JNJ16259685

Cat. No.: HY-100407

CAS No.: 409345-29-5

Molecular Formula: $C_{20}H_{23}NO_3$

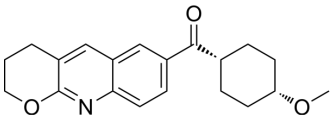
Molecular Weight: 325.4

Target: mGluR

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (307.31 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0731 mL	15.3657 mL	30.7314 mL
5 mM	0.6146 mL	3.0731 mL	6.1463 mL
10 mM	0.3073 mL	1.5366 mL	3.0731 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: ≥ 2.75 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 IC_{50} of 19 nM.

IC_{50} & Target

mGluR1

19 nM (IC_{50})

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

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

[1]. Navarro JF,et al. JNJ16259685, a selective mGlu1 antagonist, suppresses isolation-induced aggression in male mice. Eur J Pharmacol. 2008 May 31;586(1-3):217-20.

[2]. Hodgson RA, et al. Characterization of the selective mGluR1 antagonist, JNJ16259685, in rodent models of movement and coordination. Pharmacol Biochem Behav. 2011 Apr;98(2):181-7.

[3]. Lavreysen H,et al. JNJ16259685, a highly potent, selective and systemically active mGlu1 receptor antagonist. Neuropharmacology. 2004 Dec;47(7):961-72.

[4]. I Fukunaga , et al. Potent and Specific Action of the mGlu1 Antagonists YM-298198 and JNJ16259685 on Synaptic Transmission in Rat Cerebellar Slices. Br J Pharmacol. 2007 Jul;151(6):870-6.

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

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