TAK-220

Cat. No.: HY-19974

CAS No.: 333994-00-6

Molecular Formula: $C_{31}H_{41}ClN_4O_3$

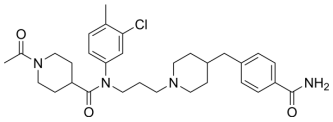
Molecular Weight: 553.14

Target: CCR; HIV

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

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (90.39 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8079 mL	9.0393 mL	18.0786 mL
	5 mM	0.3616 mL	1.8079 mL	3.6157 mL
	10 mM	0.1808 mL	0.9039 mL	1.8079 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 (4.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TAK-220 is a selective and orally bioavailable CCR5 antagonist, with IC_{50}s of 3.5 nM and 1.4 nM for inhibition on the binding of RANTES and MIP-1α to CCR5, respectively, but shows no effect on the binding to CCR1, CCR2b, CCR3, CCR4, or CCR7; TAK-220 also selectively inhibits HIV-1, with EC_{50}s of 1.2 nM (HIV-1 KK), 0.72 nM (HIV-1 CTV), 1.7 nM (HIV-1 HKW), 1.7 nM (HIV-1 HNK), 0.93 nM (HIV-1 HTN), and 0.55 nM (HIV-1 HHA), and EC_{90}s of 12 nM (HIV-1 KK), 5 nM (HIV-1 CTV), 12 nM (HIV-1 HKW), 28 nM (HIV-1 HNK), 15 nM (HIV-1 HTN), and 4 nM (HIV-1 HHA) in PBMCs.

IC_{50} & Target	MIP-1α-CCR5 1.4 nM (IC_{50}, in CHO cells)	RANTES-CCR5 3.5 nM (IC_{50}, in CHO cells)	HIV-1 (HHA) 0.55 nM (EC50, in PBMCs)	HIV-1 (CTV) 0.72 nM (EC50, in PBMCs)
	HIV-1 (HTN) 0.93 nM (EC50, in PBMCs)	HIV-1 (KK) 1.2 nM (EC50, in PBMCs)	HIV-1 (HKW) 1.7 nM (EC50, in PBMCs)	HIV-1 (HNK) 1.7 nM (EC50, in PBMCs)
	HIV-1 (HHA) 4 nM (EC90, in PBMCs)	HIV-1 (CTV) 5 nM (EC90, in PBMCs)	HIV-1 (KK) 12 nM (EC90, in PBMCs)	HIV-1 (HKW) 12 nM (EC90, in PBMCs)
	HIV-1 (HTN) 15 nM (EC90, in PBMCs)	HIV-1 (HNK) 28 nM (EC90, in PBMCs)		

In Vitro

TAK-220 is a selective CCR5 antagonist, with IC_{50}s of 3.5 nM and 1.4 nM for inhibition on the binding of RANTES and MIP-1α to CCR5 in CHO cells, respectively, but shows no effect on the binding to CCR1, CCR2b, CCR3, CCR4, or CCR7. TAK-220 (0-1000 nM) interacts with CCR5 but not with RANTES and inhibits the CCR5-mediated Casup>2+ signaling. TAK-220 inhibits R5 HIV-1 (JR-FL) envelope-mediated membrane fusion, with an IC_{50} value of 0.42 nM, but does not alter X4 HIV-1 (HXB2) envelope-mediated membrane fusion. TAK-220 also selectively inhibits HIV-1, with EC_{50}s of 1.2 nM (HIV-1 KK), 0.72 nM (HIV-1 CTV), 1.7 nM (HIV-1 HKW), 1.7 nM (HIV-1 HNK), 0.93 nM (HIV-1 HTN), and 0.55 nM (HIV-1 HHA), and EC_{90}s of 12 nM (HIV-1 KK), 5 nM (HIV-1 CTV), 12 nM (HIV-1 HKW), 28 nM (HIV-1 HNK), 15 nM (HIV-1 HTN), and 4 nM (HIV-1 HHA) in PBMCs[1]. TAK-220 shows potent inhibitory activity against the R5 isolates, with IC_{50}s of 3.12 nM against HIV-1 R5-08, 13.47 nM against HIV-1 R5-06, and 2.26 nM against HIV-1 R5-18. TAK-220 (>100 nM) has no toxicity in uninfected PBMCs[2].

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

PROTOCOL

Cell Assay [1]

PHA-stimulated PBMCs are inoculated with 1,000 to 1,400 CCID50s of R5 HIV-1 (JR-FL) or X4 HIV-1 (IIIB) or with 13 to 55 ng of p24 of HIV-1 clinical isolates per 4×10^6 cells and incubated for 4 h. The cells are washed to remove unadsorbed viral particles and seeded into a 96-well plate (2×10^5 cells/well) with culture medium containing various concentrations of TAK-220. The effects of high concentrations of human serum (HS) on the anti-HIV-1 activity of TAK-220 are examined with RPMI 1640 medium supplemented with either 20% FBS alone or 40% human type AB serum plus 10% FBS, 100 U/mL recombinant human interleukin 2, and antibiotics. On day 4 after infection, the cells are subcultured at 1:2 with culture medium containing the same concentrations of the test compounds. On day 7 after infection, the culture supernatants are collected and their p24 antigen levels are determined with a p24 antigen enzyme-linked immunosorbent assay kit[1].

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

CUSTOMER VALIDATION

- Bioact Mater. 2021 Jan 7;6(7):2039-2057.
- Brain Sci. 2023 Mar 30, 13(4), 579.

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REFERENCES

[1]. Takashima K, et al. Highly potent inhibition of human immunodeficiency virus type 1 replication by TAK-220, an orally bioavailable small-molecule CCR5 antagonist. Antimicrob Agents Chemother. 2005 Aug;49(8):3474-82.

[2]. Tremblay CL, et al. TAK-220, a novel small-molecule CCR5 antagonist, has favorable anti-human immunodeficiency virus interactions with other antiretrovirals in vitro. Antimicrob Agents Chemother. 2005 Aug;49(8):3483-5.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA