

Product Data Sheet

Product Name: Necrostatin-1

Cat. No.: GC11008

Chemical Properties

Cas. No. 4311-88-0

Chemical Name 5-(1H-indol-3-ylmethyl)-3-methyl-2-sulfanylideneimidazolidin-4-one

SMILES CN1C(=O)C(NC1=S)CC2=CNC3=CC=CC=C32

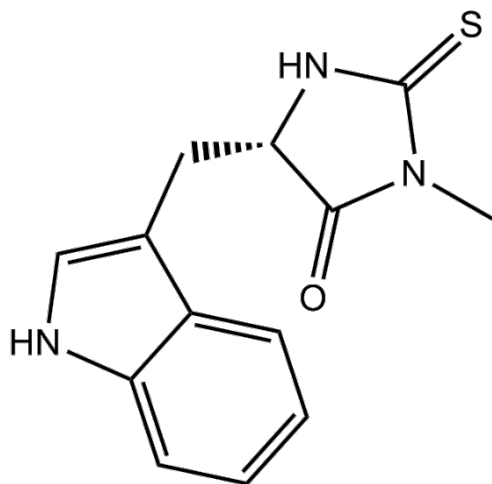
Formula $C_{13}H_{13}N_3OS$ M.Wt 259.33

Solubility ≥ 12.97 mg/mL in DMSO, ≥ 13.29 mg/mL in EtOH with ultrasonic Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ 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]:

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Cell lines	NRK-52E cells (rat tubular epithelial cell line)
Preparation Method	NRK-52E cells were maintained in RPMI-1640 medium supplemented with 10% heat-inactivated fetal bovine serum (FBS) at 37°C, 5% CO ₂ . Cells were pretreated with Necrostatin-1 (20μM) for 24 hours, followed by exposure to tumor necrosis factor-alpha (10ng/mL) and antimycin A (10μM) for 24 hours to simulate ischemia injury.
Reaction Conditions	20μM; 24h pretreatment
Applications	Necrostatin-1 significantly reduced the number of cell deaths determined by Hoechst staining and flow cytometry, increased cell viability measured by MTT assay, and decreased the protein expression of dynamin-related protein 1 (Drp1) in NRK-52E cells under simulated ischemia injury.
Animal experiment [2]:	
Animal models	12-week-old male C57BL/6 mice with destabilised medial meniscus (DMM) induced traumatic osteoarthritis
Preparation Method	Mice were divided into four groups: sham-operated + vehicle, sham-operated + Necrostatin-1, DMM-operated + vehicle, DMM-operated + Necrostatin-1 after corresponding surgery. Necrostatin-1 was injected intra-articularly twice weekly for 8 weeks, then mice were sacrificed and right knee joints were collected for micro-computed tomography, Safranin O/Fast Green staining and immunohistochemical analysis.
Dosage form	0.0468mg/kg; intra-articularly; twice weekly for 8 weeks

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Applications

Necrostatin-1 significantly reduced the OA cartilage destruction degree of DMM mice as assessed by OARSI scoring, downregulated the expression of MMP3, MMP13 and ADAMTs5 in articular cartilage, decreased serum SDF-1 α level, and reduced HMGB1 and TLR4 expression in cartilage.

References:

- [1] Zhang L, Jiang F, Chen Y, et al. Necrostatin-1 attenuates ischemia injury induced cell death in rat tubular cell line NRK-52E through decreased Drp1 expression. *Int J Mol Sci.* 2013 Dec 18;14(12):24742-54.
- [2] Liang S, Lv ZT, Zhang JM, et al. Necrostatin-1 Attenuates Trauma-Induced Mouse Osteoarthritis and IL-1 β Induced Apoptosis via HMGB1/TLR4/SDF-1 in Primary Mouse Chondrocytes. *Front Pharmacol.* 2018 Nov 27;9:1378.

Background

Necrostatin-1 is a novel small molecule inhibitor of necroptosis. Necrostatin-1 inhibits RIP1 kinase activity (EC_{50} =182nM) through allosteric binding. Necrostatin-1 inhibits necroptosis by blocking necrosome assembly and MLKL-mediated cell membrane rupture. Necrostatin-1 reduces inflammation release by inhibiting IDO. Necrostatin-1 can be used in research on cerebral ischemia-reperfusion injury, neurodegenerative diseases, inflammation, and tumors^[1-4].

In vitro, Necrostatin-1 (20 μ M) pretreated NRK-52E rat renal tubular epithelial cells for 24h, followed by treatment with TNF- α (10ng/mL) combined with antimycin A (10 μ M) for 24h. Necrostatin-1 significantly reduced cell death, increased cell viability, and decreased Drp1 protein expression^[5]. Necrostatin-1 (1-40 μ M) pretreated human neuroblastoma SH-SY5Y cells and mouse hippocampal HT-22 cells for 30min, followed by treatment with hydrogen peroxide (0.25-0.5mM)/6-hydroxydopamine (0.1-0.2mM) on SH-SY5Y cells for 24h. Necrostatin-1 significantly attenuated hydrogen peroxide/6-hydroxydopamine-induced cell death and increased cell viability^[6].

In vivo, Necrostatin-1 (0.0468mg/kg) was injected intra-articularly into C57BL/6 mice with a traumatic osteoarthritis model, twice a week for 8 weeks. Necrostatin-1 significantly alleviated knee OA cartilage degeneration in the model mice, reduced OARSI scores, and downregulated the expression of MMP3, MMP13, ADAMTs5, HMGB1, and TLR4 in cartilage tissue, and decreased serum SDF-1 α

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levels^[7]. Necrostatin-1 (1 µg; 50 µL; single injection) was administered intracerebroventricularly to C57BL/6 mice with an intracerebral hemorrhage model, 1h before modeling. Necrostatin-1 significantly reduced the expression of RIP1, RIP3, MLKL, p-RIP3, and p-MLKL in the periventricular tissue of the model mice. Necrostatin-1 inhibited cell necrosis and microglial activation. Necrostatin-1 downregulated the expression of interleukin-1β, interleukin-6, and tumor necrosis factor-α^[8].

References:

- [1] Cao L, Mu W. Necrostatin-1 and necroptosis inhibition: Pathophysiology and therapeutic implications. *Pharmacol Res.* 2021 Jan;163:105297.
- [2] Chen KQ, Wang SZ, Lei HB, et al. Necrostatin-1: a promising compound for neurological disorders. *Front Cell Neurosci.* 2024 Jun 27;18:1408364.
- [3] Cao Y, Wang HB, Ni CJ, et al. Necrostatin-1 prevents skeletal muscle ischemia reperfusion injury by regulating Bok-mediated apoptosis. *J Chin Med Assoc.* 2023 Jan 1;86(1):26-33.
- [4] Yu C, Wang X, Qin J. Effect of necrostatin-1 on sciatic nerve crush injury in rat models. *J Orthop Surg Res.* 2023 Jan 30;18(1):74.
- [5] Zhang L, Jiang F, Chen Y, et al. Necrostatin-1 attenuates ischemia injury induced cell death in rat tubular cell line NRK-52E through decreased Drp1 expression. *Int J Mol Sci.* 2013 Dec 18;14(12):24742-54.
- [6] Jantas D, Chwastek J, Grygier B, et al. Neuroprotective Effects of Necrostatin-1 Against Oxidative Stress-Induced Cell Damage: an Involvement of Cathepsin D Inhibition. *Neurotox Res.* 2020 Mar;37(3):525-542.
- [7] Liang S, Lv ZT, Zhang JM, et al. Necrostatin-1 Attenuates Trauma-Induced Mouse Osteoarthritis and IL-1β Induced Apoptosis via HMGB1/TLR4/SDF-1 in Primary Mouse Chondrocytes. *Front Pharmacol.* 2018 Nov 27;9:1378.
- [8] Liu C, Cao Y, Wang HX, et al. Necrostatin-1 decreases necroptosis and inflammatory markers after intraventricular hemorrhage in mice. *Neural Regen Res.* 2022 Dec;17(12):2710-2716.

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