CA-074 methyl ester

Cat. No.: HY-100350

CAS No.: 147859-80-1

Molecular Formula: $C_{19}H_{31}N_3O_6$

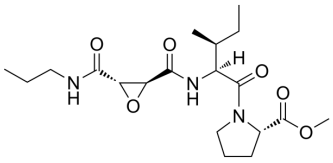
Molecular Weight: 397.47

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 : 100 mg/mL (251.59 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5159 mL	12.5796 mL	25.1591 mL
5 mM	0.5032 mL	2.5159 mL	5.0318 mL
10 mM	0.2516 mL	1.2580 mL	2.5159 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: ≥ 2.5 mg/mL (6.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CA-074 methyl ester is a specific inhibitor of Cathepsin B, which has potent bioactivities such as neuroprotective, anti-cancer, and anti-inflamatory effects.

IC_{50} & Target

Cathepsin B

In Vitro

CA-074Me (5 μM and 50 μM) inhibits RANKL-induced osteoclastogenesis in BMM cells derived from C57BL/6J and NOD/ShiLtJ mice. CA-074Me exerts its anti-osteoclastogenic effect within 24 hours post-RANKL stimulation in vitro. CA-074Me does not

	exert its anti-osteoclastogenic effect via the MAPK-ERK signaling cascade. CA-074Me inhibits c-FOS upregulation and subsequent NFATc1 autoamplification following RANKL stimulation.[2]. CA-074Me reduces apoptosis induced by CVB1[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Hippocampal CA1 neuronal programmed necrosis induced by global cerebral I/R injury is prevented by CA074-me (1 μg, 10 μg) both pre-treatment and post-treatment. The rupture of lysosomal membrane and the leakage of cathepsin-B, and this is strongly inhibited by CA074-me pre-treatment. The overexpression and nuclear translocation of RIP3 and the reduction of NAD^+ level after I/R injury are also inhibited, while the upregulation of Hsp70 is strengthened by CA074-me pre-treatment[1]. CA-074Me (30 mg/kg) is capable of inhibiting osteoclastogenesis and bone degradation in vivo[2]. In the CVB+CA-074Me (4 mg/kg/day i.m.) guinea pigs group, the scores of inflammation significantly decrease in comparison with the CVB+None group. In CVB+CA-074Me group, the number of $CD8^+$T cells decrease in comparison with the sham group [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	After seven days of cell culture and osteoclast generation, the media is removed and washed three times with PBS. BMMs are fixed with a fixing solution supplied by the manufacturer. The cells are incubated at 37°C with a solution containing deionized water, Fast Garnet GBC, Napthol phosphate, Acetate, and Tartrate for 1 h. The staining solution is removed, washed with PBS (3×), and air-dried. TRAP positive cells with three or more nuclei across whole culture area are counted as multinucleated osteoclasts using light microscopy. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	RANKL (0.08 mg/kg) with and without CA-074Me (10 mg/kg or 30 mg/kg) are mixed in sterile, nonimmunogenic 1% Extracel-HP gel. The gel is composed of thiol-modified sodium hyaluronate, thiol-modified heparin, thiol-modified gelatin, and degassed deionized sterile water. The hydrogel mixture is prepared in an aseptic hood using a sterile syringe. The control sham hydrogel contained sterile Phosphate Buffered Saline (PBS) without any cytokines. The osteolysis group is given 0.08 mg/kg RANKL in a hydrogel to induce pathologic bone loss. The hydrogel-only, hydrogel-RANKL, and hydrogel-RANKL-CA-074Me mixture is injected into 8-week old male mice calvarium in an aseptic hood (n = 5) following general anesthesia (80 mg/kg of ketamine and 7 mg/kg of xylazine). After four days, the calvaria are excised, fixed in 4% formaldehyde for 24 h, decalcified in 20% EDTA for one week, and sectioned into slides from paraffin blocks. The slides undergo Tartrate-Resistant Acid Phosphatase (TRAP) staining to identify osteoclasts. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Mol Immunol. 2020 Mar;17(3):283-299.
- Adv Funct Mater. 2023 Apr 28.
- Emerg Microbes Infect. 2022 Dec;11(1):483-497.
- Sci Adv. 2022 Nov 11;8(45):eabn9912.
- J Hazard Mater. 2022 May 10;436:129093.

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REFERENCES

[1]. Xu Y, et al. Protective mechanisms of CA074-me (other than cathepsin-B inhibition) against programmed necrosis induced by global cerebral ischemia/reperfusion injury in rats. Brain Res Bull. 2016 Jan;120:97-105

[2]. Patel N, et al. CA-074Me compound inhibits osteoclastogenesis via suppression of the NFATc1 and c-FOS signaling pathways. J Orthop Res. 2015 Oct;33(10):1474-86

[3]. Zhang L, et al. Treatment with CA-074Me, a Cathepsin B inhibitor, reduces lung interstitial inflammation and fibrosis in a rat model of polymyositis. Lab Invest. 2015 Jan;95(1):65-77

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