ZK756326 dihydrochloride

Cat. No.: HY-101038A

CAS No.: 1780259-94-0

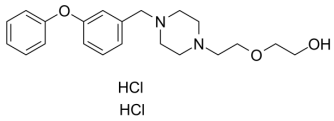
Molecular Formula: $C_{21}H_{30}Cl_2N_2O_3$

Molecular Weight: 429.38

Target: CCR

Pathway: GPCR/G Protein; Immunology/Inflammation

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

H_2O : 50 mg/mL (116.45 mM; Need ultrasonic)
DMSO : 27.5 mg/mL (64.05 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3289 mL	11.6447 mL	23.2894 mL
	5 mM	0.4658 mL	2.3289 mL	4.6579 mL
	10 mM	0.2329 mL	1.1645 mL	2.3289 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (116.45 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.75 mg/mL (6.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (6.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description ZK756326 dihydrochloride is a nonpeptide chemokine receptor agonist for the CC chemokine receptor CCR8.

IC_{50} & Target

CCR8 1.8 μM (IC_{50}, in U87 cells)	5-HT_{2B} 4.4 μM (IC_{50})	5-HT_{1A} 5.4 μM (IC_{50})	5-HT_6 5.9 μM (IC_{50})
5-HT_{5A} 16 μM (IC_{50})	5-HT_{2C} 34.8 μM (IC_{50})	α_{2A} <20 μM (IC_{50})	

In Vitro	ZK 756326 inhibits the binding of the CCR8 ligand I-309 (CCL1), with an IC_{50} value of 1.8 μM. ZK 756326 is a full agonist of CCR8, dose-responsively eliciting an increase in intracellular calcium and cross-desensitizing the response of the receptor to CCL1. ZK 756326 stimulates extracellular acidification in cells expressing human CCR8. Binding competition assays are performed on a series of other G-protein-coupled receptors to determine whether the interaction of ZK 756326 is specific for CCR8. In these assays, ZK 756326 is tested at 50 μM for inhibition of radiolabeled ligand binding. At this concentration, ZK 756326 shows >28 fold specificity for CCR8 compared with 26 other GPCRs, all with IC_{50} values of >50 μM. There is less selectivity when ZK 756326 is tested against the serotonergic receptors 5-HT_{1A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_{5A}, 5-HT_6, and the adrenergic receptor α2A, in which IC_{50} values of 5.4, 4,4, 34.8, 16, 5.9, and <20 μM (at 20 μM 65% inhibition), respectively, are observed. The compound is unlikely to be an agonist on these biogenic amine receptors, because when tested at concentrations up to 10 μM on a representative receptor, 5-HT_{1A}, it shows no agonist activity in a GTPγS binding assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	U87 MG cells expressing CCR8 are plated on poly-D-lysine-coated black 96-well plates at 10,000 cells/well and are cultured overnight. Cells are then loaded with Calcium 3, a Ca^{2+}-sensitive non-wash fluorescence dye, for 60 min at 37°C in Hanks' balanced salts solution containing 20 mM HEPES, 3.2 mM $CaCl_2$, 1% (v/v) fetal bovine serum, and 2.5 mM probenecid. Changes in intracellular free-Ca^{2+} concentration are measured with Fluorometric Imaging Plate Reader (FLIPR 3) immediately after the addition of agonist at room temperature. Cross-desensitization experiments are performed by a first addition of the agonist (CCL1 at 30 nM or ZK 756326 at 3 μM), immediately followed by a second addition of 100 nM CCL1[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biochem Pharmacol. 2021, 114565.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Haskell CA, et al. Identification and characterization of a potent, selective nonpeptide agonist of the CC chemokine receptor CCR8. Mol Pharmacol. 2006 Jan;69(1):309-16.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA