Product Data Sheet

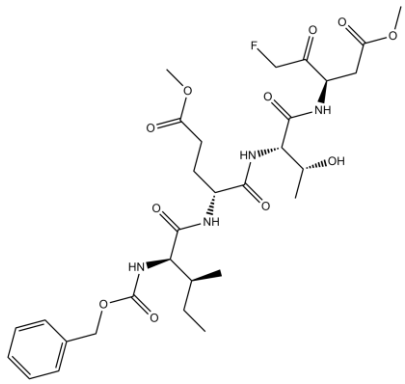
Chemical Properties

Product Name: Z-IETD-FMK

Cas No.: 210344-98-2

M.Wt: 654.68

Formula: C30H43FN4O11



Synonyms: Benzyloxycarbonyl-Ile-Glu(OMe)-Thr-Asp(OMe)-fluoromethyl ketone, Z-Ile-Glu(OMe)-Thr-Asp(OMe)-FMK

Chemical Name: methyl 5-[[1-[(5-fluoro-1-methoxy-1,4-dioxopentan-3-yl)amino]-3-hydroxy-1-oxobutan-2-yl]amino]-4-[[3-methyl-2-(phenylmethoxycarbonylamino)pentanoyl]amino]-5-oxopentanoate

Canonical SMILES: CCC(C)C(C(=O)NC(CCC(=O)OC)C(=O)NC(C(C)O)C(=O)NC(CC(=O)OC)C(=O)CF)NC(=O)OCC1=CC=CC=C1

Solubility: >32.7mg/mL 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-IETD-FMK is an inhibitor of caspase 8 [1].
Z-IETD-FMK inhibits T cell proliferation induced by PHA or anti-CD3 plus anti-CD28 without toxicity of resting T cells. The mechanism of this inhibition of Z-IETD-FMK has been proved not through the effect on IL-2 secretion or IFN-γ production but the decrease of CD25 expression. Experiments show that Z-IETD-FMK has no effect on normal cell growth when there is no activation signal. Z-IETD-FMK has also been found to significantly inhibit NF-κB activation when the concentration is 100μM [1].
Apart from the ability of inhibiting cell proliferation, Z-IETD-FMK is reported to inhibit TRAIL-mediated killing in cells. It protects the procaspases 9, 2, and 3, and protects PARP to a similar extent in both HCT116 and SW480 cells [2].

***Reference**:*

[1] C.P. Lawrence, S.C. Chow. Suppression of human T cell proliferation by the caspase inhibitors, z-VAD-FMK and z-IETD-FMK is independent of their caspase inhibition properties. Toxicology and Applied Pharmacology. 2012, 265: 103-112.
[2] Nesrin Özören, Kunhong Kim, Timothy F. Burns, 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 Research. 2000, 60: 6259-6265.

Protocol

Cell experiment:

Cell lines	Purified CD4+ and CD8+ T cells.
Preparation method	Limited solubility. 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	24 h
Applications	T cell proliferation was assayed using [3H]-thymidine incorporation. z-IETD-FMK (100 μM) inhibits T cell proliferation. About 9% of control activated T cells took up PI after activation and in the presence of 100 μM of z-IETD-FMK cell death increases to 23%. In addition, 100 μM z-IETD-FMK decreases the nuclear translocation of p65 in activated T cells.

Animal experiment [3]:

Animal models	SHIP1-/- (CD45.1) mice
Dosage form	5 mg/kg three times each week for 3 weeks
Applications	There is a significant diminution of anatomical pathology in both the

	small intestine and lungs of Z-IETD-FMK-treated mice compared with vehicle-administered controls. There is also a prominent recovery of viable CD3+ T-cell numbers in small intestine and lung of the Z-IETD-FMK-treated SHIP1-/- hosts, whereas the vehicle-treated SHIP1-/- hosts exhibit the T-cell paucity.
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. Lawrence CP, Chow SC. Suppression of human T cell proliferation by the caspase inhibitors, z-VAD-FMK and z-IETD-FMK is independent of their caspase inhibition properties. Toxicol Appl Pharmacol. 2012 Nov 15;265(1):103-12.

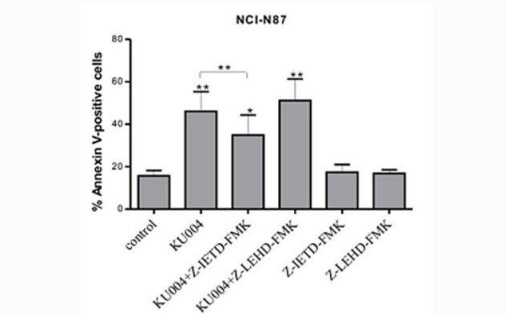
2. Park MY, Srivastava N, Sudan R et al. Impaired T-cell survival promotes mucosal inflammatory disease in SHIP1-deficient mice. Mucosal Immunol. 2014 Nov;7(6):1429-39.

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



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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