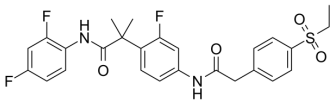
S18-000003

Cat. No.:	HY-119366
CAS No.:	2068119-11-7
Molecular Formula:	$C_{26}H_{25}F_3N_2O_4S$
Molecular Weight:	518.55
Target:	ROR
Pathway:	Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (192.85 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9285 mL	9.6423 mL	19.2845 mL
	5 mM	0.3857 mL	1.9285 mL	3.8569 mL
	10 mM	0.1928 mL	0.9642 mL	1.9285 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 (4.82 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 (4.82 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

S18-000003 is a potent, selective and orally active inhibitor of retinoic acid receptor-related orphan receptor-gamma-t (RORγt), with an IC_{50} of <30 nM towards human RORγt in competitive binding assays. S18-000003 shows selectivity for RORγt over other ROR family members (IC_{50}>10 μM). S18-000003 can be used for the research of psoriasis with low risk of thymic aberrations[1][2].

IC_{50} & Target

RORγt
<30 nM (IC_{50})

In Vitro	S18-000003 inhibits human and mouse RORγt-dependent transactivation, with IC_{50}s of 0.029 and 0.34 μM respectively in cell-based GAL4 promoter reporter assays[1]. S18-000003 (0.003-0.3 μM; 7 d) dose-dependently inhibits Th17 cell differentiation from human naive $CD4^+$T cells, with an IC_{50} of 0.024 μM[2]. S18-000003 (0.1-3 μM; 4 d) inhibits the differentiation of mouse Th17 cells from splenic naive $CD4^+$T cells, with an IC_{50} of 0.20 μM[2]. S18-000003 (0.03-1 μM; 3 d) reduces the IL-17 production in human PBMCs in a dose-dependent manner, and does not inhibit either the production of other cytokines (IL-2, IL-4, IL-10 and IFN-g) or cell proliferation[2]. S18-000003 (0.1-3 μM; 3 d) reduces IL-17 and IL-22 production in PBMCs from psoriatic mice in a dose-dependent manner[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	S18-000003 (30-100 mg/kg; p.o.) inhibits IL-17 production in the skin of IL-23-treated mice in a dose-dependent manner[1]. S18-000003 (0.1-8%; 100mL; topically administration once daily for 14 days) ameliorates psoriasis-like lesions in TPA-induced K14.Stat3C transgenic mice, and has little impact on the thymus[2]. S18-000003 (0.5 mg/kg; i.v.) exhibits the half-life (3.2 h), AUC (1930 ng•h/mL), CL_{tot} (4.33 mL/min/kg) and Vd_{ss} in rats[1]. S18-000003 (1 mg/kg; p.o.) exhibits the oral bioavailability (54.5%), C_{max} (185 ng/mL), AUC (2110 ng•h/mL) and T_{max} (4 h) in rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sasaki Y, et, al. Discovery of a potent orally bioavailable retinoic acid receptor-related orphan receptor-gamma-t (RORγt) inhibitor, S18-000003. Bioorg Med Chem Lett. 2018 Dec 1;28(22):3549-3553.

[2]. Imura C, et, al. A novel RORγt inhibitor is a potential therapeutic agent for the topical treatment of psoriasis with low risk of thymic aberrations. J Dermatol Sci. 2019 Mar;93(3):176-185.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA