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产品名称：ZK756326（dihydrochloride）
产品别名：ZK756326 dihydrochloride

生物活性：

Description

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

IC_{50} & Target

CCR8	$5\text{-}HT_{1A}$	$5\text{-}HT_{2B}$	$5\text{-}HT_{2C}$
1.8 μM (IC_{50}, in U87 cells)	5.4 μM (IC_{50})	4.4 μM (IC_{50})	34.8 μM (IC_{50})
$5\text{-}HT_{5A}$	$5\text{-}HT_{6}$	α_{2A}	
16 μM (IC_{50})	5.9 μM (IC_{50})	<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 $5\text{-}HT_{1A}$, $5\text{-}HT_{2B}$, $5\text{-}HT_{2C}$, $5\text{-}HT_{5A}$, $5\text{-}HT_{6}$, 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, $5\text{-}HT_{1A}$, it shows no agonist activity in a GTPγS binding assay[1].

Solvent&Solubility

In Vitro:

DMSO : 6 mg/mL (13.97 mM; Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / 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

*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。

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.

实验参考：

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%

Cell Assay	(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].
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.