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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

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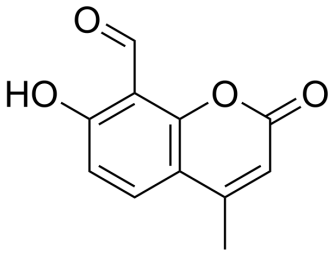
4μ8C

Cat. No.:	HY-19707
CAS No.:	14003-96-4
Molecular Formula:	$C_{11}H_8O_4$
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 : ≥ 27 mg/mL (132.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (10.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

4μ8C (IRE1 Inhibitor III) is a small-molecule inhibitor of IRE1α.

In Vitro

When applies to the media of ER stressed cultured cells, 4μ8C (IRE1 Inhibitor III) inhibits Xbp1 splicing in a concentration-dependent manner. 4μ8C dissociates slowly from IRE1, but ishout of inhibitor leads to rapid recovery of Xbp1 splicing in cells [1].The IRE1 endoribonuclease inhibitor 4μ8c prevents the splicing of the XBP1 mRNA in response to ER stress caused by mutant proinsulin production[2]. The inositol-requiring enzyme 1α (IRE1α) is a serine-threonine kinase that plays crucial roles in activating the unfolded protein response. 4μ8C 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 4μ8C treatment. In addition, both IL-5 and IL-13 production are significantly reduced upon treatment with 4μ8C[3].

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

In Vivo

4μ8c (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 EC_{50} 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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REFERENCES

[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 Sykactivation by 8-formyl-7-hydroxy-4-methylcoumarin, 4μ8C. Toxicol Appl Pharmacol. 2017 Oct 1;332:25-31.

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