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产品名称：INCB8761(PF-4136309)
产品别名：PF-4136309

生物活性：

Description

PF-4136309 is a potent, selective, and orally bioavailable CCR2 antagonist, with IC_{50}s of 5.2 nM, 17 nM and 13 nM for human, mouse and rat CCR2.

IC_{50} & Target

Human CCR2	Mouse CCR2	Rat CCR2	
5.2 nM (IC_{50})	13 nM (IC_{50})	17 nM (IC_{50})	

In Vitro

PF-4136309 is potent in human chemotaxis activity (IC_{50}=3.9 nM) and in the whole blood assay (IC_{50}=19 nM), with IC_{50} of 16 and 2.8 nM in mouse and rat chemotaxis assays. PF-4136309 is potent in inhibiting CCR2 mediated signaling events such as intracellular calcium mobilization and ERK (extracellular signal-regulated kinase) phosphorylation with IC_{50} values of 3.3 and 0.5 nM, respectively. In hERG patch clamp assay, PF-4136309 inhibits hERG potassium current with an IC_{50} of 20 μM. PF-4136309 is not a cytochrome P450 (CYP) inhibitor, with IC_{50}values of >30 μM against five major CYP isozymes CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Moreover, PF-4136309 is not a CYP inducer at concentrations up to 30 μM[1].

In Vivo

PF-4136309 (2 mg/kg) exhibits a moderate half-life in both species after iv administration (2.5 and 2.4 h). When administered orally, PF-4136309 (10 mg/kg) is absorbed rapidly, with peak concentration time (T_{max}) at 1.2 h for rats and 0.25 h for dogs. A similar half-life is observed in both species between iv dosing and po dosing. PF-4136309 is well absorbed, with an oral bioavailability of 78% in both species[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 34 mg/mL (59.80 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7587 mL	8.7937 mL	17.5874 mL
5 mM	0.3517 mL	1.7587 mL	3.5175 mL
10 mM	0.1759 mL	0.8794 mL	1.7587 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.08 mg/mL (3.66 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (3.66 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (3.66 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.66 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Xue CB, et al. Discovery of INCB8761/PF-4136309, a Potent, Selective, and Orally Bioavailable CCR2 Antagonist. ACS Med. Chem. Lett., 2011, 2 (12), pp 913-918.