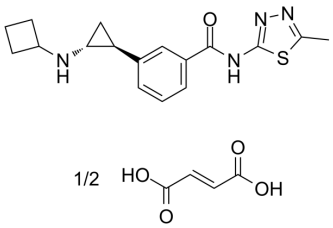
T-448

Cat. No.:	HY-122635A
CAS No.:	1597426-53-3
Molecular Formula:	$C_{17}H_{20}N_4OS.{}_1/_2C_4H_4O_4$
Molecular Weight:	386.5
Target:	Histone Demethylase
Pathway:	Epigenetics
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (43.13 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5873 mL	12.9366 mL	25.8732 mL
	5 mM	0.5175 mL	2.5873 mL	5.1746 mL
	10 mM	0.2587 mL	1.2937 mL	2.5873 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: ≥ 1.67 mg/mL (4.32 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (4.32 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (4.32 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

T-448 is a specific, orally active and irreversible inhibitor of lysine-specific demethylase 1 (LSD1, an H3K4 demethylase), with an IC_{50} of 22 nM. T-448 enhances H3K4 methylation in primary cultured rat neurons[1].

IC_{50} & Target

IC50: 22 nM (LSD1)[1].

In Vitro

T-448 enhances the levels of H3K4 methylation, increased mRNA expression of neural plasticity-related genes including brain derived neurotrophic factor (Bdnf), and ameliorated learning dysfunction[1].

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

RT-PCR[1].

Cell Line:	Primary cultured rat neurons.
Concentration:	0-10 μM.
Incubation Time:	1 day treatment.
Result:	Increased Ucp2 H3K4me2 and Ucp2 mRNA significantly.

In Vivo

T-448 has minimal impact on the LSD1-GFI1B complex and a superior hematological safety profile in mice via the generation of a compact formyl-FAD adduct. T-448 increases brain H3K4 methylation and partially restored learning function in mice with NMDA receptor hypofunction[1].

T-448 increases H3K4 methylation in the brain without causing hematological side effects even at 100 mg/kg[1].

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

Animal Model:	NR1-hypo mice[1].
Dosage:	1, 10 mg/kg.
Administration:	Orally, 3 weeks.
Result:	Dose-dependently increased the H3K4me2 levels around Bdnf, Arc, and Fos genes inthe mouse hippocampus. Resulted in partial but statistically significant and dosedependent rescue effects on the rate of correct choices in NR1-hypo mice.

REFERENCES

[1]. Matsuda S, et al. T-448, a specific inhibitor of LSD1 enzyme activity, improves learning function without causing thrombocytopenia in mice. Neuropsychopharmacology. 2018 Dec 22.

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