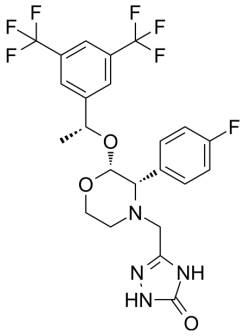
Aprepitant



Cat. No.: HY-10052

CAS No.: 170729-80-3

Molecular Formula: $C_{23}H_{21}F_7N_4O_3$

Molecular Weight: 534.43

Target: Neurokinin Receptor; Bacterial; HIV; Antibiotic

Pathway: GPCR/G Protein; Neuronal Signaling; Anti-infection

Storage: 4°C, protect from light

* In solvent : -80°C, 1 years; -20°C, 6 months (protect from light)

SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (187.12 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.8712 mL	9.3558 mL	18.7115 mL
5 mM	0.3742 mL	1.8712 mL	3.7423 mL
10 mM	0.1871 mL	0.9356 mL	1.8712 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 (4.68 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Aprepitant (MK-0869) is a selective and high-affinity neurokinin 1 receptor antagonist with a K_d of 86 pM.

IC_{50} & Target

Kd: 86 pM (Neurokinin 1 receptor)[1]

In Vitro

Aprepitant decreases the metabolic activity with an estimated IC_{50} value of 20 μM. Aprepitant induces cell-growth inhibition and G1 cell-cycle arrest. Aprepitant significantly induces apoptosis in Nalm-6 cells, and the apoptosis is mediated through caspase-3 activation. Aprepitant (20 μM) induces p53 accumulation and expression of pro-apoptotic p53 target genes[2]. Aprepitant (1, 5, 10 μM) inhibits HIV infection in MDM from both depressed and not depressed HIV negative individuals ex vivo in a dose-dependent manner. IC_{90} value of aprepitant is equivalent to 10 μM, and the IC_{50} value is about 5 μM[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	Aprepitant prevents the increase of NK-1R expression induced by in vivo NHP infection with B. burgdorferi. Aprepitant treatment prevents B. burgdorferi-induced increases in CCL2 protein levels in the CSF of NHPs. Aprepitant treatment prevents B. burgdorferi-induced increases in CCL2 and CXCL13 mRNA expression in the dorsal root ganglia of NHPs, prevents B. burgdorferi-induced increases in CCL2, CXCL13, IL-17A, and IL-6 mRNA expression in the spinal cord of NHPs. Aprepitant treatment attenuates B. burgdorferi infection-induced reductions in astrocyte activity/numbers[1]. Aprepitant (10 mg/kg, i.p.) significantly attenuates the CPP expression and locomotor activation produced by AMPH and cocaine in mice. Aprepitant does not induce significant CPP or conditioned place aversion or locomotor activation or suppression[3]. Aprepitant (125 mg/day, p.o.) results in 1 log reduction in plasma levels of viral RNA as compared to non-treated controls[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The inhibitory effect of aprepitant on metabolic activity of Nalm-6 cells is assessed by uptake of thiazolyl blue tetrazolium bromide (MTT) by viable cells. Cells are plated onto 96-well plates at a density of 5000 cells/well. After treatment with aprepitant at 5, 10, 15, 20 and 30 μM for 24, 36 and 48 h, the cells are further incubated with 100 μL of MTT (0.5 mg/mL) at 37°C for 3 h. Untreated cells are defined as the control group. Following solubilization of precipitated formazan with 100 μL of DMSO, the optical densitometry is measured with an ELISA reader at a wavelength of 578 nm. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Fifteen rhesus macaques are anesthetized and inoculated intrathecally with 1×10^8 live spirochetes into the cisterna magna, whereas five rhesus macaques are left uninfected and receive 1 mL of RPMI 1640 medium after removing an equivalent volume of CSF. The establishment of in vivo B. burgdorferi infection is confirmed by positive culture from at least necropsy tissue sample. The first set of animals are studied for 2 weeks and included two control animals (one of which is treated with aprepitant), two infected and untreated animals, and two infected animals that are treated with aprepitant. The second set of animals are studied for 4 weeks and included three control animals (one of which is treated with aprepitant), five infected and untreated animals, and four infected animals treated with aprepitant. Animals receive an average dose of aprepitant of 28 ± 6 mg/kg per day p.o. daily, and drug treatments are started 2 days before inoculation. These doses are consistent with standard veterinary regimens for the chosen drugs in NHP, and the 4-week duration of the study precludes the development of neural pathology that occurs at 8 weeks following B. burgdorferi infection. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2023 Jun 29;14(6):384.
- Cell Death Dis. 2022 Jan 10;13(1):41.
- Korean J Pain. 2022 Apr 1;35(2):173-182.
- Research Square Print. 2023 Mar 2.
- Research Square Print. 2023 Feb 2.

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REFERENCES

[1]. Martinez AN, et al. Aprepitant limits in vivo neuroinflammatory responses in a rhesus model of Lyme neuroborreliosis. J Neuroinflammation. 2017 Feb 15;14(1):37.

[2]. Bayati S, et al. Inhibition of tachykinin NK1 receptor using aprepitant induces apoptotic cell death and G1 arrest through Akt/p53 axis in pre-B acute lymphoblastic leukemia cells. Eur J Pharmacol. 2016 Nov 15;791:274-283.

[3]. Mannangatti P, et al. Differential effects of aprepitant, a clinically used neurokinin-1 receptor antagonist on the expression of conditioned psychostimulant versus opioid reward. Psychopharmacology (Berl). 2017 Feb;234(4):695-705.

[4]. Barrett JS, et al. Pharmacologic rationale for the NK1R antagonist, aprepitant as adjunctive therapy in HIV. J Transl Med. 2016 May 26;14(1):148.

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