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产品名称：Otenabant
产品别名：奥替那班； CP-945598

生物活性：

Description	Otenabant is a potent and selective cannabinoid receptor CB1 antagonist with Ki of 0.7 nM, exhibits 10,000-fold greater selectivity against human CB2 receptor.
IC_{50} & Target	Ki: 0.7 nM (CB1)
In Vitro	Otenabant HCl has low affinity with Ki of 7.6 μM for human CB2 receptors[1]. Otenabant HCl inhibits CB1 receptor with moderate unbound microsomal clearance, low hERG affinity, and adequate CNS penetration[2].
In Vivo	Otenabant acutely stimulates energy expenditure in rats and decreases the respiratory quotient indicating a metabolic switch to increased fat oxidation. Otenabant (10 mg/kg, p.o.) promotes a 9%, vehicle adjusted weight loss in a 10 day weight loss study in diet-induced obese mice[1]. Otenabant HCl reverses four cannabinoid agonistmediated behaviors (locomotor activity, hypothermia, analgesia, and catalepsy) following administration of the synthetic CB1 receptor agonist CP-55940. Otenabant HCl exhibits dose-dependent anorectic activity in a model of acute food intake in rodents and increased energy expenditure and fat oxidation[2].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**195.92 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9592 mL	9.7959 mL	19.5917 mL
	5 mM	0.3918 mL	1.9592 mL	3.9183 mL
	10 mM	0.1959 mL	0.9796 mL	1.9592 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: ≥ 3 mg/mL (5.88 mM); Clear solution

此方案可获得 ≥ 3 mg/mL (5.88 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 30.0 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: ≥ 3 mg/mL (5.88 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (5.88 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 30.0 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: ≥ 3 mg/mL (5.88 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (5.88 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 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. John R. Hadcock, et al. In vitro and in vivo pharmacology of CP-945,598, a potent and selective cannabinoid CB1 receptor antagonist for the management of obesity. Biochemical and Biophysical Research Communications, 2010; 394;366-371. [2]. Griffith DA, et al. Discovery of 1-[9-(4-chlorophenyl) -8-(2-chlorophenyl)- 9H-purin-6-yl] -4-ethylaminopiperidine-4-carboxylic acid amide hydrochloride (CP-945,598), a novel, potent, and selective cannabinoid type 1 receptor antagonist. JMedChem. 2009 ;5

实验参考：

Animal Administration	Male, 14 week old C57/Bl6/6J mice which has been maintained on a high fat diet (45% kcal from fat) for 6 weeks are selected for the DIO weight loss study. The animals body weights range at least five standard deviations from age-matched chow-fed control animals mean body weight. Mice are singly housed. The mean starting weight of all animals is 38.9±0.5 g. On day 0, mice are randomLy assigned to treatment groups (n=10 per group). Mice are dosed daily with vehicle or 10 mg/kg (p.o.) CP-945,598 over 10 days, starting approximately at 30 min before the start of the 12 h dark cycle. BW and food intake are recorded daily. Analysis of variance and comparison of means are calculated for daily and cumulative FI and cumulative BW measurements. $P < 0.05$ is considered statistically significant. [1]
Kinase Assay	Membranes are prepared from CHOK1 cells stably transfected with the human CB-1 receptor cDNA. GTPγ [^{35}S] binding assays are performed in a 96-well FlashPlate format in duplicate using 100 pM GTPγ [^{35}S] and 10μg membrane per well in assay buffer composed of 50 mM Tris HCl, pH 7.4, 3 mM $MgCl_2$, pH 7.4, 10 mM $MgCl_2$, 20 mM EGTA, 100 mM NaCl, 30 μM GDP, 0.1% bovine serum albumin, and the following protease inhibitors: 100 μg/mL bacitracin, 100 μg/mL benzamidine, 5 μg/mL aprotinin, 5 μg/mL leupeptin. The assay mix is then incubated with increasing concentrations of antagonist (10^{-10} M to 10^{-5} M) for 10 min and challenged with the cannabinoid agonist CP-55,940 (10 μM). Assays are performed at 30°C for 1 h. The FlashPlates are then centrifuged at 2000 g for 10 min. Stimulation of GTPγ [^{35}S] binding is then quantified using a Wallac Microbeta. EC_{50} calculations are done using Prism by GraphPad. Inverse agonism is measured in the absence of agonist. [2]
	[1]. John R. Hadcock, et al. In vitro and in vivo pharmacology of CP-945,598, a potent and selective cannabinoid CB1 receptor antagonist for the management of obesity. Biochemical and Biophysical Research Communications, 2010; 394;366-371.

References	[2]. Griffith DA, et al. Discovery of 1-[9-(4-chlorophenyl) -8-(2-chlorophenyl)- 9H-purin-6-yl] -4-ethylaminopiperidine-4-carboxylic acid amide hydrochloride (CP-945,598), a novel, potent, and selective cannabinoid type 1 receptor antagonist. JMedChem. 2009 ;5