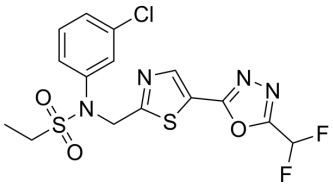
TYA-018

Cat. No.:	HY-153392
CAS No.:	2653254-31-8
Molecular Formula:	$C_{15}H_{13}ClF_2N_4O_3S_2$
Molecular Weight:	434.87
Target:	HDAC; Oxidative Phosphorylation
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (229.95 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2995 mL	11.4977 mL	22.9954 mL
5 mM	0.4599 mL	2.2995 mL	4.5991 mL
10 mM	0.2300 mL	1.1498 mL	2.2995 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 (5.75 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.75 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.75 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

TYA-018 is an orally active, potent and highly selective HDAC6 inhibitor. TYA-018 can protect heart function in mice. TYA-018 also enhances energetics in mice by increasing expression of targets associated with fatty acid metabolism, protein metabolism, and oxidative phosphorylation[1].

IC_{50} & Target

HDAC6

In Vivo

TYA-018 (15 mg/kg, Oral gavage, daily, for 8 weeks) protects against sarcomere damage and reduced Nppb expression in

BAG3^{cKO} mice[1].

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

Animal Model:	BAG3^{cKO} mice[1]
Dosage:	15 mg/kg
Administration:	Oral gavage, daily, starting at 2 months old, for 8 weeks
Result:	Conferred cardioprotection in mice. Significantly reduced Nppb expression to near WT. Reduced fibrosis in BAG3^{cKO} mice, albeit not significantly. partially restored protein expression of FLNC, PINK1, VDAC2, and p62 to amounts similar to WT mice. Significantly reduced the percentage of cardiomyocytes with damaged and reduced sarcomeres in BAG3^{cKO} mice. Significantly reduced mitochondrial content to amounts similar to WT mice.

REFERENCES

[1]. Yang J, et al. Phenotypic screening with deep learning identifies HDAC6 inhibitors as cardioprotective in a BAG3 mouse model of dilated cardiomyopathy. Sci Transl Med. 2022 Jul 6;14(652):eabl5654.

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