

Product Data Sheet

Product Name: LHVS
Cat. No.: GC38809

Chemical Properties

Cas. No. 170111-28-1

SMILES O=C(N1CCOCC1)N[C@H](C(N[C@@H](CCC2=CC=CC=C2)/C=C/S(=O)(C3=CC=CC=C3)=O)CC(C)C

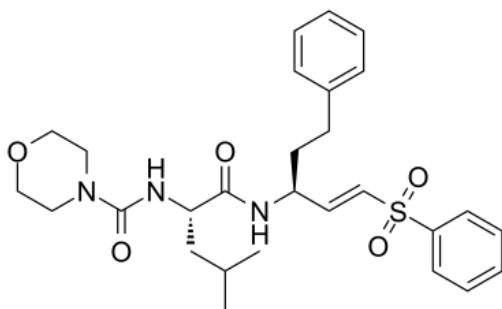
Formula $C_{28}H_{37}N_3O_5S$ M.Wt 527.68

Solubility DMSO : 100 mg/mL (189.51 mM; Need ultrasonic) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

Cell lines HOM2 cells (human B lymphoblastoid cell line)

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method HOM2 cells were maintained in RPMI medium supplemented with 10% fetal bovine serum (FBS), penicillin, streptomycin, and glutamine. HOM2 cells were preincubated with LHVS (1-5nM) prior to a pulse-chase metabolic labeling experiment with [³⁵S]methionine/cysteine.

Reaction Conditions 1-5nM; 1h.

Applications LHVS inhibited cathepsin S in HOM2 cells. LHVS prevented the complete proteolysis of the invariant chain (li), resulting in the accumulation of a class II-associated 13kDa li fragment. Consequently, the formation of SDS-stable αβ dimers (representing peptide-loaded complexes) was markedly reduced.

Animal experiment [2]:

Animal models Male ICR mice

Preparation Method Mice received a single intracerebroventricular (i.c.v.) injection of LHVS (10, 30, or 50nM in 6μL of 20% Cremophor EL/saline vehicle) 10 minutes before the induction of traumatic brain injury (TBI) using a weight-drop model. Mice were sacrificed at 24 hours post-TBI for the analysis of brain tissue (cytokines, edema, neuronal degeneration) and their neurobehavioral function was evaluated at 24 hours and 3 days.

Dosage form 10, 30, or 50nM (in 6μL vehicle); i.c.v.; single injection 10 min pre-TBI.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Applications LHSV pretreatment significantly reduced the levels of proinflammatory cytokines (IL-1 β and TNF- α) in the injured cortex, alleviated brain edema, suppressed neuronal degeneration in the cortex, and improved neurobehavioral scores at 24 hours after TBI

References:

- [1] Riese RJ, Wolf PR, Brömme D, et al. Essential role for cathepsin S in MHC class II-associated invariant chain processing and peptide loading. *Immunity*. 1996 Apr;4(4):357-66.
- [2] Xu J, Wang H, Ding K, et al. Inhibition of cathepsin S produces neuroprotective effects after traumatic brain injury in mice. *Mediators Inflamm*. 2013;2013:187873.

Background

LHSV is a potent, non-selective, irreversible, and cell-permeable cysteine protease and cathepsin inhibitor. LHSV also inhibits *T. gondii* invasion ($IC_{50}=10\mu M$)^[1-2]. Through its vinyl sulfone moiety, LHSV covalently modifies the thiol group at the active site of cathepsin S, thereby achieving high selectivity in inhibiting cathepsin S activity. LHSV can be used in research related to neuropathic pain and the autophagy/lysosomal degradation pathway^[3-4].

In vitro, treatment of the B-lymphoblastoid cell line HOM2 with LHSV (1–5nM) for 1 hour specifically inhibited cathepsin S activity, prevented complete proteolysis of the invariant chain, and significantly reduced the formation of SDS-stable $\alpha\beta$ dimers^[5]. Treatment of MCF7 tumor cells and U-937 macrophage-like cells with LHSV (10nM) for 72 hours did not show a significant effect on cell proliferation^[6].

In vivo, a single intracerebroventricular (i.c.v.) injection of LHSV (10–50nM; 6 μ L) was administered to male ICR mice 10 minutes before the induction of traumatic brain injury (TBI). LHSV significantly reduced the levels of the pro-inflammatory cytokines IL-1 β and TNF- α in the injured cortex, alleviated brain edema at 24 hours post-TBI, suppressed neuronal degeneration in the cortex, and improved neurobehavioral scores in mice at 24 hours after injury^[7]. Daily intraperitoneal injection of LHSV (25mg/kg), starting from day 0 to day 15 of MOG_{35–55} immunization to induce experimental autoimmune encephalomyelitis (EAE), was administered to both wild-type (WT) and cathepsin S-

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

deficient (Cat S^{-/-}) C57BL/6 mice. LHVS completely prevented the clinical onset of MOG₃₅₋₅₅-induced EAE in both WT and Cat S^{-/-} mice and significantly reduced the number of infiltrating macrophages, microglia, CD4⁺ T cells, CD8⁺ T cells, and B cells in the spinal cord^[8].

References:

- [1] Wilson SR, Peters C, Saftig P, et al. Cathepsin K activity-dependent regulation of osteoclast actin ring formation and bone resorption. J Biol Chem. 2009 Jan 23;284(4):2584-92.
- [2] Teo CF, Zhou XW, Bogyo M, et al. Cysteine protease inhibitors block Toxoplasma gondii microneme secretion and cell invasion. Antimicrob Agents Chemother. 2007 Feb;51(2):679-88.
- [3] Barclay J, Clark AK, Ganju P, et al. Role of the cysteine protease cathepsin S in neuropathic hyperalgesia. Pain. 2007 Aug;130(3):225-234.
- [4] Fujii H, Ivison SM, Shimizu H, et al. Inhibition of cathepsin S reduces allogeneic T cell priming but not graft-versus-host disease against minor histocompatibility antigens. Biol Blood Marrow Transplant. 2012 Apr;18(4):546-56.
- [5] Riese RJ, Wolf PR, Brömme D, et al. Essential role for cathepsin S in MHC class II-associated invariant chain processing and peptide loading. Immunity. 1996 Apr;4(4):357-66.
- [6] Mitrović A, Senjor E, Jukić M, et al. New inhibitors of cathepsin V impair tumor cell proliferation and elastin degradation and increase immune cell cytotoxicity. Comput Struct Biotechnol J. 2022 Aug 28;20:4667-4687.
- [7] Xu J, Wang H, Ding K, et al. Inhibition of cathepsin S produces neuroprotective effects after traumatic brain injury in mice. Mediators Inflamm. 2013;2013:187873.
- [8] Allan ER, Yates RM. Redundancy between Cysteine Cathepsins in Murine Experimental Autoimmune Encephalomyelitis. PLoS One. 2015 Jun 15;10(6):e0128945.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA