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产品名称：TAK-220
产品别名：TAK-220

生物活性：

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

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

In Vitro:

DMSO : ≥ 50 mg/mL (90.39 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

Solvent&Solubility	储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。 ***In Vivo:*** 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.52 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.52 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.52 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.
实验参考：	
Cell Assay	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.