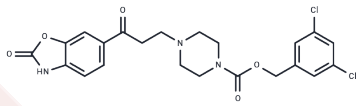
Data Sheet (Cat.No.T3631)

TargetMol

PF-8380

Chemical Properties



CAS No. : 1144035-53-9

Formula: C22H21Cl2N3O5

Molecular Weight: 478.33

Appearance: no data available

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

Biological Description

Description	PF-8380 is an effective and orally available autotaxin inhibitor (IC50: 2.8 nM, in isolated enzyme assay; 101 nM, in the human whole blood). It modulates lysophosphatidic acid (LPA) levels in vivo/vitro by directly inhibiting autotaxin; reduces LPA levels both in plasma and at the site of inflammation.
Targets(IC50)	PDE
In vitro	Pre-treatment with PF-8380 before radiotherapy can inhibit radiation-induced angiogenesis in tumor endothelial cells and delay the growth and development of intracranial glioma tumors. In a rat air pouch inflammation model, PF8380 (30 mg/kg, p. o.) reduced inflammatory pain sensitivity and decreased LPA levels in plasma and inflamed tissues by more than 95% within 3 hours.
In vivo	PF-8380 inhibits autotoxin in rat substrates (IC50: 1.16 nM) and demonstrates inhibition in human whole blood with an IC50 of 101 nM after 2 hours of treatment [1]. Furthermore, PF-8380 suppresses autotoxin in GBM cells, subsequently reducing their invasion and migration capabilities while enhancing radiation sensitization.
Kinase Assay	FS-3 substrate is solubilized in assay buffer at 500 μM and frozen at -20°C in single-use aliquots for up to 4 weeks. Recombinant autotaxin is diluted in Tris-buffered saline (140 mM NaCl, 5 mM KCl, 1 mM CaCl2, 1 mM MgCl2, 50 mM Tris, pH 8.0) and incubated with compound in DMSO or DMSO alone (final 1% DMSO) for 15 min at 37°C, and the reaction is started with the addition of FS-3 at a final concentration of 1 μM. The reaction is allowed to proceed at 37°C for 30 min and monitored at 520 nm until the uninhibited control compared with a no-enzyme control gave a Z′≥0.5. IC50s are determined in triplicate by using a four-parameter fit[1].
Cell Research	GL261 or U87-MG cells are plated in triplicate onto 6 cm plates and allowed to grow to 70% confluence. The semi-confluent cell layer is scratched with a sterile 200 μL pipette tip to create a scratch devoid of cells and plates are washed once with PBS to remove non-adherent cells and debris. For radiosensitization drug studies, cells are treated with 1 μM PF-8380 or DMSO for 45 min prior to irradiation with 4 Gy, and then incubated at 37°C in 5% CO2. Control plates are monitored for cell migration (20–24 h). Cells are fixed with 70% ethanol and stained with 1% methylene blue. To quantify migration, cells in three randomly selected high power fields (HPFs) in the scratched area are counted and normalized for surrounding cell density.(Only for Reference)

Solubility Information

Solubility	DMSO: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0906 mL	10.453 mL	20.9061 mL
5 mM	0.4181 mL	2.0906 mL	4.1812 mL
10 mM	0.2091 mL	1.0453 mL	2.0906 mL
50 mM	0.0418 mL	0.2091 mL	0.4181 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

Gierse J, et al. J Pharmacol Exp Ther. 2010, 334(1):310-317.
Bhave SR, et al. Front Oncol. 2013, 3:236.