上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：1,5-酐-2,3-双脱氧-3-[[(1R,3S)-3-[[7,8-二氢-3-(三氟甲基)-1,6-萘啶-6(5H)-基]羰基]-3-(1-甲基乙基)环己基]氨基]-4-O-甲基-D-赤式-戊糖醇
产品别名：MK-0812

生物活性：	
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].
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].
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.

实验参考：	
Animal Administration	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.
Kinase Assay	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].
	[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

References	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.