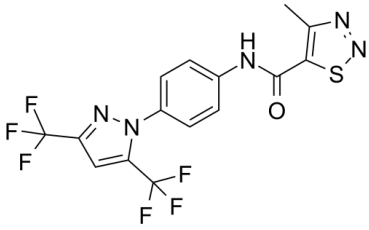
Data Sheet

Product Name:	YM-58483
Cat. No.:	CS-6047
CAS No.:	223499-30-7
Molecular Formula:	C15H9F6N5OS
Molecular Weight:	421.32
Target:	CRAC Channel
Pathway:	Membrane Transporter/Ion Channel
Solubility:	DMSO : ≥ 32 mg/mL (75.95 mM)



BIOLOGICAL ACTIVITY:

YM-58483 is the first selective and potent inhibitor of **CRAC channels** and subsequent Ca^{2+} 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 IC_{50} 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 IC_{50} 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 IC_{50} 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]. M-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 broncoconstriction and eosinophil infiltration in actively sensitized guinea pigs[4].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: YM-58483 is suspended in 0.5% methylcellulose solution for oral administration at a volume of 10 mL/kg.[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).

References:

[1]. Qi Z, et al. The Central Analgesic Mechanism of YM-58483 in Attenuating Neuropathic Pain in Rats. Cell Mol Neurobiol. 2016 Oct;36(7):1035-43

[2]. Ohga K, et al. Characterization of YM-58483/BTP2, a novel store-operated Ca2+ entry blocker, on T cell-mediated immune responses in vivo. Int Immunopharmacol. 2008 Dec 20;8(13-14):1787-9

[3]. Ohga K, et al. The suppressive effects of YM-58483/BTP-2, a store-operated Ca2+ entry blocker, on inflammatory mediator release in vitro and airway responses in vivo. Pulm Pharmacol Ther. 2008;21(2):360-9

[4]. Yoshino T, et al. YM-58483, a selective CRAC channel inhibitor, prevents antigen-induced airway eosinophilia and late phase asthmatic responses via Th2 cytokine inhibition in animal models. Eur J Pharmacol. 2007 Apr 10;560(2-3):225-33

CAIndexNames:

1,2,3-Thiadiazole-5-carboxamide, N-[4-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]-4-methyl-

SMILES:

O=C(C1=C(C)N=NS1)NC2=CC=C(N3N=C(C(F)(F)F)C=C3C(F)(F)F)C=C2

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

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