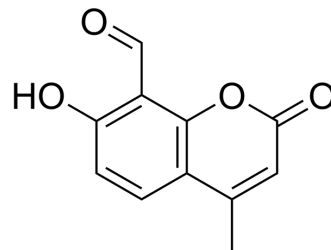


4 μ 8C

Cat. No.:	HY-19707	
CAS No.:	14003-96-4	
Molecular Formula:	C ₁₁ H ₈ O ₄	
Molecular Weight:	204.18	
Target:	IRE1	
Pathway:	Cell Cycle/DNA Damage	
Storage:	Powder	-20°C 3 years
	In solvent	-80°C 1 year
		-20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : \geq 27 mg/mL (132.24 mM)
 * " \geq " means soluble, but saturation unknown.

Concentration	Solvent	Mass	1 mg	5 mg	10 mg
			1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		4.8976 mL	24.4882 mL	48.9764 mL
	5 mM		0.9795 mL	4.8976 mL	9.7953 mL
	10 mM		0.4898 mL	2.4488 mL	4.8976 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 15% Cremophor EL >> 85% Saline
 Solubility: 25 mg/mL (122.44 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

4 μ 8C (IRE1 Inhibitor III) is a small-molecule inhibitor of IRE1 α .

In Vitro

When applied to the media of ER stressed cultured cells, 4 μ 8C (IRE1 Inhibitor III) inhibits Xbp1 splicing in a concentration-dependent manner. 4 μ 8C dissociates slowly from IRE1, but washout of inhibitor leads to rapid recovery of Xbp1 splicing in cells [1]. The IRE1 endoribonuclease inhibitor 4 μ 8c prevents the splicing of the XBP1 mRNA in response to ER stress caused by mutant proinsulin production [2]. The inositol-requiring enzyme 1 α (IRE1 α) is a serine-threonine kinase that plays crucial roles in activating the unfolded protein response. 4 μ 8C treatment dramatically inhibits IL-4 production by CD4⁺ T cells under Th0 conditions because both the IL-4 levels in the culture supernatant and the percentage of IL-4 positive cells are reduced by 4 μ 8C treatment. In addition, both IL-5 and IL-13 production are significantly reduced upon treatment with 4 μ 8C [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

4 μ 8c (IRE1 Inhibitor III) (i.p. injection; 10 mg/kg/day for 4 more weeks) leads to a significant reduction (45.2%) in

atherosclerotic lesion area in en face aorta preparations. 4μ8c can effectively mitigate plaque development in mice^[4]. 4μ8C (orally; 10, 50, or 100 mg/kg) suppresses passive cutaneous anaphylaxis (PCA) in mice (ED50 = 25.1 mg/kg)^[5]. 4μ8C reverses the ER stress-dependent loss of several known RIDD targets, with an EC₅₀ of approximately 4 μM, approximating that of inhibition of XBP1 target gene activation^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	ApoE ^{-/-} mice ^[4]
Dosage:	10 mg/kg
Administration:	I.p. injection; daily; for 4 more weeks
Result:	Led to a significant reduction (45.2%) in atherosclerotic lesion area in en face aorta preparations.

CUSTOMER VALIDATION

- Nature. 2023 Apr;616(7956):348-356.
- Nat Cell Biol. 2023 May;25(5):726-739.
- Nat Metab. 2022 Sep;4(9):1166-1184.
- J Exp Med. 2022 Apr 4;219(4):e20211498.
- Acta Pharm Sin B. 5 January 2022.

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- [1]. Cross BC, et al. The molecular basis for selective inhibition of unconventional mRNA splicing by an IRE1-binding small molecule. Proc Natl Acad Sci U S A. 2012 Apr 10;109(15):E869-78.
- [2]. Zhang L, et al. IRE1 inhibition perturbs the unfolded protein response in a pancreatic β-cell line expressing mutant proinsulin, but does not sensitize the cells to apoptosis. BMC Cell Biol. 2014 Jul 10;15:29.
- [3]. Kemp K, et al. The serine-threonine kinase inositol-requiring enzyme 1α (IRE1α) promotes IL-4 production in T helper cells. J Biol Chem. 2013 Nov 15;288(46):33272-82.
- [4]. Tufanli O, et al. Targeting IRE1 with small molecules counteracts progression of atherosclerosis. Proc Natl Acad Sci U S A. 2017 Feb 21;114(8):E1395-E1404.
- [5]. Nam ST, et al. Suppression of IgE-mediated mast cell activation and mouse anaphylaxis via inhibition of Syk activation by 8-formyl-7-hydroxy-4-methylcoumarin, 4μ8C. Toxicol Appl Pharmacol. 2017 Oct 1;332:25-31.

Caution: Product has not been fully validated for medical applications. For research use only.

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