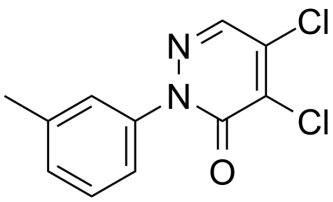
LCS-1

Cat. No.:	HY-115445
CAS No.:	41931-13-9
Molecular Formula:	$C_{11}H_8Cl_2N_2O$
Molecular Weight:	255.1
Target:	Apoptosis; SOD
Pathway:	Apoptosis; Immunology/Inflammation
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (196.00 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.9200 mL	19.6002 mL	39.2003 mL
	5 mM	0.7840 mL	3.9200 mL	7.8401 mL
	10 mM	0.3920 mL	1.9600 mL	3.9200 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (9.80 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LCS-1 is a superoxide dismutase 1 (SOD1) inhibitor. LCS-1 inhibits SOD1 activity with an IC_{50} value of 1.07 μM. LCS-1 induces the early- and late-stage apoptosis of multiple myeloma (MM.1S) cells[1][2][3].

IC_{50} & Target

SOD1
1.07 μM (IC_{50})

In Vitro

LCS-1 (1-10000 nM; 24 hours) has selective cytotoxicity towards bloom syndrome gene product (BLM) -proficient and BLM-deficient HCT116 cells[1].
LCS-1 shows growth inhibitory effect on 10/27 adenocarcinoma cell lines (median IC_{50}=0.20 μM; such as H23, H2347, HCC827 cell lines) and normal human bronchial epithelial (NHBE) cells (IC_{50}=2.66 μM)[2].
LCS-1 (0, 1.25, 2 μM; 4 h) in a concentration-dependent manner triggers significant inhibition of SOD1 enzymatic activity in multiple myeloma (MM) cells[3].

LCS-1 (0, 1.25, 2.5, 5 μM; 48 h) in a dose-dependent manner reduces the viability of various MM cell lines, including MM.1R (Dexamethasone-resistant), Dox40 (Doxorubicin-resistant), or LR5 (Melphalan-resistant) cell lines[3].
LCS-1 (48 h) has IC_{50} values of 2.5 and 4.6 μM for cell viability of ANBL6-WT (Bortezomib-sensitive) and ANBL6-BR (Bortezomib- resistant) cells, respectively[3].
LCS-1 (1.25 μM; 16 h) induces a significant increase in ROS levels and O_2 levels in MM.1S cells[3].
LCS-1 (1.25 μM; 16 h) shows a significant decrease in GSH/GSSG ratio in MM.1S cells[3].
LCS-1 (1.25 μM; 24h) induces the release of mitochondrial cytochrome-c into the cytosol, and enriches the proteins (HSP60/CLPP) mediating mtUPR signaling in MM.1S cells[3].
LCS-1-induced O_2 (1.25 μM; 5 h) triggers a marked decrease in both RP_2CP and RP_1CP forms of 26S proteasomes[3].
LCS-1 (2 μM; 16 h) induces the early- and late-stage apoptosis of MM.1S cells[3].
LCS-1 (0, 0.5, 1, 1.5, 2 μM) upregulates p53/p21 signaling, as well as downregulates survival pathway proteins MCL-1, BclxL, or c-Myc in MM.1S cells[3].
LCS-1 (0, 4, 8, 16, 24 h; 2 μM) shows a rapid and robust induction of mitochondrial unfolded protein response (UPR) proteins (BIP, PERK, phosphorylated eIF2α, or a lectin protein calnexin) in MM.1S and ANBL6-BR cells[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	BLM-proficient and BLM-deficient HCT116 cells
Concentration:	1-10000 nM
Incubation Time:	24 hours
Result:	Had IC_{50} values of 1462 nM and 24.92 nM for the viability of BLM-proficient and BLM-deficient HCT116 cells, respectively.

Western Blot Analysis[3]

Cell Line:	MM.1S and ANBL6-BR cells
Concentration:	2 μM
Incubation Time:	16 hours
Result:	Decreased the expression of cell-cycle regulatory proteins (cyclin-B1, CDC25C, and CDC2).

Western Blot Analysis[3]

Cell Line:	MM.1S cells
Concentration:	0, 0.5, 1, 1.5, 2 μM
Incubation Time:	
Result:	Upregulated p53/p21 signaling, as well as downregulated survival pathway proteins MCL-1, BclxL, or c-Myc.

Western Blot Analysis[3]

Cell Line:	MM.1S cells
Concentration:	2 μM
Incubation Time:	0, 4, 8, 16, 24 hours
Result:	Showed a rapid and robust induction of UPR proteins (BIP, PERK, phosphorylated eIF2α, or a lectin protein calnexin).

In Vivo

LCS-1 (20 mg/kg; i.p. every other day for 14 days) inhibits MM growth and prolongs host survival in MM.1S-bearing mice[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	5-week-old female CB17 SCID mice (MM.1S tumors volume=100 mm^3)[3]
Dosage:	20 mg/kg (diluted in saline)
Administration:	Intraperitoneal injections; treated on an every other day schedule for 14 days
Result:	Inhibited MM growth and prolongs host survival.

REFERENCES

[1]. Gupta A, et al. Nanocarrier Composed of Magnetite Core Coated with Three Polymeric Shells Mediates LCS-1 Delivery for Synthetic Lethal Therapy of BLM-Defective Colorectal Cancer Cells. Biomacromolecules. 2018 Mar 12;19(3):803-815.

[2]. Somwar R, et al. Superoxide dismutase 1 (SOD1) is a target for a small molecule identified in a screen for inhibitors of the growth of lung adenocarcinoma cell lines. Proc Natl Acad Sci U S A. 2011;108(39):16375-16380.

[3]. Du T, et al. Proteomic analysis identifies mechanism(s) of overcoming bortezomib resistance via targeting ubiquitin receptor Rpn13. Leukemia. 2021 Feb;35(2):550-561.

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