ACHP Hydrochloride

Cat. No.: HY-13060

CAS No.: 406209-26-5

Molecular Formula: $C_{21}H_{25}ClN_4O_2$

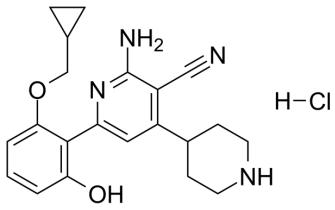
Molecular Weight: 400.9

Target: IKK

Pathway: NF-κB

Storage: 4°C, stored under nitrogen

* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (249.44 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4944 mL	12.4719 mL	24.9439 mL
5 mM	0.4989 mL	2.4944 mL	4.9888 mL
10 mM	0.2494 mL	1.2472 mL	2.4944 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 (6.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ACHP Hydrochloride (IKK-2 Inhibitor VIII) is a highly potent and selective IKK-β inhibitor with an IC_{50} of 8.5 nM.

IC_{50} & Target

IKK-β	IKK-α
8.5 nM (IC_{50})	250 nM (IC_{50})

In Vitro

ACHP Hydrochloride (Compound 4j) exhibits potent IKK-β inhibitory (IC_{50}: 8.5 nM) and cellular activities (IC_{50}=40 nM, in A549 cells). ACHP moderately inhibits IKK-α with an IC_{50} of 250 nM but exhibits good selectivity towards other kinases, such as IKK3, Syk and MKK4 (IC_{50}>20,000 nM). Moreover, ACHP demonstrates quite potent activity in various cellular assays. ACHP inhibits NF-κB-dependent reporter gene activation in TNFα-activated HEK293 cells and PMA/calcium ionophore-activated Jurkat T cells. ACHP fails to inhibit PMA-induced AP-1 activation in MRC-5 cells and PMA/calcium ionophore induced NF-κB

	dependent reporter gene transcription in Jurkat cells even at concentrations exceeding 10 μM. ACHP selectively interferes with the NF-κB signaling cascade by inhibition of IKK-β in living cells[1]. ACHP inhibits the growth of these cells in a dose-dependent manner. Tax-active cell lines are more susceptible to ACHP than Tax-inactive cell lines and Jurkat (IC_{50} values in Tax-active cell lines, Tax-inactive cell lines or Jurkat are 3.1±1.3 μM, 10.7±1.7 μM and 23.6 μM, respectively), suggesting that the growth of Tax-active cells depends on NF-κB more than Tax-inactive cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ACHP (Compound 4j) is orally bioavailable in mice and rats and demonstrates significant in vivo activity in anti-inflammatory models (arachidonic acid-induced mouse ear edema model). ACHP has reasonable aqueous solubility (0.12 mg/mL in pH 7.4 isotonic buffer) and excellent Caco-2 permeability (P_{app} 62.3×10^{-7} cm/s), and demonstrates orally bioavailability in mice (BA: 16%) and rats (BA: 60%). The favourable bioavailability of ACHP in rats is likely due to its low clearance (0.33 L/h/kg). In an acute inflammation model, ACHP exhibits oral efficacy at 1 mg/kg in a dose-dependent manner[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	HTLV-1-infected T-cell lines, ATL-35T, 81-66/45, MJ, and MT-2 cells, human ATL cell lines established from ATL patients, ATL-102, ED-40515(−) and TL-Om1 cells, and a HTLV-1-negative T-cell leukemia cell line Jurkat are used in this study. Approximately 1.5×10^4 cells are cultured in 96-well plate in triplicates at 37°C. Growth inhibitory effect of ACHP (0.01, 0.1, 1, 5, 10, 50 and 100 μM) is determined using MTT assay. Optical densities (OD) at 570 and 630 nm are measured with multiplate reader. Cell viability (%) is calculated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] In vivo arachidonic acid-induced ear edema in mice: ear edema is induced by topical application of arachidonic acid (500 μg/ear). ACHP (0.3, 1 and 3 mg/kg, p.o.), vehicle (10% cremophor in saline) are given po 60 min before the arachidonic acid application. Ear thickness is measured at 0, 1, 3 and 6 h after the arachidonic acid application. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2020 Jul 9;11(1):3427.
- Cell Death Dis. 2020 Oct 15;11(10):863.
- J Bone Miner Res. 2019 Oct;34(10):1880-1893.
- Am J Sports Med. 2021 Jan 28;363546520985203.
- Sci Rep. 2021 Jul 28;11(1):15319.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Murata T, et al. Synthesis and structure-activity relationships of novel IKK-beta inhibitors. Part 3: Orally active anti-inflammatory agents. Bioorg Med Chem Lett. 2004 Aug 2;14(15):4019-22.

[2]. Sanda T, et al. Induction of cell death in adult T-cell leukemia cells by a novel IkappaB kinase inhibitor. Leukemia. 2006 Apr;20(4):590-8.

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

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