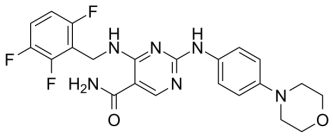
YM-341619

Cat. No.:	HY-134771
CAS No.:	643082-52-4
Molecular Formula:	$C_{22}H_{21}F_3N_6O_2$
Molecular Weight:	458.44
Target:	STAT
Pathway:	JAK/STAT Signaling; Stem Cell/Wnt
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 : 50 mg/mL (109.07 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1813 mL	10.9066 mL	21.8131 mL
	5 mM	0.4363 mL	2.1813 mL	4.3626 mL
	10 mM	0.2181 mL	1.0907 mL	2.1813 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 (5.45 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.45 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.45 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

YM-341619 (AS1617612) is a potent and orally active STAT6 inhibitor with an IC_{50} of 0.70 nM. YM-341619 inhibits Th2 differentiation in mouse spleen T cells induced by IL-4 (IC_{50}=0.28 nM) without affecting Th1 cell differentiation[1]. YM-341619 is a promising compound for the the research of allergic diseases, such as allergic asthma[2].

IC_{50} & Target

STAT6
0.70 nM (IC_{50})

In Vitro

YM-341619 (0.1-100 nM; pretreatment 30 min before IL-4) inhibits IL-4-increased STAT6 luciferase gene activity in a concentration dependent manner, exhibiting an IC_{50} value of 1.5 nM in FW4 cells[2].
YM-341619 (0.1-10 nM; pretreatment 30 min before IL-4) concentration-dependently decreases the production of IL-4 and the expression of GATA-3 mRNA in T cells cultured with IL-4. And it has no effects on the production of IFN-γ or the expression of T-bet (a Th1 transcription factor) mRNA in T cells cultured with IL-12[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[2]

Cell Line:	T cells
Concentration:	0.1 nM, 1 nM, 10 nM
Incubation Time:	Pretreatment 30 min before IL-4, then IL-4 treated for 16 hours
Result:	Decreased IL-4 and GATA-3 mRNA expression.

In Vivo

YM-341619 (intravenous injection; 1 mg/kg) exhibits CL_{tot}, $t_{1/2}$, V_d values of 36.1 mL/min/kg, 1.0 hour, 3117 mL/kg, respectively. And it exhibits C_{max}, T_{max}, AUC, and F% values of 80 ng/mL, 0.5h, 114 ng h/mL and 25%, respectively in 8-week-old female balb/c mice[1].
YM-341619 (oral administration; 0.003-0.03 mg/kg) suppresses the IgE level in a dose-dependent manner, but not the IgG2a level, and the ED_{50} value of YM-341619 for the suppression of IgE production is 0.026 mg/kg. YM-341619 tends to decrease IL-4 production and decrease IL-13 production in a dose-dependent manner (both 57%), but does not affect IFN-γ production in DNP-Ascaris-sensitized rats[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	DNP-Ascaris-sensitized rats[1]
Dosage:	0.003-0.03 mg/kg
Administration:	Oral administration; 0.003-0.03 mg/kg
Result:	Suppressed IL-4 and IL-13 production in splenocytes derived from DNP-ascaris-sensitized rats without reducing IFN-γ production.

REFERENCES

[1]. Shinya Nagashima, et al. Identification of 4-benzylamino-2-[(4-morpholin-4-ylphenyl)amino]pyrimidine-5-carboxamide derivatives as potent and orally bioavailable STAT6 inhibitors. Bioorg Med Chem. 2008 Jul 1;16(13):6509-21. 9.15

[2]. Keiko Ohga,et al.YM-341619 suppresses the differentiation of spleen T cells into Th2 cells in vitro, eosinophilia, and airway hyperresponsiveness in rat allergic models. Eur J Pharmacol. 2008 Aug 20;590(1-3):409-16.

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