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产品名称：ACHP (Hydrochloride)
产品别名：IKK-2 Inhibitor VIII

生物活性：

Description	ACHP Hydrochloride (IKK-2 Inhibitor VIII) is a highly potent and selective IKK-β inhibitor with an IC50 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].	
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].	

In Vitro:

DMSO : 50 mg/mL (124.72 mM; Need ultrasonic)

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

*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。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现

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Solvent&Solubility	用现配，当天使用： 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (6.24 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.24 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.24 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.24 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。
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.

实验参考：

Cell Assay	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].
Animal Administration	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.), Dexamethasone and 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.
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.