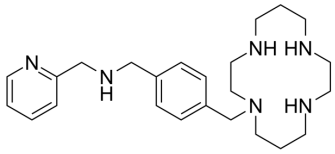
AMD 3465

Cat. No.:	HY-15971A
CAS No.:	185991-24-6
Molecular Formula:	$C_{24}H_{38}N_6$
Molecular Weight:	410.6
Target:	CXCR; HIV
Pathway:	GPCR/G Protein; Immunology/Inflammation; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AMD 3465 (GENZ-644494) is a potent antagonist of CXCR4, inhibits binding of 12G5 mAb and $CXCL12^{AF647}$ to CXCR4, with IC_{50}s of 0.75 nM and 18 nM in SupT1 cells; AMD 3465 also potently inhibits the replication of X4 HIV strains (IC_{50}: 1-10 nM), but has no effect on CCR5-using (R5) viruses.

IC_{50} & Target

12G5 mAb-CXCR4 0.75 nM (IC_{50}, in SupT1 cells)	$CXCL12^{AF647}$-CXCR4 18 nM (IC_{50}, in SupT1 cells)	X4 HIV-1 (III_B) 12.3 nM (IC_{50}, in MT-4 cells)	X4 HIV-1 (NL4.3) 6.1 nM (IC_{50}, in MT-4 cells)
X4 HIV-1 ($NL4.3^{AMD3100}$) 2822 nM (IC_{50}, in MT-4 cells)	X4 HIV-1 (RF) 7.4 nM (IC_{50}, in MT-4 cells)	X4 HIV-1 (HE) 9.8 nM (IC_{50}, in MT-4 cells)	HIV-2 (ROD) 12.3 nM (IC_{50}, in MT-4 cells)
HIV-2 (EHO) 12.3 nM (IC_{50}, in MT-4 cells)			

In Vitro	AMD 3465 is a potent antagonist of CXCR4, inhibits binding of 12G5 mAb and $CXCL12^{AF647}$ to CXCR4, with IC_{50}s of 0.75 nM and 18 nM in SupT1 cells. AMD 3465 (50 nM) totally blocks CXCL12-induced calcium mobilization, with an IC_{50} of 17 nM, but shows no effect on the intracellular calcium fluxes elicited by the CCR5 ligands RANTES, LD78β and MIP-1β in U87.CD4.CCR5 cells. AMD 3465 also potently inhibits the replication of X4 HIV strains (IC_{50}: 1-10 nM), but has no effect on CCR5-using (R5) viruses. AMD3465 is cytotoxic to the X4 HIV-1 strains IIIB, NL4.3, RF and HE with an IC_{50} ranging from 6 to 12 nM. The IC_{50} for suppression of the HIV-2 strains ROD and EHO is 12.3 nM[1]. AMD 3465 inhibits CXCL-12-induced growth in U87 and Daoy cells. AMD 3465 treatment stimulates the phosphorylation of Erk1/2 in U87 and Daoy cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AMD 3465 (2.5 mg/kg/d, s.c. for 5 weeks) significantly blocks the growth of U87 GBM and Daoy xenografts[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Following serum starvation for 24 h, astrocytes, granule cells, U87 cells, and Daoy cells are treated with 1 μg/mL CXCL12, 2.5 ng/mL AMD 3465, 200 μM rolipram, or 10 μM forskolin. Daoy and U87 cell growth in culture is measured by trypan blue

	exclusion after 24 and 48 h of treatment, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Mice are imaged at least twice after implantation of cells to identify those with equivalent tumor growth rates. Two weeks after tumor cell implantation, cohorts of mice with approximately equivalent tumor bioluminescence are divided into equal control and treatment groups. Animals in AMD 3465 experiments receive s.c. osmotic pumps loaded with 10 mg/mL AMD 3465 in sterile PBS or PBS alone. The infusion rate is 0.25 μL/h (50 μg/d). For the experiments with rolipram or caffeine, mice in the treatment groups receive oral administration of rolipram (5 μg/g/d) or caffeine (100 μg/g/d). The concentration of drug in the water is determined from daily measurements of water consumption by each animal over the course of 7 days. Concentrations are adjusted based on water consumption to provide the prescribed dose[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biomed Pharmacother. 2021 Mar 24;138:111476.
- J Labelled Comp Radiopharm. 2018 May 15;61(5):438-446.
- Patent. US20180263995A1.

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REFERENCES

[1]. Hatse S, et al. AMD3465, a monomacrocyclic CXCR4 antagonist and potent HIV entry inhibitor. Biochem Pharmacol. 2005 Sep 1;70(5):752-61.

[2]. Yang L, et al. Blocking CXCR4-mediated cyclic AMP suppression inhibits brain tumor growth in vivo. Cancer Res. 2007 Jan 15;67(2):651-8.

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