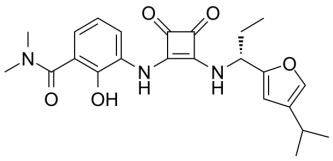
SCH 563705

Cat. No.:	HY-10011
CAS No.:	473728-58-4
Molecular Formula:	$C_{23}H_{27}N_3O_5$
Molecular Weight:	425.48
Target:	CXCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 30 mg/mL (70.51 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.3503 mL	11.7514 mL	23.5029 mL
5 mM	0.4701 mL	2.3503 mL	4.7006 mL
10 mM	0.2350 mL	1.1751 mL	2.3503 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

SCH 563705 is a potent and orally available CXCR2 and CXCR1 antagonist, with IC_{50}s of 1.3 nM, 7.3 nM and K_is of 1 and 3 nM, respectively.

IC_{50} & Target

CXCR2 1 nM (Ki)	CXCR1 3 nM (Ki)	CXCR2 1.3 nM (IC_{50})	CXCR1 7.3 nM (IC_{50})
Mouse CXCR2 5.2 nM (IC_{50})			

In Vitro

SCH 563705 (Compound 16) is a potent and orally available CXCR2 and CXCR1 antagonist, with IC_{50}s of 1.3 nM, 7.3 nM and K_is of 1 and 3 nM, respectively. SCH 563705 shows potent inhibition against both Gro-a and IL-8 induced human neutrophil migration (chemotaxis IC_{50} = 0.5 nM, against 30 nM of Gro-a; chemotaxis IC_{50} = 37 nM, against 3 nM of IL-8)[1]. SCH 563705 potently inhibits mouse CXCR2 (IC_{50} = 5.2 nM)[2].

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

In Vivo	SCH 563705 has good oral pharmacokinetic profiles in rats, mice, monkeys and dogs[1]. SCH 563705 (50 mg/kg p.o) reduces blood $Ly6G^+$ $Ly6C^+$ neutrophil frequency and unchanged levels of Ly6GLy6Chi monocytes. SCH563705 (3-30 mg/kg p.o) treatment causes a dosedependent elevation in plasma levels of CXCL1[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice[2] Induction of anti-collagen antibody-induced arthritis. Anti-collagen antibody-induced arthritis (ABIA) is induced in BALB/c mice (n = 8 mice per treatment group) as follows. On day 0, mice are injected intraperitoneally with 4 mg ArthritoMAB Arthritis-inducing Antibody Cocktail. On day 3, mice are boosted intraperitoneally with 50 μg of lipopolysaccharide from Escherichia coli 055:B5 in 200 μL sterile PBS. In all studies, SCH 563705 is administered in a vehicle consisting of 0.4% METHOCEL E15 premium hydroxypropyl methylcellulose (MC). Clinical scores are determined daily as follows. Each paw is assigned a score of 0-4 based on the following criteria: asymptomatic, 0; slight redness, 1; one or more swollen digits in addition to redness, 2; swelling of entire paw, 3; ankylosing of joints and residing of swelling, 4. The sum of the four paw scores for each mouse (0-16) are plotted against time to calculate the area under the curve (AUC) of disease activity. Paw hickness measurements are made daily using a micrometer caliper over the metatarsals of the paw. The percent change in paw thickness relative to baseline (day 0) measurements is then calculated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Allergy Clin Immunol. 2015 Sep;136(3):781-791.e9.
- Dev Cell. 2018 Nov 19;47(4):409-424.e9.
- Mucosal Immunol. 2016 Nov;9(6):1372-1383.

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REFERENCES

[1]. Chao J, et al. C(4)-alkyl substituted furanyl cyclobutenediones as potent, orally bioavailable CXCR2 and CXCR1 receptor antagonists. Bioorg Med Chem Lett. 2007 Jul 1;17(13):3778-83.

[2]. Min SH, et al. Pharmacological targeting reveals distinct roles for CXCR2/CXCR1 and CCR2 in a mouse model of arthritis. Biochem Biophys Res Commun. 2010 Jan 1;391(1):1080-6.

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