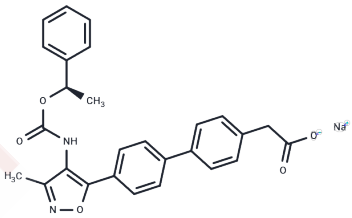
Data Sheet (Cat.No.T2000)

TargetMol

AM095

Chemical Properties



CAS No. : 1345614-59-6

Formula: C27H23N2NaO5

Molecular Weight: 478.47

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AM095 is a potent LPA1 receptor antagonist with IC50 values of 0.98 and 0.73 μM for recombinant human or mouse LPA1 respectively.
Targets(IC50)	LPA Receptor,LPL Receptor
In vitro	AM095 is a potent LPA1 receptor antagonist because it inhibits GTPγS binding to Chinese hamster ovary (CHO) cell membranes overexpressing recombinant human or mouse LPA1 with IC50 values of 0.98 and 0.73 μM, respectively. AM095 inhibits LPA-driven chemotaxis of CHO cells overexpressing mouse LPA1 (IC50=778 nM) and human A2058 melanoma cells (IC50=233 nM). The IC50 of AM095 in the human LPA1 GTPγS binding assay is comparable with that of our previously published compound AM966 (IC50=0.98±0.17 μM) and the Debio-0719 compound (IC50=0.60±0.04 μM)[1]. AM095 inhibits the LPA-induced calcium flux of CHO cells stably transfected with human or mouse LPA1. The IC50 for AM095 antagonism of LPA-induced calcium flux of human or mouse LPA1-transfected CHO cells is 0.025 and 0.023 μM, respectively[2].
In vivo	AM095 exhibits high oral bioavailability and moderate half-life, demonstrating tolerability in both rats and dogs following oral and intravenous administration. In rats, an oral dose (10 mg/kg) of AM095 results in peak plasma concentrations (Cmax) of 41 μM at 2 hours, decreasing to 10 nM by 24 hours. Conversely, an intravenous dose (2 mg/kg) leads to a Cmax of 12 μM within 15 minutes, similarly diminishing to approximately 10 nM by 24 hours, with a half-life (t1/2) of 1.79 hours. In dogs, an oral administration of 5 mg/kg achieves a peak plasma concentration of 21 μM within 15 minutes, falling to 10 nM by 24 hours, whereas an intravenous dosage (2 mg/kg) yields a Cmax of 11 μM in 15 minutes, reducing to 15 nM by 8 hours, and a t1/2 of 1.5 hours[1].
Kinase Assay	Known amounts of AM095 (diluted in DMSO) or vehicle (DMSO) are added to 25 to 40 μg of hLPA1/CHO or mLPA1/CHO membranes and 0.1 nM [35S]-GTPγS in buffer (50 mM HEPES, 0.1 mM NaCl, 10 mM MgCl2, 50 μg/mL saponin, pH 7.5) containing 0.2% fatty acid-free human serum albumin and 5 μM GDP. To test for LPA1 antagonist activity, the ability of AM095 to inhibit GTPγS binding stimulated by 900 nM LPA (18:1) is measured. Alternatively, to test for agonist effects, the ability of AM095 to stimulate GTPγS binding in the absence of LPA is measured. Reactions are incubated for 30 min at 30°C, before harvesting membranes onto glass filter binding plates (UniFilter GF/B) and washing three times with cold buffer containing 50 mM HEPES, pH 7.4, 100 mM NaCl, 10 mM MgCl2 using a Brandel 96-tip cell harvester. Plates are dried and then cpm are evaluated

Kinase Assay	by using a Packard TopCount NXT microplate scintillation counter[1].

Solubility Information

Solubility	DMSO: 5.5 mg/mL (11.49 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (2.09 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.090 mL	10.450 mL	20.900 mL
5 mM	0.418 mL	2.090 mL	4.180 mL
10 mM	0.209 mL	1.045 mL	2.090 mL
50 mM	0.0418 mL	0.209 mL	0.418 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Swaney JS, et al. Pharmacokinetic and pharmacodynamic characterization of an oral lysophosphatidic acid type 1 receptor-selective antagonist. J Pharmacol Exp Ther. 2011 Mar;336(3):693-700.

Castelino FV, et al. Amelioration of dermal fibrosis by genetic deletion or pharmacologic antagonism of lysophosphatidic acid receptor 1 in a mouse model of scleroderma. Arthritis Rheum. 2011 May;63(5):1405-15.