TAK-418

Cat. No.: HY-138830

CAS No.: 1818252-53-7

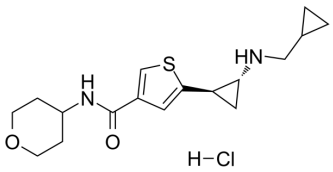
Molecular Formula: $C_{17}H_{25}ClN_2O_2S$

Molecular Weight: 356.91

Target: Histone Demethylase

Pathway: Epigenetics

Storage: -20°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 55 mg/mL (154.10 mM; ultrasonic and warming and heat to 60°C)

H_2O : ≥ 16.67 mg/mL (46.71 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8018 mL	14.0091 mL	28.0183 mL
5 mM	0.5604 mL	2.8018 mL	5.6037 mL
10 mM	0.2802 mL	1.4009 mL	2.8018 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: ≥ 5.5 mg/mL (15.41 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5.5 mg/mL (15.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TAK-418 is a selective, orally active LSD1 (KDM1A) enzyme inhibitor with an IC_{50} of 2.9 nM. TAK-418 unlocks aberrant epigenetic machinery and improves autism symptoms in neurodevelopmental disorder models[1][2].

In Vivo

TAK-418 (1 mg/kg; p.o.; once daily for 14 days) ameliorates some autism spectrum disorder (ASD) -like behaviors in neurodevelopmental disorder model rodents[1].

TAK-418 increases H3K4me1/2/3 and H3K9me2 levels at the Ucp2 gene and induced Ucp2 mRNA expression in primary cultured rat neurons. TAK-418 also increases H3K4me1/2/3 at the Bdnf gene. TAK-418 avoids the steric interference with GFI1B in the binding pocket through the generation of a compact formylated adduct form of coenzyme flavin adenine dinucleotide (FAD). TAK-418 shows a good pharmacokinetic profile in rodents and inhibits LSD1 enzyme activity in the brain

	without causing hematological toxicity in rodents[1]. Single administration of TAK-418 at 1 or 3 mg/kg increases H3K4me2 levels at Ucp2 gene in the mouse brain[1]. TAK-418 can ameliorate neurological problems at the cellular, molecular, gene expression, and functional levels in a mouse model of KS ($Kmt2d^{+/\beta Geo}$ mice)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Baba R, et al. LSD1 enzyme inhibitor TAK-418 unlocks aberrant epigenetic machinery and improves autism symptoms in neurodevelopmental disorder models. Sci Adv. 2021;7(11):eaba1187. Published 2021 Mar 12.

[2]. Zhang L, et al. Inhibition of KDM1A activity restores adult neurogenesis and improves hippocampal memory in a mouse model of Kabuki syndrome. Mol Ther Methods Clin Dev. 2021;20:779-791. Published 2021 Feb 18

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