

Product Data Sheet

Product Name: AM-095 free base

Cat. No.: GC15908

Chemical Properties

Cas. No. 1228690-36-5

Chemical Name 2-[4-[4-[3-methyl-4-[[[(1R)-1-phenylethoxy]carbonylamino]-1,2-oxazol-5-yl]phenyl]phenyl]phenyl]acetic acid

SMILES CC1=NOC(=C1NC(=O)OC(C)C2=CC=CC=C2)C3=CC=C(C=C3)C4=CC=C(C=C4)CC(=O)O

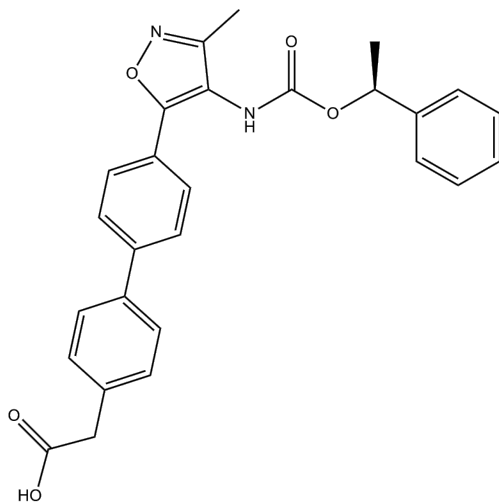
Formula $C_{27}H_{24}N_2O_5$ M.Wt 456.49

Solubility DMSO : 67.3 mg/mL (147.43 mM; Storage Store at -20°C
Need ultrasonic and warming)

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

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

**Kinase
experiment:**

Assays are conducted using both hLPA1/CHO and mLPA1/CHO cells. A cell pellet of hLPA1/CHO or mLPA1/CHO cells is resuspended in appr 20 mL of ice-cold membrane buffer containing 10 mM HEPES, pH 7.4, 1 mM dithiothreitol, and protease inhibitors. Cells are sonicated, and the cell lysate is centrifuged at 2000 rpm for 10 min at 4°C. The supernatant is further centrifuged at 25,000 rpm for 70 min at 4°C. The membrane pellet is resuspended in 5 mL of ice-cold membrane buffer and homogenized using a Potter-Elvehjem tissue grinder. Final protein concentration is determined using the Bradford Protein Assay Kit. Known amounts of AM095 (diluted in dimethyl sulfoxide) or vehicle (dimethyl sulfoxide) 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 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 by using a Packard TopCount NXT microplate scintillation counter.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal experiment:

Mice underwent UUO or sham surgery to the left kidney. In brief, a longitudinal, upper left incision is performed to expose the left kidney. The renal artery is located and a 6/0 silk thread is passed between the artery and the ureter. The thread is looped around the ureter and knotted three times insuring full ligation of ureter. The kidney is returned to abdomen, the abdominal muscle is sutured, and the skin is closed with staples. The contralateral (right) kidney served as an uninjured control. AM095 (30 mg/kg) or vehicle (water) is given 1 to 4 h before UUO and then b.i.d. thereafter by oral gavage. After 8 days, mice are euthanized using inhaled CO₂, and the kidneys are harvested and cut in half for histopathological and biochemical analysis of fibrosis. To assess fibrosis, half of the kidney is fixed in 10% neutral buffered formalin and stained using Masson's trichrome. The other half of the kidney is frozen at -80°C for subsequent biochemical analysis of collagen content.

References:

- [1]. 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.
- [2]. Ruisanchez E, et al. Lysophosphatidic acid induces vasodilation mediated by LPA1 receptors, phospholipase C, and endothelial nitric oxide synthase. *FASEB J.* 2014 Feb;28(2):880-90.
- [3]. Swaney, J. S., et al. Pharmacokinetic and pharmacodynamic characterization of an oral lysophosphatidic acid type 1 receptor-selective antagonist. *Journal of Pharmacology and Experimental Therapeutics* (2011), 336(3), 693-700.

Background

AM095 is a novel, potent and orally bioavailable antagonist of lysophosphatidic acid type 1 receptor (LPA1) with IC₅₀ values of 0.73 and 0.98 µM for mouse or recombinant human LPA1, respectively [1].

In vitro, AM095 has shown to inhibit LPA1-induced chemotaxis of both mouse LPA1/CHO cells and human A2058 melanoma cells with IC₅₀ values of 0.78 µM and 0.23µM [1].

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

In vivo, AM095 could dose-dependently block LPA-induced histamine release with an ED50 value of 8.3 mg/kg in mice. Additionally, AM095 has been revealed to remarkably reduce the BALF collagen and protein with an ED50 value of 10 mg/kg in lungs. AM095 has also shown to decrease both macrophage and lymphocyte infiltration induced by bleomycin in mice [1].

References:

[1] Swaney JS1, Chapman C, Correa LD, Stebbins KJ, Broadhead AR, Bain G, Santini AM, Darlington J, King CD, Baccei CS, Lee C, Parr TA, Roppe JR, Seiders TJ, Ziff J, Prasit P, Hutchinson JH, Evans JF, Lorrain DS. Pharmacokinetic and pharmacodynamic characterization of an oral lysophosphatidic acid type 1 receptor-selective antagonist. J Pharmacol Exp Ther. 2011 Mar;336(3):693-700.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA