Product Data Sheet

Product Name: SCH 563705
Cat. No.: GC15401

Chemical Properties

Cas. No.	473728-58-4		
Chemical Name	3-[[3,4-dioxo-2-[[(1R)-1-(4-propan-2-ylfuran-2-yl)propyl]amino]cyclobuten-1-yl]amino]-2-hydroxy-N,N-dimethylbenzamide		
SMILES	CCC(C1=CC(=CO1)C(C)C)NC2=C(C(=O)C2=O)NC3=CC=CC(=C3O)C(=O)N(C)C		
Formula	$C_{23}H_{27}N_3O_5$	M.Wt	425.48
Solubility	DMSO : 125 mg/mL (293.79 mM; Need ultrasonic)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	SCH 563705		

Protocol

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Animal experiment:

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].

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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.

Background

SCH 563705 is a potent and orally available CXCR2 and CXCR1 antagonist, with IC50s of 1.3 nM, 7.3 nM and Kis of 1 and 3 nM, respectively.

SCH 563705 (Compound 16) is a potent and orally available CXCR2 and CXCR1 antagonist, with IC50s of 1.3 nM, 7.3 nM and Kis of 1 and 3 nM, respectively. SCH 563705 shows potent inhibition against both Gro-a and IL-8 induced human neutrophil migration (chemotaxis IC50 = 0.5 nM, against 30 nM of Gro-a; chemotaxis IC50 = 37 nM, against 3

nM of IL-8)[1]. SCH 563705 potently inhibits mouse CXCR2 (IC50 = 5.2 nM)[2].

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].

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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