K777

Cat. No.: HY-119293

CAS No.: 233277-99-1

Molecular Formula: $C_{32}H_{38}N_4O_4S$

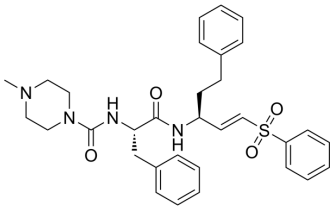
Molecular Weight: 575

Target: Cathepsin; CCR; Cytochrome P450; Parasite; SARS-CoV; Filovirus

Pathway: Metabolic Enzyme/Protease; GPCR/G Protein; Immunology/Inflammation; Anti-infection

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (173.91 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7391 mL	8.6957 mL	17.3913 mL
	5 mM	0.3478 mL	1.7391 mL	3.4783 mL
	10 mM	0.1739 mL	0.8696 mL	1.7391 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 (4.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.35 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

K777 is a potent, orally active and irreversible cysteine protease inhibitor. K777 is also a potent CYP3A4 inhibitor with an IC_{50} of 60 nM and a selective CCR4 antagonist featuring the potent chemotaxis inhibition. K777 irreversibly inhibits Cruzain, the major cysteine protease of Trypansoma cruzi, and cathepsins B and L. K777 is a broad-spectrum antiviral by targeting cathepsin-mediated cell entry. K777 inhibits SARS-CoV and EBOV pseudovirus entry with IC_{50} values of 0.68 nM and 0.87 nM, respectively[1][2][3].

IC_{50} & Target			
	CYP3	CCR4	Trypanosoma

In Vitro

K777 (K11777) can inhibit entry driven by other viral envelope proteins, including HIV-based pseudotypes bearing spikes from coronaviruses (SARS-CoV, HCoV-229E, NL63, MERS-CoV) or glycoproteins from filoviruses (EBOV, SUDV, TAFV, RESTV, BEBOV and MARV).

K777 inhibits SARS-CoV, HCoV-229E, NL63, MERS-CoV, EBOV, SUDV, TAFV, RESTV, BEBOV, MARV and Nipah pseudovirus entry with IC_{50} values of 0.68 nM, 1.48 nM, 6.78 nM, 46.12 nM, 0.87 nM, 1.14 nM, 2.26 nM, 3.37 nM, 5.91 nM, 1.9 nM and 0.42 nM, respectively.

In contrast, 100 nM K777 does not inhibit infection mediated by envelope glycoproteins from an alphavirus (CHIKV), a rhabdovirus (VSV), a flavivirus (HCV), the retroviruses MLV-A and XMRV or two arenaviruses, Lassa and Junin virus[1].

K777 alone demonstrates up to ~ 70% inhibition of 229E-S-mediated transduction. Simultaneous treatment with Camostat and K777 increases inhibition to ~ 90%. Similar inhibition patterns are obtained using the human intestinal epithelial cell line Caco-2, which express endogenous TMPRSS2 and cathepsins[1].

K777 inhibits both CCL17 binding and CCL17-induced chemotaxis in Hut78 cells (IC_{50} of 57 and 8.9 nM, respectively). The K777-mediated inhibition of chemotaxis is potent even in the presence of a 10-fold higher concentration of CCL17.

K777 induces CCR4 internalization, with a ⊠50% reduction of cell surface CCR4. K777 does not inhibit CXCR4-induced chemotaxis or internalization and did not bring about Ca^{2+} mobilization by itself[3].

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

In Vivo

K777 (K11777; 35-105 mg/kg; oral administration; twice a day; for 10 days; C57BL/6 IFN-γR-KO mice) treatment rescues mice from otherwise lethal infections[4] .

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

Animal Model:	C57BL/6 IFN-γR-KO mice (6-8 weeks of age) injected with Cryptosporidium parvum[4]
Dosage:	35 mg/kg, 70 mg/kg, and 105 mg/kg
Administration:	Oral administration; twice a day; for 10 days
Result:	Rescued mice from otherwise lethal infections.

CUSTOMER VALIDATION

- bioRxiv. 2023 Nov 5.

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REFERENCES

[1]. Zhou Y, et al. Protease inhibitors targeting coronavirus and filovirus entry. Antiviral Res. 2015 Apr;116:76-84.

[2]. Jacobsen W, et al. In vitro evaluation of the disposition of A novel cysteine protease inhibitor. Drug Metab Dispos. 2000 Nov;28(11):1343-51.

[3]. Sato T, et al. Internalization of CCR4 and inhibition of chemotaxis by K777, a potent and selective CCR4 antagonist. Pharmacology. 2013;91(5-6):305-13.

[4]. Ndao M, et al. A cysteine protease inhibitor rescues mice from a lethal Cryptosporidium parvum infection. Antimicrob Agents Chemother. 2013 Dec;57(12):6063-73.

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