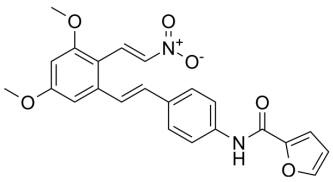
NLRP3-IN-8

Cat. No.:	HY-146594
CAS No.:	2768650-56-0
Molecular Formula:	$C_{23}H_{20}N_2O_6$
Molecular Weight:	420.41
Target:	NOD-like Receptor (NLR)
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

NLRP3-IN-8 (compound 27) is an orally active, directly binding NLRP3 inflammasome inhibitor with an IC_{50} value of 1.23 μM against IL-1 β. NLRP3-IN-8 has good metabolic stability to liver microsomes ($t_{1/2}$ = 138.63 min), and has almost no toxicity (against L02: IC_{50} > 100 μM)[1].

IC_{50} & Target	NLRP3	NLRP3 inflammasome

In Vitro

NLRP3-IN-8 (compound 27) exhibits prominent anti-inflammatory activity with an IC_{50} of 1.23 μM[1].
NLRP3-IN-8 exhibits good metabolic stability through human liver microsomes ($t_{1/2}$ = 138.63 min)[1].
NLRP3-IN-8 (0-10 μM, 1 h) significantly inhibits pyrolysis rate in a concentration-dependent manner[1].
NLRP3-IN-8 only inhibits the activation of NLRP3 inflammasomes, and could inhibit the activation of inflammasome by a variety of inducer[1].
NLRP3-IN-8 blocks NLRP3-induced ASC oligomerization[1].
NLRP3-IN-8 inhibits NLRP3 inflammasome assembly by blocking the interaction of NLRP3-NEK7 and NLRP3-ASC[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	BMDMs cells
Concentration:	0.5, 1, and 2 μM
Incubation Time:	30 min, pretreated with LPS (200 ng/mL) for 3 h
Result:	Dose-dependently blocked IL-1 b secretion and caspase-1 cleavage at concentrations of 0.5-2 μM. Inhibited the maturation of intracellular caspase-1 (p20), and did not affect the expression of other constituent proteins of NLRP3 inflammasome, such as pro-IL-1 β, pro-caspase-1 (p45), NLRP3, ASC and NEK7.

In Vivo

NLRP3-IN-8 (compound 27) (DSS-induced C57BL/6 male mice; 0-20 mg/kg; intragastric; once a day, 7 days) effectively alleviates the severity of DSS-induced colitis in mouse[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	DSS-induced acute colitis model in C57BL/6 male mice[1].

Dosage:	20 mg/kg and 10 mg/kg dissolved in 0.5% sodium carboxymethyl cellulose aqueous solution.
Administration:	Intragastric administration, once a day, 7 days.
Result:	Reduced the weight loss during the onset of colitis in mice, and decreased the disease activity index (DAI) in a dose-dependent manner. Reduced colon shortening, pathological index score, the expression of TNF-a, IL-6 and IL-1 β in the tissues and inhibited the decrease of goblet cells.

REFERENCES

[1]. Xing Xing Zhang, et al. Discovery of 4-((E)-3,5-dimethoxy-2-((E)-2-nitrovinyl)styryl)aniline derivatives as potent and orally active NLRP3 inflammasome inhibitors for colitis. Eur J Med Chem. 2022 Apr 7;236:114357.

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