CA-074

Cat. No.: HY-103350

CAS No.: 134448-10-5

Molecular Formula: $C_{18}H_{29}N_3O_6$

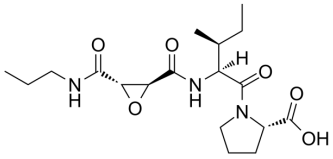
Molecular Weight: 383.44

Target: Cathepsin

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (326.00 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6080 mL	13.0399 mL	26.0797 mL
	5 mM	0.5216 mL	2.6080 mL	5.2159 mL
	10 mM	0.2608 mL	1.3040 mL	2.6080 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 (5.42 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.42 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CA-074 is a potent inhibitor of cathepsin B with a K_i of 2 to 5 nM.

IC_{50} & Target

Ki: 2 to 5 nM (Cathepsin B)[1]

In Vitro

CA-074 is a synthetic analogue of E-64, a natural peptidyl epoxide that irreversibly inhibits most known lysosomal cysteine proteinases, and is developed by means of rational drug design, exploiting the dipeptidylcarboxypeptidase activity of cathepsin B. CA-074 can be used to selectively inhibit cathepsin B within living cells, as long as the experimental conditions permit significant fluid-phase endocytosis of the drug[2]. CA-074 inhibits cathepsin B with a K_i of 2 to 5 nM, whereas the

	initial K_is for cathepsin H and L are about 40-200 μM. CA-074 exhibits 10000-30000 times greater inhibitory effects on purified rat cathepsin B than on cathepsin H and L[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Intraperitoneally injection of compound CA-074 into rats potently and selectively inhibits cathepsin B activity[1]. Intravenously administration of CA-074 immediately after the ischaemic insult saves 67% of CA1 neurons from delayed neuronal death on day 5 in eight monkeys undergoing 20 min brain ischaemia: the extent of inhibition is excellent in three of eight and good in five of eight monkeys[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats: Compound CA-074 or CA-030 or E-64 is injected intraperitoneally as a solution in saline containing DMSO. A dose of 8 mg/100 g body weight is injected. The rats are killed by a blow to the head 6 h after the injection, and their liver is perfused with saline, removed, weighed and chilled on ice. Samples of 4 g of liver are minced and homogenized. The homogenate is centrifuged at 800 xg for 15 min and the supernatant is centrifuged at 12000 xg for 30 min. The precipitate is suspended in 2 mL of 0.05 M acetate buffer, pH 5,0, and freeze-thawed for measurements of cathepsin B, H and L activities[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2020 Mar 27;11(1):1620.
- Biomaterials. 2022: 121887.
- Neoplasia. 2018 Oct;20(10):1008-1022.
- Int J Mol Sci. 2022, 23(14), 7544.
- Sci Rep. 2022 Jul 16;12(1):12197.

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REFERENCES

[1]. Towatari T, et al. Novel epoxysuccinyl peptides. A selective inhibitor of cathepsin B, in vivo. FEBS Lett. 1991 Mar 25;280(2):311-5.

[2]. Montaser M, et al. CA-074, but not its methyl ester CA-074Me, is a selective inhibitor of cathepsin B within living cells. Biol Chem. 2002 Jul-Aug;383(7-8):1305-8.

[3]. Yamashima T, et al. Inhibition of ischaemic hippocampal neuronal death in primates with cathepsin B inhibitor CA-074: a novel strategy for neuroprotection based on 'calpain-cathepsin hypothesis'. Eur J Neurosci. 1998 May;10(5):1723-33.

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