GSK-7975A

Cat. No.: HY-12507  
CAS No.: 1253186-56-9  
Molecular Formula: C₁₈H₁₂F₅N₃O₂  
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 6 months  
                     -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO: ≥ 90 mg/mL (226.53 mM)  
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Concentration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mM</td>
<td></td>
<td>2.5170 mL</td>
<td>12.5849 mL</td>
<td>25.1699 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.5034 mL</td>
<td>2.5170 mL</td>
<td>5.0340 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.2517 mL</td>
<td>1.2585 mL</td>
<td>2.5170 mL</td>
</tr>
</tbody>
</table>

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: ≥ 10 mg/mL (25.17 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 10 mg/mL (25.17 mM); Clear solution

3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
   Solubility: ≥ 10 mg/mL (25.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

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

In Vitro

GSK-7975A reduces FcεRI-dependent Ca²⁺ 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
GSK-7975A inhibits toxin-induced activation of ORAI1 and/or activation of Ca\textsuperscript{2+} currents after Ca\textsuperscript{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\textsuperscript{[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\textsuperscript{[3]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**PROTOCOL**

**Animal Administration** \textsuperscript{[3]}

Mice: Acute pancreatitis is induced in C57BL/6J mice by ductal injection of tauroliothocholic 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\textsuperscript{[3]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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**REFERENCES**


