Product Data Sheet

Product Name: IKK-16 (hydrochloride)
Cat. No.: GC12370

Chemical Properties

Cas. No.	1186195-62-9		
Chemical Name	[4-[(4-benzo[b]thien-2-yl-2-pyrimidinyl)amino]phenyl][4-(1-pyrrolidinyl)-1-piperidinyl]-methanone, monohydrochloride		
SMILES	O=C(N1CCC(N2CCCC2)CC1)C3=CC=C(C=C3)NC4=NC=CC(C5=CC(C=CC=C6)=C6S5)=N4.Cl		
Formula	$C_{28}H_{29}N_5OS$ • HCl	M.Wt	520.1
Solubility	≤10mg/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	IKK-16 (hydrochloride)		

Protocol

Cell experiment [1]:

Cell lines	HepG2 cells (human hepatocellular carcinoma cell line)
Preparation Method	HepG2 cells were cultured in Dulbecco’s Modified Eagle’s Medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 100U/mL penicillin, and 100μg/mL streptomycin at 37°C under 5% CO_2. Cells were treated with IKK-16 at 5μM, either alone or in combination with Deoxyelephantopin (DET; 30–50μM) or gemcitabine (GEM; 40–50μM) for 24 hours.
Reaction Conditions	5μM; 24 hours.

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Applications	IKK-16 significantly enhanced the cytotoxicity of DET and gemcitabine in HepG2 cells by further suppressing constitutive and TNF-α-induced NF-κB nuclear translocation. IKK-16 alone reduced NF-κB p65 subunit localization to the nucleus and synergized with DET to inhibit phosphorylation of IκBα, leading to increased apoptosis via mitochondrial dysfunction (e.g., cytochrome c release, caspase-3 activation, and PARP cleavage).

Animal experiment [2]:

Animal models	C57BL/6 mice with chronic kidney disease (CKD) induced by 5/6 nephrectomy.
Preparation Method	CKD mice were subjected to LPS-induced endotoxemia (2mg/kg; i.p.) or cecal ligation and puncture (CLP)-induced polymicrobial sepsis. IKK-16 (1mg/kg) was administered intravenously 1 hour after LPS injection or CLP surgery. Cardiac function, inflammatory markers, and organ injury were assessed at 18–24 hours.
Dosage form	1mg/kg; i.v.; Single injection.
Applications	IKK-16 attenuated sepsis-aggravated cardiac dysfunction (improved ejection fraction, fractional shortening, and fractional area change), reduced lung inflammation (decreased myeloperoxidase activity), and suppressed systemic proinflammatory cytokine levels (TNF-α, IL-1β, IL-6, IL-10). Mechanistically, IKK-16 inhibited cardiac IKKα/β phosphorylation, IκBα degradation, NF-κB p65 nuclear translocation, and inducible nitric oxide synthase (iNOS) expression, while modulating Akt and ERK1/2 signaling pathways.

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References:
[1] Mehmood T, Maryam A, Zhang H, et al. Deoxyelephantopin induces apoptosis in HepG2 cells via oxidative stress, NF-κB inhibition and mitochondrial dysfunction. Biofactors. 2017 Jan 2;43(1):63-72.
[2] Chen J, Kieswich JE, Chiazza F, et al. IκB Kinase Inhibitor Attenuates Sepsis-Induced Cardiac Dysfunction in CKD. J Am Soc Nephrol. 2017 Jan;28(1):94-105.

Background

IKK-16 (hydrochloride) is a novel, orally active selective inhibitor of IκB kinase (IKK), with IC_{50} values of 40nM, 70nM, and 200nM against IKK-2, IKK complex, and IKK-1[1-2]. IKK-16 shows potential applications in research areas such as sepsis, acute inflammation models, and prostate cancer[3-4].

In vitro, treatment of SKBR3 cells with 5μM IKK-16 for 24 hours significantly inhibited cell viability, reduced interactions between PTPIP51 and RelA/IκB, enhanced the association of PTPIP51 with the Her2 receptor, and weakened the interaction between PTPIP51 and PTP1B[5]. In HepG2 cells, combined treatment with 5μM IKK-16 and deoxyelephantopin (DET; 10–100μM) for 24 hours, IKK-16 further enhanced DET-induced cytotoxicity and synergistically suppressed nuclear translocation of NF-κB p65[6].

In vivo, in LPS/PepG-induced multiple organ dysfunction models and cecal ligation and puncture (CLP)-induced sepsis models, intravenous administration of IKK-16 (1mg/kg) 1 hour after induction, IKK-16 significantly alleviated sepsis-related cardiac dysfunction, renal impairment, hepatocellular injury, and pulmonary inflammation. IKK-16 also reduced phosphorylation of IκBα, nuclear translocation of NF-κB p65 subunit, and expression of inducible nitric oxide synthase (iNOS) in cardiac and hepatic tissues[7]. In a 5/6 nephrectomy-induced chronic kidney disease (CKD) mouse model, intravenous administration of IKK-16 (1mg/kg) 1 hour after LPS challenge (2mg/kg) or CLP surgery, IKK-16 markedly attenuated sepsis-aggravated cardiac dysfunction and pulmonary inflammation, lowered plasma levels of proinflammatory cytokines (TNF-α, IL-1β, IL-6, IL-10), and suppressed phosphorylation of IKKα/β and IκBα, nuclear translocation of p65 NF-κB, and iNOS expression in cardiac tissues[8].

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[1] Waelchli R, Bollbuck B, Bruns C, et al. Design and preparation of 2-benzamido-pyrimidines as inhibitors of IKK. Bioorg Med Chem Lett. 2006 Jan 1;16(1):108-12.
[2] Mu Y, Cory TJ. Suppression of HIV-1 Viral Replication by Inhibiting Drug Efflux Transporters in Activated Macrophages. Curr HIV Res. 2021;19(2):128-137.
[3] Galbraith NJ, Manek S, Walker S, et al. The effect of IκK-16 on lipopolysaccharide-induced impaired monocytes. Immunobiology. 2018 Apr-May;223(4-5):365-373.
[4] Zhang K, Yang J, Yang QQ, et al. ER stress genes (COL1A1, LOXL2, VWF) predicts IKK-16 as a Candidate therapeutic target for colitis-related inflammation and fibrosis suppression. Front Immunol. 2025 Jun 18;16:1587860.
[5] Dietel E, Brobeil A, Tag C, et al. PTPIP51 crosslinks the NFκB signaling and the MAPK pathway in SKBR3 cells. Future Sci OA. 2020 Mar 4;6(5):FSO463.
[6] Mehmood T, Maryam A, Zhang H, et al. Deoxyelephantopin induces apoptosis in HepG2 cells via oxidative stress, NF-κB inhibition and mitochondrial dysfunction. Biofactors. 2017 Jan 2;43(1):63-72.
[7] Coldewey SM, Rogazzo M, Collino M, et al. Inhibition of IκB kinase reduces the multiple organ dysfunction caused by sepsis in the mouse. Dis Model Mech. 2013 Jul;6(4):1031-42.
[8] Chen J, Kieswich JE, Chiazza F, et al. IκB Kinase Inhibitor Attenuates Sepsis-Induced Cardiac Dysfunction in CKD. J Am Soc Nephrol. 2017 Jan;28(1):94-105.

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