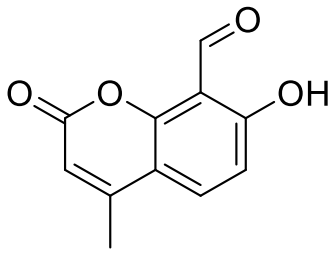
Product data sheet

MedKoo Cat#: 530969 Name: 4μ8C CAS#: 14003-96-4 Chemical Formula: $C_{11}H_8O_4$ Exact Mass: 204.0423 Molecular Weight: 204.181	
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:
4μ8C, also known as IRE1 Inhibitor III, is a IRE1 Inhibitor. 4μ8C inhibits IRE1α splicing of Xbp1 mRNA (IC50 = 6.8 μM) and reduces subsequent gene expression of Erdj4 (IC50 = 3.4 μM) in stress-cultured MEF cells but does not block IRE1α autophosphorylation.

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	19	93.06

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	4.90 mL	24.49 mL	48.98 mL
5 mM	0.98 mL	4.90 mL	9.80 mL
10 mM	0.49 mL	2.45 mL	4.90 mL
50 mM	0.10 mL	0.49 mL	0.98 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. Kemp KL, Lin Z, Zhao F, Gao B, Song J, Zhang K, Fang D. 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. doi: 10.1074/jbc.M113.493171. Epub 2013 Oct 7. PMID: 24100031; PMCID: PMC3829173.

2. Zhang L, Nosak C, Sollazzo P, Odisho T, Volchuk A. 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. doi: 10.1186/1471-2121-15-29. PMID: 25011481; PMCID: PMC4118655.

In vivo study

1. Tufanli O, Telkoparan Akillilar P, Acosta-Alvear D, Kocaturk B, Onat UI, Hamid SM, Çimen I, Walter P, Weber C, Erbay E. Targeting IRE1 with small molecules counteracts progression of atherosclerosis. Proc Natl Acad Sci U S A. 2017 Feb 21;114(8):E1395-E1404. doi: 10.1073/pnas.1621188114. Epub 2017 Jan 30. PMID: 28137856; PMCID: PMC5338400.

7. Bioactivity
Biological target:
4μ8C (IRE1 Inhibitor III) is a small-molecule inhibitor of IRE1α.

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In vitro activity

To further confirm the role of IRE1α in IL-4 production, the effects of an IRE1α inhibitor, 4μ8C, was investigated on IL-4 expression in an in vitro culture system. On average, an ~60% reduction in Xbp-1 splicing was confirmed by qRT-PCR (Fig. 4A) upon treatment of CD4+ T cells with the inhibitor. It was found that 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 were reduced by 4μ8C treatment (Fig. 4, B–D). In contrast, the expression of IFN-γ did not appear to be affected by IRE1α inhibitor 4μ8C (Fig. 4, B–D). These led us to conclude that the suppression of IRE1α functions in T cells blocks IL-4 production. In addition, both IL-5 and IL-13 production were significantly reduced upon treatment with 4μ8C (Fig. 4D). In contrast, cytokines IFN-γ and IL-17 appeared to be normal (Fig. 3D). Therefore, the pharmacological suppression of IRE1α inhibits the production of all Th2 cytokines analyzed in CD4 T cells, whereas diminished expression of IRE1α leads to reduced IL-4 but not IL-5 and IL-13.

Reference: J Biol Chem. 2013 Nov 15;288(46):33272-82. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24100031/

In vivo activity

4μ8c treatment led to a significant reduction (45.2%; $P < 0.001$) in atherosclerotic lesion area in en face aorta preparations (Fig. 4E) and a significant reduction in the spliced Xbp1 mRNA (Fig. S7A) ($P < 0.05$) but no change in IRE1 phosphorylation in the spleens (Fig. S7B). Furthermore, 4μ8c treatment led to a reduced foam cell area (Fig. 4F) without overt differences in body weight, blood glucose levels (Table S4), liver morphology, and plasma ALT activity between the inhibitor-treated and control mice (Fig. S7 C and D). These in vivo findings show that pharmacological inhibition of IRE1 can effectively mitigate plaque development in mice.

Reference: Proc Natl Acad Sci U S A. 2017 Feb 21;114(8):E1395-E1404. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/28137856/