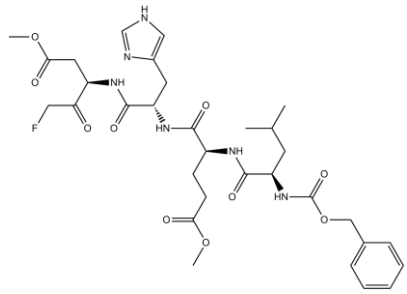
Product Name: Z-LEHD-FMK

Revision Date: 6/30/2016

Product Data Sheet

Chemical Properties



Product Name: Z-LEHD-FMK

Cas No.: 210345-04-3

M.Wt: 690.72

Formula: C32H43FN6O10

Chemical Name: methyl (4S)-5-[[(2S)-1-[[(3S)-5-fluoro-1-methoxy-1,4-dioxopentan-3-yl]amino]-3-(1H-imidazol-5-yl)-1-oxopropan-2-yl]amino]-4-[[(2S)-4-methyl-2-(phenylmethoxycarbonylamino)pentanoyl]amino]-5-oxopentanoate

Canonical SMILES: CC(C)CC(C(=O)NC(CCC(=O)OC)C(=O)NC(CC1=CN=CN1)C(=O)NC(CC(=O)OC)C(=O)CF)NC(=O)OCC2=CC=CC=C2

Solubility: Soluble 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.

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

Biological Activity

Targets : Caspase

Pathways: Apoptosis >> Caspase

Description:

Z-LEHD-FMK is a specific and irreversible inhibitor of caspase-9 [1].
Caspase-9 is an initiator caspase and plays an important role in the mitochondrial death pathway. Caspase-9 is activated during programmed cell death and cleaves procaspase-7 and procaspase-3.

Z-LEHD-FMK is a specific and irreversible caspase-9 inhibitor. In HCT116 human colon cancer cell line and 293 human embryonic kidney cell line, Z-LEHD-FMK inhibited apoptosis mediated by tumor necrosis factor-related apoptosis-inducing ligand (TRAIL). These results suggested that TRAIL induced death through the mitochondrial pathway in some human cells. In a colony assay, Z-LEHD-FMK inhibited the reduction of colony growth of HCT116 induced by TRAIL. In normal human hepatocytes, Z-LEHD-FMK protected cells from TRAIL-induced apoptosis. These results suggested that a combination of Z-LEHD-FMK and TRAIL selectively killed cancer cells while protecting normal liver cells [1].
In rats with focal ischemia/reperfusion, Z-LEHD-FMK improved neurological outcome by 63% and reduced infarction volume by 49% [2]. In spinal cord trauma rat model, Z-LEHD-FMK reduced apoptotic cell count and protected neurons, myelin, axons, glia and intracellular organelles in the spinal cord [3].

***Reference**:*
[1]. Ozoren N, Kim K, Burns TF, et al. The caspase 9 inhibitor Z-LEHD-FMK protects human liver cells while permitting death of cancer cells exposed to tumor necrosis factor-related apoptosis-inducing ligand. Cancer Res, 2000, 60(22): 6259-6265.
[2]. Mouw G, Zechel JL, Zhou Y, et al. Caspase-9 inhibition after focal cerebral ischemia improves outcome following reversible focal ischemia. Metab Brain Dis, 2002, 17(3): 143-151.
[3]. Colak A, Karaoğlan A, Barut S, et al. Neuroprotection and functional recovery after application of the caspase-9 inhibitor z-LEHD-fmk in a rat model of traumatic spinal cord injury. J Neurosurg Spine, 2005, 2(3): 327-334.

Protocol

Cell experiment:

Cell lines	Human colon cancer, HCT116, human embryonic fibroblastand 293 cell lines
Preparation method	Soluble in DMSO > 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 conditions	20 μM Z-LEHD-FMK for 30 mins followed by 20ng/ml TRAIL for 4 hours
Applications	Z-LEHD-FMK completely protects HCT116 and 293 cells from TRAIL-induced toxicity. Z-LEHD-FMK also protected human hepatocytes from TRAIL-induced apoptosis. The colony growth of HCT116 is reduced in the presence of TRAIL, and there are significantly more colonies present when the HCT116 cells were incubated in the presence of TRAIL and Z-LEHD-FMK.

Animal experiment [3]:

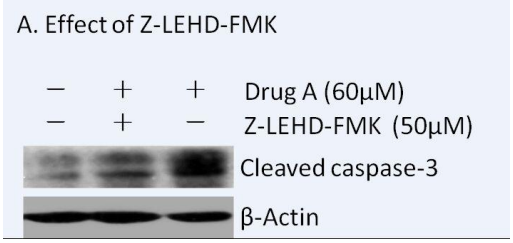
Animal models	Adult male Wistar albino rats, 250 to 350 g, spinal cord injury model
Dosage form	Intravenous 0.8-mM/kg injection of z-LEHD-fmk.
Applications	At 24 hours post-injury, the mean apoptotic cell count in trauma-only controls was significantly higher than that in z-LEHD-fmk–treated group. Electron microscopy results also show Z-LEHD-FMK treatment protected neurons, glia, myelin, axons, and intracellular organelles. The specimens treated with z-LEHD-fmk displays significantly fewer apoptotic cells and diminished axonal demyelination.
Preparation method	Dry-form z-LEHD-fmk was dissolved in dimethylsulfoxide prepared with phosphatebuffered saline.
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.

***Reference**:*
1. Ozoren N, Kim K, Burns TF, et al. The caspase 9 inhibitor Z-LEHD-FMK protects human liver cells while permitting death of cancer cells exposed to tumor necrosis factor-related apoptosis-inducing ligand. Cancer Res, 2000, 60(22): 6259-6265.
2. Colak A, Karao lan A, Barut S, et al. Neuroprotection and functional recovery after application of the caspase-9 inhibitor z-LEHD-fmk in a rat model of traumatic spinal cord injury. J Neurosurg Spine, 2005, 2(3): 327-334.

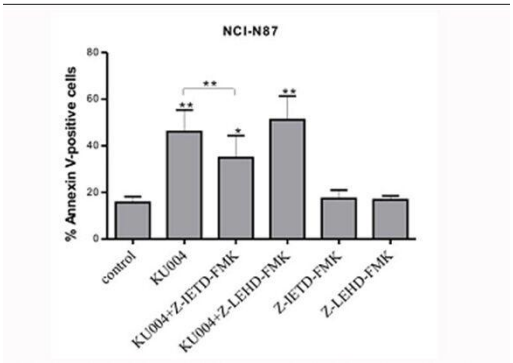
Product Citations

1. Chen Y, Sun M, et al, "a novel PAC-1 derivative, activates procaspase-3 and causes cancer cell apoptosis." Cancer Chemother Pharmacol. 2016 Aug 3. PMID:27488460
2. Tian, Chongchong, et al. "A novel dual EGFR/HER2 inhibitor KU004 induces cell cycle arrest and apoptosis in HER2-overexpressing cancer cells." Apoptosis 20.12 (2015): 1599-1612. PMID:26437915

Product Validation



We used 60 μM Drug A to treat A549 cells, which were pre-treated with 50 μM Z-LEHD-FMK or not. After 24 hours, we detected the protein levels of cleaved Caspase-3 by Western Blot. The result showed that Z-LEHD-FMK could significantly inhibit the activation of Caspase-3 induced by Drug A, which indicated that activation of Caspase-3 induced by Drug A is Caspase-9 dependent.



KU004 induces apoptosis mainly via the extrinsic pathway. (C) NCI-N87 cells were pre-incubated with Z-IETD-FMK and Z-LEHD-FMK for 1 h followed by 1 μM KU004 for 48 h. Annexin V-FITC positive cell rates were detected by flow cytometry.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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