

Product Data Sheet

Product Name: YM 58483

Cat. No.: GC14665

Chemical Properties

Cas. No. 223499-30-7

Chemical Name N-(4-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)-4-methyl-1,2,3-thiadiazole-5-carboxamide

SMILES FC(F)(C1=CC(C(F)(F)F)=NN1C(C=C2)=CC=C2NC(C3=C(C)N=NS3)=O)F

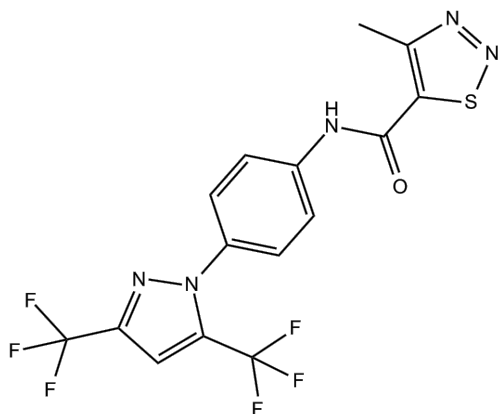
Formula $C_{15}H_9F_6N_5OS$ M.Wt 421.32

Solubility ≥ 50 mg/mL in EtOH, ≥ 90 mg/mL in DMSO Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Patient-derived glioblastoma stem cells (GSCs)

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Preparation Method GSCs were grown in DMEM/HAM-F12 medium with 2mM glutamine, 10% (v/v) fetal bovine serum (FBS), 2µg/ml heparin, 20ng/ml EGF and 25ng/ml bFGF, 100U/ml penicillin and 100µg/ml streptomycin at 37°C in 5% CO₂/atmosphere. GSCs (3×10^4 cells) were seeded on 96-well plates, incubated for 24h, and then treated with different concentrations of YM 58483 (0.1, 1, 10, 20, and 30µM) at 37°C. After 24h, cell viability was measured.

Reaction Conditions 0.1, 1, 10, 20, and 30µM; 24h

Applications YM 58483 treatment significantly reduced the cell viability of GSCs in a concentration-dependent manner.

Animal experiment [2]:

Animal models Male DBA/1 mice

Preparation Method Male DBA/1 mice (7 weeks old) were housed singly in a standard environment with food and water ad libitum. Mice were acclimated for a week before starting the experiment. 100µg chicken type II collagen (CII) was mixed with 100µl complete Freund's adjuvant and injected i.d. on day 0 at the base of the tail. On day 21, a booster injection of 100µg chicken CII in 100µl of PBS was administered (i.p.). YM 58483 (10mg/kg) or vehicle was administered daily from days 28 to 37. The effect of YM 58483 on paw oedema in mice was measured.

Dosage form 10mg/kg/day for 10 days; i.p.

Applications YM 58483 treatment significantly reduced the CII-induced paw oedema in mice.

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References:

- [1] Terrié E, Déliot N, Benzidane Y, et al. Store-operated calcium channels control proliferation and self-renewal of cancer stem cells from glioblastoma[J]. Cancers, 2021, 13(14): 3428.
- [2] Gao X H, Gao R, Tian Y Z, et al. A store-operated calcium channel inhibitor attenuates collagen-induced arthritis[J]. British journal of pharmacology, 2015, 172(12): 2991-3002.

Background

YM 58483 is a pyrazole-derived inhibitor of CRAC channels that inhibits Ca^{2+} signals with an IC_{50} value of 100nM [1]. YM 58483 suppresses the CRAC, TRPC3, and TRPC5 channels and facilitates the TRPM4 channel, reducing cytokine production and NFAT dephosphorylation [2]. YM 58483 has been widely used as a potent analgesic to alleviate thermal hyperalgesia and mechanical hyperalgesia in mice[3].

In vitro, YM 58483 treatment for 48 hours significantly inhibited the production of IL-5 and IL-13 in human peripheral blood cells induced by phytohemagglutinin-P (PHA), with IC_{50} values of 125nM and 148nM, respectively[4]. The pretreatment of YM 58483 for 1 hour inhibited the production of IL-4 and IL-5 in conalbumin-stimulated D10.G4.1 cells, with IC_{50} values of 200nM and 180nM, respectively[5]. Treatment with 30 μM YM 58483 for 24 hours significantly reduced the proliferation of glioblastoma stem cells (GSC) and decreased the expression of SOX2[6].

In vivo, YM 58483 treatment via oral administration at a dose of 30mg/kg/day for 10 consecutive days significantly inhibited the activity of donor anti-host cytotoxic T lymphocytes (CTL) and the production of IFN- γ , and reduced the number of donor T cells in the spleen within the mouse model of graft-versus-host disease (GVHD)[7]. Oral administration of 10mg/kg dose of YM 58483 daily for 10 consecutive days significantly inhibited the development of collagen-induced paw edema in mice, alleviated joint damage in mice, and improved spontaneous movement defects[8].

References:

- [1] Parekh A B. Store-operated CRAC channels: function in health and disease[J]. Nature reviews Drug discovery, 2010, 9(5): 399-410.
- [2] Rubaiy H N. ORAI calcium channels: regulation, function, pharmacology, and therapeutic

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targets[J]. Pharmaceuticals, 2023, 16(2): 162.

[3] Gao R, Gao X, Xia J, et al. Potent analgesic effects of a store-operated calcium channel inhibitor[J]. PAIN®, 2013, 154(10): 2034-2044.

[4] Ohga K, Takezawa R, Yoshino T, 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[J]. Pulmonary pharmacology & therapeutics, 2008, 21(2): 360-369.

[5] Yoshino T, Ishikawa J, Ohga K, 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[J]. European journal of pharmacology, 2007, 560(2-3): 225-233.

[6] Terrié E, Déliot N, Benzidane Y, et al. Store-operated calcium channels control proliferation and self-renewal of cancer stem cells from glioblastoma[J]. Cancers, 2021, 13(14): 3428.

[7] Ohga K, Takezawa R, Arakida Y, et al. Characterization of YM-58483/BTP2, a novel store-operated Ca²⁺ entry blocker, on T cell-mediated immune responses in vivo[J]. International immunopharmacology, 2008, 8(13-14): 1787-1792.

[8] Gao X H, Gao R, Tian Y Z, et al. A store-operated calcium channel inhibitor attenuates collagen-induced arthritis[J]. British journal of pharmacology, 2015, 172(12): 2991-3002.

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