YM-58483

Cat. No.: HY-100831
CAS No.: 223499-30-7
Molecular Formula: C₁₅H₉F₆N₅OS
Molecular Weight: 421.32
Target: CRAC Channel
Pathway: Membrane Transporter/Ion Channel
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 : ≥ 32 mg/mL (75.95 mM)
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Mass 1 mg</th>
<th>Solvent Mass 5 mg</th>
<th>Solvent Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.3735 mL</td>
<td>11.8675 mL</td>
<td>23.7349 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4747 mL</td>
<td>2.3735 mL</td>
<td>4.7470 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2373 mL</td>
<td>1.1867 mL</td>
<td>2.3735 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: ≥ 2.5 mg/mL (5.93 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
YM-58483 is the first selective and potent inhibitor of CRAC channels and subsequent Ca²⁺ signals.

In Vitro
YM-58483 can decrease the levels of P-ERK and P-CREB, without affecting the expression of CD11b and GFAP. YM-58483 also inhibits the release of spinal cord IL-1β, TNF-α, and PGE2[1]. YM-58483 and cyclosporine A inhibits T cell proliferation in a one-way mixed lymphocyte reaction (mLR) with IC₅₀ values of 330 and 12.7 nM, respectively[2]. YM-58483 inhibits DNP antigen-induced histamine release from and leukotrienes (LTs) production in IgE-primed RBL-2H3 cells, a rat basophilic leukemia cell line, with IC₅₀ values of 460 and 310 nM, respectively. YM-58483 also inhibits phytohemagglutinin-P (PHA)-stimulated IL-5 and IL-13 production in human peripheral blood cells with IC₅₀ values
of 125 and 148 nM, respectively, which is approximately 5 times less potent than prednisolone[3]. YM-58483 inhibits IL-4 and IL-5 production in a conalbumine-stimulated murine Th2 T cell clone (D10.G4.1), and IL-5 production in phytohemagglutinin-stimulated human whole blood cells with IC_{50} values comparable to those reported for its CRAC channel inhibition (around 100 nM)[4].

In Vivo

Intrathecal YM-58483 at the concentration of 300 μM (1.5 nmol) and 1000 μM (10 nmol) produces a significant central analgesic effect on the SNL rats[1]. In the mouse graft-versus-host disease (GVHD) model, YM-58483 (1-30 mg/kg, p.o.) and cyclosporine A (1-30 mg/kg, p.o.) inhibit donor anti-host cytotoxic T lymphocyte (CTL) activity and IFN-γ production, and also reduce the number of donor T cells, especially donor CD8+ T cells, in the spleen. YM-58483 (1-10 mg/kg, p.o.) and cyclosporine A (2, 10 mg/kg, p.o.) inhibit the sheep red blood cell (SRBC)-induced delayed type hypersensitivity (DTH) response[2]. YM-58483 (30 mg/kg, p.o.) significantly suppresses ovalbumin (OVA)-induced bronchoconstriction in OVA-sensitized guinea pigs, whereas prednisolone does not. YM-58483 (3-30 mg/kg, p.o.) and prednisolone (100 mg/kg, p.o.) both significantly and completely suppress airway hyperresponsiveness (AHR) caused by OVA exposure[3]. YM-58483 inhibits antigen-induced eosinophil infiltration into airways, and decreases IL-4 and cysteinyl-leukotrienes content in inflammatory airways induced in actively sensitized Brown Norway rats. Orally administered YM-58483 prevents antigen-induced late phase asthmatic bronchoconstriction and eosinophil infiltration in actively sensitized guinea pigs[4].

PROTOCOL

Animal Administration[2]

Male Balb/c mice are immunized by subcutaneous injection of SRBC (2×10^7 cells) on day 0. Immunized mice are challenged with 30 μL of 1×10^8 SRBC into the left hind footpad on day 5. Footpad swelling is measured 24 h after the challenge using a thickness gauge and expressed as the difference between the thickness of the left footpad and that of the right one, which receives an equal volume of 0.9% saline. As a negative control, male Balb/c mice are injected with 0.9% saline and challenged with SRBC. YM-58483 and cyclosporine A are administered orally once daily from day 0 to day 5 (6 consecutive days).

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

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REFERENCES


