Product Data Sheet

Chemical Properties

Product Name: INCB3344
Cas No.: 1262238-11-8
M.Wt: 577.24
Formula: C29H34F3N3O6
Synonyms: INCB 3344; INCB-3344
Chemical Name: N-[2-[[3S,4S)-1-[4-(1,3-benzodioxol-5-yl)-4-hydroxycyclohexyl]-4-et hoxypyrrolidin-3-yl]amino]-2-oxoethyl]-3-(trifluoromethyl)benzamide
Canonical SMILES: CCOC1CN(CC1NC(=O)CNC(=O)C2=CC(=CC=C2)C(F)(F)F)C3CCC(CC3)(C4=CC5=C(C=C4)OCO5)O
Solubility: ≥25.9mg/mL in DMSO
Storage: Store at -20°C
General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: GPCR/G protein
Pathways: CCR2
Description:
INCB3344 is a novel potent and selective antagonist of CCR2 receptor, which possesses an IC 50 of 10 nM for CCL2. [1]
CCR2 is a chemokine receptor mainly expressed on monocytes which acts as the key receptor in mediating their tissue influx in the context of immune-based inflammation. CCR2 is a G
protein-coupled receptor (GPCR), whose ligands include the chemokines MCP family, including CCL2, CCL7, CCL8. These ligands bind CCR2 receptor with high affinity and elicit a chemotactic signal which leads to directed migration of the receptor-bearing cells. CCL2 has been shown to be relevant in high concentrations in various inflammatory lesions, implicating this chemokine as a physiologically important chemotactic signal for monocytes. [1]

Characterization of the pharmacological activity of INCB3344 was first evaluated by testing its ability to inhibit CCL2 binding to CCR2 in a whole cell binding assay using a murine monocyte cell line, WEHI-274.1 and 125I-labeled mCCL2 as a tracer. The binding IC 50 of INCB3344 in this assay was determined to be 10±5 nM, and inhibition greater than 90% binding was observed at a concentration of 90nM. The chemotaxis inhibitory activity of different concentrations of INCB3344 was evaluated using 30nM mCCL2 as the agonist. The result showed a similar potency to the binding assay. Selectivity of INCB3344 was evaluated against a panel of GPCRs including several human chemokine receptors using radioligand binding assays. Results from these studies demonstrate at least 100-fold selectivity of INCB3344 against all of the receptors tested. [1] INCB3344 treatment results in a dose-dependent inhibition of macrophage influx in a mouse delayed-type hypersensitivity model. The histopathological analysis of tissues from the delayed-type hypersensitivity model illustrates that inhibitory activity of CCR2 leads to a substantial reduction in tissue inflammation. [1]

Reference:

Protocol

Cell experiment:

Cell lines
WEHI-274.1 cells

Preparation method
Dissolved in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.

Reacting conditions
0.3-300 nM; 6 min.

Applications
In WEHI-274.1 cells, INCB3344 inhibits monocyte chemotaxis with IC50 value of 10 nM using 30 nM mCCL2 as the agonist. INCB3344 blocks ERK phosphorylation in response to mCCL2 with IC50 value of 3-10 nM, which is mediated by CCR2 signaling.

Animal experiment [3]:
Animal models | Female BALB/c mice (20 g) received i.p. injection of thioglycolate.
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Dosage form | 30, 60, or 100 mg/kg BID; 48 h; administrated orally.
Applications | INCB3344 dose-dependently reduces total cell number in the lavage fluid and inhibits monocyte influx by 36%, 55% and 73% at 30 mg/kg, 60 mg/kg and 100 mg/kg, respectively.
Other notes | Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Caution
FOR RESEARCH PURPOSES ONLY.
NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.