ALX 40-4C

Cat. No.:	HY-P7061
CAS No.:	143413-49-4
Molecular Formula:	$C_{56}H_{113}N_{37}O_{10}$
Molecular Weight:	1464.74
Sequence:	Ac-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-NH2
Sequence Shortening:	Ac-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-{d-Arg}-NH2
Target:	CXCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description	ALX 40-4C is a small peptide inhibitor of the chemokine receptor CXCR4, inhibits SDF-1 from binding CXCR4 with a K_i of 1 μM, and suppresses the replication of X4 strains of HIV-1; ALX 40-4C Trifluoroacetate also acts as an antagonist of the APJ receptor, with an IC_{50} of 2.9 μM.	
IC_{50} & Target	SDF-1-CXCR4 1 μM (Ki)	APJ receptor 2.9 μM (IC_{50})
In Vitro	ALX 40-4C is a small peptide inhibitor of the chemokine receptor CXCR4, interacts with the second extracellular loop of CXCR4 and inhibits infection exclusively by blocking direct virus-CXCR4 interactions[1]. ALX 40-4C shows potent anti HIV-1 effect, with EC_{50}s of 0.34 ± 0.04 μg/mL, 0.37 ± 0.01 μg/mL for HIV-1 NL4-3, NC10, and 0.18 ± 0.11 μg/mL, 0.06 ± 0.02 μg/mL for HIV-1 HXB2, HC43, respectively, and with a CC_{50} (50% cytotoxic concentration) of 21 μg/mL. ALX 40-4C also exhibits potent activity against env-recombinant HIV, with EC_{50}s of 0.38 ± 0.01 μg/mL, 0.40 ± 0.0 μg/mL for HIV-1 NL4-3 env, NC10, and 1.34 ± 0.06 μg/mL, 1.02 ± 0.29 μg/mL for HIV-1 HXB2 env, HC43, and a CC_{50} of 21 μg/mL[2]. ALX 40-4C binds to APJ with an IC_{50} of 2.9 μM. ALX 40-4C inhibits HIV-1 gp120/APJ-mediated cell membrane fusion, with an IC_{50}s of 3.41 μM and 3.1 μM for IIIB isolate and 89.6 isolate, respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

PROTOCOL

Kinase Assay [3]	The stably transfected cells are harvested in PBS (Ca^{2+} and Mg^{2+} free) plus 0.5 nM EDTA and washed twice with PBS. Ligand binding experiments are performed using a single concentration (0.2 nM) of ^{125}I-Apelin-13 in the absence or presence of increasing concentrations of unlabeled Apelin-13 or ALX 40-4C in a final volume of 100 μL of binding buffer (50 nM Hepes, pH 7.4, 1 nM $CaCl_2$, 5 nM $MgCl_2$, 0.1% bovine serum albumin) containing 5 × 10^5 cells. Nonspecific binding is determined by the addition of 1 μM unlabeled Apelin-13. Samples are incubated for 90 min at room temperature. The incubation is terminated by separating the cells from the binding buffer by centrifugation and washing once with 500 μL of cold binding buffer. Bound ligands are determined by counting gamma emissions. At least three independent experiments are performed[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Doranz BJ, et al. Safe use of the CXCR4 inhibitor ALX40-4C in humans. AIDS Res Hum Retroviruses. 2001 Apr 10;17(6):475-86.

[2]. Armand-Ugón M, et al. HIV-1 resistance to the gp41-dependent fusion inhibitor C-34. Antiviral Res. 2003 Jul;59(2):137-42.

[3]. Zhou N, et al. Binding of ALX40-4C to APJ, a CNS-based receptor, inhibits its utilization as a co-receptor by HIV-1. Virology. 2003 Jul 20;312(1):196-203.

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