

Product Data Sheet

Product Name: IMD 0354

Cat. No.: GC17830

Chemical Properties

Cas. No. 978-62-1

Chemical Name N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide

SMILES C1=CC(=C(C=C1Cl)C(=O)NC2=CC(=CC(=C2)C(F)(F)F)C(F)(F)F)O

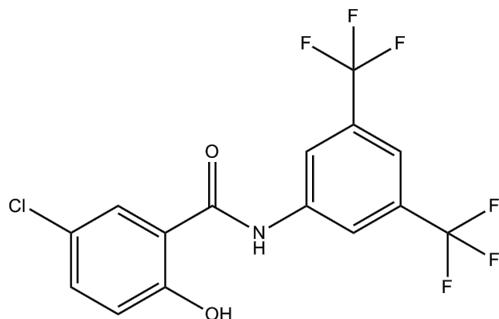
Formula $C_{15}H_8ClF_6NO_2$ M.Wt 383.67

Solubility $\geq 100.8\text{mg/mL}$ 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.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines HMC-1 cells

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

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Preparation method	The solubility of this compound in DMSO is >100.8mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting condition	0-10 µM; 24, 48 and 72 h
Applications	In HMC-1 cells transfected with pNF-κB-TA-Luc plasmid, IMD 0354 dose-dependently reduced luciferase activity, which represented transcriptional activation of NF-κB. Treatment with IMD 0354 for 24h completely suppressed the translocation of NF-κB to the nucleus. IMD-0354 significantly inhibited cell proliferation in a time- and dose-dependent way. IMD-0354 almost inhibited the proliferation of IC-2G559 cells and IC-2V814 cells at 0.5 µM. In HMC-1 cells, IMD-0354 arrested the cell cycle at the G0/G1 phase.
Animal experiment [2]:	
Animal models	a mouse model of allergic inflammation
Dosage form	5 or 20 mg/kg; administered intraperitoneally from day 8 to day 18
Application	In OVA-/OVA mice and OVA/CMC/OVA mice, IMD-0354 (20 mg/kg) significantly decreased the amount of activated NF-κB in the lungs. IMD-0354 at 5 mg/kg also significantly decreased NF-κB, but the magnitude of the decrease was lower than with 20 mg/kg IMD-0354. IMD-0354 at 20 mg/kg significantly reduced airway resistance, suggesting that administration of IMD-0354 improved the airway hyperresponsiveness (AHR). IMD-0354 at 20 mg/kg also significantly reduced eosinophil infiltration.

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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.

References:

[1]Tanaka A, Konno M, Muto S, Kambe N, Morii E, Nakahata T, Itai A and Matsuda H. A novel NF- κ B inhibitor, IMD-0354, suppresses neoplastic proliferation of human mast cells with constitutively activated c-kit receptors. Blood. 2005 Mar; 105(6): 2324-31.

[2]Sugita A, Ogawa H, Azuma M, Muto S, Honjo A, Yanagawa H, Nishioka Y, Tani K, Itai A and Sone S. Antiallergic and anti-inflammatory effects of a novel I κ B kinase beta inhibitor, IMD-0354, in a mouse model of allergic inflammation. Int Arch Allergy Immunol. 2009; 148(3): 186-98.

Background

IC50: IMD-0354 showed anti-tumor effect on seven hematologic malignancy cells with IC50 ranged from 0.1M to 0.6 M.

IMD-0354, serving as an IKK β inhibitor, inhibits I κ B α phosphorylation in NF- κ B pathway. [1]

In vitro: IMD-0354, at the concentration of less than 5 M, down-regulated the expression of NF- κ B and blocked the translocation of NF- κ B to the nucleus in HMC-1 cells. Study from HMC-1 cells also showed that IMD-0354 inhibited cell proliferation in a time and dose dependent manner. In addition, IMD-0354 at the concentration of 0.5 μ M inhibited the proliferation of IC-2G559 cells and IC-2V814 cells. This agent was also reported to arrest the cell cycle at the G0/G1 phase and decreased the ratio of cells in S and G2/M phases in HMC-1 cells. 1 μ M IMD-0354 was reported to decrease Cyclin D3 expression and reduce pRb phosphorylation level in a time-dependent manner in HMC-1 cells. [1]

In vivo: A study from lungs of OVA-sensitized mice showed that 5 mg/kg IMD-0354 significantly inhibited NF- κ B, although the magnitude of inhibition is lower than that caused by 20 mg/kg IMD-0354. 20 mg/kg IMD-0354 ameliorated airway hyper-responsiveness and decreased the numbers of bronchial eosinophils and mucus-producing cells in OVA-sensitized mice. In addition, the total

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numbers of cells and eosinophils was also reduced by IMD-0354 in OVA-sensitized mice. Moreover, IMD-0354 suppressed the production of Th2 cytokines including IL-5, IL-13 and eotaxin in the airways and/or lungs of OVA-sensitized mice, whereas it did not alter the restoration of Th1 cytokines under the same experimental conditions. [2]

Clinical trial: So far, a phase I clinical trial of a topical formulation of IMD-0354 for treatment of atopic dermatitis had been successfully completed. [3]

References:

- [1] Tanaka A, Konno M, Muto S, Kambe N, Morii E, Nakahata T, Itai A and Matsuda H. A novel NF- κ B inhibitor, IMD-0354, suppresses neoplastic proliferation of human mast cells with constitutively activated c-kit receptors. *Blood*. 2005 Mar; 105(6): 2324-31.
- [2] Sugita A, Ogawa H, Azuma M, Muto S, Honjo A, Yanagawa H, Nishioka Y, Tani K, Itai A and Sone S. Antiallergic and anti-inflammatory effects of a novel I κ B kinase beta inhibitor, IMD-0354, in a mouse model of allergic inflammation. *Int Arch Allergy Immunol*. 2009; 148(3): 186-98.
- [3] Verstrepen L and Beyaert R. Receptor proximal kinases in NF- κ B signaling as potential therapeutic targets in cancer and inflammation. *Biochem Pharm*. 2014; 92: 519-29.

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