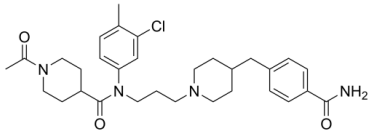
Data Sheet

Product Name:	TAK-220
Cat. No.:	CS-5579
CAS No.:	333994-00-6
Molecular Formula:	$C_{31}H_{41}ClN_4O_3$
Molecular Weight:	553.14
Target:	CCR; HIV
Pathway:	Anti-infection; GPCR/G Protein; Immunology/Inflammation
Solubility:	DMSO : ≥ 50 mg/mL



BIOLOGICAL ACTIVITY:

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. IC50 & Target:IC50: 3.5 nM (RANTES-CCR5, in CHO cells), 1.4 nM (MIP-1α-CCR5, in CHO cells)[1]

EC50: 1.2 nM (HIV-1 KK, in PBMCs), 0.72 nM (HIV-1 CTV, in PBMCs), 1.7 nM (HIV-1 HKW, in PBMCs), 1.7 nM (HIV-1 HNK, in PBMCs), 0.93 nM (HIV-1 HTN, in PBMCs), 0.55 nM (HIV-1 HHA, in PBMCs)[1]

EC90: 12 nM (HIV-1 KK, in PBMCs), 5 nM (HIV-1 CTV, in PBMCs), 12 nM (HIV-1 HKW, in PBMCs), 28 nM (HIV-1 HNK, in PBMCs), 15 nM (HIV-1 HTN, in PBMCs), 4 nM (HIV-1 HHA, in PBMCs)[1] ***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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

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.

CAIndexNames:

4-Piperidinecarboxamide, 1-acetyl-N-[3-[4-[[4-(aminocarbonyl)phenyl]methyl]-1-piperidinyl]propyl]-N-(3-chloro-4-methylphenyl)-

SMILES:

O=C(C1CCN(C(C)=O)CC1)N(CCCN2CCC(CC3=CC=C(C(N)=O)C=C3)CC2)C4=CC=C(C)C(Cl)=C4

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