NIC-0102

Cat. No.: HY-151252

CAS No.: 2806031-94-5

Molecular Formula: $C_{21}H_{25}BF_2N_2O_4$

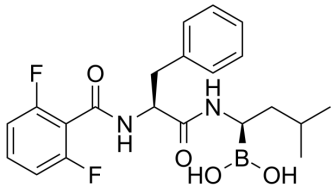
Molecular Weight: 418.24

Target: Proteasome; NOD-like Receptor (NLR)

Pathway: Metabolic Enzyme/Protease; Immunology/Inflammation

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (239.10 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3910 mL	11.9549 mL	23.9097 mL
	5 mM	0.4782 mL	2.3910 mL	4.7819 mL
	10 mM	0.2391 mL	1.1955 mL	2.3910 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.98 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.98 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

NIC-0102 is an orally active proteasome inhibitor (pIC_{50}=7.55) that specifically inhibits NLRP3 inflammatory vesicle activation. NIC-0102 shows potent anti-inflammatory effects in a model of dextran sulfate sodium (DSS)-induced ulcerative colitis. NIC-0102 also inhibits production of pro-IL-1β[1].

IC_{50} & Target

proteasom β5	proteasom β2	proteasom β1
3.7 nM (IC_{50})	100.5 nM (IC_{50})	113.6 nM (IC_{50})

In Vitro

NIC-0102 (compound 27) (7.5, 15, 30, 60 nM; 1h) specifically suppresses NLRP3 inflammasome activation in LPS-primed J774A.1 and BMDM cells[1].

NIC-0102 (7.5, 15, 30, 60 nM; 1h) induces polyubiquitination of NLRP3 via inhibition of the proteasome during the activation

step in LPS-primed J774A.1 cells[1].
NIC-0102 (7.5, 15, 30, 60 nM; 1h) exhibits inhibitory effects on NF-κB in the priming step of the NLRP3 pathway in LPS-primed J774A.1 cells[1].
NIC-0102 (15, 60 nM; 1h) blocks NLRP3-ASC interaction and ASC oligomerization in LPS-primed J774A.1 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	J774A.1 and BMDM cells (LPS-primed)
Concentration:	7.5, 15, 30, 60 nM
Incubation Time:	1 h
Result:	Inhibited the release of IL-1β in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	J774A.1 cells (LPS-primed)
Concentration:	7.5, 15, 30, 60 nM
Incubation Time:	1 h
Result:	Dose-dependently inhibited the release of mature IL-1β and the caspase-1 p20 subunit in supernatants from J774A.1 cells but did not affect pro-IL-1β, pro-caspase-1, NLRP3, or ASC in cell lysates. Increased the polyubiquitinated NLRP3 protein in adose-dependent manner, and significantly increased the amount of c-Cbl and Cbl-b. Showed an inhibitory effect on the NF-κB subunit p65, phosphorylated p65, and NLRP3 protein at 60 nM, at which NF-κB-dependent TNF-α secretion was slightly decreased.

Western Blot Analysis[1]

Cell Line:	J774A.1 cells (LPS-primed)
Concentration:	15, 60 nM
Incubation Time:	1 h
Result:	Inhibited the interaction between NLRP3and ASC stimulated by LPS and nigericin. Showed a concentration-dependent suppression effect on ASC oligomerization.

In Vivo

NIC-0102 (0.125, 0.25, 0.5 mg/kg; p.o.; single every 72 h for 10 days) shows strong protection against DSS-induced acute colitis in mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL/6 mice (6 to 8-week-old; DSS-induced ulcerative colitis model)[1].
Dosage:	0.125, 0.25, and 0.5 mg/kg
Administration:	Oral gavage; single every 72 h for 10 days.
Result:	Significantly suppressed weight and fecal occult blood. Decreased colonic length in a dose-dependent manner. Resulted in a dose-dependent reduction in tissue-associated IL-1β concentration and significantly inhibited pro-IL-1β.

Animal Model:	Male C57BL/6 mice (6 to 8-week-old)[1].
Dosage:	0.5 mg/kg (for i.v.); 1 mg/kg (for p.o.)
Administration:	Intravenous injection; Oral gavage; single.
Result:	Pharmacokinetic Parameters of NIC-0102 in male C57BL/6 mice[1].

	IV (0.5 mg/kg)	PO (1 mg/kg)
$T_{1/2}$ (h)	4.73	8.36
T_{max} (h)	0.08	0.25
C_{max} (ng/mL)	376.6	207.7
$AUC_{0-\infty}$ (h•ng/mL)	448.8	489.2
$MRT_{0-\infty}$ (h)	6.14	-
V_z (L/kg)	7.7	-
CL (mL/min/kg)	18.8	-
F (%)	-	48.1%

REFERENCES

[1]. Wu X, et al. Discovery of a Novel Oral Proteasome Inhibitor to Block NLRP3 Inflammasome Activation with Anti-inflammation Activity. J Med Chem. 2022 Sep 5.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA