Rho-Kinase-IN-2

Cat. No.: HY-150640

CAS No.: 2573071-18-6

Molecular Formula: $C_{20}H_{25}FN_4O_2$

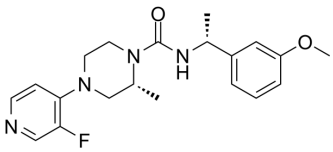
Molecular Weight: 372.44

Target: ROCK

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Stem Cell/Wnt; TGF-beta/Smad

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 : 50 mg/mL (134.25 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6850 mL	13.4250 mL	26.8500 mL
5 mM	0.5370 mL	2.6850 mL	5.3700 mL
10 mM	0.2685 mL	1.3425 mL	2.6850 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 mg/mL (5.37 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2 mg/mL (5.37 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (5.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rho-Kinase-IN-2 (Compound 23) is an orally active, selective, and central nervous system (CNS)-penetrant Rho Kinase (ROCK) inhibitor (ROCK2 IC_{50}=3 nM). Rho-Kinase-IN-2 can be used in Huntington's research[1].

IC_{50} & Target

ROCK2
3 nM (IC_{50})

In Vitro

Rho-Kinase-IN-2 (0-10 mM, 1 hour) treatment shows an increase in AKT phosphorylation and a decrease in MYPT1

phosphorylation[1].

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

Western Blot Analysis[1]

Cell Line:	A7r5 and PANC1 cells
Concentration:	0-10 mM
Incubation Time:	1 hour
Result:	Showed concentration-dependent effects, leading to an increase in AKT phosphorylation (EC_{50}=28 nM) and a decrease in MYPT1 phosphorylation (IC_{50}=14 nM).

In Vivo

Rho-Kinase-IN-2 (oral adiministration; 10 mg/kg; 6 times; 0.5, 1, 2, 4, 8, and 12 h) treatment shows dose- and time-dependent ROCK1 and ROCK2 target engagement[1].

Rho-Kinase-IN-2 (oral adiministration; 10 or 20 mg/kg; QD or BID; 2 weeks) treatment shows excellent tolerability assessment[1].

Rho-Kinase-IN-2 (oral adiministration; 1-20 mg/kg; once) treatment shows a direct dose- and time-dependent relationship between brain exposure and MYPT1 phosphorylation status[1].

Rho-Kinase-IN-2 (oral adiministration; 10 or 20 mg/kg; once) treatment decreases in the mean arterial, systolic, diastolic blood pressure, and heart rate[1].

Rho-Kinase-IN-2 (oral adiministration; 10 mg/kg; twice a day; 90 days) treatment leads to lower-than-expected brain concentrations[1].

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

Animal Model:	Male C57BL/6 mice[1]
Dosage:	10 mg/kg
Administration:	Oral adiministration; 10 mg/kg; 6 times; 0.5, 1, 2, 4, 8, and 12 h
Result:	Observed dose- and time-dependent ROCK1 and ROCK2 TE, with a free brain KiNativ ROCK1 and ROCK2 IC_{50}=Ø6 nM.

Animal Model:	3−4 months old heterozygote Q175DN KI and wild-type littermate mice[1]
Dosage:	10 or 20 mg/kg
Administration:	Oral adiministration; 10 or 20 mg/kg; once a day or twice a day; 2 weeks
Result:	Scored neurological index normally at all doses although a slight loss in bodyweight (Ø2%) in the 20 mg/kg treatment group.

Animal Model:	Heterozygote HTT zQ175DN knock-in mice[1]
Dosage:	1-20 mg/kg
Administration:	Oral adiministration; 1-20 mg/kg; once
Result:	Remained over MYPT1 IC_{50} for over 2 h of the free brain at 10 mg/kg, and observed the dose- and time-dependent inhibition of MYPT1 phosphorylation in the striatum following acute in vivo dosing.

Animal Model:	CD1 mice[1]
Dosage:	10 and 20 mg/kg
Administration:	Oral adiministration; 10 or 20 mg/kg; once
Result:	Observed the decreases in the mean arterial (maximum change of 61.0 ± 8.5 mmHg from baseline), systolic (maximum change of 59.5 ± 8.4 mmHg from baseline), diastolic blood pressure (maximum change of 56.4 ± 9.0 mmHg from baseline), and heart rate (maximum change from predose of 107 bpm) when compared to the control group from 0.5 to 2 h post dose.

Animal Model:	Heterozygote Q175DN KI mouse model of HD[1]
Dosage:	10 mg/kg
Administration:	Oral adiministration; 10 mg/kg; twice a day; 90 days
Result:	Led to lower-than-expected brain concentrations compared to single dosing.

REFERENCES

[1]. Tammy Ladduwahetty, et al. Identification of a Potent, Selective, and Brain-Penetrant Rho Kinase Inhibitor and its Activity in a Mouse Model of Huntington's Disease. J Med Chem. 2022 Jul 11.

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