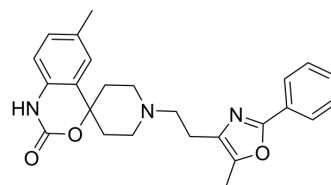


RS 504393

Cat. No.:	HY-15418		
CAS No.:	300816-15-3		
Molecular Formula:	C ₂₅ H ₂₇ N ₃ O ₃		
Molecular Weight:	417.5		
Target:	CCR		
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 : 10 mg/mL (23.95 mM; ultrasonic and warming and heat to 60°C)
 H₂O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.3952 mL	11.9760 mL	23.9521 mL
	5 mM	0.4790 mL	2.3952 mL	4.7904 mL
	10 mM	0.2395 mL	1.1976 mL	2.3952 mL

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

In Vivo

- Add each solvent one by one: 50% DMSO >> 15% EtOH >> 35% PEG300
 Solubility: 31.25 mg/mL (74.85 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 1.25 mg/mL (2.99 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 1.25 mg/mL (2.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RS 504393 is a selective CCR2 chemokine receptor antagonist (IC₅₀ values are 89 nM and > 100 μM for inhibition of human recombinant CCR2 and CCR1 receptors respectively).

IC₅₀ & Target

CCR2 89 nM (IC ₅₀)	Human α _{1a} receptor 72 nM (IC ₅₀)	Human α _{1d} receptor 460 nM (IC ₅₀)	5HT-1a receptor 1070 nM (IC ₅₀)
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In Vitro	RS 504393 inhibits the MCP-1-induced chemotaxis with an IC ₅₀ of 330 nM. RS 504393 treatment suppresses allergen induced β -hexosaminidase release significantly. Without allergen priming, MCP-1 induces mast cell degranulation, which is completely suppressed by RS 504393 ^[4] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	RS504393 (0.3-3 μ g) with CCL2 progressively blocks thermal hyperalgesia dose-dependently in mice ^[1] . RS 504393 (5 mg/kg, i.v.) suppresses the elevated numbers of leukocytes and increased total protein content in BALF induced by The LPS. RS504393 significantly down regulates the LPS-induced elevation of IL-1 β , PAI-1 mRNA and protein expressions. RS504393 significantly suppresses induced lung edema, protein-rich fluid, polymorphonuclear accumulation and bronchial wall thickening induced by LPS ^[2] . RS-504393 significantly reduces renal pathology, especially the extensive interstitial fibrosis mediated by decrease in type I collagen synthesis in a UUO model ^[3] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[4]

Isolated mast cells are sensitized by incubation with anti-DNP IgE in RPMI1640 containing 10 ng/mL of murine recombinant IL-3, 10 ng/mL of recombinant SCF, and 5% murine serum. The cells are then washed with HBSS containing 10 ng/mL of murine recombinant IL-3, 10 ng/mL of recombinant SCF, 0.04% BSA, and 10 mM HEPES. Resuspended cells at a concentration of 2 to 8 \times 10⁴ cells/100 μ L are transferred into triplicate wells of a 96 well U-bottom plate and allowed to equilibrate at 37°C for 10 minutes before the addition of DNP-albumin or compound 48/80. After 45 minutes, the plate is centrifuged at 290 g for 5 minutes at 4°C. The β -hexosaminidase activity of the culture supernatant is determined using a Published protocol. Fifty- μ L aliquots of the supernatant are placed in wells of another 96-well plate together with 100 μ L of 2.5 mM p-nitrophenyl-N-acetyl β -d glucosaminide solubilized in 0.04mol/L citrate buffer adjusted to pH 4.5 with disodium phosphate. After incubation at 37°C for 90 minutes, the reactions are terminated by addition of 50 μ L of 0.4mol/L glycine adjusted to pH 10.7 with sodium hydroxide. The colored product is measured at 405 nm with a reference filter of 570 nm. The relative release of β -hexosaminidase is defined as the activity in the supernatant of the tested cells divided by the activity in the positive control cell supernatant, multiplied by 100. Compound 48/80 stimulus is used for assay control. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[2]

Male C57BL/6J mice (n=30) and male homozygote CCR1, CCR2 and CCR3 knockout mice (n=12, in each phenotype), 6-8 weeks old and weighing 20 \pm 2 g. Intranasal administration of PBS or LPS (5 mg/kg) is performed in a volume of 1 mL/kg body weight. C57BL/6J mice are treated with vehicle or RS504393 (5 mg/kg) intraperitoneally 30 min before LPS challenge. Four hours after LPS challenge, mice are terminated by an intraperitoneal injection of an overdose of pentobarbitone. The mice are kept on a 12-h light/dark cycle with access to mice chow and water ad libitum. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2023 Sep 12;9(1):94.
- ACS Nano. 2024 Feb 21.
- Nat Commun. 2022 Nov 26;13(1):7281.
- J Exp Med. 2023 Aug 7;220(8):e20220509.
- Sci Adv. 2023 Nov 3;9(44):eadi7337.

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REFERENCES

[1]. Baamonde, Ana., et al. Involvement of glutamate NMDA and AMPA receptors, glial cells and IL-1 β in the spinal hyperalgesia evoked by the chemokine CCL2 in mice. *Neuroscience Letters* (2011), 502(3), 178-181.

[2]. Yang, Dong., et al. Roles of CC chemokine receptors (CCRs) on lipopolysaccharide-induced acute lung injury. *Respiratory Physiology & Neurobiology* (2010), 170(3), 253-259.

[3]. Kitagawa, Kiyoki., et al. Blockade of CCR2 ameliorates progressive fibrosis in kidney. *American Journal of Pathology* (2004), 165(1), 237-246.

[4]. Tominaga T, et al. Blocking mast cell-mediated type I hypersensitivity in experimental allergic conjunctivitis by monocyte chemoattractant protein-1/CCR2. *Invest Ophthalmol Vis Sci*. 2009 Nov;50(11):5181-8.

[5]. Mirzadegan T, et al. Identification of the binding site for a novel class of CCR2b chemokine receptor antagonists: binding to a common chemokine receptor motif within the helical bundle. *J Biol Chem*. 2000 Aug 18;275(33):25562-71.

Caution: Product has not been fully validated for medical applications. For research use only.

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