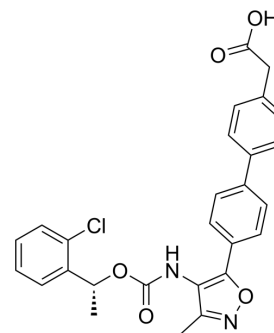


AM966

Cat. No.:	HY-15277		
CAS No.:	1228690-19-4		
Molecular Formula:	C ₂₇ H ₂₃ ClN ₂ O ₅		
Molecular Weight:	490.93		
Target:	LPL Receptor		
Pathway:	GPCR/G Protein		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (203.70 mM; Need ultrasonic)					
	Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg	10 mg
		Concentration				
		1 mM		2.0370 mL	10.1848 mL	20.3695 mL
5 mM			0.4074 mL	2.0370 mL	4.0739 mL	
	10 mM		0.2037 mL	1.0185 mL	2.0370 mL	
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 50% PEG300 >> 50% saline Solubility: 10 mg/mL (20.37 mM); Suspended solution; Need ultrasonic Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: 2.5 mg/mL (5.09 mM); Suspended solution; Need ultrasonic Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.09 mM); Clear solution 					

BIOLOGICAL ACTIVITY

Description	AM966 is a high affinity, selective, oral LPA ₁ -antagonist, inhibits LPA-stimulated intracellular calcium release (IC ₅₀ =17 nM).
IC₅₀ & Target	LPA ₁ ^[1]
In Vitro	AM966 is a potent, selective, orally bioavailable LPA ₁ receptor antagonist. AM966 inhibits LPA ₁ -mediated chemotaxis of human A2058 melanoma cells (IC ₅₀ =138±43 nM), IMR-90 human lung fibroblasts (IC ₅₀ =182±86 nM) and CHO mLPA ₁ cells (IC ₅₀ =469±54 nM) ^[1] . LPA-induced ERK1/2 activation is completely blocked by AM966 (100 nM), which selectively antagonizes LPA

¹ over LPA₂₋₅, with an IC₅₀ value of 3.8±0.4 nM. Pre-treatment with AM966 (100 nM) completely blocks ERK1/2 phosphorylation induced by Mianserin^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

AM966 (30 mg/kg, BID) reduces vascular leakage, inflammation and lung injury and inflammation in a 3 day Bleomycin (HY-108345) model. AM966 inhibits lung fibrosis, maintains mouse body weight and decreases lung inflammation 14 days after Bleomycin lung injury. AM966 reduces vascular leakage, tissue injury and pro-fibrotic cytokine production in the 14 day Bleomycin study. AM966 demonstrates greater efficacy compared to Pirfenidone (HY-B0673) in the 14 day Bleomycin model. AM966 decreases mortality and fibrosis at late time points after Bleomycin injury^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

CHO-K1 cells are grown to 80% confluency in 12-well plates, serum-starved for 24 h and incubated in serum-free medium with AM966. After 21 h, [³H]thymidine (0.5 µCi/well) is added and the incubation is continued for 3 h. The medium is then removed, and the cells are placed on ice and washed twice with 1 mL of ice-cold PBS containing 5% trichloroacetic acid. Cells are solubilized and [³H]thymidine incorporation is determined by liquid scintillation counting. Assays are performed in triplicate^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[1]

Mice^[1]

The oral exposure of AM966 is determined in fasted mice. Animals received AM966 (10 mg/kg) in vehicle (water) by oral gavage and are then killed by CO₂ inhalation at 1, 2, 4, 8 and 24 h post dose (n=2 animals per time point for each test compound). Blood (approximately 300 µL) is collected via cardiac puncture into EDTA-containing tubes and centrifuged at 1450×g for 10 min. The plasma is removed and analysed for AM966 content by liquid chromatography-mass spectrometry (LCMS). Briefly, known amounts of AM966 are added to thawed mouse plasma to yield a concentration range from 0.8 to 4000 ng/mL. Mouse plasma samples are precipitated using acetonitrile (1:4, v:v) containing the internal standard buspirone. A 10 µL aliquot of the analyte mixture is injected using a Leap PAL autosampler. Analyses are performed using an Agilent Zorbax SB-C8 column (2.1×50 mm; 5 µm) linked to a Shimadzu LC-10AD VP with SCL-10A VP system controller. Tandem mass spectrometric detection is carried out on a PE Sciex API3200 in the positive ion mode (ESI) by multiple reaction monitoring. The calibration curves are constructed by plotting the peak-area ratio of analysed peaks against known concentrations. The lower limit of quantitation is 0.8 ng/mL. The data are subjected to linear regression analysis with 1/x² weighting.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2022 Mar 10;S1550-4131(22)00083-3.
- Autophagy. 2022 Feb 27;1-22.
- Cell Commun Signal. 2023 Sep 25;21(1):257.
- Neuropsychopharmacol Rep. 2019 Sep;39(3):156-163.
- Apoptosis. 2019 Jun;24(5-6):478-498.

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REFERENCES

[1]. Swaney, JS, et al. A novel, orally active LPA1 receptor antagonist inhibits lung fibrosis in the mouse bleomycin model. Br J Pharmacol. 2010 Aug;160(7):1699-713.

[2]. Olianas MC, et al. Antidepressants activate the lysophosphatidic acid receptor LPA(1) to induce insulin-like growth factor-I receptor transactivation, stimulation of ERK1/2 signaling and cell proliferation in CHO-K1 fibroblasts. *Biochem Pharmacol.* 2015 Jun 15;95(4):311-23.

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

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