LMK-235

Cat. No.: HY-18998

CAS No.: 1418033-25-6

Molecular Formula: $C_{15}H_{22}N_2O_4$

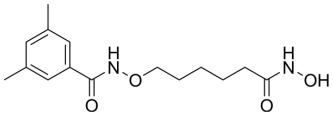
Molecular Weight: 294.35

Target: HDAC

Pathway: Cell Cycle/DNA Damage; Epigenetics

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 : ≥ 30 mg/mL (101.92 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.3973 mL	16.9866 mL	33.9732 mL
5 mM	0.6795 mL	3.3973 mL	6.7946 mL
10 mM	0.3397 mL	1.6987 mL	3.3973 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 (7.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.07 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LMK-235 is a potent and selective HDAC4/5 inhibitor, inhibits HDAC5, HDAC4, HDAC6, HDAC1, HDAC2, HDAC11 and HDAC8, with IC_{50}s of 4.22 nM, 11.9 nM, 55.7 nM, 320 nM, 881 nM, 852 nM and 1278 nM, respectively, and is used in cancer research.

IC_{50} & Target

HDAC5 4.22 nM (IC_{50})	HDAC4 11.9 nM (IC_{50})	HDAC6 55.7 nM (IC_{50})	HDAC1 320 nM (IC_{50})
HDAC11	HDAC2	HDAC8	

	852 nM (IC_{50})	881 nM (IC_{50})	1278 nM (IC_{50})

In Vitro

LMK-235 shows cytotoxic activity against human ovarian cancer cell lines A2780 and A2780 CisR, with IC_{50}s of 0.49 μM and 0.32 μM, respectively. LMK-235 inhibits HDAC in A2780 and A2780 CisR cell lines, with IC_{50}s of 0.65 μM and 0.32 μM, respectively. LMK-235 produces a higher reduction in cell viability in comparison to the combination of cisplatin and vorinostat in all cell lines[1]. LMK-235 (0, 0.625, 1.25, 2.5, 5, 10, and 20 μM) reduces the proliferation of BC cells in a dose- and time-dependent manner. LMK-235 (0-800 nM) also inhibits the growth of BC cells. Moreover, LMK-235 synergizes with bortezomib in BC cell lines[2]. LMK235 (2, 20?nM) decreases in HDAC4 nuclear accumulation in Cdkl5 -/Y NPCs, completely restores the reduced number of neurons generated from Cdkl5 -/Y NPCs. LMK235 also restores histone 3 acetylation in Cdkl5 -/Y NPCs. LMK235 causes a notable increase in the isoform IV, but does not affect BDNF isoforms I or II[3].

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

In Vivo

LMK235 (5 and 20?mg/kg) restores survival and maturation of postmitotic granule neurons in Cdkl5 -/Y mice. LMK235 also restores synapse development in the dentate gyrus and hippocampus of Cdkl5 -/Y mice. Furthermore, LMK235 restores hippocampus-dependent learning and memory in Cdkl5 -/Y mice[3].

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PROTOCOL

Cell Assay [1]

The rate of cell survival under the action of test substances is evaluated by an improved MTT assay. The assay is based on the ability of viable cells to metabolize yellow 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) to violet formazan that can be detected spectrophotometrically. In brief, A2780, Cal27, Kyse510, and MDA-MB-231 cell lines are seeded at a density of 5000, 7000, 8000, and 10 000 cells/well in 96-well plates. After 24 h, cells are exposed to increased concentrations of the test compounds. Incubation is ended after 72 h, and cell survival is determined by addition of MTT solution (5 mg/mL in phosphate buffered saline). The formazan precipitate is dissolved in DMSO. Absorbance is measured at 544 and 690 nm in a FLUOstar microplate reader[1].

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

CUSTOMER VALIDATION

- Theranostics. 2022 Jan 31;12(5):2080-2094.
- Cancer Lett. 2023 Apr 4;216158.
- Acta Biomater. 2022 Jun;145:297-315.
- JCI Insight. 2021 Dec 7;e153948.
- J Transl Med. 2021 Jun 12;19(1):258.

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REFERENCES

[1]. Marek L, et al. Histone deacetylase (HDAC) inhibitors with a novel connecting unit linker region reveal a selectivity profile for HDAC4 and HDAC5 with improved activity against chemoresistant cancer cells. J Med Chem. 2013 Jan 24;56(2):427-36.

[2]. Li A, et al. HDAC5, a potential therapeutic target and prognostic biomarker, promotes proliferation, invasion and migration in human breast cancer. Oncotarget. 2016 Jun 21;7(25):37966-37978.

[3]. Trazzi S, et al. HDAC4: a key factor underlying brain developmental alterations in CDKL5 disorder. Hum Mol Genet. 2016 Sep 15;25(18):3887-3907.

Caution: Product has not been fully validated for medical applications. For research use only.

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