Eeyarestatin I

Cat. No.: HY-110078

CAS No.: 412960-54-4

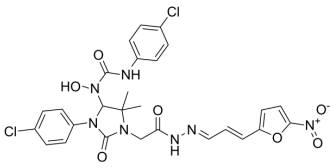
Molecular Formula: $C_{27}H_{25}Cl_2N_7O_7$

Molecular Weight: 630.44

Target: p97; Apoptosis

Pathway: Cell Cycle/DNA Damage; Apoptosis

Storage: -20°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (39.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5862 mL	7.9310 mL	15.8619 mL
	5 mM	0.3172 mL	1.5862 mL	3.1724 mL
	10 mM	0.1586 mL	0.7931 mL	1.5862 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: 1.25 mg/mL (1.98 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Eeyarestatin I, a potent endoplasmic reticulum-associated protein degradation (ERAD) inhibitor, is a potent protein translocation inhibitor. Eeyarestatin I inhibits Sec61 translocon. Eeyarestatin I targets the p97-associated deubiquitinating process (PAD) and inhibits atx3-dependent deubiquitination. Eeyarestatin I interferes at a step prior to proteasomal degradation. Eeyarestatin I induces cell death via the proapoptotic protein NOXA and has anticancer effects[1][2][3][4][5].

IC_{50} & Target

Endoplasmic reticulum-associated protein degradation (ERAD)[1][2]

In Vitro

Eeyarestatin I (2.5-40 μM; 48 hours; A549 and H358 cells) treatment causes a dose-dependent cell death of both A549 and H358 cells[1].
Eeyarestatin I (2.5-40 μM; 48 hours; A549 and H358 cells) treatment increases endoplasmic reticulum (ER) stress markers including Bip and CHOP as low as 20 μM. Eeyarestatin I treatment shows a dose dependent ubiquitination of key proteins including PERK and IRE1α[1].
Eeyarestatin I (20 μM; 48 hours; A549 and H358 cells) treatment induces cell migration and cell invasion[1].
Eeyarestatin 1 prevents the transfer of nascent proteins from the membrane-targeting complex to the ER translocation

machinery, most probably by inactivating the Sec61 complex[2].

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

Cell Viability Assay[1]

Cell Line:	A549 and H358 cells
Concentration:	2.5 μM, 5 μM, 10 μM, 20 μM, 40 μM
Incubation Time:	48 hours
Result:	Caused dose dependent cell death of both A549 and H358 cells.

Western Blot Analysis[1]

Cell Line:	A549 and H358 cells
Concentration:	2.5 μM, 5 μM, 10 μM, 20 μM, 40 μM
Incubation Time:	48 hours
Result:	Increased ER stress markers including Bip and CHOP.

REFERENCES

[1]. Pauwels E, et al. Inhibitors of the Sec61 Complex and Novel High Throughput Screening Strategies to Target the Protein Translocation Pathway. Int J Mol Sci. 2021 Nov 5;22(21):12007.

[2]. Parag P Shah, et al. Regulation of VCP/p97 demonstrates the critical balance between cell death and epithelial-mesenchymal transition (EMT) downstream of ER stress. Oncotarget. 2015 Jul 10;6(19):17725-37.

[3]. Benedict C S Cross, et al. Eeyarestatin I inhibits Sec61-mediated protein translocation at the endoplasmic reticulum. J Cell Sci. 2009 Dec 1;122(Pt 23):4393-400.

[4]. Qiuyan Wang, et al. Inhibition of p97-dependent protein degradation by Eeyarestatin I. J Biol Chem. 2008 Mar 21;283(12):7445-54.

[5]. Qiuyan Wang, et al. ERAD inhibitors integrate ER stress with an epigenetic mechanism to activate BH3-only protein NOXA in cancer cells. Proc Natl Acad Sci U S A. 2009 Feb 17;106(7):2200-5.

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