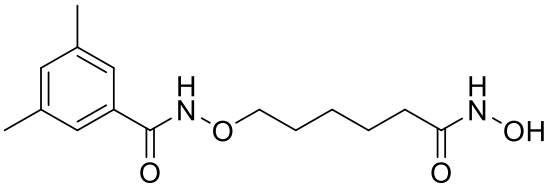
Product data sheet

MedKoo Cat#: 406579 Name: LMK-235 CAS#: 1418033-25-6 Chemical Formula: $C_{15}H_{22}N_2O_4$ Exact Mass: 294.15796 Molecular Weight: 294.35	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
LMK-235 is a selective histone deacetylase (HDAC) 4 and HDAC5 inhibitor. LMK-235 demonstrates activity against chemoresistant cancer cell lines in an MTT assay for cytotoxicity using human ovarian cancer cell lines A2780 and cisplatin resistant A2780CisR (IC50 = 0.49 and 0.32 μ M respectively).

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	29.43	100
Ethanol	29.43	100

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	3.40 mL	16.99 mL	33.97 mL
5 mM	0.68 mL	3.40 mL	6.79 mL
10 mM	0.34 mL	1.70 mL	3.40 mL
50 mM	0.07 mL	0.34 mL	0.68 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Li X, Guo Y, Kuang X, Zhao L, Li H, Cheng B, Wang W, Zhang Z, Liu P, Wang J. Histone deacetylase inhibitor LMK-235-mediated HO-1 expression induces apoptosis in multiple myeloma cells via the JNK/AP-1 signaling pathway. Life Sci. 2019 Apr 15;223:146-157. doi: 10.1016/j.lfs.2019.03.011. Epub 2019 Mar 12. PMID: 30876940.

2. Li A, Liu Z, Li M, Zhou S, Xu Y, Xiao Y, Yang W. 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. doi: 10.18632/oncotarget.9274. Erratum in: Oncotarget. 2017 May 2;8(18):30619-30620. PMID: 27177225; PMCID: PMC5122364.

In vivo study

1. Trazzi S, Fuchs C, Viggiano R, De Franceschi M, Valli E, Jedynak P, Hansen FK, Perini G, Rimondini R, Kurz T, Bartesaghi R, Ciani E. HDAC4: a key factor underlying brain developmental alterations in CDKL5 disorder. Hum Mol Genet. 2016 Sep 15;25(18):3887-3907. doi: 10.1093/hmg/ddw231. Epub 2016 Jul 27. PMID: 27466189.

7. Bioactivity
Biological target:

Product data sheet

LMK-235 is a potent and selective HDAC4/5 inhibitor, inhibits HDAC5, HDAC4, HDAC6, HDAC1, HDAC2, HDAC11 and HDAC8, with IC50s of 4.22 nM, 11.9 nM, 55.7 nM, 320 nM, 881 nM, 852 nM and 1278 nM, respectively.

In vitro activity

It was found that LMK-235, a selective inhibitor of class IIA HDAC4/5, induced apoptosis of MM cells by downregulating HO-1 that is closely related to HDAC4. LMK-235 increased phosphorylation of JNK and c -Jun in MM cells. Downregulation of HO-1 expression in combination with LMK-235 expression further activated phosphorylation of JNK and c-Jun and induced apoptosis in MM cells. When the JNK inhibitor SP600125 was used in combination, the apoptosis phenomenon was reversed. However, when HO-1 was upregulated, LMK-235-mediated phosphorylation of JNK and c-Jun was inhibited, and apoptosis of MM cells began to decrease. These data suggest that LMK-235 has potent anti-myeloma activity through regulation of HO-1-induced apoptosis via the JNK/AP-1 pathway. This provides a new concept for the treatment of multiple myeloma.

Reference: Life Sci. 2019 Apr 15;223:146-157. https://linkinghub.elsevier.com/retrieve/pii/S0024-3205(19)30169-9

In vivo activity

The effects of 2 doses (5 and 20 mg/kg) of LMK235 on H3 acetylation were examined. It was found that an 8-day treatment with the lowest dose (5 mg/kg) was sufficient to fully restore H3 acetylation in the hippocampus of Cdkl5 -/Y mice (Fig. 7B). A moderate increase in H3 acetylation was also found in control mice (data not shown). Based on these results, Cdkl5 -/Y and control Cdkl5 +/Y male mice were treated daily with the lowest dose of LMK235 or vehicle. Some mice were sacrificed after 8 days of treatment. Other mice were treated for 8 days plus additional 8 days during which they were behaviorally tested. These mice were sacrificed immediately after behavioral testing (i.e. 16 days after initiation of treatment; Fig. 7A). The effects of treatment on the neuroanatomy of the hippocampal region were examined in mice treated for 8 and 16 days. It was found that both 8 and 16 days of treatment had no adverse effect on body weight in both genotypes indicating that LMK235 does not impair animals' well-being (Supplementary Material, Table 1).

Reference: Hum Mol Genet. 2016 Sep 15;25(18):3887-3907. https://academic.oup.com/hmg/article-lookup/doi/10.1093/hmg/ddw231