Org 27569

Cat. No.: HY-13288

CAS No.: 868273-06-7

Molecular Formula: $C_{24}H_{28}ClN_3O$

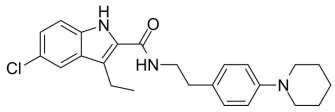
Molecular Weight: 409.95

Target: Cannabinoid Receptor

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 : ≥ 52.2 mg/mL (127.33 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4393 mL	12.1966 mL	24.3932 mL
	5 mM	0.4879 mL	2.4393 mL	4.8786 mL
	10 mM	0.2439 mL	1.2197 mL	2.4393 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 (6.10 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.10 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Org 27569 is a potent CB1 receptor allosteric modulator, which increases agonist binding, yet blocks agonist-induced CB1 signaling.

In Vitro

Org 27569 enhances agonist (CP55940) binding, promotes agonist binding to CB1 yet inhibits agonist-induced G protein activation and blocks the agonist-induced conformational changes in TM6. Org 27569 inhibits agonist-induced TM6 movement in CB1 detected by a fluorescent probe on site 342[2]. Org 27569 produces a significant, but saturable, increase in

	the level of specific [^{3}H]CP 55,940 binding. Org 27569 (1 μM) inhibits electrically evoked contractions of the mouse vas deferens with the pEC_{50} and E_{max} being 8.66±0.11 and 77% (95% confidence limits, 70.6-82.7), respectively[4]. In hCB1R cells, Org 27569 (1 and 10 μM) behaves as a weak inverse agonist producing a small but significant decrease in basal [^{35}S]GTPγS binding. Org 27569 is less effective as an inhibitor of WIN55212-mediated inhibition of forskolin-stimulated cAMP production. Org 27569 induces a small but significant level of ERK1/2 phosphorylation with an E_{max} of 19% and pEC_{50} value of 8.55±0.99[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ORG 27569 (3.2 and 5.6 mg/kg, i.p.) significantly attenuates cocaine associated cue-induced reinstatement, cocaine priming-induced reinstatement, methamphetamine associated cue-induced reinstatement and methamphetamine priming-induced reinstatement in rat[1]. Org27569 (30 mg/kg, i.p.) produces CB1-independent hypophagic effects and does not affect the discriminative stimulus effects of anandamide (AEA). Org27569 (100 μg intracerebroventricularly) does not affect the pharmacologic effects of systemically administered CP55,940 compared with vehicle[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [4]	Binding assays are performed with the CB1 receptor agonist [^{3}H]CP 55,940 (0.7 nM) and the CB1 receptor antagonist [^{3}H]SR 141716A (1.2 nM), 1 mg/mL BSA and 50 mM Tris buffer containing 0.1 mM EDTA and 0.5 mM $MgCl_2$, pH 7.4, in a total assay volume of 500 μL. Binding is initiated by the addition of mouse brain membranes (30 μg). Assays are carried out at 37°C for 60 min before termination by addition of ice-cold wash buffer (50 mM Tris buffer and 1 mg/mL BSA) and vacuum filtration using a 24-well sampling manifold and Whatman GF/B glass-fiber filters that have been soaked in wash buffer at 4°C for 24 h. Each reaction tube is washed five times with a 4-mL aliquot of buffer. The filters are oven-dried for 60 min and then placed in 5 mL of scintillation fluid, and radioactivity is quantitated by liquid scintillation spectrometry. Specific binding is defined as the difference between the binding that occurs in the presence and absence of 1 μM concentrations of the corresponding unlabeled ligand and is 70 to 80% of the total binding. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Following a 1-week acclimation period, CB1 (+/+) and (−/−) mice are food-deprived, given an intraperitoneal injection of Org27569 (30 mg/kg), rimonabant (10 mg/kg; positive control), or vehicle at 23 h, and placed in a plastic cage with access to water. A premeasured amount (2.3-2.6 g) of sweet cereal or standard chow is placed in the test cage from 24 to 26h. All mice receive each treatment condition in a counterbalanced design, with at least 96 h between test days. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Jing L, et al. Effects of the cannabinoid CB? receptor allosteric modulator ORG 27569 on reinstatement of cocaine- and methamphetamine-seeking behavior in rats. Drug Alcohol Depend. 2014 Oct 1;143:251-6.

[2]. Fay JF, et al. A key agonist-induced conformational change in the cannabinoid receptor CB1 is blocked by the allosteric ligand Org 27569. J Biol Chem. 2012 Jul 30.

[3]. Gamage TF, et al. In-vivo pharmacological evaluation of the CB1-receptor allosteric modulator Org-27569. Behav Pharmacol. 2014 Apr;25(2):182-5.

[4]. Price MR, et al. Allosteric modulation of the cannabinoid CB1 receptor. Mol Pharmacol. 2005 Nov;68(5):1484-95.

[5]. Baillie GL, et al. CB(1) receptor allosteric modulators display both agonist and signaling pathway specificity. Mol Pharmacol. 2013 Feb;83(2):322-38.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA