

Product Data Sheet

Product Name: EX 527 (SEN0014196)

Cat. No.: GC10635

Chemical Properties

Cas. No. 49843-98-3

Chemical Name 6-chloro-2,3,4,9-tetrahydro-1H-carbazole-1-carboxamide

SMILES C1CC(C2=C(C1)C3=C(N2)C=CC(=C3)Cl)C(=O)N

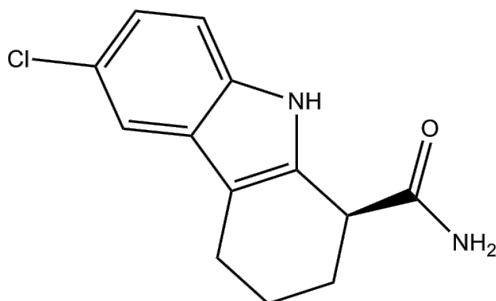
Formula $C_{13}H_{13}ClN_2O$ M.Wt 248.71

Solubility ≥ 12.4 mg/mL in DMSO, ≥ 25.45 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	C2C12 cells (mouse skeletal muscle myoblast cell line)
Preparation Method	C2C12 cells were cultured in DMEM with 10% FBS and 1% penicillin-streptomycin at 37°C, 5% CO ₂ , switched to differentiation medium (2% horse serum) at 80-90% confluence, treated with 30g/L D-gal for 48h to induce senescence, then co-treated with TRIM16-overexpressing lentivirus and 100μM EX 527 for 48h. After treatment, intracellular ROS, antioxidant proteins (Nrf-2, HO-1, SOD1) and muscle markers (MHC, MyoD, MyoG, Atrogin-1, MuRF-1), myotube diameter/fusion index, and PI3K/AKT/mTOR/FOXO3 pathway proteins were measured.
Reaction Conditions	100μM; 48h
Applications	EX 527 reversed the antioxidant effect of TRIM16 overexpression in D-gal-induced senescent C2C12 cells, increasing ROS levels. EX 527 counteracted TRIM16 overexpression-mediated upregulation of Nrf-2, HO-1 and SOD1. EX 527 offset the protective effect of TRIM16 overexpression on myotube atrophy, reversing MHC, MyoD, MyoG upregulation and Atrogin-1, MuRF-1 downregulation. EX 527 compromised TRIM16 overexpression-mediated upregulation of PI3K/AKT/mTOR pathway proteins and partial suppression of FOXO3 activation.
Animal experiment [2]:	
Animal models	Male Balb/C mice (6-8 weeks old, 18-22g)

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Preparation Method	Mice were intraperitoneally administered a single dose of EX 527 at 10mg/kg 0.5h prior to a single intraperitoneal injection of LPS (10mg/kg); mice were sacrificed 18h after LPS challenge for plasma ELISA (TNF- α , IL-6), left lung histopathology (H&E), lung MPO activity assay, and Western blot of TF, PAI-1, 4E-BP1 and p-4E-BP1. In a separate mechanism arm, mice received 100mg/kg 3BDO i.p. 0.5h before EX 527, then LPS 0.5h later, same endpoints at 18h.
Dosage form	10mg/kg; i.p.; single injection 0.5h before LPS
Applications	EX 527 suppressed LPS-induced elevation of plasma TNF- α and IL-6. EX 527 attenuated LPS-induced lung histological abnormalities including leukocyte infiltration, hemorrhage, bronchial wall thickening and alveolar edema. EX 527 decreased lung MPO activity. EX 527 suppressed LPS-induced upregulation of tissue factor and plasminogen activator inhibitor-1 in lung tissue. EX 527 suppressed LPS-induced phosphorylation of 4E-BP1. Co-administration of 3BDO abolished the inhibitory effect of EX 527 on 4E-BP1 phosphorylation and partially reversed the suppressive effect of EX 527 on IL-6 induction and the beneficial effect of EX 527 on lung injury.
References: [1] Guo A, Huang K, Lu Q, et al. TRIM16 facilitates SIRT-1-dependent regulation of antioxidant response to alleviate age-related sarcopenia. J Cachexia Sarcopenia Muscle. 2024;15(5):2056-2070. [2] Huang J, Tian R, Yang Y, et al. Selective inhibition of SIRT1 by EX-527 alleviates endotoxemia-associated acute lung injury via suppression of mTOR in mice. Innate Immun. 2017;23(8):669-677.	

Background

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EX 527 (SEN0014196) is a cell-permeable SIRT1 inhibitor ($IC_{50}=123nM$). EX 527 binds to the SIRT1-NAD⁺ complex and blocks the deacetylase activity of SIRT1 toward substrates such as p53. EX 527 can be used in studies related to cancer, Huntington's disease, diabetic nephropathy, and neurodegenerative diseases^[1-4].

In vitro, treatment of TRIM16-overexpressing senescent C2C12 myotubes with 100 μ M EX 527 for 48 hours reversed the inhibitory effect of TRIM16 on oxidative stress, increased intracellular ROS levels, and counteracted the protective effect of TRIM16 on myotube atrophy in senescent muscle cells^[5]. Co-treatment of OGD/R-injured HT22 cells with 1 μ M EX 527 and 10 μ M Vitexin for 24 hours reduced cell viability, increased apoptosis rate, decreased mitochondrial membrane potential, and elevated mitochondrial ROS levels^[6]. Treatment of streptozotocin-pretreated INS-1 cells with 10 μ M EX 527 for 48 hours, followed by Astragaloside IV treatment for 4 hours, reversed the protective effect of Astragaloside IV against streptozotocin-induced reduction in INS-1 cell viability^[7].

In vivo, C57BL/6J mice received a single intraperitoneal injection of 5mg/kg EX 527 immediately after cecal ligation and puncture (CLP). This reduced dead cells in the hippocampal dentate gyrus and activated microglia^[8]. C57BL/6J T2DM mice induced by high-fat diet plus streptozotocin received intravenous tail vein injections of human umbilical cord mesenchymal stem cells (1×10^6 cells per mouse; once every 7 days for 6 doses). During this intervention period, intraperitoneal injection of 10mg/kg EX 527 every 3 days for 6 consecutive weeks weakened the improvement effect of human umbilical cord mesenchymal stem cells on glucose tolerance and failed to effectively rescue islet structure and the imbalance of α -cell and β -cell ratios^[9]. Male Balb/C mice received a single intraperitoneal injection of 10mg/kg EX 527 0.5 hours before lipopolysaccharide (LPS; 10mg/kg)-induced endotoxemia. This reduced plasma TNF- α and IL-6 levels and alleviated histological abnormalities including lung leukocyte infiltration, hemorrhage, bronchial wall thickening, and alveolar edema^[10].

References:

[1] Smith MR, Syed A, Lukacsovich T, et al. A potent and selective Sirtuin 1 inhibitor alleviates pathology in multiple animal and cell models of Huntington's disease. Hum Mol Genet. 2014 Jun 1;23(11):2995-3007.

[2] Napper AD, Hixon J, McDonagh T, et al. Discovery of indoles as potent and selective inhibitors of

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the deacetylase SIRT1. J Med Chem. 2005 Dec 15;48(25):8045-54.

[3] Sivakumar KK, Stanley JA, Behlen JC, et al. Inhibition of Sirtuin-1 hyperacetylates p53 and abrogates SIRT1-p53 interaction in Cr(VI)-Induced Apoptosis in the ovary. Reprod Toxicol. 2022 Apr;109:121-134.

[4] Wang X, Su L, Liu S, et al. Paeoniflorin Inhibits the Activation of Microglia and Alleviates Depressive Behavior by Regulating SIRT1-NF- κ B-NLRP3/Pyroptosis Pathway. Int J Mol Sci. 2024 Nov 22;25(23):12543..

[5] Guo A, Huang K, Lu Q, et al. TRIM16 facilitates SIRT-1-dependent regulation of antioxidant response to alleviate age-related sarcopenia. J Cachexia Sarcopenia Muscle. 2024;15(5):2056-2070.

[6] Chen C, Zhang Z, Du B, et al. Vitexin alleviates cerebral ischemia/reperfusion injury by regulating mitophagy via the SIRT1/PINK1/Parkin pathway. Brain Res Bull. 2025;227:111404.

[7] Lin Y, Xu Y, Zheng X, et al. Astragaloside IV Ameliorates Streptozotocin Induced Pancreatic β -Cell Apoptosis and Dysfunction Through SIRT1/P53 and Akt/GSK3 β /Nrf2 Signaling Pathways. Diabetes Metab Syndr Obes. 2022 Jan 13;15:131-140.

[8] Li HR, Liu Q, Zhu CL, et al. β -Nicotinamide mononucleotide activates NAD⁺/SIRT1 pathway and attenuates inflammatory and oxidative responses in the hippocampus regions of septic mice. Redox Biol. 2023;63:102745.

[9] Song J, Wang L, Wang LM, et al. Mesenchymal stromal cells ameliorate mitochondrial dysfunction in α cells and hyperglucagonemia in type 2 diabetes via SIRT1/FoxO3a signaling. Stem Cells Transl Med. 2024 Aug;13(8):776-790.

[10] Huang J, Tian R, Yang Y, et al. Selective inhibition of SIRT1 by EX-527 alleviates endotoxemia-associated acute lung injury via suppression of mTOR in mice. Innate Immun. 2017;23(8):669-677.

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