Product Data Sheet

Product Name: ACHP
Cat. No.: GC17416

Chemical Properties

Cas. No.	406208-42-2		
Chemical Name	(E)-2-amino-6-(2-(cyclopropylmethoxy)-6-oxocyclohexa-2,4-dien-1-ylidene)-4-(piperidin-4-yl)-1,6-dihydropyridine-3-carbonitrile		
SMILES	O=C1/C(C(OCC2CC2)=CC=C1)=C3NC(N)=C(C#N)C(C4CCNCC4)=C/3		
Formula	$C_{21}H_{24}N_4O_2$	M.Wt	364.44
Solubility	<7.29mg/ml in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	ACHP		

Protocol

Cell experiment [1]:

Cell lines	U266 and NCUMM-2 myeloma cell lines
Preparation method	The solubility of this compound in DMSO is > 10 mM. 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 condition	0-50 μM; 8 h

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Applications	In U266 and NCUMM-2 myeloma cell lines, ACHP (>10 μmol/L) inhibited the DNA binding activity of NF-κB after only 4 hours. ACHP also efficiently inhibited the phosphorylation of IκBαand p65 at 1 μmol/L after 20 minutes treatment. ACHP (10 μmol/L, 24h) also inhibited cell cycle progression and induced apoptosis. In NCUMM-2 cells, ACHP (10 μmol/L) efficiently induced apoptosis (15.8%) and a higher concentration of ACHP (50 μmol/L) induced apoptosis in 43.7% of the cells.

References:

[1] Sanda T, Iida S, Ogura H, Asamitsu K, Murata T, Bacon KB, Ueda R, Okamoto T. Growth inhibition of multiple myeloma cells by a novel IkappaB kinase inhibitor. Clin Cancer Res. 2005 Mar 1;11(5):1974-82.

Background

IC50: 8.5 and 250 nM for IKKβ and IKKα, respectively

ACHP is an IκB kinase inhibitor. Nuclear factor-KB (NF-KB) involved in cell survival and proliferation of multiple myeloma has been well established.

In vitro: ACHP is selective for IKKα and IKKβ over IKK3, Syk and MAPKKK4 (IC50 > 20 μM), DNA binding activity of NF-κB is inhibited. ACHP is an effective blockade NF-κB pathway in multiple myeloma cell lines, and induces cell growth arrest and apoptosis. It was observed that NF-KB is constitutively activated in all human myeloma cell lines, thus confirming the previous studies. In addition, It was found the phosphorylation of p65

subunit of NF-KB besides the phosphorylation of IKBA and the activation of NF-KB DNA binding and that various target genes of NF-KB including bcl-xL, XIAP, c-IAP1, cyclin D1, and IL-6 are up-regulated. 2-amino-6-[2-(cyclopropylmethoxy)-6-hydroxyphenyl]-4-piperidin-4-yl nicotinenitrile (ACHP) is a novel IKB kinase inhibitor. Treatment of myeloma cells with ACHP showed the cell growth was efficiently inhibited (IC50 values ranging from 18 to 35 Mmol/L) concomitantly with inhibition of the phosphorylation of IKBA/p65 and NF-KB DNA-binding, down-regulation of the NF-KB target genes, and then induction of apoptosis. In addition, the treatment of ACHP potentiated the cytotoxic effects of vincristine and melphalan (L-phenylalanine mustard), conventional antimyeloma drugs. These findings suggest that by blocking the antiapoptotic nature of myeloma cells endowed by the constitutive activation of NF-KB, IKB kinase inhibitors such as ACHP can sensitize myeloma cells to the cytotoxic effects of chemotherapeutic agents.

In vivo: So far, no study in vivo has been conducted.

Clinical trial: Clinical study has been conducted.

Reference:
[1] Sanda T, Iida S, Ogura H, Asamitsu K, Murata T, Bacon KB, Ueda R, Okamoto T. Growth inhibition of multiple myeloma cells by a novel IkappaB kinase inhibitor. Clin Cancer Res. 2005 Mar 1;11(5):1974-82.

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