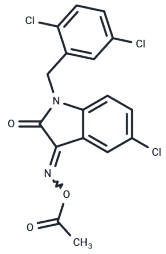
Data Sheet (Cat.No.T1924)

TargetMol

LDN-57444

Chemical Properties



CAS No. : 668467-91-2

Formula: C17H11Cl3N2O3

Molecular Weight: 397.64

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	LDN-57444 is a reversible, competitive inhibitor of the proteasome Uch-L1 with an IC50 of 0.88 μM.
Targets(IC50)	Apoptosis,DUB
In vitro	In vivo, LDN-57444 significantly alters the distribution of synaptic proteins and the morphology of dendritic spines. It leads to a reduction in UCH-L1 activity but does not affect the protease inhibition of cAMP levels.
In vivo	LDN-57444 (25-50 μM) reduces cell viability in a dose-dependent manner by inhibiting the activity of the ubiquitin-proteasome system and increasing the levels of highly ubiquitinated proteins, thereby inducing apoptosis.
Kinase Assay	HTS screen: To start an assay, 0.5 μL of 5 mg/mL test compound (about 50 μM final reaction concentration) or DMSO control is aliquoted into each well. Both enzyme and substrate are prepared in UCH reaction buffer (50 mM Tris-HCl [pH 7.6], 0.5 mM EDTA, 5 mM DTT, and 0.5 mg/mL ovalbumin). 25 μL of 0.6 nM UCH-L1 is then added to each well except substrate control wells, followed by plate shaking for 45-60 s on an automatic shaker. The enzyme/compound mixture is incubated at room temperature for 30 min before 25 μL of 200 nM Ub-AMC is added to initiate the enzyme reaction. The reaction mixture (300 pM UCH-L1, 100 nM Ubiquitin-AMC with 2.5 μg test compound) is incubated at room temperature for 30 additional minutes prior to quenching the reaction by the addition of 10 μL 500 mM acetic acid per well. The fluorescence emission intensity is measured on a LJL Analyst using a coumarin filter set (ex = 365 nm, em = 450 nm) and is subtracted by the intrinsic compound fluorescence to reveal the enzyme activity. A DMSO control (0.5 μL of DMSO, 25 μL of UCH-L1, 25 μL of ubiquitin-AMC, 10 μL of acetic acid), enzyme control (25 μL of UCH-L1, 25 μL of buffer, 10 μL of acetic acid), substrate control (25 μL of buffer, 25 μL of ubiquitin-AMC, 10 μL of acetic acid), and inhibitor control (0.5 μL of ubiquitin aldehyde [100 nM stock], 25 μL of UCH-L1, 25 μL of ubiquitin-AMC, 10 μL of acetic acid) are also performed in each assay plate to ensure quality and reproducibility. Potential UCH-L1 inhibitors are selected if the compounds demonstrated greater than 60% inhibition compared to the controls. The UCH-L1 enzymatic reactions are manually repeated twice using the same protocol to confirm the results for the hit compounds from the primary robot-assisted screen.
Cell Research	MTT assay(Only for Reference)

Solubility Information

Solubility	DMSO: 19.9 mg/mL (50.05 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 1.5 mg/mL (3.77 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5148 mL	12.5742 mL	25.1484 mL
5 mM	0.503 mL	2.5148 mL	5.0297 mL
10 mM	0.2515 mL	1.2574 mL	2.5148 mL
50 mM	0.0503 mL	0.2515 mL	0.503 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Liu Y, et al. Chem Biol, 2003, 10(9), 837-846.
Wu W, Xu H, Liao C, et al. Blockade of USP14 potentiates type I interferon signaling and radiation-induced antitumor immunity via preventing IRF3 deubiquitination. Cellular Oncology. 2022: 1-15
Yue X, Liu T, Wang X, et al.Pharmacological inhibition of BAP1 recruits HERC2 to competitively dissociate BRCA1-BARD1, suppresses DNA repair and sensitizes CRC to radiotherapy.Acta Pharmaceutica Sinica B.2023
Cartier AE, et al. PLoS One, 2012, 7(4), e34713.
Gong B, et al. Cell, 2006, 126(4), 775-788.
Liu S, Chai T, Garcia-Marques F, et al.UCHL1 is a potential molecular indicator and therapeutic target for neuroendocrine carcinomas.Cell Reports Medicine.2024
Tan YY, et al. Mol Cell Biochem, 2008, 318(1-2), 109-115.