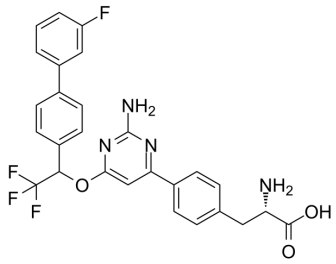
LP-533401

Cat. No.:	HY-15849
CAS No.:	945976-43-2
Molecular Formula:	$C_{27}H_{22}F_4N_4O_3$
Molecular Weight:	526.48
Target:	Tryptophan Hydroxylase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



BIOLOGICAL ACTIVITY

Description	LP-533401 is a Tryptophan hydroxylase 1 inhibitor that regulates serotonin production in the gut.
IC_{50} & Target	Tryptophan hydroxylase[1]
In Vitro	LP-533401 completely inhibits serotonin production in Tph1–expressing cells (RBL2H3 cells) at a dose of 1 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral administration once daily for up to 6 weeks of this small molecule prevents the development of and fully rescues, in a dose-dependent manner, 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 LP533401 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 LP533401 to mice injected with EL4 cells inhibits the decrement in osteoblast numbers and trabecular bone volume, prolongs survial, and decreases leukemic infiltration[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: 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.

CUSTOMER VALIDATION

- Life Sci. 2021 Sep 29;285:120002.
- Cell Signal. 2023 Jan 26;105:110612.

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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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