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：INCB 3284
产品别名：INCB 3284

生物活性：

Description	INCB 3284 is a potent, selective and orally bioavailable human CCR2 antagonist, inhibiting monocyte chemoattractant protein-1 binding to hCCR2, with an IC50 of 3.7 nM. INCB 3284 can be used in the research of acute liver failure.
IC_{50} & Target	MCP-1-hCCR2
	3.7 nM (IC_{50})
In Vitro	INCB 3284 is a pentent, selective and orally bioavailable human CCR2 antagonist, inhibiting monocyte chemoattractant protein-1 binding to hCCR2, with an IC50 of 3.7 nM. INCB 3284 also causes an IC50 of 4.7 nM in antagonism of chemotaxis activity, an IC50 of 84 μM in inhibition of the hERG potassium current. However, INCB 3284 has no effec on CCR1, CCR3, CCR5, CXCR3, and CXCR5, or additional GPCRs at a concentration of 1 μM. Moreover, INCB 3284 potently inhibits CCR2-mediated signaling events such as intracellular calcium mobilization and ERK phosphorylation with IC50 values of 6 and 2.6 nM, respectively[1].
In Vivo	INCB 3284 (1 mg/kg/day, ip) reduces liver damage, and decreases microglia activation in AOM-treated mice via inhibition on CCR2. INCB 3284 also significantly reduces the pERK1/2 to tERK1/2 ratio, as well as G-protein signaling pathway activity and proinflammatory cytokine production in cortex lysates from mice administed with azoxymethane[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 83.3 mg/mL (160.03 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9211 mL	9.6054 mL	19.2108 mL
	5 mM	0.3842 mL	1.9211 mL	3.8422 mL
	10 mM	0.1921 mL	0.9605 mL	1.9211 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: ≥ 2.5 mg/mL (4.80 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.80 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 25.0 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% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.80 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.80 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 25.0 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 INCB3284, a Potent, Selective, and Orally Bioavailable hCCR2 Antagonist. ACS Med Chem Lett. 2011 Mar 31;2(6):450-4. [2]. McMillin M, et al. Neuronal CCL2 is upregulated during hepatic encephalopathy and contributes to microglia activation and neurological decline. J Neuroinflammation. 2014 Jul 10;11:121.

实验参考：

Animal Administration	Mice[2] Male C57Bl/6 mice (20 to 25 g) are given free access to water and rodent chow and are housed in constant temperature, humidity, and 12 h light-dark cycling. Acute liver failure is induced via a single intraperitoneal (ip) injection of 100 mg/kg of azoxymethane (AOM). In parallel, systemic inhibition of CCR2 and CCR4 activity is accomplished via pretreatment with INCB 3284 (1 mg/kg/day ip) or C021 (1 mg/kg/day ip) for 3 days prior to injection of AOM. Following injection, mice are placed on heating pads adjusted to 37°C and monitored frequently for signs of neurological decline. To reduce the impacts of hypoglycemia and dehydration, cage floors are supplied with hydrogel and rodent chow and after 12 h, and every subsequent 4 h, mice are injected subcutaneously with 5% dextrose in 250 μL of saline. If mice undergo a 20% or greater weight loss they are removed from the study[2].
References	[1]. Xue CB, et al. Discovery of INCB3284, a Potent, Selective, and Orally Bioavailable hCCR2 Antagonist. ACS Med Chem Lett. 2011 Mar 31;2(6):450-4. [2]. McMillin M, et al. Neuronal CCL2 is upregulated during hepatic encephalopathy and contributes to microglia activation and neurological decline. J Neuroinflammation. 2014 Jul 10;11:121.