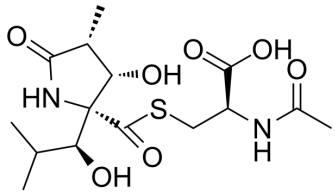
Lactacystin

Cat. No.:	HY-16594
CAS No.:	133343-34-7
Molecular Formula:	$C_{15}H_{24}N_2O_7S$
Molecular Weight:	376.43
Target:	Proteasome; Apoptosis; ROS Kinase
Pathway:	Metabolic Enzyme/Protease; Apoptosis; Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (53.13 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6565 mL	13.2827 mL	26.5654 mL
	5 mM	0.5313 mL	2.6565 mL	5.3131 mL
	10 mM	0.2657 mL	1.3283 mL	2.6565 mL

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

BIOLOGICAL ACTIVITY

Description

Lactacystin is a potent, orally active, irreversible, cell-permeable, selective 20S proteasome inhibitor (IC_{50} = 4.8 μM). Lactacystin also inhibits the lysosomal enzyme cathepsin A. Lactacystin inhibits cell growth and induces apoptosisand cell cycle arrest, and has antiviral and antioxidative activity. Lactacystin induces neurite outgrowth and hypertension. Lactacystin has the potential for the research of cancer, Neurological Disease, hypertension and Malaria, and so on[1] [2] [3] [4] [5] [6] [7] [8] [9] [10] .

IC_{50} & Target

IC50: 4.8 μM (proteasome)[1]

In Vitro

Lactacystin (up to 25.6 μM, 1 h) has no cytotoxicity to HeLa or SH-SY5Y cells, and decreases RVP infection by 63.8% in HeLa and by 74.5% in SH-SY5Y cells[2].

Lactacystin (2.5 μM) in combination with Parthenolide (HY-N0141) (5 μM) causes a synergistic increase in the apoptotic fraction of the drug-resistant L1210 cells[3].

Lactacystin（2.5, 5 and 10 μM, 24 h）inhibits the proliferation (IC_{50} value of 10 μ M) and increases the apoptotic in C6 cells[4].

Lactacystin (10μM, 24 h) increases Cisplatin (HY-17394)-induced ER stress-associated apoptosis in Hela cells[5].

Lactacystin (7.5 μM, 4-48 h) increased reactive oxygen species and GSH levels in HT-29 cells[6].

Lactacystin (1, 2.5, 5 μM, 24 h) induces stellation in astrocytes from neonatal rat cortex[7].

Lactacystin (10μM, 8-24 h) induces apoptosis, G2/M cell cycle arrest in the PC12 cells[10].

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

Cell Viability Assay[4]

Cell Line:	C6 cells
Concentration:	0, 2.5, 5, 10 μM
Incubation Time:	24 h
Result:	Suppressed cell growth and viability to 28.9%, and increased the apoptotic in C6 cells.

Cell Viability Assay[10]

Cell Line:	PC12
Concentration:	5, 10, 20 μM
Incubation Time:	24 h
Result:	Declined cell viability in a concentration-dependent manner (79.47% at 5 mM, 49.31% at 10 μM and 31.20% at 20 μM.

Apoptosis Analysis[10]

Cell Line:	PC12
Concentration:	10 μM
Incubation Time:	4, 8, 16, 24h
Result:	Increased significantly apoptotic in a time-dependent manner from 8 to 24 h (14.10% at 8 h, 24.90% at 16 h and 39.41% at 24 h).

Cell Cycle Analysis[10]

Cell Line:	PC12
Concentration:	10 μM
Incubation Time:	4, 8, 16, 24h
Result:	Reduced in the number of cells in the G2-phase (from 17.45% to 30.94%, 31.80% and 32.18%, respectively.) of the cell cycle for 8, 16 and 24h.

RT-PCR[4][6]

Cell Line:	C6 cells, HT-29 cells
Concentration:	0, 2.5, 5, and 10 μM (C6 cells), 7.5 μM in HT-29 cells
Incubation Time:	24-48 h
Result:	Increased the mRNA in the ratio of Bax to Bcl-2 in C6cells. Increased the expression of GGT, GCLC, xCT and Nrf2 in HT-29 cells.

Western Blot Analysis[4][4]

Cell Line:	C6 cells, HT-29 cells

Concentration:	0, 2.5, 5, and 10 μM (C6 cells), 7.5 μM in HT-29 cells
Incubation Time:	24-48h
Result:	Increased the expression in the ratio of Bax to Bcl-2 in C6cells. Increased protein levels of GGT, GCLC, xCT in HT-29 cells.

In Vivo

Lactacystin (2 μg for ICV) induces a Parkinson's disease-like motor phenotype 5-7 days after injection in young and adult mice[8].
Lactacystin (1.0 ug or 5.0 μg/20g for 7days) results in significantly smaller tumor and promotes apoptosis than control in C6 orthotopic xenograft tumor models[4].
Lactacystin (5 mg/kg/day, dissolved in drinking water, six weeks) induces model of hypertension in male adult Wistar rats[9].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57Bl/6RccHsd mice with 8-9 weeks (young) and 12-14 months (adult) old[2]
Dosage:	2 μg
Administration:	Microinjection
Result:	Induced a Parkinson's disease-like motor phenotype 5-7 days after injection in young and adult mice.

Animal Model:	Male C57Bl/6RccHsd mice[8]
Dosage:	2 μg, 7days
Administration:	Intracerebroventricular injection (ICV)
Result:	Induced spontaneous contralateral rotating behavior.

Animal Model:	C6 orthotopic xenograft tumor models[4]
Dosage:	1.0 ug or 5.0 μg/20g for 7days
Administration:	Intravenous injection (i.p.)
Result:	Reduced the tumor volume. Showed polygonal condensed nuclei with brown Tunnel staining indicating apoptosis in tumor tissue. Increased the mRNA and protein level in the ratio of Bax to Bcl-2 in tumor tissue.

CUSTOMER VALIDATION

- Cell Mol Gastroenterol Hepatol. 2022 Oct 13;S2352-345X(22)00216-8.
- iScience. 2023 Feb.

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REFERENCES

[1]. Shaobo Wang, et al. The ubiquitin-proteasome system is essential for the productive entry of Japanese encephalitis virus. Virology. 2016 Nov;498:116-127.

[2]. Ann H Cory, et al. Lactacystin, a proteasome inhibitor, potentiates the apoptotic effect of parthenolide, an inhibitor of NFkappaB activation, on drug-resistant mouse leukemia L1210 cells. Anticancer Res 2002 Nov-Dec;22(6C):3805-9.

[3]. Haifeng Wang, et al. The proteasome inhibitor lactacystin exerts its therapeutic effects on glioma via apoptosis: an in vitro and in vivo study. J Int Med Res. 2013 Feb;41(1):72-81.

[4]. Ye Xu, et al. Proteasome inhibitor lactacystin enhances cisplatin cytotoxicity by increasing endoplasmic reticulum stress-associated apoptosis in HeLa cells. Mol Med Rep. 2015 Jan;11(1):189-95.

[5]. Nils-Erik Huseby, et al. The proteasome inhibitor lactacystin enhances GSH synthesis capacity by increased expression of antioxidant components in an Nrf2-independent, but p38 MAPK-dependent manner in rat colorectal carcinoma cells. Free Radic Res. 2016;50(1):1-13. https://pubmed.ncbi.nlm.nih.gov/26530909/

[6]. Qing-Guo Ren, et al. Lactacystin stimulates stellation of cultured rat cortical astrocytes. Neurochem Res. 2009 May;34(5):859-66.

[7]. Fedor Simko, et al. Lactacystin-Induced Model of Hypertension in Rats: Effects of Melatonin and Captopril. Int J Mol Sci. 2017 Jul 25;18(8):1612.

[8]. Zhentao Zhang, et al. Cell cycle events mediate lactacystin-induced apoptotic death of neuronal PC12 cells. Cell Biol Int. 2010 Dec;34(12):1181-7.

[9]. Csizmadia V, et al. Effect of proteasome inhibitors with different chemical structures on the ubiquitin-proteasomesystem in vitro. Vet Pathol. 2010 Mar;47(2):358-67.

[10]. Savolainen MH, et al. Nigral injection of a proteasomal inhibitor, lactacystin, induces widespread glial cell activationand shows various phenotypes of Parkinson's disease in young and adult mouse. Exp Brain Res. 2017 Jul;235(7):2189-2202.

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