Remodelin hydrobromide

Cat. No.: HY-16706A

CAS No.: 1622921-15-6

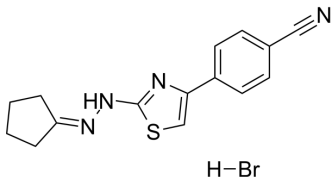
Molecular Formula: $C_{15}H_{15}BrN_4S$

Molecular Weight: 363.28

Target: Histone Acetyltransferase

Pathway: Epigenetics

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 44 mg/mL (121.12 mM)
H_2O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7527 mL	13.7635 mL	27.5270 mL
5 mM	0.5505 mL	2.7527 mL	5.5054 mL
10 mM	0.2753 mL	1.3763 mL	2.7527 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 15% Cremophor EL >> 85% Saline
   Solubility: 10 mg/mL (27.53 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.88 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.88 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Remodelin hydrobromide is an orally active and selective inhibitor of acetyltransferase NAT10. Remodelin hydrobromide inhibits NAT10 activitity and slows DNA replication and suppresses growth of prostate cancer cells. Remodelin hydrobromide inhibits the growth of prostate cancer and hepatocellular carcinoma in xenograft model. Remodelin hydrobromide enhances the healthspan in hutchinson-gilford progeria syndrome (HGPS) mouse model[1][2][3][4].

In Vitro

Remodelin hydrobromide (10-40 μM, 1-7 days) inhibits NAT10 activity and cell proliferation with a dose-dependent manner in both AR-positive and AR-negative prostate cancer cells[2].
Remodelin hydrobromide (20 μM, 24 hours) inhibits NAT10 and slows DNA replication in prostate cancer cells[2].
Remodelin hydrobromide (1 μM, 7 days) decreases nuclear shape defects and increase genomic stability in Lmna$^{G609G/G609G}$ fibroblasts[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	Prostate cancer cell lines VCaP, PC3, and DU145
Concentration:	0,10,20,40 μM
Incubation Time:	1,2,7 days
Result:	Inhibited NAT10 and suppressed the growth of both AR-positive and AR-negative prostate cancer cells. Displayed significantly decreased cell proliferation activity over time, compared to the control group. Decreased colony formation ability with a dose-dependent manner.

Immunofluorescence[2]

Cell Line:	Prostate cancer cell lines VCaP, PC3, and DU145
Concentration:	20 μM
Incubation Time:	24 h
Result:	Showed a significant decrease in both the positive labeling rate and the fluorescence intensity compared to the control group. Significantly reduced both the staining foci of IdU and the staining foci of CldU compared to control group.

Western Blot Analysis[3]

Cell Line:	Skin fibroblasts from Lmna$^{G609G/G609G}$ and wildtype (WT) littermates
Concentration:	1 μM
Incubation Time:	7 days
Result:	Decreased the higher level of the DNA double-strand break (DSB) marker gamma H2AX (γ H2AX, Ser-139 phosphorylated histone H2AX).

In Vivo

Remodelin hydrobromide (2 or 20 mg/kg, i.p., once every two days for 4 weeks) significantly reduces AR-negative prostate cancer tumor growth in tumor xenograft nude mice model[2].
Remodelin hydrobromide (100 mg/kg, p.o.) inhibits NAT10 and significantly enhances the healthspan in aLmna$^{G609G/G609G}$ hutchinson-gilford progeria syndrome (HGPS) mouse model. Remodelin hydrobromide (5 mg/kg, p.o.) shows a $T_{1/2}$ of 1.81 hours and oral bioavailability (F%) of 43.5% in mice[3].
Pharmacokinetic parameters for Remodelin hydrobromide in Mice[1]
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Route	Dose (mg/kg)	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-t} (ng/h/mL)	$AUC_{0-\infty}$ (ng/h/mL)	MRT_last (h)	F(%)

p.o.	5	1.81	0.25	409	235	259	0.84	43.5%

Animal Model:	PC-3 cells tumor xenograft model in nude athymic BALB/c nu/nu mice[2]
Dosage:	2 or 20 mg/kg
Administration:	Intraperitoneal injection (i.p.), once every two days for 4 weeks
Result:	Significantly reduced AR-negative prostate cancer tumor growth. In the high-dose group, xenograft tumor weight at the endpoint was much smaller than that in the low-dose group.

Animal Model:	$Lmna^{G609G/G609G}$ hutchinson-gilford progeria syndrome (HGPS) mouse model[3]
Dosage:	100 mg/kg
Administration:	Oral gavage (p.o.), daily schedule for 3 weeks of age onward, until the end-point
Result:	Ameliorated age-dependent weight loss. Ameliorated cardiac pathology. Led to the dramatic amelioration of HGPS cardiac pathologies, including reduction of adventitial fibrosis of the aorta, rescue of vascular smooth muscle cell loss, and salvage of smooth muscle actin (SMA) loss, both in the aorta and the coronary arteries.

Animal Model:	WT Mice (Pharmacokinetic assay)[3]
Dosage:	5 mg/kg
Administration:	Oral gavage (p.o.)
Result:	Showed a $T_{1/2}$ of 1.81 hours and oral bioavailability (F%) of 43.5% in mice[3].

CUSTOMER VALIDATION

- Cell Death Dis. 2023 Nov 1;14(11):712.
- Cell Rep. 2023 Jul 17;42(7):112810.
- Acta Pharmacol Sin. 2023 Jun 5.
- Oncogene. 2021 Apr;40(15):2711-2724.
- Life Sci. 2023 Jul 17;121948.

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REFERENCES

[1]. Larrieu D, et al. Chemical inhibition of NAT10 corrects defects of laminopathic cells. Science. 2014 May 2;344(6183):527-32.

[2]. Ma N, et.al. Inhibition of N-Acetyltransferase 10 Suppresses the Progression of Prostate Cancer through Regulation of DNA Replication. Int J Mol Sci. 2022 Jun 12;23(12):6573.

[3]. Balmus G, et.al. Targeting of NAT10 enhances healthspan in a mouse model of human accelerated aging syndrome. Nat Commun. 2018 Apr 27;9(1):1700.

[4]. Zhang X, et.al. N-Acetyltransferase 10 Enhances Doxorubicin Resistance in Human Hepatocellular Carcinoma Cell Lines by Promoting the Epithelial-to-Mesenchymal Transition. Oxid Med Cell Longev. 2019 Jul 1;2019:7561879.

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