Ilacirnon

Cat. No.: HY-101713

CAS No.: 1100318-47-5

Molecular Formula: $C_{20}H_{13}ClF_3N_5O_3S$

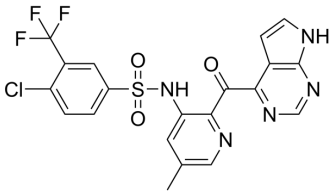
Molecular Weight: 495.86

Target: CCR

Pathway: GPCR/G Protein; Immunology/Inflammation

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (201.67 mM)

H_2O : 0.25 mg/mL (0.50 mM; Need ultrasonic and warming)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0167 mL	10.0835 mL	20.1670 mL
5 mM	0.4033 mL	2.0167 mL	4.0334 mL
10 mM	0.2017 mL	1.0083 mL	2.0167 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 (5.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CCX140 (CCX140-B) is a potent CCR2 antagonist.

IC_{50} & Target

hCCR2	CCR2	CCR5
2.3 nM (Kd, in monocytes)	3 nM (IC_{50}, in THP-1 cells)	7 μM (IC_{50}, in Activated T lymphocytes)

In Vitro

CCX140 (CCX140-B) potently inhibits CCL2-induced chemotaxis of purified human blood monocytes with IC_{50} values of 8 nM in buffer and 200 nM in the presence of 100% human serum. CCX140 also inhibits CCL2-induced Ca^{2+} mobilization in monocytes with an IC_{50} value of 3 nM. CCX140 inhibits the binding of ^{125}I-CCL2 to monocytes with an IC_{50} value of 17 nM. CCX140 has a K_d value of 2.3 nM toward hCCR2. CCX140 also inhibits monocyte chemotaxis mediated by the other CCR2 ligands: CCL8/MCP-2, CCL7/MCP-3, and CCL13/MCP-4[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Treatment of hCCR2 KI mice with CCX140 (CCX140-B) causes a dose-dependent reduction in the number of peritoneal leukocytes after thioglycollate challenge: CCX140 strongly blocks leukocyte infiltration at 30 mg/kg, partially blocks leukocyte infiltration at 10 mg/kg, and fails to block leukocyte infiltration at 3 mg/kg. In DIO hCCR2 KI mice, treatment with 100 mg/kg CCX140 blocks the progressive increase in UAER and ACR. CCX140 maintains lower UAER and ACR values during the entire 8-wk dosing regimen[1]. In DIO mice, the CCR2 antagonist completely blocks the recruitment of inflammatory macrophages to visceral adipose tissue. The mice exhibit reduced hyperglycemia and insulinemia, improved insulin sensitivity, increased circulating adiponectin levels, decreased pancreatic islet size and increased islet number. CCX140 also reduces urine output, glucose excretion, hepatic glycogen and triglyceride content and glucose 6-phosphatase levels[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: CCX140 is formulated as a solution in 1% hydroxypropyl methylcellulose. Male uninephrectomized hCCR2 KI mice are rendered diabetic with the high-fat diet and dosed with 100 mg/kg CCX140, but for 8 wk of dosing. Eight-week-old male hCCR2 KI Lepr db/db mice are similarly dosed with 100 mg/kg CCX140 for 6 wk[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2019 Oct 14;10(10):781.

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REFERENCES

[1]. Sullivan T, et al. CCR2 antagonist CCX140-B provides renal and glycemic benefits in diabetic transgenic human CCR2 knockin mice. Am J Physiol Renal Physiol. 2013 Nov 1;305(9):F1288-97.

[2]. Sullivan TJ, et al. Experimental evidence for the use of CCR2 antagonists in the treatment of type 2 diabetes. Metabolism. 2013 Nov;62(11):1623-32.

Caution: Product has not been fully validated for medical applications. For research use only.

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