Mocetinostat

Cat. No.: HY-12164

CAS No.: 726169-73-9

Molecular Formula: $C_{23}H_{20}N_6O$

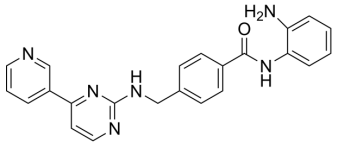
Molecular Weight: 396.44

Target: HDAC; Autophagy; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (126.12 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5224 mL	12.6122 mL	25.2245 mL
5 mM	0.5045 mL	2.5224 mL	5.0449 mL
10 mM	0.2522 mL	1.2612 mL	2.5224 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 (5.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mocetinostat (MGCD0103) is a potent, orally active and isotype-selective HDAC (Class I/IV) inhibitor with IC_{50}s of 0.15, 0.29, 1.66 and 0.59 μM for HDAC1, HDAC2, HDAC3 and HDAC11, respectively. Mocetinostat shows no inhibition on HDAC4, HDAC5, HDAC6, HDAC7, or HDAC8.

IC_{50} & Target

HDAC1	HDAC2	HDAC11	HDAC3
0.15 μM (IC_{50})	0.29 μM (IC_{50})	0.59 μM (IC_{50})	1.66 μM (IC_{50})

In Vitro

Mocetinostat is a potent, orally active and isotype-selective HDAC (Class I/IV) inhibitor with IC_{50}s of 0.15, 0.29, 1.66 and 0.59 μM for HDAC1, HDAC2, HDAC3 and HDAC11, respectively. Mocetinostat shows no inhibition on HDAC4, HDAC5, HDAC6, HDAC7, or HDAC8. Mocetinostat (MGCD0103) exhibits potent and selective antiproliferative activities against a broad spectrum of

	human cancer cell lines in vitro, and HDAC inhibitory activity is required for these effects. In all cell lines tested, Mocetinostat (MGCD0103) partially inhibits cellular HDAC enzyme activity although the maximal inhibition of activity varies among cell lines from 75% to 85% of total activity. The IC_{50} of Mocetinostat in intact cancer cells is independent of tissue origin. In A549 cells, MGCD0103 shows dose-dependent inhibition of HDAC activity in whole cells. At high concentrations in A549 cells, Mocetinostat inhibits a maximum of 80% of total activity. In HCT116 cells, Mocetinostat induces a significant S-phase depletion and both G_1 and G_2-M accumulation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Mocetinostat (MGCD0103) significantly inhibits growth of human tumor xenografts in nude mice in a dose-dependent manner and the antitumor activity correlated with induction of histone acetylation in tumors. The p.o. administration of Mocetinostat (MGCD0103) (2HBr salt) significantly reduces growth of implanted advanced A549 tumors in nude mice in a dose-dependent manner after 13 days of daily administration. Mocetinostat (170 mg/kg for 2HBr salt, corresponding to 120 mg/kg of free base) significantly blocks growth of tumors compared with vehicle treatment alone ($P<0.05$ in post-ANOVA Dunnett's test) with no change in body weight[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells in 96-well plates are incubated with Mocetinostat at various concentrations for 72 h at 37°C in 5% CO_2. MTT is added at a final concentration of 0.5 mg/mL and incubated with the cells for 4 h before an equal volume of solubilization buffer [50% N,N-dimethylformamide, 20% SDS (pH 4.7)] is added. After overnight incubation, solubilized dye is quantified by reading at 570 nm using a reference at 630 nm. Absorbance values are converted to cell numbers according to a standard growth curve of the relevant cell line. The concentration which reduces cell numbers to 50% relative to DMSO-treated cells is determined as MTT IC_{50}[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][2]	Mice[1] Female CD-1 nude mice, ages 8 to 10 wk are used. Tumor fragments (30 mg), which have been serially passaged thrice in vivo in minimal, are implanted s.c. through a small surgical incision on the flank of the mice while under general anesthesia. Mocetinostat is dissolved in vehicle (PBS acidified with 0.1 N HCl or PEG400/0.2 N HCl saline, 40:60) and dosed p.o. as solutions daily. Tumor volumes and body weight are monitored thrice weekly for at least 2 wk. Each experimental group containe six to eight animals. For pharmacokinetic study, blood is collected from animals at various time points, and plasma samples are analyzed. Rats[2] Forty rats (220±20 g) are randomly divided into four different dosages of Mocetinostat groups (Low group, Medium group, High group, and control group with 10 rats in each group). Mocetinostat is dissolved in corn oil as suspension at three different concentrations (20, 40, and 80 mg/mL). Three different Mocetinostat groups (Low group, Medium group, and High group) are respectively given Mocetinostat 20, 40, and 80 mg/kg one time by intragastric administration at every morning and last for 7 days. Control group are given saline by same administration method. At 8 days morning, six probe drugs, Bupropion, Phenacetin, Tolbutamide, Metoprolol, Testosterone, and Omeprazole, are mixed in corn oil and given to the rats of three Mocetinostat groups and control group by intragastric administration at a single dosage of 10 mg/kg for Bupropion, Phenacetin, Metoprolol, Testosterone, and Omeprazole and 1 mg/kg for Tolbutamide. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2022 Sep 14;8(1):92.
- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.

- Oncogene. 2023 Aug 31.
- Int J Oncol. 2020 Jun;56(6):1429-1441.

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REFERENCES

[1]. Fournel M, et al. MGCD0103, a novel isotype-selective histone deacetylase inhibitor, has broad spectrum antitumor activity in vitro and in vivo. Mol Cancer Ther. 2008 Apr;7(4):759-68.

[2]. Cai J, et al. The Effect of MGCD0103 on CYP450 Isoforms Activity of Rats by Cocktail Method. Biomed Res Int. 2015;2015:517295.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA