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产品名称：INF39
产品别名：INF39

生物活性：

Description	INF39 is an irreversible and noncytotoxic NLRP3 inhibitor.
In Vitro	INF39 is able to significantly inhibit ATP- and nigericin-induced IL-1β release at 10 μM. INF39 reduces caspase-1 activation and pyroptosis in the macrophages. INF39 can block not only NLRP3 activation but also the NF-κB pathway. INF39 potentially reacts with Cys-SH residues in the active site of cysteine protease caspase-1, but does not directly target caspase-1 activity. INF39 is able to reduce the steady state (or basal) BRET signal of NLRP3 without affecting the viability of cells, meaning that it can interfere with the basal NLRP3 conformation. INF39 does not block the initial conformational changes suffered by NLRP3 upon sensing the decrease of intracellular K^+; however, it affects a second step of NLRP3 conformational change that could be related with the ATPase activity of the receptor and be independent of the decrease of intracellular K^+. INF39 reaches the intestinal epithelium without undergoing chemical modifications. After absorption into epithelial cells, it is likely to act locally at the mucosal epithelial level[1].
In Vivo	Oral administration of INF39 reduces systemic and colonic inflammation in rats treated with 2,4-dinitrobenzenesulfonic acid. Significant increments of body weight are observed in inflamed rats under treatment with INF39 (12.5, 25, and 50 mg/ kg). Treatment with DNBS results in a significant increment of spleen weight (+39.3%). Such an increase is significantly reduced by administration of INF39 (+2.2, +4.3 and +4.8% at 12.5, 25, 50 mg/kg, respectively). The inhibition of NLRP3 inflammasome complex with INF39 dose-dependently attenuates the decrease in colonic length (−19, −13 and −8% at 12.5, 25, 50 mg/kg, respectively). Rats treated with INF39 displays a significant reduction of macroscopic damage score (4.7 at 12.5 mg/kg, 3.1 at 25 mg/kg, and 2.8 at 50 mg/kg). Oral administration of INF39 reduces colonic myeloperoxidase, IL-1β, and TNF Levels in DNBS-treated rats[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 1 mg/mL (4.45 mM;** Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.4508 mL	22.2539 mL	44.5077 mL
5 mM	---	---	---
10 mM	---	---	---

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References	[1]. Cocco M, et al. Development of an Acrylate Derivative Targeting the NLRP3 Inflammasome for the Treatment of Inflammatory Bowel Disease.J Med Chem. 2017 May 11;60(9):3656-3671.

实验参考：

	Rats: DNBS-untreated and DNBS treated animals are assigned to the following treatment groups: INF39

Animal Administration	(12.5, 25, 50 mg/kg/day) or dexamethasone (DEX, 1 mg/kg/day). INF39 and dexamethasone are suspended in olive oil and 1% methylcellulose, respectively, and administered in a volume of 0.2 mL/rat. DNBS-untreated animals (control group) and DNBS-treated rats (colitis group) received drug vehicle to serve as controls. Body weight is monitored daily starting from the onset of drug treatments[1].
Kinase Assay	INF39 (100 μM final concentration, 2% DMSO) is added to wells containing immobilized NALP3 protein and preincubated for 55 min at 37°C to mimic normal experimental time (15 min preincubation+40 min incubation with ATP); in the control wells a mixture of buffer and DMSO is added. After the preincubation time the wells areished three times with reaction buffer, and ATP (250 μM) is added for 40 min at 37°C. ADP formation is measured with ADP-Glo-Assay[1].
References	[1]. Cocco M, et al. Development of an Acrylate Derivative Targeting the NLRP3 Inflammasome for the Treatment of Inflammatory Bowel Disease.J Med Chem. 2017 May 11;60(9):3656-3671.