产品名称：Org 27569
产品别名：Org 27569

生物活性：

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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 52.2 mg/mL (127.33 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 2.5 mg/mL (6.10 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (6.10 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (6.10 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.10 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.10 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Jing L, et al. Effects of the cannabinoid CB_1 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.

实验参考：

Animal Administration	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. [3]
Kinase Assay	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. [4]
	[1]. Jing L, et al. Effects of the cannabinoid CB_1 receptor allosteric modulator ORG 27569 on

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