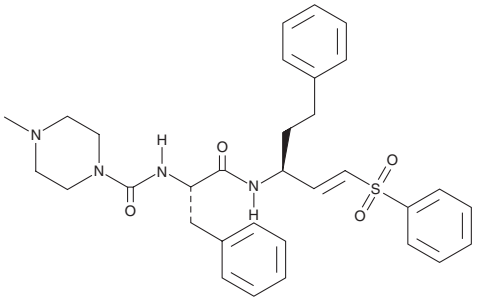
PRODUCT INFORMATION

K777

Item No. 19114

CAS Registry No.: 233277-99-1
Formal Name: 4-methyl-N-[(1S)-2-oxo-2-[[(1S)-1-(2-phenylethyl)-3-(phenylsulfonyl)-2-propen-1-yl]amino]-1-(phenylmethyl)ethyl]-1-piperazinecarboxamide
Synonyms: APC-3316, CRA-3316, K11777, MePip-Phe-hPhe-VSφ
MF: $C_{32}H_{38}N_4O_4S$
FW: 574.7
Purity: ≥98% (mixture of isomers)
Supplied as: A solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

K777 is supplied as a solid. A stock solution may be made by dissolving the K777 in the solvent of choice, which should be purged with an inert gas. K777 is soluble in DMSO.

Description

K777 is a cysteine protease inhibitor.[1] It inhibits human cathepsin S (K_i = 0.002 µM) and human cathepsin L (K_i = 0.05 µM), which cleaves the severe acute respiratory coronavirus 2 (SARS-CoV-2) spike glycoprotein, also known as the surface glycoprotein. K777 is selective for these proteases over human cathepsin K, -B, and -C (K_is = 0.4, 3, >100 µM, respectively), as well as the SARS-CoV-2 cysteine proteases papain-like protease (PL^{pro}) and main protease (M^{pro}), also known as the 3C-like protease ($3CL^{pro}$; K_is = >100 µM for both). It prevents cleavage of the spike protein S1 subunit *in vitro* and reduces the cytopathic effect of SARS-CoV-2 in infected Vero E6, HeLa/ACE2, and A549/ACE2 cells (EC_{50}s = <0.074, 0.004, and <0.080 µM, respectively). K777 induces mortality in *T. b. brucei* trypanosomes (IC_{50} = 0.1 µM) and reduces myocardial damage in a canine model of *T. cruzi* infection when administered at a dose of 50 mg/kg twice per day.[2,3] It also inhibits chemokine (C-C motif) ligand 17 (CCL17) binding to, and CCL17-induced chemotaxis of, HuT 78 cells (IC_{50}s = 0.057 and 0.0089 µM, respectively), as well as induces chemokine (C-C motif) receptor 4 (CCR4) internalization.[4]

References

1. Mellott, D.M., Tseng, C.-T., Drelich, A., *et al.* A clinical-stage cysteine protease inhibitor blocks SARS-CoV-2 infection of human and monkey cells. *ACS Chem. Biol.* **16(4)**, 642-650 (2021).
2. Troeberg, L., Morty, R.E., Pike, R.N., *et al.* Cysteine proteinase inhibitors kill cultured bloodstream forms of *Trypanosoma brucei brucei*. *Exp. Parasitol.* **91(4)**, 349-355 (1999).
3. Barr, S.C., Warner, K.L., Kornreic, B.G., *et al.* A cysteine protease inhibitor protects dogs from cardiac damage during infection by *Trypanosoma cruzi*. *Antimicrob. Agents Chemother.* **49(12)**, 5160-5161 (2005).
4. Sato, T., Iwase, M., Miyama, M., *et al.* Internalization of CCR4 and inhibition of chemotaxis by K777, a potent and selective CCR4 antagonist. *Pharmacology* **91(5-6)**, 305-313 (2013).

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