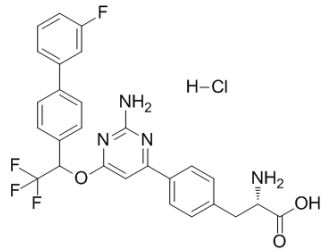
LP-533401 hydrochloride

Cat. No.:	HY-15849A
CAS No.:	1040526-12-2
Molecular Formula:	$C_{27}H_{23}ClF_4N_4O_3$
Molecular Weight:	562.94
Target:	Tryptophan Hydroxylase
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (**44.41 mM;** Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7764 mL	8.8819 mL	17.7639 mL
	5 mM	0.3553 mL	1.7764 mL	3.5528 mL
	10 mM	0.1776 mL	0.8882 mL	1.7764 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 (4.44 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: 2.5 mg/mL (4.44 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description	LP-533401 hydrochloride is a **tryptophan hydroxylase 1** inhibitor that regulates serotonin production in the gut.
IC_{50} & Target	Tryptophan hydroxylase 1[1]
In Vitro	LP-533401 hydrochloride is a tryptophan hydroxylase 1 inhibitor. LP-533401 (1 μM) completely inhibits serotonin production in Tph1-expressing cells (RBL2H3 cells) after treatment for 3 days[1].
In Vivo	Oral administration once daily for up to 6 weeks of LP-533401 (25, 100 or 250 mg/kg) dose-dependently prevents the development of and fully rescues, osteoporosis in ovariectomized rodents because of an isolated increase in bone

formation. Pharmacokinetic studies in rodents show that LP-533401 level in the brain is negligible following oral administration, indicating that it is virtually unable to cross the blood-brain barrier[1]. Mice treated repeatedly with LP-533401 (30-250 mg/kg per day) exhibit marked 5-HT content reductions in the gut, lungs, and blood, but not in the brain. After a single LP-533401 dose (250 mg/kg), lung and gut 5-HT contents decrease by 50%, whereas blood 5-HT levels remain unchanged, suggesting gut and lung 5-HT synthesis[2]. Adult, healthy mice treated with the Tph-1 inhibitor LP-533401 show 30% decrease in circulating serotonin levels, with a consequent 30% increase in osteoblast numbers. Administration of LP-533401 to mice injected with EL4 cells inhibits the decrement in osteoblast numbers and trabecular bone volume, prolongs survial, and decreases leukemic infiltration[3].

PROTOCOL

Animal Administration [1]

Mice[1]

Mice are treated from day 1 post-ovariectomy for 4 weeks with **LP-533401 (1, 10, 100 or 250 mg per kg body weight per day)** or vehicle. Next mice are treated for 4 weeks starting 2 weeks post-ovariectomy with **LP-533401 (250 mg per kg body weight per day)** or vehicle. lastly, mice are treated for 6 weeks starting 6 weeks post-ovariectomy with **LP-533401 (25, 100 or 250 mg per kg body weight per day)** or vehicle[1].

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

REFERENCES

[1]. Yadav, V.K., et al. Inhibition of gut-derived serotonin synthesis: A potential bone anabolic treatment. Nat. Med. 16(3), 308-312 (2010).

[2]. Abid S, et al. Inhibition of gut- and lung-derived serotonin attenuates pulmonary hypertension in mice. Am J Physiol Lung Cell Mol Physiol. 2012 Sep 15;303(6):L500-8.

[3]. Krevvata M, et al. Inhibition of leukemia cell engraftment and disease progression in mice by osteoblasts. Blood. 2014 Oct 30;124(18):2834-46.

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