Product Data Sheet

Product Name: LDN 57444
Cat. No.: GC10510

Chemical Properties

Cas. No.	668467-91-2		
Chemical Name	[(Z)-[5-chloro-1-[(2,5-dichlorophenyl)methyl]-2-oxoindol-3-ylidene]amino] acetate		
SMILES	CC(=O)ON=C1C2=C(C=CC(=C2)Cl)N(C1=O)CC3=C(C=CC(=C3)Cl)Cl		
Formula	$C_{17}H_{11}Cl_3N_2O_3$	M.Wt	397.64
Solubility	≥ 16.7 mg/mL in DMSO with gentle warming	Storage	Desiccate at 4°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	LDN 57444		

Protocol

Cell experiment [1]:

Cell lines	SK-N-SH cells
Preparation Method	SK-N-SH cells were incubated with DMEM-H medium supplemented with 10% fetal calf serum (FCS), and 1% penicillin/streptomycin in a humidified atmosphere at 37°C with 5% CO_2. Cells were cultured in a 96-well culture plate at 5×10^4 cells/well. After 24h cultured at 37°C in the atmosphere of 5% CO_2, cells were treated with different concentrations of LDN 57444 (0, 5, 10, 25, 50, 75, and 100μM) and incubated for 24h. Cell viability was measured.

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Reaction Conditions	0, 5, 10, 25, 50, 75, and 100μM; 24h
Applications	LDN 57444 treatment significantly reduced the cell viability of SK-N-SH cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	Spontaneously hypertensive rats
Preparation Method	Spontaneously hypertensive rats (2-month-old; 240-280g) were kept in an air-conditioned room at 24-25°C with a 12-h light/dark cycle. LDN 57444 was administered intraperitoneally in rats from 2 months of age for 4 months at the dose of 20μg/kg/day. Blood pressure was measured in all rats every month, and the hearts of rats were collected for analysis.
Dosage form	20μg/kg/day for 4 months; i.p.
Applications	LDN 57444 treatment reduced blood pressure and attenuated cardiac hypertrophy and fibrosis in rats.

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References:
[1] Tan Y Y, Zhou H Y, Wang Z Q, et al. Endoplasmic reticulum stress contributes to the cell death induced by UCH-L1 inhibitor[J]. Molecular and cellular biochemistry, 2008, 318(1): 109-115.
[2] Han X, Zhang Y L, Fu T, et al. Blockage of UCHL1 activity attenuates cardiac remodeling in spontaneously hypertensive rats[J]. Hypertension Research, 2020, 43(10): 1089-1098.

Background

LDN 57444 is a small molecular inhibitor that can block UCHL1 deubiquitinase activity (K_i=0.40μM; IC_{50}=0.88μM), with an IC_{50} value of 25μM for inhibiting UCHL3[1]. LDN 57444 suppresses mouse oocyte maturation by improving oxidative stress, attenuating mitochondrial function, curbing spindle body formation and down-regulating extracellular signal-related kinases (ERK1/2) expression [2]. LDN 57444 has been widely used to inhibit the invasive ability of nasopharyngeal cancer cells and reduce the adhesion of cancer cells[3].

In vitro, LDN 57444 treatment (50μM) for 24 hours significantly triggered apoptosis in SK-N-SH cells and inhibited the ubiquitin-proteasome system and induced endoplasmic reticulum stress[4]. Treatment with 10μM LDN 57444 for 24 hours significantly inhibited the migration of human dermal fibroblasts (HDFs) and upregulated the phosphorylation

of Smad2 and Smad3[5].

In vivo, LDN 57444 treatment via daily intraperitoneal injection at a dose of 40μg/kg for 3 weeks significantly reduced atrial fibrillation induced by angiotensin II in mice[6]. Daily intraperitoneal injection of 5mg/kg dose of LDN 57444 for 14 days can result in a reduced number of metastatic foci in the lungs and liver of mice with DU-145 xenograft tumors[7]. Daily intraperitoneal injection of 20μg/kg dose of LDN 57444 for 4 months can lower the blood pressure of spontaneously hypertensive rats and improve the cardiac function[8].

References:
[1] Liu Y, Lashuel H A, Choi S, et al. Discovery of inhibitors that elucidate the role of UCH-L1 activity in the H1299 lung cancer cell line[J]. Chemistry & biology, 2003, 10(9): 837-846.
[2] Yuan P, Zhou L, Zhang X, et al. UCH-L1 inhibitor LDN-57444 hampers mouse oocyte maturation by regulating oxidative stress and mitochondrial function and reducing ERK1/2 expression[J]. Bioscience Reports, 2020, 40(10): BSR20201308.
[3] Kobayashi E, Hwang D, Bheda-Malge A, et al. Inhibition of UCH-L1 deubiquitinating activity with two forms of LDN-57444 has anti-invasive effects in metastatic carcinoma cells[J]. International journal of molecular sciences, 2019, 20(15): 3733.
[4] Tan Y Y, Zhou H Y, Wang Z Q, et al. Endoplasmic reticulum stress contributes to the cell death induced by UCH-L1 inhibitor[J]. Molecular and cellular biochemistry, 2008, 318(1): 109-115.
[5] Pan H, Song J, An Q, et al. Inhibition of Ubiquitin C-Terminal Hydrolase L1 Facilitates Cutaneous Wound Healing via Activating TGF-β/Smad Signalling Pathway in Fibroblasts[J]. Experimental Dermatology, 2024, 33(10): e15186.
[6] Bi H L, Zhang Y L, Yang J, et al. Inhibition of UCHL1 by LDN-57444 attenuates Ang II–Induced atrial fibrillation in mice[J]. Hypertension Research, 2020, 43(3): 168-177.
[7] Liu S, Garcia-Marques F J, Shen M, et al. Ubiquitin C-terminal hydrolase L1 is a regulator of tumor growth and metastasis in double-negative prostate cancer[J]. American Journal of Clinical and Experimental Urology, 2024, 12(5): 306.
[8] Han X, Zhang Y L, Fu T, et al. Blockage of UCHL1 activity attenuates cardiac remodeling in spontaneously hypertensive rats[J]. Hypertension Research, 2020, 43(10): 1089-1098.

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