Vicriviroc maleate

Cat. No.: HY-17377

CAS No.: 599179-03-0

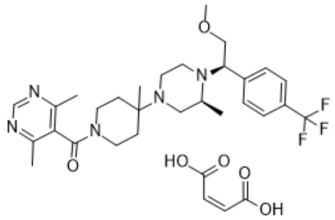
Molecular Formula: $C_{32}H_{42}F_3N_5O_6$

Molecular Weight: 649.7

Target: CCR; HIV

Pathway: GPCR/G Protein; Immunology/Inflammation; Anti-infection

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 : 50 mg/mL (76.96 mM; Need ultrasonic)
H_2O : 25 mg/mL (38.48 mM; Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5392 mL	7.6959 mL	15.3917 mL
5 mM	0.3078 mL	1.5392 mL	3.0783 mL
10 mM	0.1539 mL	0.7696 mL	1.5392 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 (3.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.85 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.85 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vicriviroc maleate (SCH-417690 maleate; SCH-D maleate) is a potent, selective, oral bioavailable and CNS penetrated antagonist of CCR5, with a K_i of 2.5 nM, and also inhibits HIV-1 in PBMC cells, with IC_{90}s of 3.3 nM (JrFL), 2.8 nM (ADA-M), 1.8 nM (301657), 4.9 nM (JV1083) and 10 nM (RU 570).

IC_{50} & Target

CCR5	HIV-1 (301657)	HIV-1 (ADA-M)	HIV-1 (JrFL)
2.5 nM (Ki)	1.8 nM (IC90, in PBMC cells)	2.8 nM (IC90, in PBMC cells)	3.3 nM (IC90, in PBMC cells)

	HIV-1 (JV1083) 4.9 nM (IC90, in PBMC cells)	HIV-1 (RU 570) 10 nM (IC90, in PBMC cells)
In Vitro	Vicriviroc maleate (SCH-417690 maleate; SCH-D maleate) is a potent, selective and oral bioavailable inhibitor of CCR5, with a K_i of 2.5 nM, and also inhibits HIV-1 in PBMC cells, with IC_{90}s of 3.3 (JrFL), 2.8 (ADA-M), 1.8 (301657), 4.9 (JV1083) and 10 nM (RU 570). In addition, Vicriviroc maleate shows a mean IC_{50} and IC_{90} of 0.45 nM and 4 nM for a panel of HIV isolates, and has weak activity against hERG activity (IC_{50}, 5.8 μM)[1]. Vicriviroc maleate inhibits chemotactic response to MIP-1α with IC_{50} values below 1 nM, and suppresses RANTES-induced signaling with a mean IC_{50} of 4.2 ± 1.3 nM. Vicriviroc maleate potently suppresses all the viral isolates tested, with geometric mean EC_{50}s of 0.04-2.3 nM and IC_{90}s of 0.45-18 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
In Vivo	Vicriviroc maleate (SCH-417690 maleate; SCH-D maleate; 10 mg/kg) has good oral availablity in rats and monkeys, with no acute CNS or GI effects in rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

PROTOCOL

Cell Assay [2]

Ficoll-purified peripheral blood mononuclear cells (PBMCs) are stimulated in vitro with phytohemagglutinin (PHA) (5 μg/mL) and interleukin-2 (IL-2) (50 U/mL) for 3 to 7 days. The cells are resuspended at 4×10^6/mL in complete medium (RPMI, 10% fetal bovine serum [FBS], 50 U/mL IL-2), seeded into 96-well plates (2×10^5/well), incubated with an equal volume of culture medium containing compound (Vicriviroc) for 1 h at 37°C, and infected in triplicate with 25 to 100 50% tissue culture infectious doses (TCID50) per well of viral inoculum for 3 to 4 h. Cells are washed twice in phosphate-buffered saline (PBS) to remove residual virus and are cultured with compound for 4 to 6 days. HIV-1 replication is quantified by measurement of extracellular p24 antigen in the supernatants by enzyme-linked immunosorbent assay. The 50% effective concentrations (EC_{50}s) and EC_{90}s for each virus are determined using Graphpad PRISM software[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Tagat JR, et al. Piperazine-based CCR5 antagonists as HIV-1 inhibitors. IV. Discovery of 1-[(4,6-dimethyl-5-pyrimidinyl)carbonyl]- 4-[4-[2-methoxy-1(R)-4-(trifluoromethyl)phenyl]ethyl-3(S)-methyl-1-piperazinyl]- 4-methylpiperidine (Sch-417690/Sch-D), a potent, highly selective, and orally bioavailable CCR5 antagonist. J Med Chem. 2004 May 6;47(10):2405-8.

[2]. Strizki JM, et al. Discovery and characterization of vicriviroc (SCH 417690), a CCR5 antagonist with potent activity against human immunodeficiency virus type 1. Antimicrob Agents Chemother. 2005 Dec;49(12):4911-9.

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