Product Data Sheet

Product Name: AMD-070
Cat. No.: GC12196

Chemical Properties

Cas. No.	558447-26-0		
Chemical Name	N'-(1H-benzimidazol-2-ylmethyl)-N'-[(8S)-5,6,7,8-tetrahydroquinolin-8-yl]butane-1,4-diamine		
SMILES	C1CC(C2=C(C1)C=CC=N2)N(CCCCN)CC3=NC4=CC=CC=C4N3		
Formula	$C_{21}H_{27}N_5$	M.Wt	349.48
Solubility	≥ 17.45 mg/mL in DMSO, ≥ 44.5 mg/mL in EtOH, ≥ 7.47 mg/mL in Water with gentle warming	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-070		

Protocol

Cell experiment [1,2]:

Cell lines	Melanoma cells CHL-1 and A375, HOS cells

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Preparation method	The solubility of this compound in DMSO is >17.5mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting condition	6.6 μM, 24h
Applications	In melanoma cells CHL-1 and A375, treatment of AMD-070 significantly inhibited the migration of cells. Besides that, the void sizes of cells were also increased by the inhibitor treatment. In HOS cells expressing human CXCR4, AMD-070 inhibited HIV-1 infection with IC50 value of 10 nM.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1] O'boyle G, Swidenbank I, Marshall H, et al. Inhibition of CXCR4–CXCL12 chemotaxis in melanoma by AMD11070[J]. British journal of cancer, 2013, 108(8): 1634.

[2] Gudmundsson K S, Sebahar P R, Richardson L D A, et al. Amine substituted N-(1H-benzimidazol-2ylmethyl)-5, 6, 7, 8-tetrahydro-8-quinolinamines as CXCR4 antagonists with potent activity against HIV-1[J]. Bioorganic & medicinal chemistry letters, 2009, 19(17): 5048-5052.

Background

AMD-070 is a selective and oral bioavailable antagonist of chemokine receptor CXCR4 with IC50 value of 13 nM [1].
CXCR4 is a G-protein-coupled receptor that plays important roles in tumor development. It affects the migration, proliferation and survival of cancer cells through the CXCL12-mediated MAPK signaling. AMD-070 is an orally bioavailable antagonist of CXCR4 and is found to be an inhibitor of tumor cell migration. CXCR4 is also one of the two chemokine receptors that are used by virus for infecting human cells. As a CXCR4 inhibitor, AMD-070 can repress the replication of X4 (T-tropic) HIV-1 and the interaction of gp120/CXCR4 potently. The mechanistic studies demonstrate that AMD-070 is an allosteric inhibitor. It was found that a hydrogen bond was formed between the benzimidazole of AMD-070 and the Tyr45 residue of CXCR4 whereas the residues Asp262, Asp171 and Glu288 were not involved in the direct interactions with AMD-070 [1, 2 and 3].
AMD-070 is selective against CXCR4 over other related G-protein-coupled chemokine receptors including CXCR1, CXCR2, CCR1, CCR2b, CCR4 and CCR5. The IC50 values of AMD-070 against these GPCRs were all above 10 μM. In HOS cells expressing human CXCR4, AMD-070 inhibited HIV-1 infection with IC50 value of 10 nM. In CD4+CXCR4+T cells, AMD-070 showed anti-HIV-1 activity (IC50 value of 2 nM) through inhibiting the SDF-1 induced calcium flux with IC50 value of 12 nM. In addition, AMD-070 inhibited the

competitive binding of 125I-SDF-1with IC50 value of 13 nM. In melanoma cells CHL-1 and A375, treatment of AMD-070 significantly inhibited the migration of cells. Besides that, the void sizes of cells were also increased by the inhibitor treatment [1, 2 and 4].

References:

[1] Skerlj RT, Bridger GJ, Kaller A, McEachern EJ, Crawford JB, Zhou Y, Atsma B, Langille J, Nan S, Veale D, Wilson T, Harwig C, Hatse S, Princen K, De Clercq E, Schols D. Discovery of novel small molecule orally bioavailable C-X-C chemokine receptor 4 antagonists that are potent inhibitors of T-tropic (X4) HIV-1 replication. J Med Chem. 2010 Apr 22;53(8):3376-88.

[2] O'Boyle G, Swidenbank I, Marshall H, Barker CE, Armstrong J, White SA, Fricker SP, Plummer R, Wright M, Lovat PE. Inhibition of CXCR4-CXCL12 chemotaxis in melanoma by AMD11070. Br J Cancer. 2013 Apr 30;108(8):1634-40.

[3] Wong RS, Bodart V, Metz M, Labrecque J, Bridger G, Fricker SP. Comparison of the potential multiple binding modes of bicyclam, monocylam, and noncyclam small-molecule CXC chemokine receptor 4 inhibitors. Mol Pharmacol. 2008 Dec;74(6):1485-95.

[4] Gudmundsson KS, Sebahar PR, Richardson LD, Miller JF, Turner EM, Catalano JG, Spaltenstein A, Lawrence W, Thomson M, Jenkinson S. Amine substituted N-(1H-benzimidazol-2ylmethyl)-5,6,7,8-tetrahydro-8-quinolinamines as CXCR4 antagonists with potent activity against HIV-1. Bioorg Med Chem Lett. 2009 Sep 1;19(17):5048-52.