

Product Data Sheet

Product Name: Ulinastatin

Cat. No.: GC19805

Chemical Properties

Cas. No. 80449-31-6

Formula M.Wt

Solubility H₂O : 10 mg/mL (Need ultrasonic); Storage -20°C, protect from light
DMSO : 1 mg/mL (Need ultrasonic)

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 SH-SY5Y cells (human neuroblastoma cell line) and PC12 cells (rat adrenal pheochromocytoma cell line)

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SH-SY5Y cells were cultured in DMEM supplemented with 10% FBS. PC12 cells were maintained in RPMI-1640 medium with 5% FBS and differentiated Preparation Method using nerve growth factor (NGF; 50ng/mL) for 4 days. Cells were pretreated with Ulinastatin (100–500µM) for 6 hours, followed by exposure to MPP⁺ (100µM) for 24 hours to establish a Parkinson's disease (PD) model.

Reaction
Conditions 100–500µM; pretreatment for 6h

Applications Ulinastatin significantly attenuated MPP⁺-induced cytotoxicity by enhancing cell viability and reducing lactate dehydrogenase (LDH) release. Ulinastatin suppressed apoptosis and inhibited the secretion of pro-inflammatory cytokines. Ulinastatin also restored dopamine (DA) secretion (HPLC) and tyrosine hydroxylase (TH) expression in MPP⁺-treated cells. Mechanistically, Ulinastatin downregulated the NLRP3 pathway, reducing the expression of NLRP3, caspase-1, ASC, IL-1β, and IL-18. The protective effects were reversed by the NLRP3 activator Nigericin, confirming NLRP3 inhibition as a key mechanism.

Animal experiment [2]:

Animal models 21-day-old male C57BL/6 mice

Mice in the chronic Ketamine (CK) group were intraperitoneally injected with ketamine (30mg/kg) three times daily (30-minute intervals) for 7 consecutive Preparation Method days. Mice in the Ulinastatin pretreatment group received Ulinastatin (50000U/kg) intraperitoneally 30 minutes before the first Ketamine injection each day.

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Dosage form 50000U/kg; i.p.; once daily for 7 days

Applications Repetitive Ketamine exposure induced cognitive impairment and anxiety-like behaviors. Ulinastatin pretreatment significantly improved cognitive performance, as evidenced by shorter escape latency and increased platform-crossing times in the MWM test, and alleviated anxiety-like behaviors by increasing center duration time in the OFT. Ulinastatin also suppressed neuroinflammation by reducing hippocampal levels of IL-1 β and IL-6. Furthermore, Ulinastatin downregulated the expression of dementia-related proteins, including Tau, phosphorylated Tau (pS396), and A β , in the hippocampus.

References:

- [1] Hong Y, Meng S, Wang S, et al. Ulinastatin Alleviates Repetitive Ketamine Exposure-Evoked Cognitive Impairment in Adolescent Mice. *Neural Plast.* 2022 Dec 12;2022:6168284.
[2] Mohankumar K, Li X, Sung N, et al. Bis-Indole-Derived Nuclear Receptor 4A1 (NR4A1, Nur77) Ligands as Inhibitors of Endometriosis. *Endocrinology.* 2020 Apr 1;161(4):bqaa027.

Background

Ulinastatin is a broad-spectrum protease inhibitor that suppresses the activity of various hydrolases, including trypsin, chymotrypsin, and elastase^[1-2]. Ulinastatin mitigates tissue injury and excessive inflammatory responses through stabilization of lysosomal membranes, inhibition of inflammatory mediator release, scavenging of oxygen free radicals, and modulation of immune reactions. Ulinastatin is indicated for the treatment of acute pancreatitis, acute exacerbations of chronic recurrent pancreatitis, and as adjunctive therapy in acute circulatory failure (e.g., septic shock, traumatic shock)^[3-4].

In vitro, pretreatment of SH-SY5Y cells and NGF-differentiated PC12 cells with Ulinastatin (100-500 μ M) for 6 hours, followed by incubation in an MPP⁺ (100 μ M)-induced Parkinson's disease cell model for 24 hours, Ulinastatin significantly suppressed MPP⁺-induced NLRP3 inflammasome

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activation, reduced lactate dehydrogenase release and apoptosis, and enhanced dopamine secretion and tyrosine hydroxylase expression^[5]. In an LPS (1µg/mL)-induced acute kidney injury model using podocytes (MPC5), treatment with Ulinastatin (100U/mL) for 48 hours, Ulinastatin markedly inhibited LPS-induced ferroptosis, upregulated SLC7A11 and GPX4 protein expression, promoted cell proliferation, and improved cytoskeletal structure^[6].

In vivo, intraperitoneal pretreatment of adolescent mice with Ulinastatin (50000U/kg, once daily) for 7 days prior to repetitive ketamine exposure (30mg/kg, three times daily at 30-minute intervals, for 7 days), Ulinastatin significantly decreased escape latency and increased platform-crossing counts in the Morris water maze test and alleviated anxiety-like behaviors in the open-field test. Ulinastatin also reduced hippocampal levels of IL-1β and IL-6 inflammatory cytokines, as well as the expression of Tau, Tau-pS396, and Aβ proteins^[7]. In aged (18-month-old) rats undergoing tibial fracture fixation under sevoflurane anesthesia, a single intraperitoneal dose of Ulinastatin (100000U/kg, administered 30 minutes before surgery), Ulinastatin significantly increased spontaneous alternation rates in the Y-maze and discrimination indices in the novel object recognition test. Moreover, Ulinastatin downregulated hippocampal TRPM4 channel expression, reduced neuronal apoptosis, and improved mitochondrial structure^[8].

References:

- [1] Luo Q, Tang Y, Jiang Z, et al. hUCMSCs reduce theca interstitial cells apoptosis and restore ovarian function in premature ovarian insufficiency rats through regulating NR4A1-mediated mitochondrial mechanisms. *Reprod Biol Endocrinol*. 2022 Aug 19;20(1):125.
- [2] Lv ZT, Huang JM, Zhang JM, et al. Effect of Ulinastatin in the Treatment of Postoperative Cognitive Dysfunction: Review of Current Literature. *Biomed Res Int*. 2016;2016:2571080.
- [3] Lv B, Jiang XM, Wang DW, et al. Protective Effects and Mechanisms of Action of Ulinastatin against Cerebral Ischemia-Reperfusion Injury. *Curr Pharm Des*. 2020;26(27):3332-3340.
- [4] Atal SS, Atal S. Ulinastatin - a newer potential therapeutic option for multiple organ dysfunction syndrome. *J Basic Clin Physiol Pharmacol*. 2016 Mar;27(2):91-9.
- [5] Lin Y, Xu D, Gao F, et al. Ulinastatin inhibits NLRP3-induced apoptosis in a PD cell model. *Ann Transl Med*. 2021 Jun;9(11):924.
- [6] Yang X, Guo N. Ulinastatin ameliorates podocyte ferroptosis via regulating miR-144-3p/SLC7A11 axis in acute kidney injury. *In Vitro Cell Dev Biol Anim*. 2023 Oct;59(9):697-705.
- [7] Hong Y, Meng S, Wang S, et al. Ulinastatin Alleviates Repetitive Ketamine Exposure-Evoked Cognitive Impairment in Adolescent Mice. *Neural Plast*. 2022 Dec 12;2022:6168284.

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[8] Xia X, Li J, Zhang M, et al. Ulinastatin modulates TRPM4 expression and apoptosis to mitigate cognitive dysfunction in aged perioperative neurocognitive disorder rats. Sci Rep. 2025 May 22;15(1):17774.

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