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ProductInformation

Z-Ala-Glu(OMe)-Val-Asp(OMe) Fluoromethyl Ketone

Product Number **C 8484**
Storage Temperature –20 °C

Product Description

Molecular Formula: $C_{28}H_{39}FN_4O_{10}$
Molecular Weight: 610.6

Z-Ala-Glu(OMe)-Val-Asp(OMe) Fluoromethyl Ketone is the methylated, cell permeable derivative of the caspase inhibitor Z-Ala-Glu-Val-Asp Fluoromethyl Ketone (Z-AEVD-FMK, Z = benzyloxycarbonyl).

Z-AEVD-FMK is a potent irreversible inhibitor of caspase-10 and, with lower efficiency, activated caspase-8. Caspases are a group of cysteine aspartate-specific proteases that play a role in apoptosis.[1,2] Caspase 10 can activate the NF-κB pathway.[3] It contains two death effector domains and with caspase-8 is implicated in apoptosis signaling complexes associated with TNFR-like death receptors including Fas.[4,5]

Methylation of the acidic amino acids Glu and Asp enhances the cell membrane permeability of Z-AEVD-FMK. Once in the cell, endogenous esterase activity hydrolyzes the methyl groups to form the biological active form. For *in vitro* studies an esterase needs to be included in the reaction mix to generate the active form of the molecule.

FMK is a trapping group responsible for irreversible inhibition and is also non-cytotoxic. Inhibition occurs when the FMK group covalently bonds to the –SH of an adjacent cysteine residue on the target protein.

Z-Ala-Glu(OMe)-Val-Asp(OMe)-Fluoromethyl Ketone is supplied as a white solid.

Preparation Instructions

Prepare 20 mM stock solutions in dry (≥ 99.9 %) DMSO to maintain product stability. Also soluble in DMF.

Storage/Stability

Store at –20 °C. The product is reported to be stable at room temperature for one year in a desiccator.

References

1. Nicholson, D.W., and Thornberry, N.A., Caspases: killer proteases. Trends Biochem. Sci., **22,** 299 (1997).
2. Cohen, G.M., Caspases: the executioners of apoptosis. Biochem. J., **326,** 1-16 (1997).
3. Chaudhary, P.M., et al. Activation of the NF-κB pathway by caspase 8 and its homologs. Oncogene, **19,** 4451-4460 (2000).
4. Fernandes-Alnemri, T. et al., In vitro activation of CPP32 and Mch3 by Mch4, a novel human apoptotic cysteine protease containing two FADD-like domains. Proc. Natl. Acad. Sci. USA, **93,** 7464-7469 (1996).
5. Vincenz, C., and Dixit, V. M., Fas-associated death domain protein interleukin-1beta-converting enzyme 2 (FLICE2), an ICE/Ced-3 homologue, is proximally involved in CD95- and p55-mediated death signaling. J. Biol. Chem., **272**, 6578-6583 (1997).

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