

Product Data Sheet

Product Name: NU6300
Cat. No.: GC32829

Chemical Properties

Cas. No. 2070015-09-5

SMILES O=S(C(C=C1)=CC=C1NC2=NC(OCC3CCCCC3)=C4C(NC=N4)=N2)(C=C)=O

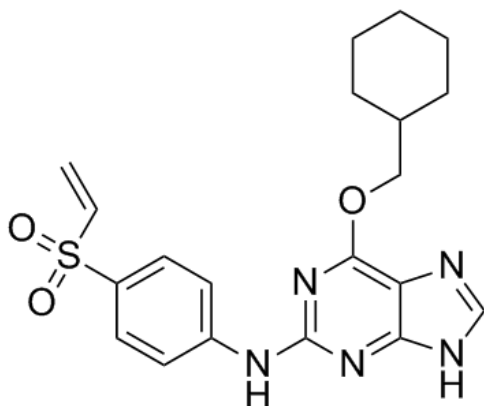
Formula $C_{20}H_{23}N_5O_3S$ M.Wt 413.49

Solubility DMSO : ≥ 32 mg/mL (77.39 mM) 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]:

Cell lines THP-1 cells (human monocytic cell line), mouse bone marrow-derived macrophages (BMDMs), HEK-293T cells (human embryonic kidney cell line)

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THP-1 cells were maintained in RPMI 1640 medium supplemented with 10% FBS and 1% penicillin/streptomycin. BMDMs were differentiated from bone marrow cells in DMEM supplemented with 10% FBS and 20% L929-conditioned medium. HEK-293T cells were maintained in DMEM supplemented with 10% FBS. Cells were pretreated with NU6300 (0.5-10 μ M) for 40 minutes to 16 hours, followed by Nigericin (10 μ M; 1h), Poly(dA:dT) (1 μ g/mL; 6h), or Flagellin (1 μ g/mL; 6h) stimulation.

Reaction Conditions 0.5-10 μ M; 40min-16h pretreatment

Applications NU6300 significantly inhibited GSDMD cleavage and palmitoylation, blocked GSDMD membrane localization and oligomerization, and reduced pyroptosis and IL-1 β release in AIM2, NLRC4, and NLRP3 inflammasome-activated cells. NU6300 also feedback inhibited ASC oligomerization and caspase-1 activation under NLRP3 inflammasome activation conditions.

Animal experiment [1]:

Animal models C57BL/6J mice, BALB/c mice

Preparation Method For the colitis model, male C57BL/6J mice were administered 3.25% dextran sulfate sodium (DSS) in drinking water for 6 days, followed by normal water. NU6300 (5, 10, 20mg/kg) or Necrosulfonamide (NSA, 20mg/kg) was intraperitoneally administered daily for 5 consecutive days concurrently with the return to normal water. For the sepsis model, mice were intraperitoneally administered NU6300 (5, 10mg/kg) or NSA (10mg/kg) 1 hour before LPS (8mg/kg for BALB/c, 50mg/kg for C57BL/6J) injection.

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Dosage form	5-20mg/kg; i.p.; Daily administration for 5 days (colitis) or single injection (sepsis).
Applications	NU6300 administration significantly attenuated body weight loss, disease activity index, colon shortening, and pathological damage (epithelial/mucosal damage, crypt dilation, goblet cell depletion) in DSS-induced colitis.

References:

[1] Jiang X, Zhang X, Cai X, et al. NU6300 covalently reacts with cysteine-191 of gasdermin D to block its cleavage and palmitoylation. Sci Adv. 2024 Feb 9;10(6):eadi9284.

Background

NU6300 is a small molecule compound that specifically inhibits pyroptosis by covalently binding to the C191 site of the Gasdermin D (GSDMD) protein^[1]. NU6300 can covalently react with the cysteine 191 (C191) of GSDMD, a key executioner protein in pyroptosis, thereby blocking the cleavage and palmitoylation of GSDMD. This prevents the N-terminal fragment of GSDMD from forming pores in the cell membrane, ultimately inhibiting the occurrence of pyroptosis^[2].

In vitro, pretreatment of human monocytic THP-1 cells, mouse bone marrow-derived macrophages, and HEK-293T cells with NU6300 (0.5–10 μ M) for 40 minutes to 16 hours, followed by activation of AIM2, NLRC4, or NLRP3 inflammasomes via nigericin (10 μ M; 1h), poly(dA:dT) (1 μ g/mL; 6h), or flagellin (1 μ g/mL; 6h), significantly inhibited the cleavage and palmitoylation of GSDMD. This blocked its membrane localization and oligomerization, thereby reducing pyroptosis and the release of the proinflammatory cytokine IL-1 β ^[3].

In vivo, NU6300 (5mg/kg) was administered via intraperitoneal injection in DSS-induced colitis mouse models (daily for five consecutive days) or LPS-induced sepsis mouse models (single injection). NU6300 significantly alleviated body weight loss, disease activity index elevation, colon shortening, and histopathological damage in DSS-induced colitis mice, while also improving epithelial and mucosal damage, crypt dilation, and goblet cell depletion. Additionally, NU6300 significantly increased the survival rate of septic mice, reduced the spleen index, and lowered the levels of

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proinflammatory cytokines^[3].

References:

- [1] Shua Y, Wang Q, Wang Y, et al. Progress in small-molecule inhibitors of gasdermin D. Eur J Med Chem. 2025 Dec 15;300:118171.
- [2] Anscombe E, Meschini E, Mora-Vidal R, et al. Identification and Characterization of an Irreversible Inhibitor of CDK2. Chem Biol. 2015 Sep 17;22(9):1159-64.
- [3] Jiang X, Zhang X, Cai X, et al. NU6300 covalently reacts with cysteine-191 of gasdermin D to block its cleavage and palmitoylation. Sci Adv. 2024 Feb 9;10(6):ead9284.

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