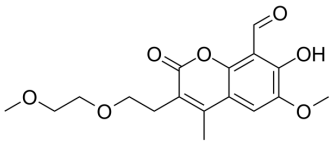
MKC9989

Cat. No.:	HY-12399
CAS No.:	1338934-20-5
Molecular Formula:	$C_{17}H_{20}O_7$
Molecular Weight:	336.34
Target:	IRE1
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (148.66 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9732 mL	14.8659 mL	29.7318 mL
5 mM	0.5946 mL	2.9732 mL	5.9464 mL
10 mM	0.2973 mL	1.4866 mL	2.9732 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 (7.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MKC9989 is a Hydroxy aryl aldehydes (HAA) inhibitor and also inhibits IRE1α with an IC_{50} of 0.23 to 44 μM.

IC_{50} & Target

IC50: 0.23 to 44 μM (IRE1α)[1]

In Vitro

At 10 μM concentration, MKC9989 completely inhibits both basal and thapsigargin induced splicing of XBP1 mRNA. These effects are observed even in cells pre-treated with thapsigargin, indicating that MKC9989 can fully reverse the onset of XPB1 splicing after the UPR is initiated. In parallel analysis, MKC9989, significantly stabilizes the RIDD target CD59 mRNA when co-administered with thapsigargin relative to thapsigargin treatment alone and modestly increases levels of CD59 mRNA in non-stressed cells, the latter likely reflects the inhibition of baseline RIDD activity. In contrast to effects on XBP1 splicing, MKC9989 moderately stabilizes CD59 levels when administered 2 hour post treatment with thapsigargin. Finally, the potency of MKC9989 against the splicing of XBP1 mRNA (EC_{50}=0.33 μM) is comparable to its potency against RNA cleavage in

vitro[1].

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

PROTOCOL

Cell Assay [1]

Human RPMI 8226 plasmacytoma cells are grown in monolayer culture using medium (DMEM) supplemented with 10% fetal calf serum (FCS) at 37°C and 5% CO_2. MKC9989 is prepared as 10 mM stocks in DMSO, stored at -20°C, and diluted in medium. Thapsigargin (Tg) is resuspended in DMSO and diluted in medium. Cells are grown to 50% confluency, treated with 1 μM Tg and/or 10 μM MKC9989 at the indicated time points. After incubation of cells for the indicated periods, cells are harvested[1].

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

REFERENCES

[1]. Sanches M, et al. Structure and mechanism of action of the hydroxy-aryl-aldehyde class of IRE1 endoribonuclease inhibitors. Nat Commun. 2014 Aug 28;5:4202.

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