GSK-7975A

Cat. No.: HY-12507

CAS No.: 1253186-56-9

Molecular Formula: $C_{18}H_{12}F_5N_3O_2$

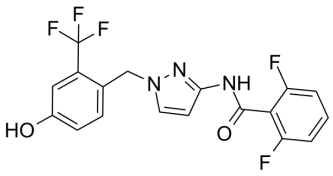
Molecular Weight: 397.3

Target: Calcium Channel

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

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 : ≥ 90 mg/mL (226.53 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5170 mL	12.5849 mL	25.1699 mL
5 mM	0.5034 mL	2.5170 mL	5.0340 mL
10 mM	0.2517 mL	1.2585 mL	2.5170 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK-7975A is a potent and orally available CRAC channel inhibitor.

In Vitro

GSK-7975A reduces FcεRI-dependent Ca^{2+} influx and 3 μM GSK-7975A reduces the release of histamine, leukotriene C4, and cytokines (IL-5/-8/-13 and TNFα) by up to 50%[1]. GSK-7975A inhibits mediator release from mast cells, and pro-inflammatory cytokine release from T-cells in a variety species. GSK-7975A completely inhibits calcium influx through CRAC channels. This leads to inhibition of the release of mast cell mediators and T-cell cytokines from multiple human and rat preparations. Mast cells from guinea-pig and mouse preparations are not inhibited by GSK-7975A; however cytokine release

	is fully blocked from T-cells in a mouse preparation[2]. GSK-7975A inhibits toxin-induced activation of ORAI1 and/or activation of Ca^{2+} currents after Ca^{2+} release, in a concentration-dependent manner, in mouse and human pancreatic acinar cells (inhibition >90% of the levels observed in control cells). GSK-7975A also prevents activation of the necrotic cell death pathway in mouse and human pancreatic acinar cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GSK-7975A inhibits local and systemic features of acute pancreatitis in TLCS-AP, CER-AP, FAEE-AP, in dose- and time-dependent manners. GSK-7975A significantly reduces increases in serum amylase, IL6, and pancreatic MPO levels; lung MPO is reduced significantly by low dose only. GSK-7975A markedly reduces pancreatic histopathology in TLCS-AP, CER-AP, and FAEE-AP[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3]	Mice: Acute pancreatitis is induced in C57BL/6J mice by ductal injection of taurolithocholic acid 3-sulfate or intravenous' administration of cerulein or ethanol and palmitoleic acid. Some mice then are given GSK-7975A, which inhibit ORAI1, at different time points to assess local and systemic effects. Sampling of GSK-7975A is at 1, 2, 4, 10, and 22 hours after osmotic minipump insertion from 3 mice/time point. Immediately after humane killing, blood is collected into a heparinized tube, diluted 1:1 with sterile water, and the pancreas is removed and homogenized. Standards and study samples (50 µL from blood and 100 µL from pancreas) are extracted by protein precipitation and centrifuged. Supernatants are dried under heated nitrogen (40°C). Levels of GSK-7975A and GSK-6288B are determined[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Front Pharmacol. 2022 Feb 23;13:816133.
- Front Pharmacol. 23 February 2022.
- Front Pharmacol. 2021 Jul 14;12:684538.
- J Cell Physiol. 2021 Mar 11.
- Front Physiol. 2021 Mar 9;12:639857.

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REFERENCES

[1]. Ashmole I, et al. CRACM/Orai ion channel expression and function in human lung mast cells. J Allergy Clin Immunol. 2012 Jun;129(6):1628-35.e2.

[2]. Rice LV, et al. Characterization of selective Calcium-Release Activated Calcium channel blockers in mast cells and T-cells from human, rat, mouse and guinea-pig preparations. Eur J Pharmacol. 2013 Mar 15;704(1-3):49-57.

[3]. Wen L, et al. Inhibitors of ORAI1 Prevent Cytosolic Calcium-Associated Injury of Human Pancreatic Acinar Cells and Acute Pancreatitis in 3 Mouse Models. Gastroenterology. 2015 Aug;149(2):481-92.e7.

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

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