JNJ-63533054

Cat. No.: HY-19838

CAS No.: 1802326-66-4

Molecular Formula: $C_{17}H_{17}ClN_2O_2$

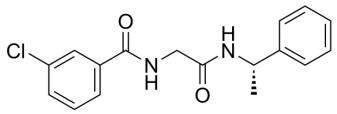
Molecular Weight: 317

Target: GPR139

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 : ≥ 50 mg/mL (157.73 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1546 mL	15.7729 mL	31.5457 mL
5 mM	0.6309 mL	3.1546 mL	6.3091 mL
10 mM	0.3155 mL	1.5773 mL	3.1546 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 (7.89 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JNJ-63533054 is a potent, selective and orally active GPR139 agonist with an EC_{50} of 16 nM for human GPR139 (hGPR139). JNJ-63533054 shows selective for GPR139 over other GPCRs, ion channels, and transporters. JNJ-63533054 can cross the blood-brain barrier (BBB)[1][2].

IC_{50} & Target

EC50: 16 nM (Human GPR139), 63 nM (Rat GPR139) and 28 nM (Mouse GPR139)[1]

In Vitro

JNJ-63533054 specifically activates human GPR139 in the calcium mobilization (EC_{50} of 16 nM) and GTPγS binding (EC_{50} of 17 nM) assays. JNJ-63533054 also activates the rat and mouse GPR139 receptor with similar potency (rat EC_{50} of 63 nM, mouse EC_{50} of 28 nM)[1].

	?In a saturation study for human GPR139, a single population of high-affinity binding sites for [3H] JNJ-63533054 is observed (K_d of 10 nM). The B_{max} value is 26 pmol/mg of protein. Saturation studies for the rat GPR139 and mouse GPR139 yielded K_d values within the same range (32 nM and 23 nM, respectively; B_{max} = 8.5 pmol/mg of protein and 6.2 pmol/mg of protein, respectively)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	JNJ-63533054 (3-30 mg/kg; oral administration; once; SD rats) treatment induces a dose-dependent reduction in locomotor activity in the first hour[1]. ?The pharmacokinetics of JNJ-63533054 (Compound 7c; 1 mg/kg iv; 5 mg/kg po) in rat is examined. The IV clearance is 53 mL/min/kg,? the C_{max} is 317 ng/mL (~1 μM), the $t_{1/2}$ is 2.5 hours,? and JNJ-63533054 is able to cross the blood-brain barrier (BBB) with a brain to plasma ratio (b/p) of 1.2[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley rats (350-450 g)[1]
Dosage:	3 mg/kg, 10 mg/kg, and 30 mg/kg
Administration:	Oral administration; once
Result:	Induced a dose-dependent reduction in locomotor activity in the first hour.

REFERENCES

[1]. Dvorak CA, et al. Identification and SAR of Glycine Benzamides as Potent Agonists for the GPR139 Receptor. ACS Med Chem Lett. 2015 Jul 20;6(9):1015-8.

[2]. Liu C, et al. GPR139, an Orphan Receptor Highly Enriched in the Habenula and Septum, Is Activated by the Essential Amino Acids L-Tryptophan and L-Phenylalanine. Mol Pharmacol. 2015 Nov;88(5):911-25.

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