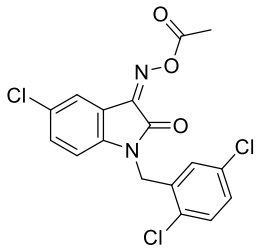
Product data sheet

MedKoo Cat#: 510324 Name: LDN-57444 CAS#: 668467-91-2 Chemical Formula: $C_{17}H_{11}Cl_3N_2O_3$ Exact Mass: 395.9835 Molecular Weight: 397.64	
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:
LDN-57444 is a Uch-L1 inhibitor (ubiquitin C-terminal hydrolase-L1) with Ki= 0.4 μ M. Ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) is an intracellular protein abundantly expressed in neurons, and a mutation in UCH-L1 has been identified in familial Parkinson's disease.

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	14.72	37.02
DMF	16.0	40.24
DMF:PBS (pH 7.2) (1:2)	0.3	0.75

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.51 mL	12.57 mL	25.15 mL
5 mM	0.50 mL	2.51 mL	5.03 mL
10 mM	0.25 mL	1.26 mL	2.51 mL
50 mM	0.05 mL	0.25 mL	0.50 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. Kobayashi E, Hwang D, Bheda-Malge A, Whitehurst CB, Kabanov AV, Kondo S, Aga M, Yoshizaki T, Pagano JS, Sokolsky M, Shakelford J. Inhibition of UCH-L1 Deubiquitinating Activity with Two Forms of LDN-57444 Has Anti-Invasive Effects in Metastatic Carcinoma Cells. Int J Mol Sci. 2019 Jul 31;20(15):3733. doi: 10.3390/ijms20153733. PMID: 31370144; PMCID: PMC6696221.
2. Tan YY, Zhou HY, Wang ZQ, Chen SD. Endoplasmic reticulum stress contributes to the cell death induced by UCH-L1 inhibitor. Mol Cell Biochem. 2008 Nov;318(1-2):109-15. doi: 10.1007/s11010-008-9862-x. Epub 2008 Jul 12. PMID: 18622688.

In vivo study

1. Liu S, Wang C, Lu J, Dai G, Che H, He W. Long-term inhibition of UCHL1 decreases hypertension and retinopathy in spontaneously hypertensive rats. J Int Med Res. 2021 Jun;49(6):3000605211020641. doi: 10.1177/03000605211020641. PMID: 34130526; PMCID: PMC8212382.

2. Gong Z, Ye Q, Wu JW, Zhou JL, Kong XY, Ma LK. UCHL1 inhibition attenuates cardiac fibrosis via modulation of nuclear factor-κB signaling in fibroblasts. Eur J Pharmacol. 2021 Jun 5;900:174045. doi: 10.1016/j.ejphar.2021.174045. Epub 2021 Mar 19. PMID: 33745956.

7. Bioactivity

Biological target:

LDN-57444 is an inhibitor of ubiquitin C-terminal hydrolase L1 (UCH-L1), with an IC50 of 0.88 μM and a Ki of 0.40 μM; LDN-57444 also suppresses UCH-L3 activity, with an IC50 of 25 μM.

In vitro activity

Initially, this study tested two forms of LDN inhibitor of UCH-L1 DUB activity on the viability and migration of the well-established nasopharyngeal NP69 parental control line, and on the NP69 cell line stably expressing EBV pro-metastatic factor, LMP1 (Figure 3). Figure 3A demonstrates a visible boost in UCH-L1 expression levels in LMP1 stably-expressing NP69 cell line.. The results of 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium salt (MTS) assay in Figure 3B show that in concentration higher than 5 μM both forms of inhibitor start inducing death in both NP69 and NP69-LMP1 cells definitely through non-specific, UCH-L1-independent pathways.

Reference: Int J Mol Sci. 2019 Aug; 20(15): 3733. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6696221/

In vivo activity

LDN57444-treated SHRs (spontaneously hypertensive rats) showed significantly reduced systolic blood pressure, although the inhibitor did not normalize the hypertension to the level observed in WKY rats ($P < 0.05$) (Figure 2b). H&E staining showed that the ganglion cell layer was loose and swollen. The thickness of the central retina (at two optic-disc diameters from the optic disc), particularly the inner plexiform, inner nuclear, and photoreceptor layers, was markedly increased in SHRs. These elevations were significantly reduced in LDN57444-treated SHRs ($P < 0.05$) (Figure 2c). However, the peripheral retinal morphology and thickness in the 4 groups were similar (Figure 2d). The accumulation of ionized calcium-binding adaptor molecule 1-positive microglia/macrophages was observed in vehicle-treated SHRs; this accumulation was significantly attenuated in LDN57444-treated SHRs ($P < 0.05$) (Figure 2e). These results suggest that LDN57444 treatment attenuates hypertension and hypertensive retinopathy in SHRs.

Reference: J Int Med Res. 2021 Jun; 49(6): 03000605211020641. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8212382/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.