Raphin1

Cat. No.: HY-123960

CAS No.: 2022961-17-5

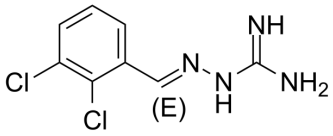
Molecular Formula: $C_8H_8Cl_2N_4$

Molecular Weight: 231.08

Target: Phosphatase

Pathway: Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (540.94 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.3275 mL	21.6375 mL	43.2751 mL
	5 mM	0.8655 mL	4.3275 mL	8.6550 mL
	10 mM	0.4328 mL	2.1638 mL	4.3275 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: ≥ 2.08 mg/mL (9.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (9.00 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (9.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Raphin1 is an orally bioavailable, selective inhibitor of the regulatory phosphatase PPP1R15B (R15B). Raphin1 binds strongly to the R15B-PP1c holophosphatase (K_d=33 nM), and shows ~30-fold selective in binding R15B-PP1c over R15A-PP1c. Raphin1 crosses the blood-brain barrier, and reduces organismal and molecular deficits in a mouse model of a protein misfolding disease[1].

IC_{50} & Target

Kd≈33 nM (R15B-PP1c holophosphatase)[1]

In Vitro

Raphin1 causes a rapid and transient accumulation of its phosphorylated substrate, resulting in a transient attenuation of protein synthesis[1].

	Raphin1 inhibits the recombinant R15B-PP1c holoenzyme, but not the closely related R15A-PP1c, by interfering with substrate recruitment[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Raphin1 improves weight of HD^{82Q} mice treated from 4 to -10 weeks of age with 2 mg/kg of Raphin1 once a day by oral gavage. Raphin1 also decreases SDS-insoluble huntingtin assemblies and nuclear inclusions in the cortex of HD^{82Q} mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Krzyzosiak A, et al. Target-Based Discovery of an Inhibitor of the Regulatory Phosphatase PPP1R15B. Cell. 2018 Aug 23;174(5):1216-1228.e19.

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