

Product Data Sheet

Product Name: HAMI3379

Cat. No.: GC17092

Chemical Properties

Cas. No. 1245653-57-9

Chemical Name 3-[[[(3-carboxycyclohexyl)amino]carbonyl]-4-[3-[4-[4-(cyclohexyloxy)butoxy]phenyl]propoxy]-benzoic acid

SMILES O=C(NC1CCCC(C(O)=O)C1)C2=CC(C(O)=O)=CC=C2OCCCC(C=C3)=CC=C3OCCCCOC4CCCCC4

Formula $C_{34}H_{45}NO_8$

M.Wt 595.7

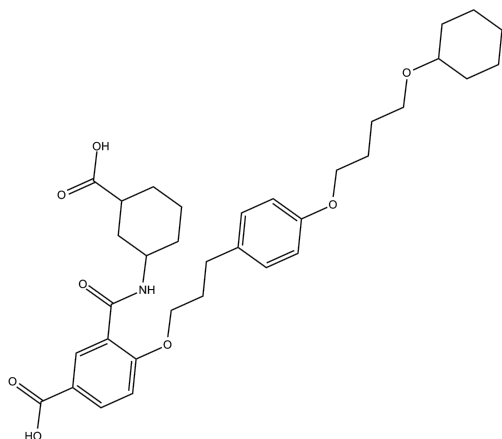
Solubility $\leq 5\text{mg/ml}$ in ethanol; 20mg/ml in DMSO; 20mg/ml in dimethyl formamide

Storage Store at -20°C

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]:

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Cell lines Murine microglial cell line BV-2 cells

Preparation Method Cells were pre-treated with or without HAMI3379 at various concentrations (0, 0.001, 0.01, 0.1, 1 μ M) for 30min before the addition of LPS, then maintained for 24h until the end of the experiments.

Reaction Conditions 0, 0.001, 0.01, 0.1, 1 μ M; 30min

Applications HAMI3379 significantly inhibited LPS-induced phagocytosis and overproduction of the proinflammatory cytokines in BV-2 cells.

Animal experiment [2]:

Animal models Male Sprague–Dawley rats

Preparation Method Diluted HAMI3379 (0.025, 0.05, 0.1, 0.2 and 0.4mg/kg) were injected intraperitoneally 30min before middle cerebral artery occlusion (MCAO), and brain injury was determined 24h after reperfusion.

Dosage form 0.025, 0.05, 0.1, 0.2 and 0.4mg/kg; i.p.; 30min before MCAO

Applications HAMI3379 at 0.1–0.4mg/kg significantly reduced the infarct volume and percentage increase in the ischemic/contralateral hemispheric ratio (an index of brain edema). HAMI3379 also significantly reduced the neurological deficit score and increased the holding angle in the inclined board test.

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References:

- [1]Chen L, Yang Y, Li C T, et al. CysLT₂ receptor mediates lipopolysaccharide-induced microglial inflammation and consequent neurotoxicity in vitro. *Brain Res.* 2015 Oct 22;1624:433-445.
- [2]Shi Q J, Wang H, Liu Z X, et al. HAMI3379, a CysLT₂R antagonist, dose- and time-dependently attenuates brain injury and inhibits microglial inflammation after focal cerebral ischemia in rats. *Neuroscience.* 2015 Apr 16;291:53-69.

Background

HAMI3379 is the first reported potent and selective cysteinyl leukotrienes (CysLT₂) receptor antagonist and also identified as an antagonist of the orphan G protein-coupled receptor GPR17. HAMI3379 was initially developed to treat cardiovascular and inflammatory disorders^{[1][2]}. HAMI3379 also exerts neuroprotective effects by modulating microglial polarization and preserving blood–brain barrier integrity^[3].

In vitro, HAMI3379 (1μM) pretreatment on HEK293 cells stably expressing human CysLT₂ receptors for 1h significantly inhibited leukotriene C₄ (100nM; 6h) induced expression of Egr-1 and IL-8 at both mRNA and protein levels, as well as IL-8 release into the culture medium^[4]. HAMI3379 pretreatment (0, 0.001, 0.01, 0.1, 1μM) on murine microglial BV-2 cells for 30min before 24h incubation of LPS (100ng/ml) significantly inhibited LPS-induced phagocytosis and overproduction of the proinflammatory cytokines (TNF-α, IL-6, and IL-1β)^[5].

In vivo, HAMI3379 (0.1mg/kg) was administered intraperitoneally into post-stroke depression (PSD) gerbil model 30 minutes before and after transient global cerebral ischemia surgery, once daily for 14 days. HAMI3379 diminished PSD-induced neurological injury and depression-like behaviors in gerbils via suppressing the NLRP3 inflammasome/pyroptosis pathway^[6]. HAMI3379 (0.025, 0.05, 0.1, 0.2 and 0.4mg/kg) was administrated into Sprague–Dawley rats via intraperitoneal injection 30min before middle cerebral artery occlusion (MCAO). HAMI3379 (0.1–0.4mg/kg) significantly reduced the infarct volume and percentage increase in the ischemic/contralateral hemispheric ratio, significantly reduced the neurological deficit score and increased the holding angle in the inclined board test at 24h in a dose-dependent manner^[7].

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- [1] Dong X W, Zhao Y M, Huang X Q, et al. Structure-based drug design using GPCR homology modeling: toward the discovery of novel selective CysLT2 antagonists. *Eur J Med Chem.* 2013 Apr;62:754-63.
- [2] Merten N, Fischer J, Simon K, et al. Repurposing HAMI3379 to Block GPR17 and Promote Rodent and Human Oligodendrocyte Differentiation. *Cell Chem Biol.* 2018 Jun 21;25(6):775-786.e5.
- [3] Chen K C, Lan K P, Lai S C. Neuroprotective effects of CysLT2R antagonist on *Angiostrongylus cantonensis*-induced edema and meningoencephalitis. *Mol Biochem Parasitol.* 2024 Dec;260:111649.
- [4] Lin K, Fang S H, Cai B L, et al. ERK/Egr-1 signaling pathway is involved in CysLT2 receptor-mediated IL-8 production in HEK293 cells. *Eur J Cell Biol.* 2014 Jul;93(7):278-88.
- [5] Chen L, Yang Y, Li C T, et al. CysLT2 receptor mediates lipopolysaccharide-induced microglial inflammation and consequent neurotoxicity in vitro. *Brain Res.* 2015 Oct 22;1624:433-445.
- [6] Zhou L, Zhang J J, Han X, et al. CysLT2R Antagonist HAMI3379 Ameliorates Post-Stroke Depression through NLRP3 Inflammasome/Pyroptosis Pathway in Gerbils. *Brain Sci.* 2022 Jul 24;12(8):976.
- [7] Shi Q J, Wang H, Liu Z X, et al. HAMI3379, a CysLT2R antagonist, dose- and time-dependently attenuates brain injury and inhibits microglial inflammation after focal cerebral ischemia in rats. *Neuroscience.* 2015 Apr 16;291:53-69.

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