# INCB 3284

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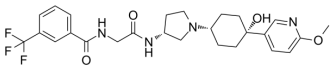
| **Cat. No.:** | HY-15450A |
| **CAS No.:** | 887401-92-5 |
| **Molecular Formula:** | $C_{26}H_{31}F_3N_4O_4$ |
| **Molecular Weight:** | 520.54 |
| **Target:** | CCR |
| **Pathway:** | GPCR/G Protein; Immunology/Inflammation |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 2 years<br>-20°C 1 year |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 83.3 mg/mL (160.03 mM)

$H_2O$ : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

* "≥" 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 |

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 (4.80 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.80 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.80 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

INCB 3284 is a potent, selective and orally bioavailable human CCR2 antagonist, inhibiting monocyte chemoattractant protein-1 binding to hCCR2, with an $IC_{50}$ 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 ($IC_{50}$)

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| **In Vitro** | INCB 3284 is a pentent, selective and orally bioavailable human CCR2 antagonist, inhibiting monocyte chemoattractant protein-1 binding to hCCR2, with an $IC_{50}$ of 3.7 nM. INCB 3284 also causes an $IC_{50}$ of 4.7 nM in antagonism of chemotaxis activity, an $IC_{50}$ 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 $IC_{50}$ values of 6 and 2.6 nM, respectively[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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| **Animal Administration [2]** | Mice[2]<br>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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## 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.





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