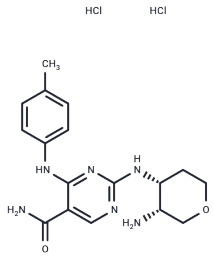
Data Sheet (Cat.No.T39874)

TargetMol
YOUR TARGET MOLECULES

GSK143 dihydrochloride

Chemical Properties



CAS No. : 2341796-81-2

Formula: C17H24Cl2N6O2

Molecular Weight: 415.32

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	GSK143 dihydrochloride is a highly selective, orally active inhibitor of spleen tyrosine kinase (SYK), exhibiting a pIC 50 value of 7.5. It effectively inhibits phosphorylated Erk (pErk) with a pIC 50 value of 7.1. The compound demonstrates anti-inflammatory properties and hinders the recruitment of immune cells in the intestinal muscularis of mice.
In vitro	GSK143 dihydrochloride (compound 20) effectively inhibits a range of kinases including ZAP-70 (pIC 50 = 4.7), LCK (pIC 50 = 5.3), LYN (pIC 50 = 5.4), JAK1/2/3 (pIC 50 = 5.8/5.8/5.7), Aurora B (pIC 50 = 4.8), hWB (pIC 50 = 6.6), and hERG (pIC 50 = 4.7). When administered at concentrations ranging from 10 to 10,000 nM every 24 hours over a three-day period, it exhibits an IC 50 of 323 nM in chronic lymphocytic leukaemia (CLL) cells. Additionally, a one-time dose of 1 μM for 30 minutes interrupts early signaling mechanisms, notably SYK phosphorylation and calcium flux. Furthermore, dosages between 0.1 to 10 μM for 30 minutes conditionally lessen cytokine production in bone marrow-derived macrophages. This compound's ability to selectively inhibit these targets, particularly its efficacy at a specific concentration in CLL cells with an IC 50 of 323 nM, underscores its potential for therapeutic applications, demonstrating varied impacts on cellular processes and signaling pathways critical in disease pathogenesis.
In vivo	GSK143 (0.1-10 mg/kg; orally; 1.5 hours) reduces inflammation and prevents recruitment of immune cells in the intestinal muscularis of 1 mg/kg[3]. GSK143 (3, 10, 30, 100 mg/kg; oral; 1 hour before ovalbumin challenge) reduces the cutaneous reverse passive Arthus reaction in a dose dependent manner by approximately 50% and 70% at 10 mg/kg and 30 mg/kg, respectively[2]. GSK143 (iv of 1 mg/kg; po of 3 mg/kg) has a T 1/2 of 4.2 hours, low clearance (16 mL/min/kg), moderate bioavailability of 30% and a V ss of 4.1 L/kg in rats[1]. Animal Model: Wild type C57NL/BL6 mice, 10-12 weeks old[3]Dosage: 0.1, 1, 3, 10 mg/kg Administration: Orally; 1.5 hours before intestinal manipulation (IM) Result: Reduced inflammation and prevented recruitment of immune cells in the intestinal muscularis. Animal Model: Male CD rats (175-200 g)[1]Dosage: 1 mg/kg of iv; 3 mg/kg of po (Pharmacokinetic Analysis) Administration: IV or PO Result: Had a T 1/2 of 4.2 hours, low clearance (16 mL/min/kg), moderate bioavailability of 30% and a V ss of 4.1 L/kg.

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4078 mL	12.0389 mL	24.0778 mL
5 mM	0.4816 mL	2.4078 mL	4.8156 mL
10 mM	0.2408 mL	1.2039 mL	2.4078 mL
50 mM	0.0482 mL	0.2408 mL	0.4816 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

John Liddle, et al. Discovery of GSK143, a Highly Potent, Selective and Orally Efficacious Spleen Tyrosine Kinase Inhibitor. Bioorg Med Chem Lett. 2011 Oct 15;21(20):6188-94.