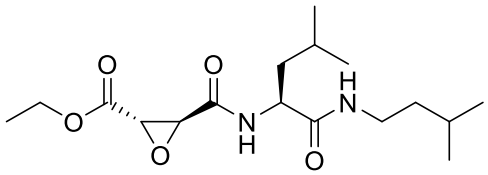
Product data sheet

MedKoo Cat#: 319511 Name: Aloxistatin (E-64d) CAS#: 88321-09-9 Chemical Formula: $C_{17}H_{30}N_2O_5$ Exact Mass: 342.21547 Molecular Weight: 342.436	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Aloxistatin (E-64d), is a selective cysteine protease inhibitor or calpain and autophagy inhibitor. E-64d prevents in vitro cerulein-induced trypsinogen activation. E-64d can enter the intact cell and inhibit calpain. E-64d has been shown safe for the treatment of Alzheimer's disease in human. E-64d is potentially useful in the treatment of developmental seizure-induced brain damage both by regulating abnormal zinc signal transduction and through the modulation of altered lipid metabolism via ApoE/clusterin pathway in hippocampus.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	50	146.02
Ethanol	33.33	97.33

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.92 mL	14.60 mL	29.20 mL
5 mM	0.58 mL	2.92 mL	5.84 mL
10 mM	0.29 mL	1.46 mL	2.92 mL
50 mM	0.06 mL	0.29 mL	0.58 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. McGowan EB, Becker E, Detwiler TC. Inhibition of calpain in intact platelets by the thiol protease inhibitor E-64d. Biochem Biophys Res Commun. 1989 Jan 31;158(2):432-5. doi: 10.1016/s0006-291x(89)80065-8. PMID: 2537073.

In vivo study

1. Hook G, Hook V, Kindy M. The cysteine protease inhibitor, E64d, reduces brain amyloid-β and improves memory deficits in Alzheimer's disease animal models by inhibiting cathepsin B, but not BACE1, β-secretase activity. J Alzheimers Dis. 2011;26(2):387-408. doi: 10.3233/JAD-2011-110101. PMID: 21613740; PMCID: PMC4317342.

2. Cheng XW, Murohara T, Kuzuya M, Izawa H, Sasaki T, Obata K, Nagata K, Nishizawa T, Kobayashi M, Yamada T, Kim W, Sato K, Shi GP, Okumura K, Yokota M. Superoxide-dependent cathepsin activation is associated with hypertensive myocardial remodeling and represents a target for angiotensin II type 1 receptor blocker treatment. Am J Pathol. 2008 Aug;173(2):358-69. doi: 10.2353/ajpath.2008.071126. Epub 2008 Jun 26. PMID: 18583318; PMCID: PMC2475774.

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7. Bioactivity

Biological target:

Aloxistatin (E64d) is a cell-permeable and irreversible broad-spectrum cysteine protease inhibitor. Aloxistatin (E64d) exhibits entry-blocking effect for MERS-CoV.

In vitro activity

E-64d, a membrane permeant derivative of E-64c, a thiol protease inhibitor, was tested for ability to inhibit calpain activity in intact platelets. Calpain activity was measured by proteolysis of actin-binding protein and talin, two known substrates of calpain. Incubation of platelets with E-64c (not permeant) or E-64d before lysis prevented proteolysis after lysis. When the platelets were incubated with E-64c or E-64d and then washed to remove the drugs before lysis, only E-64d inhibited proteolysis. When platelets were incubated with E-64c or E-64d and then activated with A23187 plus calcium, a treatment that activates intraplatelet calpain, only E-64d inhibited proteolysis. These results indicate that E-64d can enter the intact cell and inhibit calpain.

Reference: Biochem Biophys Res Commun. 1989 Jan 31;158(2):432-5. https://linkinghub.elsevier.com/retrieve/pii/S0006-291X(89)80065-8

In vivo activity

To evaluate that issue, a cysteine protease inhibitor, E64d, was orally administered to normal guinea pigs or transgenic mice expressing human AβPP, both of which express the human wild-type β-secretase site sequence. In guinea pigs, oral E64d administration caused a dose-dependent reduction of up to 92% in brain, CSF, and plasma of Aβ40 and Aβ42, a reduction of up to 50% in the C-terminal β-secretase fragment (CTFβ), and a 91% reduction in brain cathepsin B activity, but increased brain BACE1 activity by 20%. In transgenic AD mice, oral E64d administration improved memory deficits and reduced brain Aβ40 and Aβ42, amyloid plaque, brain CTFβ, and brain cathepsin B activity, but increased brain BACE1 activity. It's concluded that E64d likely reduces brain Aβ by inhibiting cathepsin B and not BACE1 β-secretase activity and that E64d therefore may have potential for treating AD patients.

Reference: J Alzheimers Dis. 2011;26(2):387-408. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/21613740/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.