Product Name: Z-DEVD-FMK

Revision Date: 6/30/2016

# Product Data Sheet

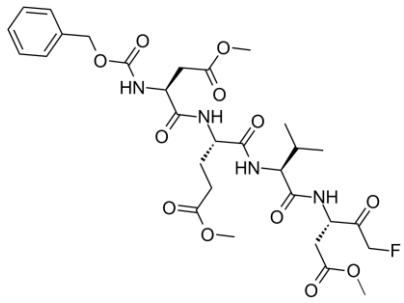
## Chemical Properties

**Product Name:** Z-DEVD-FMK

**Cas No.:** 210344-95-9

**M.Wt:** 668.66

**Formula:** C30H41N4O12F



**Synonyms:** Caspase-3 Inhibitor II,Z-Asp(OMe)-Glu(OMe)-Val-Asp(OMe)-FMK

**Chemical Name:** methyl (4S)-5-[[(2S)-1-[[(3S)-5-fluoro-1-methoxy-1,4-dioxopentan-3-yl]amino]-3-methyl-1-oxobutan-2-yl]amino]-4-[[(2S)-4-methoxy-4-oxo-2-(phenylmethoxycarbonylamino)butanoyl]amino]-5-oxopentanoate

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

**Solubility:** >33.4mg/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-DEVD-FMK is a tetrapeptide caspase inhibitor that is considered relatively selective for caspase-31, 2 and has been widely used in in vitro and in vivo models of acute injury to delineate

roles for caspase 3 in neuronal cell death. Intracerebroventricular injections of Z-DEVD-FMK improved function after LFP3. Intraparenchymal infusion of Z-DEVD-FMK over several days after combined CCI and hypoxia reduced lesion size, although functional outcome was not significantly improved in this model4 (Clark et al., 2000).
Z-DEVD-FMK was a potent inhibitor of calpain and that improvement observed after treatment with Z-DEVD-FMK may reflect, at least in part, this action.
Early treatment with Z-DEVD-FMK improved neurologic function and reduced lesion volume.
Z-DEVD-FMK reduces cell death and inhibits calpain in a model of in vitro necrosis and a cell free assay and Z-DEVD-FMK treatment inhibits calpain activity after TBI in vivo.
Z-DEVD-FMK improved neurologic function and reduced tissue damage at an injury severity that showed predominantly necrotic neuronal cell death with minimal evidence of caspase 3 activation. Moreover, effective treatment with Z-DEVD-FMK was associated with reduced calpain-mediated -spectrin degradation. Z-DEVD-FMK was also neuroprotective, at concentrations lower than those routinely used to inhibit caspase 3, in an in vitro model of necrotic neuronal cell death induced by maitotoxin.
The present data show that treatment with Z-DEVD-FMK improves behavioral recovery, reduces tissue damage and prevents accumulation of calpain-mediated α-spectrin breakdown products when administered not later than 1 hour after injury in a TBI model that primarily shows necrosis. Z-DEVD-FMK also reduces necrotic neuronal cell death in vitro, and such neuroprotection is associated with inhibition of calpain, but not caspase 3 or cathepsin B. In addition, Z-DEVD-FMK reduces calpainmediated hydrolysis of casein, which indicates that Z-DEVD-FMK can directly inhibit calpain. This nonspecificproperty of Z-DEVD-FMK may account, at least in part, for its neuroprotective actions5.

***Reference**:*

*1. Garcia-Calvo M, Peterson EP, Leiting B, Ruel R, Nicholson DW, Thornberry NA (1998) Inhibition of human caspases by peptidebased and macromolecular inhibitors. J Biol Chem 273:32608–32613*
*2. Thornberry NA, Rano TA, Peterson EP, Rasper DM, Timkey T, Garcia-Calvo M, Houtzager VM, Nordstrom PA, Roy S, Vaillancourt JP, Chapman KT, Nicholson DW (1997) A combinatorial approach defines specificities of members of the caspase family and granzyme B. Functional relationships established for key mediators of apoptosis. J Biol Chem 272:17907–17911*
*3. Yakovlev AG, Knoblach SM, Fan L, Fox GB, Goodnight R, Faden AI (1997) Activation of CPP32-like caspases contributes to neuronal apoptosis and neurological dysfunction after traumatic brain injury. J Neurosci 17:7415–7424*
*4. Clark RS, Kochanek PM, Watkins SC, Chen M, Dixon CE, Seidberg NA, Melick J, Loeffert JE, Nathaniel PD, Jin KL, Graham SH (2000) Caspase-3 mediated neuronal death after traumatic brain injury in rats. J Neurochem 74:740–753*
*5. S. M. Knoblach, D. A. Alroy et al, Caspase Inhibitor z-DEVD-fmk Attenuates Calpain and Necrotic Cell Death in Vitro and After Traumatic Brain Injury, Journal of Cerebral Blood Flow & Metabolism 24:1119–1132.*

## Protocol

**Cell experiment:**

| | |
|---|---|
| Cell lines | WM9, WM35, WM98-1 and WM793 cells |

| | |
|---|---|
| Preparation method | The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months. |
| Reacting conditions | 20 μM, 24 hours |
| Applications | To demonstrate the importance of caspase activation in TRAIL-induced apoptosis. Z-DEVD-FMK was added to melanoma cells along with TRAIL. Z-DEVD-FMK was only able to partially inhibit the cytotoxic effects of TRAIL. The decreased ability of Z-DEVD-FMK to inhibit death may result from the ability of the peptide to enter the cell. |

**Animal experiment [3]:**

| | |
|---|---|
| Animal models | Male C57Bl/6 mice with controlled cortical impact (CCI) injury |
| Dosage form | Intracerebroventricular injection, 160 ng, |
| Applications | To assess motor recovery, mice were tested for the ability to traverse a narrow, suspended beam during recovery over a 21-day period. Mice treated 1 hour after CCI performed significantly better than did vehicle controls on days 7, 14, and 21 after injury. Mice treated 4 hours after CCI performed significantly better than controls only on day 21 after injury, but this was an isolated observation, as they did not show a trend toward better performance compared with other treatment groups on any other testing day. |
| 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**:*

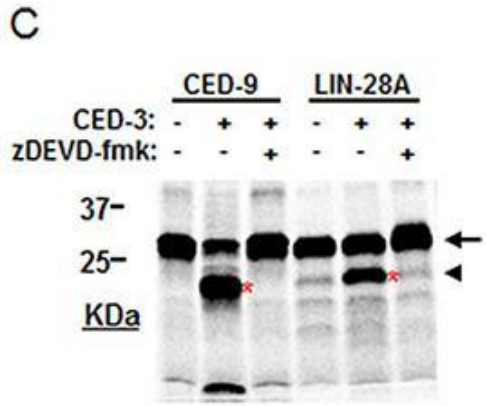
*[1] Griffith T S, Chin W A, Jackson G C, et al. Intracellular regulation of TRAIL-induced apoptosis in human melanoma cells. The Journal of Immunology, 1998, 161(6): 2833-2840.*

*[2] Knoblach S M, Alroy D A, Nikolaeva M, et al. Caspase inhibitor z-DEVD-fmk attenuates calpain and necrotic cell death in vitro and after traumatic brain injury. Journal of Cerebral Blood Flow & Metabolism, 2004, 24(10): 1119-1132.*

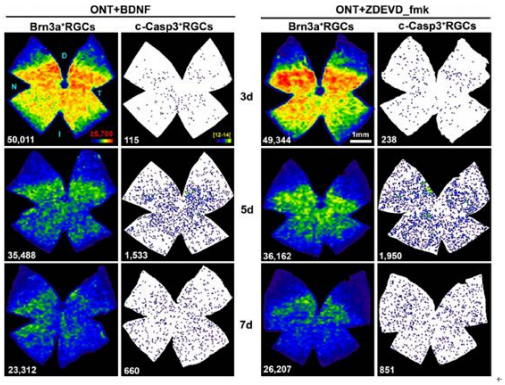
## Product Citations

*1. Russo HM, Rathkey J, et al. "Active Caspase-1 Induces Plasma Membrane Pores That Precede Pyroptotic Lysis and Are Blocked by Lanthanides." J Immunol. 2016 Aug 15;197(4):1353-67. PMID:27385778*
*2. Chen Y, Sun M, et al. "SM-1, a novel PAC-1 derivative, activates procaspase-3 and causes cancer cell apoptosis". Cancer Chemother Pharmacol. 2016 Aug 3. PMID:27488460*
*3. Benjamin P Weaver, et al. "CED-3 caspase acts with miRNAs to regulate non-apoptotic gene expression dynamics for robust development in C. elegans" Elife. 2014 Dec 30: e107010. PMID:25432023*
*4. Sánchez-Migallón MC, et al. "Apoptotic Retinal Ganglion Cell Death After Optic Nerve Transection or Crush in Mice: Delayed RGC Loss With BDNF or a Caspase 3 Inhibitor." Invest Ophthalmol Vis Sci. 2016 Jan 1;57(1):81-93. PMID:26780312*
*5. Kim DS, Jin H, et al. "p73 gene in dopaminergic neurons is highly susceptible to manganese neurotoxicity." Neurotoxicology. 2016 Apr 20. pii: S0161-813X(16)30057-2. PMID:27107493*

## Product Validation




In vitro cleavage assay with the zDEVD-fmk. The arrow and arrowhead (and red asterisks) indicate the full-length protein and a predominant CED-3 cleavage product, respectively. The specifiity of the partial LIN-28 cleavage by CED-3 and found that it was completely blocked by addition of the caspase-specific-inhibitor zDEVD-fmk.




Brain-derived neurotrophic factor or Z-DEVD_fmk treatment delays ONT-induced RGC degeneration across the retina. Isodensity and neighbor maps showing the distribution of Brn3aþRGCs and c-casp3þRGCs in retinas treated just after the injury with BDNF or Z-DEVD_fmk and analyzed at 3, 5, or 7 days after the lesion. Invest Ophthalmol Vis Sci. 2016 Jan 1;57(1):81-93.

## 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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