MK-0812 Succinate

Cat. No.: HY-50669A

CAS No.: 851916-42-2

Molecular Formula: $C_{28}H_{40}F_3N_3O_7$

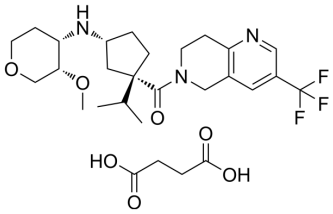
Molecular Weight: 587.63

Target: CCR

Pathway: GPCR/G Protein; Immunology/Inflammation

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (54.46 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7018 mL	8.5088 mL	17.0175 mL
5 mM	0.3404 mL	1.7018 mL	3.4035 mL
10 mM	0.1702 mL	0.8509 mL	1.7018 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 (4.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.25 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MK-0812 Succinate is a potent and selective CCR2 antagonist with high affinity at CCR2.

IC_{50} & Target

CCR2

In Vitro

MK-0812 is a potent and selective CCR2 antagonist[1]. 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, MK-0812 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[2] MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	MK-0812 (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, MK-0812 treatment causes a dose-dependent reduction in circulating $Ly6C^{hi}$ monocytes and a corresponding elevation in the CCR2 ligand CCL2[1]. MK-0812 is administered by continuous i.v. infusion to maintain a constant level of the drug in blood[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice[1] Female BALB/c mice are used between 8 and 10 weeks of age. SCH563705 or MK-0812 are administered in a 0.4% methylcellulose (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[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. 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.

[2]. 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.

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