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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

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- Trockeneiszuschlag
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- Expressversand

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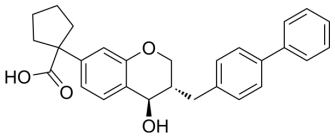
CP-105696

Cat. No.:	HY-19193
CAS No.:	158081-99-3
Molecular Formula:	$C_{28}H_{28}O_4$
Molecular Weight:	428.52
Target:	Leukotriene Receptor
Pathway:	GPCR/G Protein
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 : 100 mg/mL (233.36 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3336 mL	11.6681 mL	23.3361 mL
	5 mM	0.4667 mL	2.3336 mL	4.6672 mL
	10 mM	0.2334 mL	1.1668 mL	2.3336 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 (5.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CP-105696 is a potent and selective Leukotriene B_4 Receptor antagonist, with an IC_{50} of 8.42 nM.

IC_{50} & Target

LTB_4
8.42±0.26 nM (IC_{50})

In Vitro

CP-105696 is a structurally novel, selective and potent LTB_4 receptor antagonist. In vitro, CP-105696 inhibits [^{3}H]LTB_4 (0.3 nM) binding to high-affinity LTB_4 receptors on human neutrophils with an IC_{50} value of 8.42±0.26 nM. Scatchard analyses of [

	^{3}H]LTB$_4$ binding to these high-affinity receptors indicate that CP-105696 acts as a noncompetitive antagonist. CP-105696 inhibits human neutrophil chemotaxis mediated by LTB$_4$ (5 nM) in a noncompetitive manner with an IC$_{50}$ value of 5.0±2.0 nM. Scatchard analyses of [^{3}H]LTB$_4$ binding to low-affinity receptors on neutrophils indicate that CP-105696 acts as a competitive antagonist at this receptor, and inhibition of LTB$_4$-mediated CD11b upregulation on human neutrophils is competitively inhibited by CP-105696 (pA$_2$=8.03±0.19). CP-105696 at 10 μM does not inhibit either human neutrophil chemotaxis or CD11b upregulation mediated through alternate (i.e., C5a, lL-8, PAF) G-protein coupled chemotactic factor receptors. In isolated human monocytes, LTB$_4$ (5 nM)-mediated Ca^{2+} mobilization is inhibited by CP-105696 with an lC$_{50}$ value of 940±70 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	At a dose of 50 mg/kg/day (28 days), B10.BR (H2k) allografts transplanted into C57Bl/6 (H2b) recipients are significantly protected, as reflected by the mean survival time versus control grafts (27±20 days [n=10] vs. 12±6 days [n=14]; P=0.0146). Using an induction protocol (day -1 to day 3), CP-105696 at 100 mg/kg/day significantly prolongs allograft survival (33±23 days [n=9]; P=0.0026), but CP-105696 at 10 mg/kg/day does not (18±16 days [n=8]; P=0.1433). Syngeneic grafts survive indefinitely (n=11). Immunohistological evaluation of allografts at rejection reveals a mononuclear cell infiltrate composed primarily of CD3+ and CD11b+ (Mac-1+) cells, which are infrequent in syngeneic grafts. Allografts from mice treated with CP-105696 at 50 or 100 mg/kg/day demonstrat a selective reduction in β2-integrin (Mac-1) expression on monocytes/macrophages, as demonstrated by CD11b staining density compared with allograft controls[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice[2] Allogeneic donor hearts are harvested after intravenous heparinization of donor B10.BR mice (H2k) and are preserved via retrograde perfusion with cold cardioplegia solution into the left ventricle. Recipient C57Bl/6 mice (H2b) are prepared by ligating the lumbar vessels and isolating the abdominal aorta and vena cava; donor hearts are sutured in place by microvascular anastomoses of the donor aorta and pulmonary artery to the recipient aorta and inferior vena cava, respectively. CP-105696 is evaluated in a 28-day treatment protocol (50 mg/kg/day), a high-dose (100 mg/kg/day) induction protocol (day -1 to day 3), and a low-dose (10 mg/kg/day) induction protocol (day -1 to day 3). In all study groups, drug is administered orally in a 0.5% methylcellulose vehicle. In parallel studies, treatment of C57Bl/6 (H2b) recipients bearing B10.BR (H2k) cardiac allografts given FK506 (2 mg/kg/day for 28 days), our standard control immunosuppressant, significantly prolongs allograft survival (mean survival time [MST], 40±18 days [n=9]; P=0.0002)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Showell HJ, et al. The in vitro and in vivo pharmacologic activity of the potent and selective leukotriene B4 receptor antagonist CP-105696. J Pharmacol Exp Ther. 1995 Apr;273(1):176-84.

[2]. Weringer EJ, et al. Antagonizing leukotriene B4 receptors delays cardiac allograft rejection in mice. Transplantation. 1999 Mar 27;67(6):808-15.

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