Product Data Sheet

Product Name: GSK 3008348 hydrochloride
Cat. No.: GC32471

Chemical Properties

Cas. No.	1629249-40-6		
SMILES	O=C(O)C[C@@H](C1=CC(N2N=C(C)C=C2C)=CC=C1)CN3C[C@H](CCC(N4)=CC=C5C4=NCCC5)CC3.[x].Cl		
Formula	$C_{29}H_{37}N_5O_2$.xHCl	M.Wt	
Solubility	DMSO : 11.66 mg/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.		

Caution: Product has not been fully validated for medical applications. For research use only.
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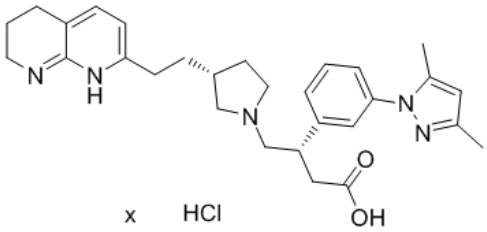
Structure



Protocol

Cell experiment [1]:

Cell lines	PK-15 cells (porcine kidney cell line)
Preparation Method	PK-15 cells were pretreated with GSK 3008348 hydrochloride (100nM) prior to or concurrently with FMDV infection.
Reaction Conditions	100nM; 1 hour before infection.

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Applications	GSK 3008348 hydrochloride suppressed viral RNA (vRNA) replication and virus production when added prior to or concurrently with virus infection. GSK 3008348 hydrochloride inhibited FMDV replication by blocking the viral entry step.

Animal experiment [2]:

Animal models	Male C57BL/6 mice with bleomycin-induced lung fibrosis
Preparation Method	In prophylactic studies, GSK 3008348 hydrochloride was administered via subcutaneously implanted osmotic mini-pumps at 15mg/kg/day for 14 days post-bleomycin. In therapeutic studies, mice were dosed twice daily by intranasal (i.n.) inhalation of 3mg/kg from day 14 to day 28 post-bleomycin.
Dosage form	3 or 15mg/kg; s.c. osmotic pump; i.n. inhalation; daily or twice for 14days.
Applications	GSK 3008348 hydrochloride was evaluated for its effect on TGF-β pathway biomarkers (e.g., Smad2 levels in lung tissue and BAL cells) in a murine model of lung fibrosis.

References:

[1] Tang J, Abdullah SW, Li P, et al. Heat Shock Protein 60 Is Involved in Viral Replication Complex Formation and Facilitates Foot and Mouth Virus Replication by Stabilizing Viral Nonstructural Proteins 3A and 2C. mBio. 2022 Oct 26;13(5):e0143422.
[2] John AE, Graves RH, Pun KT, et al. Translational pharmacology of an inhaled small molecule αvβ6 integrin inhibitor for idiopathic pulmonary fibrosis. Nat Commun. 2020 Sep 16;11(1):4659.

Background

GSK 3008348 hydrochloride is a small molecule antagonist targeting integrin αvβ6 (IC_{50}=1.50nM)

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GSK 3008348 hydrochloride is a small molecule antagonist targeting integrin αvβ6 (IC_{50}=1.50nM). GSK 3008348 hydrochloride also inhibits the activity of αvβ1 (IC_{50}=2.83nM), αvβ3 (IC_{50}=12.53nM), αvβ5 (IC_{50}=4.00nM), and αvβ8 (IC_{50}=2.26nM)[1-2]. GSK 3008348 hydrochloride can be used in research related to pulmonary fibrosis and various cancers[3-4].

In vitro, PK-15 cells were treated with GSK 3008348 hydrochloride (100nM) 1 hour before viral infection. GSK 3008348 hydrochloride significantly inhibited FMDV viral RNA (vRNA) replication and virus production[5]. NHBE cells were incubated with GSK 3008348 hydrochloride (0.26nM) for 2-24 hours. At 2 hours. GSK 3008348 hydrochloride induced the internalization of αvβ6 integrin from the cell surface; at 24 hours, GSK 3008348 hydrochloride significantly reduced the total intracellular level of αvβ6 integrin[6].

In vivo, a mouse model of bleomycin-induced pulmonary fibrosis was treated with GSK 3008348 hydrochloride (prophylactic study: 15mg/kg; s.c. osmotic pump; for 14 days; therapeutic study: 3mg/kg; intranasal inhalation; twice daily for 14 days). GSK 3008348 hydrochloride inhibited the activation of TGF-β and demonstrated a prolonged duration of action[7].

References:

[1] Procopiou PA, Anderson NA, Barrett J, et al. Discovery of (S)-3-(3-(3,5-Dimethyl-1 H-pyrazol-1-yl)phenyl)-4-((R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)pyrrolidin-1-yl)butanoic Acid, a Nonpeptidic αvβ6 Integrin Inhibitor for the Inhaled Treatment of Idiopathic Pulmonary Fibrosis. J Med Chem. 2018 Sep 27;61(18):8417-8443.
[2] Han Z, Ma Y, Cao G, et al. Integrin αVβ1 regulates procollagen I production through a non-canonical transforming growth factor β signaling pathway in human hepatic stellate cells. Biochem J. 2021 May 14;478(9):1689-1703.
[3] Maden CH, Fairman D, Chalker M, et al. Safety, tolerability and pharmacokinetics of GSK3008348, a novel integrin αvβ6 inhibitor, in healthy participants. Eur J Clin Pharmacol. 2018 Jun;74(6):701-709.
[4] Maher TM, Simpson JK, Porter JC, et al. A positron emission tomography imaging study to confirm target engagement in the lungs of patients with idiopathic pulmonary fibrosis following a single dose of a novel inhaled αvβ6 integrin inhibitor. Respir Res. 2020 Mar 26;21(1):75.
[5] Tang J, Abdullah SW, Li P, et al. Heat Shock Protein 60 Is Involved in Viral Replication Complex Formation and Facilitates Foot and Mouth Virus Replication by Stabilizing Viral Nonstructural Proteins 3A and 2C. mBio. 2022 Oct 26;13(5):e0143422.

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[6] Hryczanek HF, Barrett J, Barrett TN, et al. Core Modifications of GSK3335103 toward Orally Bioavailable αvβ6 Inhibitors with Improved Synthetic Tractability. J Med Chem. 2024 Nov 14;67(21):19689-19715.
[7] John AE, Graves RH, Pun KT, et al. Translational pharmacology of an inhaled small molecule αvβ6 integrin inhibitor for idiopathic pulmonary fibrosis. Nat Commun. 2020 Sep 16;11(1):4659.

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