Z-IETD-FMK

Cat. No.: HY-101297

CAS No.: 210344-98-2

Molecular Formula: $C_{30}H_{43}FN_4O_{11}$

Molecular Weight: 655

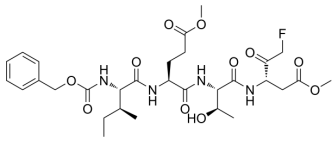
Sequence: Z-Ile-Glu-Thr-Asp-FMK

Sequence Shortening: ZIETDFMK

Target: Caspase

Pathway: Apoptosis

Storage: Sealed storage, away from moisture
Powder -80°C 2 years
-20°C 1 year
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (63.62 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5267 mL	7.6336 mL	15.2672 mL
	5 mM	0.3053 mL	1.5267 mL	3.0534 mL
	10 mM	0.1527 mL	0.7634 mL	1.5267 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.18 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.18 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.18 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Z-IETD-FMK (Z-IE(OMe)TD(OMe)-FMK) is a selective and cell permeable caspase-8 inhibitor[1]. Z-IETD-FMK is also a granzyme B inhibitor[5].

IC_{50} & Target

Caspase-8

In Vitro	T-cellZ-IETD-FMK causes full inhibition only of the proapoptotic effect of TNFα with an IC_{50} of 0.46 μM[1]. Z-IETD-FMK and Z-VAD-FMK at non-toxic doses are found to be immunosuppressive and inhibit human T cell proliferation induced by mitogens and IL-2. They are shown to block NF-κB in activated primary T cells, but have little inhibitory effect on the secretion of IL-2 and IFN-γ during T cell activation[2]. Z-IETD-FMK inhibits the cleavage of caspase-8 and only partially inhibits the cleavage of caspase-3 and PARP. Z-IETD-FMK can prevent the execution of apoptosis in retinal cells exposed to different apoptotic stimuli[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pharmacological inhibition of caspase-8 by z-IETD-FMK robustly reduces tumor growth and this is closely associated with a reduction in the release of pro-inflammatory cytokines, IL-6, TNF-α, IL-18, IL-1α, IL-33, but not IL-1β. Furthermore, inhibition of caspase-8 reduces the recruitment of innate suppressive cells, such as myeloid-derived suppressor cells, but not of regulatory T cells to lungs of tumor-bearing mice[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	T cell proliferation following mitogen stimulation is determined using [^{3}H]-thymidine incorporation. In brief, PBMCs or purified T cells are seeded at 1×10^6 cells/mL in 96 well plates and stimulated with either PHA (5 μg/mL or co-stimulated with anti-CD3 mAb (5 μg/mL) and anti-CD28 mAb (2.5 μg/mL) in the presence or absence of caspase inhibitor Z-IETD-FMK. The cells are cultured for 72 h with the last 16 h pulsed with [[^{3}H]-labelled methyl-thymidine (0.037 MBq) prior to harvest onto glass fibre filter mats using a Tomtec automated multi-well harvester[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Mice: Mice are divided into three groups: (1) naive, non-treated, mice; (2) CTR (control), i.t. instilled with NMU; and (3) lung cancer-bearing mice treated with Z-IETD-FMK (0.5 μg per mouse). The involvement of caspase-8 in lung cancer development is the determined at different time points (3, 7 and 28 days)[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Biomed Eng. 2023 Mar;7(3):281-297.
- Cell Mol Immunol. 2023 Aug 17.
- Sci Adv. 2023 Oct 6;9(40):eadi6586.
- Sci Adv. 2022 Nov 11;8(45):eabn9912.
- J Pineal Res. 2024 Jan 31.

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REFERENCES

[1]. Cowburn AS, et al. z-VAD-fmk augmentation of TNF alpha-stimulated neutrophil apoptosis is compound specific and does not involve the generation of reactive oxygen species.

[2]. Lawrence CP, et al. 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.

[3]. Tezel G, et al. Inhibition of caspase activity in retinal cell apoptosis induced by various stimuli in vitro. Invest Ophthalmol Vis Sci. 1999 Oct;40(11):2660-7.

[4]. Terlizzi M, et al. Pharmacological inhibition of caspase-8 limits lung tumour outgrowth. Br J Pharmacol. 2015 Aug;172(15):3917-28.

[5]. Yang J, et al. Granzyme B Is an Essential Mediator in CD8+ T Cell Killing of Theileria parva-Infected Cells.Infect Immun. 2018 Dec 19;87(1). pii: e00386-18.

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