259685 on Synaptic Transmission in Rat Cerebellar Slices.