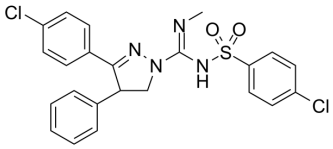
(±)-Ibipinabant

Cat. No.:	HY-14791A
CAS No.:	362519-49-1
Molecular Formula:	$C_{23}H_{20}Cl_2N_4O_2S$
Molecular Weight:	487.4
Target:	Cannabinoid Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 31 mg/mL (63.60 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent, Mass	1 mg	5 mg	10 mg
1 mM	2.0517 mL	10.2585 mL	20.5170 mL
5 mM	0.4103 mL	2.0517 mL	4.1034 mL
10 mM	0.2052 mL	1.0259 mL	2.0517 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 (5.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

(±)-Ibipinabant ((±)-SLV319) is the racemate of SLV319. (±)-Ibipinabant ((±)-SLV319) is a potent and selective cannabinoid-1 (CB-1) receptor antagonist with an IC_{50} of 22 nM.

IC_{50} & Target

IC50: 22 nM (CB-1)[1]; Ki: 7.8 nM (CB-1)[2]

In Vitro

Cannabinoid receptor 1 (CB1R) antagonists appear to be promising drugs for the treatment of obesity, however, serious side effects have hampered their clinical application. Ibipinabant is a new, potent [K_i (CB1)=7.8 nM] and selective [K_i (CB2)=7.943 nM] CB1 antagonist [pA2 for arachidonic acid release in CHO cells=9.9] with in vitro pharmacological characteristics similar to rimonabant including inverse agonism and brain penetrance[3].

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

In Vivo	(±)-Ibipinabant ((±)-SLV319) (3 mg/kg) reduces unfasted glucose to a significantly greater degree than rimonabant at the same dose on days 17, 28 and 38. Chronic treatment with (±)-Ibipinabant ((±)-SLV319) significantly attenuates the progression of diabetes in ZDF rats, blunting the increase in blood glucose and HbA1c over time. Ibipinabant also reduces the hyperinsulinemia apparent at 6-8 weeks of age and attenuates the dramatic reduction in insulin levels observed 1-2 weeks later[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3]	Rats: SLV319, rimonabant and rosiglitazone are suspended in a 10% dimethylacetamide, 10% cremophor, 10% ethanol and 70% water vehicle. Drugs are administered by oral gavage in a volume of 2 mL/kg body weight at 09:00 hours every day. Treatment groups are as follows: (i) Vehicle: ad libitum access to food (vehicle), (ii) Vehicle: restricted access to food (20% less than average food intake of ad libitum vehicle-treated group for the first 3 days of the study, then 10% less than the average food intake of the ad libitum vehicle-treated group for the remainder of the study) (restricted), (iii) Rosiglitazone (4 mg/kg), (iv) Rimonabant (3 mg/kg) (RIM 3 mg/kg), (v) Rimonabant (10 mg/kg) (RIM 10 mg/kg), (vi) (±)-Ibipinabant ((±)-SLV319) (3 mg/kg) (IBI 3 mg/kg) and (vii) Ibipinabant (10 mg/kg) (IBI 10 mg/kg). Rosiglitazone is used as a positive control for its ability to delay β-cell decline, and rimonabant is used as a positive control for CB1 antagonism[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Chorvat RJ, et al. JD-5006 and JD-5037: peripherally restricted (PR) cannabinoid-1 receptor blockers related to SLV-319 (Ibipinabant) as metabolic disorder therapeutics devoid of CNS liabilities. Bioorg Med Chem Lett. 2012 Oct 1;22(19):6173-80.

[2]. Lange JH, et al. Synthesis, biological properties, and molecular modeling investigations of novel 3,4-diarylpyrazolines as potent and selective CB(1) cannabinoid receptor antagonists. J Med Chem. 2004 Jan 29;47(3):627-43.

[3]. Rohrbach K, et al. Ibipinabant attenuates β-cell loss in male Zucker diabetic fatty rats independently of its effects on body weight. Diabetes Obes Metab. 2012 Jun;14(6):555-64.

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