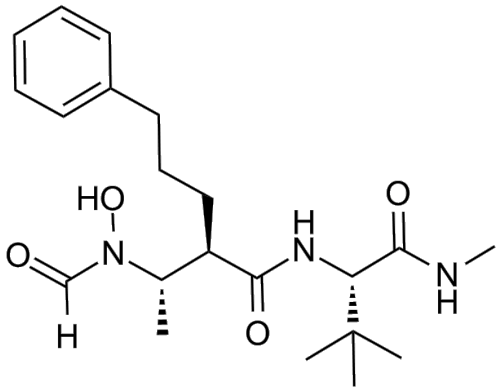
Product Data Sheet

Product Name: GI 254023X
Cat. No.: GC14578

Chemical Properties

Cas. No.	260264-93-5		
Chemical Name	(2R)-N-[(2S)-3,3-dimethyl-1-(methylamino)-1-oxobutan-2-yl]-2-[(1S)-1-[formyl(hydroxy)amino]ethyl]-5-phenylpentanamide		
SMILES	CC(C(CCCC1=CC=CC=C1)C(=O)NC(C(=O)NC)C(C)(C)C)N(C=O)O		
Formula	$C_{21}H_{33}N_3O_4$	M.Wt	391.5
Solubility	DMF: 1 mg/mL,Ethanol: 1 mg/mL,Ethanol:PBS (pH 7.2) (1:6): 0.14mg/mL	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

Cell lines	A2780 ovarian cancer cells and primary ovarian cancer (OC) cells

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Preparation Method	A2780 cells were plated at 25000 cells per well in borosilicate chambered coverglass and cultured for 48h. Primary OC cells were plated similarly. Cells were then treated with 100μM GI 254023X or solvent control for 48h. For migration assays, A2780 and primary OC cells were plated at 500000 cells per well in 6-well plates and cultured to form a monolayer. A scratch was made using a 200μl pipette tip, and cells were treated with 100μM GI 254023X or solvent control in media containing 10% FCS. Wound healing was observed after 24h.
Reaction Conditions	100μM GI 254023X; 48h for CXCL16 analysis, 24h for migration assays
Applications	GI 254023X significantly inhibited CXCL16 shedding from the cell membrane, reducing sCXCL16 levels in culture supernatants by 89.7%. GI 254023X also strongly reduced the migration potential of A2780 and primary OC cells in scratch assays.

Animal experiment [2]:

Animal models	PSAPP transgenic mice (Alzheimer's disease model)
Preparation Method	35-week-old PSAPP transgenic mice were used. The GI 254023X was administered via intraperitoneal injection at a dose of 200mg/kg once daily for 5 consecutive days. One hour after the final injection, the mice were sacrificed, and brain and plasma samples were collected for analysis.
Dosage form	200mg/kg/day for 5 days; i.p.

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Applications	GI 254023X significantly reduced brain LRP1 shedding by 60%, increased plasma Aβ40 levels by 1.45-fold.

References:
[1] Gooden MJ, Wiersma VR, Boerma A, et al. Elevated serum CXCL16 is an independent predictor of poor survival in ovarian cancer and may reflect pro-metastatic ADAM protease activity. Br J Cancer. 2014 Mar 18;110(6):1535-44.
[2] Shackleton B, Crawford F, Bachmeier C. Inhibition of ADAM10 promotes the clearance of A? across the BBB by reducing LRP1 ectodomain shedding. Fluids Barriers CNS. 2016 Aug 8;13(1):14.

Background

GI 254023X is a selective inhibitor with an IC_{50} value of 5.3nM for MMP9 (Matrix Metalloproteinase 9). The selectivity of GI 254023X for ADAM10 (A Disintegrin and Metalloproteinase 10) is 100 times higher than that for ADAM17, with an IC_{50} value of 2.5nM. GI 254023X is primarily used in the research of immunology, inflammation, and neurodegenerative diseases[1]. GI 254023X selectively binds to the catalytic domains of ADAM10 and MMP9 to inhibit their enzymatic activities[2]. GI 254023X also prevents the degradation of E-cadherin in epithelial cells, which is crucial for maintaining cell-to-cell adhesion and tissue integrity[3]. GI 254023X reduces the degradation of extracellular matrix components, thereby affecting processes such as tissue remodeling and angiogenesis[4].

In vitro, pretreatment of PAC1/RAGE cells with GI 254023X (100nM - 25mM) for 1 hour followed by stimulation with 300nM PACAP-27 for 2 hours significantly inhibited PACAP-induced RAGE shedding. The inhibition rate reached 86% at 25mM and 75% at 1mM, with a slight inhibitory effect even at the low concentration of 100nM. At a concentration of 1mM, GI 254023X inhibited basal RAGE shedding by 67%[5]. In ovarian cancer cell lines A2780 and primary ovarian cancer cells, treatment with GI 254023X (100μM) significantly inhibited the release of CXCL16 (CXC chemokine ligand 16), increased the levels of CXCL16 on the cell membrane, and reduced the release of soluble CXCL16 (sCXCL16) in the culture supernatant, with an inhibition rate of up to 89.7%. GI 254023X also significantly inhibited the migratory capacity of ovarian cancer cells[6].

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In vivo, GI 254023X (100mg/kg) was administered via intraperitoneal injection to mice 30 minutes and 24 hours after traumatic brain injury (TBI). GI 254023X significantly reduced brain tissue lesion volume in TBI mice, decreased the generation of the axonal injury marker SMI32, attenuated the upregulation of TNFα, IL-6, and LCN2, and increased the expression of the T cell marker Cd247[7]. GI 254023X (200mg/kg) was administered via intraperitoneal injection to 35-week-old PSAPP transgenic mice (an Alzheimer's disease model) for 5 consecutive days. This treatment significantly reduced the levels of LRP1 in the brain and increased Aβ40 levels in the plasma[8].

References:

[1] Hoettecke N, Ludwig A, Foro S, et al. Improved synthesis of ADAM10 inhibitor GI254023X. Neurodegener Dis. 2010;7(4):232-8.
[2] Ma S, Xu J, Wang X, et al. Effect of ADAM10 Inhibitor GI254023X on Proliferation and Apoptosis of Acute T-Lymphoblastic Leukemia Jurkat Cells In Vitro and Its Possible Mechanisms. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2015 Aug;23(4):950-5.
[3] Li J, Ouyang Q, Chen CW, et al. Neuron-Derived ADAM10 Production Stimulates Peripheral Nerve Injury-Induced Neuropathic Pain by Cleavage of E-Cadherin in Satellite Glial Cells. Pain Med. 2017 Sep 1;18(9):1752-1766.
[4] Kim YH, Jung JC. Suppression of tunicamycin-induced CD44v6 ectodomain shedding and apoptosis is correlated with temporal expression patterns of active ADAM10, MMP-9 and MMP-13 proteins in Caki-2 renal carcinoma cells. Oncol Rep. 2012 Nov;28(5):1869-74.
[5] Metz VV, Kojro E, Rat D, et al. Induction of RAGE shedding by activation of G protein-coupled receptors. PLoS One. 2012;7(7):e41823.
[6] Gooden MJ, Wiersma VR, Boerma A, et al. Elevated serum CXCL16 is an independent predictor of poor survival in ovarian cancer and may reflect pro-metastatic ADAM protease activity. Br J Cancer. 2014 Mar 18;110(6):1535-44.
[7] Appel D, Hummel R, Weidemeier M, et al. Pharmacologic Inhibition of ADAM10 Attenuates Brain Tissue Loss, Axonal Injury and Pro-inflammatory Gene Expression Following Traumatic Brain Injury in Mice. Front Cell Dev Biol. 2021 Mar 15;9:661462.
[8] Shackleton B, Crawford F, Bachmeier C. Inhibition of ADAM10 promotes the clearance of Aβ across the BBB by reducing LRP1 ectodomain shedding. Fluids Barriers CNS. 2016 Aug 8;13(1):14.

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