MK-0812

Cat. No.: HY-50669

CAS No.: 624733-88-6

Molecular Formula: $C_{24}H_{34}F_3N_3O_3$

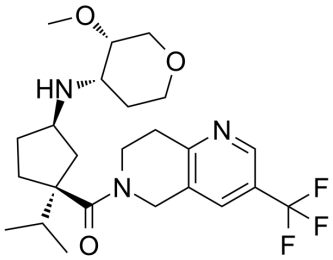
Molecular Weight: 469.54

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 : 100 mg/mL (212.97 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1297 mL	10.6487 mL	21.2974 mL
	5 mM	0.4259 mL	2.1297 mL	4.2595 mL
	10 mM	0.2130 mL	1.0649 mL	2.1297 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 (5.32 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.32 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MK-0812 is a potent and selective CCR2 antagonist with low nM affinity for CCR2.

IC_{50} & Target

CCR2

In Vitro

MK-0812 completely blocks all MCP-1 mediated response in a concentration dependent manner, with an IC_{50} of 3.2 nM. This value is similar to the potency observed for the inhibition of ^{125}I-MCP-1 binding by MK-0812 on isolated monocytes (IC_{50} 4.5 nM). In fact, the antagonist not only completely blocks the shape change response to exogenous MCP-1, but also results in a monocyte forward scatter measurement below unstimulated or basal levels. The addition of MK-0812 to rhesus blood also inhibits MCP-1 induced monocyte shape change. The IC_{50} for MK-0812 in whole blood assays is 8 nM[1] MK0812 is a potent and selective small molecule CCR2 antagonist[2].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	MK-0812 is administered by continuous i.v. infusion to maintain a constant level of the drug in blood[1]. Administration of MK0812 at 30 mg/kg, p.o. reduces the frequency of $Ly6G^{-}Ly6C^{hi}$ monocytes in the peripheral blood, while no impact on circulating $Ly6G^{+}Ly6C^{+}$ neutrophil frequency is observed. In addition, MK0812 treatment causes a dose-dependent reduction in circulating $Ly6C^{hi}$ monocytes and a corresponding elevation in the CCR2 ligand CCL2[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Human whole blood is collected in EDTA tubes and used within 1 h of blood collection. For antagonist treated samples, blood (200 μL) is pre-incubated with MK-0812 (0.1% final DMSO concentration) for 30 min at room temperature. After which, 20 μL of FITC conjugated anti-CD14 antibody and 4 μL of chemokine or buffer is added to each sample and mixed lightly. An aliquot (100 μL) of the blood mixture is incubated for 10 min at 37°C, immediately placed on ice and lightly fixed with 250 μL of ice cold fixative (49 mL PBS, 1.0 mL 4% para-formaldehyde) for 1 min. Red blood cells are lysed by adding 1.0 mL of ice cold lysis solution (0.15 M NH_4Cl_2, 10 mM sodium bicarbonate, and 1 mM EDTA), and incubated for 20 min on ice. After complete lysis of red blood cells, 100 μL of 4% para-formaldehyde is added and the samples are analyzed by flow cytometry for forward scatter measurements[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Female BALB/c mice are used between 8 and 10 weeks of age. SCH563705 or MK0812 are administered in a 0.4% MC solution by 30 mg/kg oral gavage (p.o.). Two hours later, the frequency of $CD11b^{+}Ly6G^{-}Ly6C^{hi}$ monocytes and $CD11b^{+}Ly6G^{+}Ly6C^{+}$ neutrophils is determined by flow cytometry. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wisniewski T, et al. Assessment of chemokine receptor function on monocytes in whole blood: In vitro and ex vivo evaluations of a CCR2 antagonist.J Immunol Methods. 2010 Jan 31;352(1-2):101-10.

[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.

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