

Product Data Sheet

Product Name: Ac-YVAD-CMK

Cat. No.: GC42721

Chemical Properties

Cas. No. 178603-78-6

Chemical Name N-acetyl-L-tyrosyl-L-valyl-N-[(1S)-1-(carboxymethyl)-3-chloro-2-oxo-propyl]-L-alaninamide

SMILES C1CC(=O)[C@H](CC(=O)O)NC(=O)[C@H](C)NC(=O)[C@@H](NC(=O)[C@@H](NC(=O)C)Cc1ccc(O)cc1)C(C)C

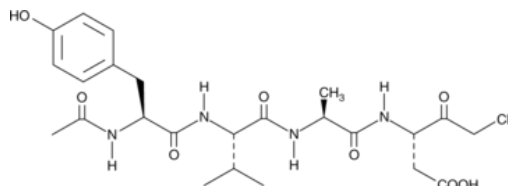
Formula $C_{24}H_{33}ClN_4O_8$ M.Wt 541

Solubility 20mg/mL in DMSO, 10mg/mL in DMF 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.

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

Structure



Protocol

Cell experiment [1]:

Cell lines	MDA-MB-231 cells (human breast cancer cell line)
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Preparation Method	MDA-MB-231 cells were maintained in RPMI-1640 medium supplemented with 10% fetal bovine serum at 37°C, 5% CO ₂ . MDA-MB-231 cells were treated with Ac-YVAD-CMK at 5-30μM for 48 hours for western blotting; at 10μM for 24, 48 or 72 hours for MTT assay; at 10μM for 24 hours for Annexin V-FITC/PI flow cytometry apoptosis assay; and at 10μM for 24 hours for Transwell invasion assay.
Reaction Conditions	5-30μM; 24h-72h
Applications	Ac-YVAD-CMK decreased Caspase-1 protein expression in MDA-MB-231 cells. Ac-YVAD-CMK increased proliferation ability of MDA-MB-231 cells at 24, 48 and 72 hours. Ac-YVAD-CMK decreased apoptotic proportion of MDA-MB-231 cells at 24 hours. Ac-YVAD-CMK increased the number of invading MDA-MB-231 cells through Matrigel-coated Transwell inserts at 24 hours.
Animal experiment [2]:	
Animal models	C57BL/6 mice
Preparation Method	Mice were intraperitoneally administered Ac-YVAD-CMK (12.5μmol/kg) 1 hour before 2% sevoflurane exposure for 5 hours. Mice were subjected to Morris water maze and novel object recognition test 24 hours after exposure, then sacrificed for hippocampal immunoblotting, immunostaining, ATP assay, MDA assay, DHE staining, and transmission electron microscopy.
Dosage form	12.5μmol/kg; i.p.; single dose

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Applications	Ac-YVAD-CMK reduced hippocampal NLRP3, cleaved caspase-1, IL-1 β and IL-18 protein levels in sevoflurane-exposed mice. Ac-YVAD-CMK decreased cleaved caspase-1 immunofluorescence in CA3 region. Ac-YVAD-CMK reduced hippocampal DHE fluorescence, MDA level, and increased ATP concentration. Ac-YVAD-CMK blocked the increase of LC3B-II/I, P62 and Tomm20 in hippocampus, and increased HSP60-LAMP2 colocalization. Ac-YVAD-CMK decreased escape latency and increased platform crossing times in Morris water maze, and rescued the decreased recognition index in novel object recognition test.
References: [1] Sun Y, Guo Y. Expression of Caspase-1 in breast cancer tissues and its effects on cell proliferation, apoptosis and invasion. <i>Oncol Lett.</i> 2018 May;15(5):6431-6435. [2] Zheng D, Wang H, Zhou Y, et al. Ac-YVAD-cmk ameliorated sevoflurane-induced cognitive dysfunction and revised mitophagy impairment. <i>PLoS ONE.</i> 2023 Jan 25;18(1):e0280914.	

Background

Ac-YVAD-CMK is a selective, irreversible caspase-1 inhibitor. Ac-YVAD-CMK covalently binds to the active site of caspase-1 to block the maturation and release of IL-1 β and IL-18, thereby inhibiting pyroptosis-related inflammation. Ac-YVAD-CMK can be used in studies related to inflammation, pyroptosis, neuroprotection, acute lung injury, acute kidney injury, and acute graft-versus-host disease^[1-4].

In vitro, during hypoxia/reoxygenation induction (culture with 30mM glucose for 24 hours, then hypoxia for 4 hours/reoxygenation for 2 hours), 50 μ M Ac-YVAD-CMK treatment of H9C2 cells reduced caspase-1 activity, decreased supernatant IL-1 β and IL-18 levels, lowered intracellular ROS production, increased cell viability, and reduced LDH release^[5]. Treatment of MDA-MB-231 cells with 5-30 μ M Ac-YVAD-CMK for 24-72 hours decreased Caspase-1 protein expression, increased cell proliferation, reduced apoptosis levels, and increased the number of Transwell invasive cells^[6]. Pretreatment of human CHP100 cells with 100 μ M Ac-YVAD-CMK for 1 hour followed by 10pM HIV-1

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gp120 for 24 hours eliminated gp120-enhanced COX-2 protein expression and reduced gp120-induced cell death^[7].

In vivo, a single intraperitoneal injection of 12.5µmol/kg Ac-YVAD-CMK in sevoflurane-exposed C57BL/6 mice reduced hippocampal NLRP3, cleaved caspase-1, IL-1β and IL-18 protein expression, decreased hippocampal ROS and MDA levels, increased ATP concentration, blocked the elevation of LC3B-II/I, P62 and Tomm20, and improved Morris water maze escape latency, platform crossing frequency, and novel object recognition index^[8]. A single intraperitoneal injection of 12.5µmol/kg Ac-YVAD-CMK in C57BL/6 mice followed by cold restraint stress for 8 hours attenuated gastric mucosal hemorrhagic erosion and ulceration, reduced gastric ulcer index, and decreased serum TNF-α, IL-1β, IL-6 and IL-18 levels^[9]. A single intraperitoneal injection of Ac-YVAD-CMK in AAV-Lung-SARS-CoV-2 N-induced C57BL/6 mice reduced serum IL-1β and IL-6 protein levels, weakened lung tissue IL-1β and IL-6 immunofluorescence intensity, and alleviated lung tissue inflammatory lesions and damage^[10].

References:

- [1] Lipinska K, Malone KE, Moerland M, et al. Applying caspase-1 inhibitors for inflammasome assays in human whole blood. J Immunol Methods. 2014 Aug;411:66-9.
- [2] Lin X, Ye H, Siaw-Debrah F, et al. AC-YVAD-CMK inhibits pyroptosis and improves functional outcome after intracerebral hemorrhage. Biomed Res Int. 2018 Oct 16;2018:3706047.
- [3] Yang M, Fang JT, Zhang NS, et al. Caspase-1-Inhibitor AC-YVAD-CMK Inhibits Pyroptosis and Ameliorates Acute Kidney Injury in a Model of Sepsis. Biomed Res Int. 2021 Jun 10;2021:6636621.
- [4] Chen W, Su G, Xu Y, et al. Caspase-1 inhibition ameliorates murine acute graft versus host disease by modulating the Th1/Th17/Treg balance. Int Immunopharmacol. 2021 May;94:107503.
- [5] Qiu Z, He Y, Ming H, et al. Lipopolysaccharide (LPS) Aggravates High Glucose- and Hypoxia/Reoxygenation-Induced Injury through Activating ROS-Dependent NLRP3 Inflammasome-Mediated Pyroptosis in H9C2 Cardiomyocytes. J Diabetes Res. 2019;2019:8151836.
- [6] Sun Y, Guo Y. Expression of Caspase-1 in breast cancer tissues and its effects on cell proliferation, apoptosis and invasion. Oncol Lett. 2018 May;15(5):6431-6435.

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- [7] Corasaniti MT, Bellizzi C, Russo R, et al. Caspase-1 inhibitors abolish deleterious enhancement of COX-2 expression induced by HIV-1 gp120 in human neuroblastoma cells. *Toxicol Lett.* 2003 Mar 31;139(2-3):213-9.
- [8] Zheng D, Wang H, Zhou Y, et al. Ac-YVAD-cmk ameliorated sevoflurane-induced cognitive dysfunction and revised mitophagy impairment. *PLoS ONE.* 2023 Jan 25;18(1):e0280914.
- [9] Zhang F, Wang L, Wang J, et al. The caspase-1 inhibitor AC-YVAD-CMK attenuates acute gastric injury in mice: involvement of silencing NLRP3 inflammasome activities. *Sci Rep.* 2016 Apr 7;6:24166.
- [10] Pan P, Shen M, Yu Z, et al. SARS-CoV-2 N protein promotes NLRP3 inflammasome activation to induce hyperinflammation. *Nat Commun.* 2021 Aug 2;12:4664.

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