Product Data Sheet

Product Name: AMD 3465
Cat. No.: GC10473

Chemical Properties

Cas. No.	185991-24-6		
Chemical Name	N-(pyridin-2-ylmethyl)-1-[4-(1,4,8,11-tetrazacyclotetradec-1-ylmethyl)phenyl]methanamine		
SMILES	C1CNCCNCCCN(CCNC1)CC2=CC=C(C=C2)CNCC3=CC=CC=N3		
Formula	$C_{24}H_{38}N_6$	M.Wt	410.6
Solubility	H_2O : ≥ 100 mg/mL (243.55 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	AMD 3465		

Protocol

Cell experiment:

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].

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Animal experiment:	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].

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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.

Background

IC50: 10.38 ± 1.99 nM for CXCR4 activation as measured by GTP binding

CXCR4 is widely expressed in multiple cell types, and involved in neonatal development, hematopoiesis, and lymphocyte trafficking and homing. Additionally CXCR4 is a co-receptor for HIV. Small molecule antagonists of CXCR4 thus have therapeutic potential. AMD3465 is an N-pyridinylmethylene monocyclam CXCR4 antagonist blocking infection of T-tropic, CXCR4-using HIV.

In vitro: Using the CCRF-CEM T-cell line expressing CXCR4 previous authors have demonstrated that AMD3465 is an antagonist of SDF-1 ligand binding, and inhibits SDF-1

mediated signaling as shown by inhibition of GTP binding, calcium flux, and inhibition of chemotaxis. AMD3465 does not inhibit chemokine-stimulated calcium flux in cells expressing CXCR3, CCR1, CCR2b, CCR4, CCR5 or CCR7, nor does it inhibit binding of LTB4 to its receptor, BLT1 [1].

In vivo: AMD3465 caused leukocytosis when subcutaneously administered in mice and dogs, with peak mobilization occurring between 0.5 and 1.5 h following subcutaneous dosing in mice and with maximum peak plasma concentration of compound preceding peak mobilization in dogs, demonstrating that AMD3465 has the potential to mobilize hematopoietic stem cells. These data demonstrate the therapeutic potential for the CXCR4 antagonist AMD3465 [1].

Clinical trials: Currenlty no clinical data are available.

Reference:
[1] Bodart V, Anastassov V, Darkes MC, Idzan SR, Labrecque J, Lau G, Mosi RM, Neff KS, Nelson KL, Ruzek MC, Patel K, Santucci Z, Scarborough R, Wong RS, Bridger GJ, Macfarland RT, Fricker SP. Pharmacology of AMD3465: a small molecule antagonist of the chemokine receptor CXCR4. Biochem Pharmacol. 2009;78(8):993-1000.