Resminostat hydrochloride

Cat. No.: HY-14718A

CAS No.: 1187075-34-8

Molecular Formula: $C_{16}H_{20}ClN_3O_4S$

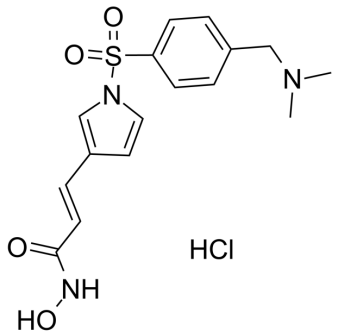
Molecular Weight: 385.87

Target: HDAC

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage: 4°C, sealed storage, away from moisture

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (129.58 mM)

H_2O : 7.14 mg/mL (18.50 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5915 mL	12.9577 mL	25.9155 mL
5 mM	0.5183 mL	2.5915 mL	5.1831 mL
10 mM	0.2592 mL	1.2958 mL	2.5915 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 (5.39 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (5.39 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Resminostat hydrochloride is a potent inhibitor of HDAC1, HDAC3 and HDAC6, with mean IC_{50} values of 42.5, 50.1, 71.8 nM, respectively, and shows less potent activities against HDAC8, with an IC_{50} of 877 nM.

IC_{50} & Target

HDAC1	HDAC3	HDAC6	HDAC8
42.5 nM (IC_{50})	50.1 nM (IC_{50})	71.8 nM (IC_{50})	877 nM (IC_{50})

In Vitro

Resminostat hydrochloride (Resminostat [HCl], 5 μM) induces histone acetylation in myeloma cells. Resminostat

hydrochloride displays a substrate competitive binding mode with a mean K_i value of 27 nM. Resminostat hydrochloride (5 μM) induces histone hyperacetylation in myeloma cells. Resminostat inhibits cell growth, induces apoptosis and inhibits MM cell proliferation. Resminostat (5 μM) also modulates expression of bcl-2 family proteins and inhibits Akt pathway signalling downstream of Akt. Resminostat exerts synergistic activity against myeloma cells when combined with common and new anti-myeloma agents[1]. Resminostat inhibits cell growth in head and neck squamous cell carcinoma cell lines, with IC_{50}s ranging from 0.775 μM to 1.572 μM (IC_{50} for SCC25: 0.775 μM; CAL27: 1.572 μM; and FaDu: 0.899 μM). Resminostat (1.25 and 2.5 μM) has a synergistic effect with irradiation on HNSCC cell lines. Resminostat in combination with cisplatin induces a downregulation of survivin. However, Resminostat shows no effect on Mcl-1 and p-AKT expression[2]. Resminostat reduces viability of HCC cells with the co-treatment of AZD-2014, with IC_{50}s ranging from 0.89 ± 0.12 μM to 0.07 ± 0.01 μM[3].

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

PROTOCOL

Kinase Assay [1]

Forty microliter enzyme buffer (15 mM Tris HCl pH 8.1, 0.25 mM EDTA, 250 mM NaCl, 10% v:v glycerol) containing HDAC1, 3, 6 or 8 activity, 29 μL enzyme buffer and 1 μL resminostat [HCl] at different concentrations are added to a 96-well microtitre plate and the reaction started by the addition of 30 μL substrate peptide Ac-NH-GGK(Ac)-AMC (HDAC1, 3 and 6 assays, final concentrations 6 μM for HDAC1, 10 μM for HDAC6 and 25 μM for HDAC3/DAD) or Ac-RHK(Ac)K(Ac)-AMC (HDAC8 assay, final concentration 50 μM). After incubation for 180 min (HDAC1, HDAC6, HDAC8) or 120 min (HDAC3) at 30°C, the reaction is terminated by the addition of 25 μL stop solution (50 mM Tris HCl pH 8, 100 mM NaCl, 0.5 mg/mL trypsin and 2 μM trichostatin A [TSA]). After incubation at room temperature for further 40 min, fluorescence is measured using a Wallac Victor2 1420 multilabel counter (extinction 355 nm, emission 460 nm) for quantification of AMC generated by tryptic cleavage of the deacetylated peptide. For the calculation of the 50% inhibitory concentration (IC_{50}) values the fluorescence in wells without test compound (1% DMSO, negative control) is set as 100% enzymatic activity and the fluorescence in wells with 2 μM TSA (positive control) are set at 0% enzymatic activity (background fluorescence substracted)[1].

Cell Assay [2]

A CCK-8 cell proliferation assay is used to investigate the antiproliferative effect of resminostat on HNSCC cells. Cells are seeded into 96-well plates at a density of 3×10^5/well. After 24 hours of growth, the cells are treated with resminostat and cisplatin, either alone or in combination and incubated for 72 hours. Untreated cells maintained in RPMI and equal concentrations of dimethylsulfoxide served as control. After 72 hours, cell proliferation is measured by CCK-8. Experiments are carried out in triplicate 3 times[2].

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CUSTOMER VALIDATION

- Acta Pharmacol Sin. 2021 Apr 13.
- Methods Mol Biol. 2018;1711:351-398.

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REFERENCES

[1]. Mandl-Weber S, et al. The novel inhibitor of histone deacetylase resminostat (RAS2410) inhibits proliferation and induces apoptosis in multiple myeloma (MM) cells. Br J Haematol. 2010 May;149(4):518-28.

[2]. Enzenhofer E, et al. Effect of the histone deacetylase inhibitor resminostat on head and neck squamous cell carcinoma cell lines. Head Neck. 2017 May;39(5):900-907.

[3]. Peng X, et al. mTOR inhibition sensitizes human hepatocellular carcinoma cells to resminostat. Biochem Biophys Res Commun. 2016 Sep 2;477(4):556-562.