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Produktinformation

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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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AA147

Cat. No.: HY-124293

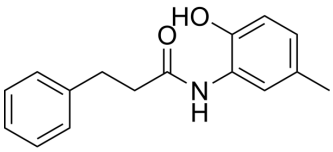
CAS No.: 393121-74-9

Molecular Formula: $C_{16}H_{17}NO_2$

Molecular Weight: 255.31

Target: ATF6; Reactive Oxygen Species

Pathway: Cell Cycle/DNA Damage; Immunology/Inflammation; Metabolic Enzyme/Protease; NF-κB



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 (195.84 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.9168 mL	19.5840 mL	39.1681 mL
	5 mM	0.7834 mL	3.9168 mL	7.8336 mL
	10 mM	0.3917 mL	1.9584 mL	3.9168 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: ≥ 5 mg/mL (19.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 5 mg/mL (19.58 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

AA147 is a endoplasmic reticulum (ER) proteostasis regulator. AA147 promotes protection against oxidative damage in neuronal cells and prevents endothelial barrier dysfunction by activating ATF6 arm (selectively) of the unfolded protein response (UPR) and the NRF2 oxidative stress response. AA147 can rebalances XBP1s expression in vivo, and also induces survival motor neuron (SMN) expression and spinal motorneuron (MN) protection[1][2][3][4].

In Vitro

AA147 (20-0.078 μM (dilution in half); 6 or 16 h) protects against glutamate-induced oxidative toxicity in HT22 cells by decreasing the reactive oxygen species (ROS)-associated damage[1].
AA147 (10 μM; 16 h) induces NRF2-dependent upregulation of oxidative stress response genes in HT22 cells[1].
AA147 (10 μM; 16 h) covalently modifies KEAP1 to promote NRF2 activation in HT22 cells[1].

AA147 (5, 10, 15 μM; 4, 8, 16, 24, 48 h) induces ATF6 activation and upregulates phosphorylation of cofilin in BPAEC[2].
AA147 (10 μM; 24 h) reduces LPS-induced endothelial barrier disruption in BPAEC[2].
AA147 (5, 10 μM; 135 h) enhances lung endothelial barrier integrity[2].

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

Cell Viability Assay[1]

Cell Line:	HT22 cells
Concentration:	0.078, 0.156, 0.312, 0.625, 1.25, 2.5, 5, 10, 20 μM
Incubation Time:	6 or 16 h (pre-incubation)
Result:	Showed dose-dependent increases in the viability of glutamate-treated HT22 cells when pretreated with AA147 for 6 or 16 h prior to the glutamate challenge (addition concurrently with the glutamate challenge did not improve the viability of glutamate-treated cells). Reduced ROS accumulation in cells when pre-incubation of 16 h.

Cell Viability Assay[1]

Cell Line:	HT22 cells
Concentration:	10 μM
Incubation Time:	16 h
Result:	Significant increased the expression of genes associated with antioxidant activity in neuronal models, including prolactins and glutathione transferases. Activated NRF2 through a mechanism involving metabolic activation and covalent KEAP1 protein modification.

Cell Viability Assay[2]

Cell Line:	BPAEC
Concentration:	5, 10 μM
Incubation Time:	135 h
Result:	Decreased permeability of cells by activation of ATF6.

Western Blot Analysis[2]

Cell Line:	BPAEC
Concentration:	5, 10, 15 μM
Incubation Time:	4, 8, 16, 24, 48 h
Result:	Significantly induced ATF6 activation and upregulated cofilin phosphorylation (in a concentration-dependent manner).

Western Blot Analysis[2]

Cell Line:	BPAEC
Concentration:	10 μM
Incubation Time:	24 h

Result:	Reduced LPS-induced cATF6 suppression (Fig.5A) and VE-cadherin phosphorylation. Inhibited cofilin and MLC2 activation in the inflamed cells. Inhibited LPS-induced hyperpermeability in BPAEC.

In Vivo

AA147 (intrathecal injection; single for 3 days) can rebalance XBP1s expression in severe SMA-like mice by activating ATF6, and also induce survival motor neuron expression and spinal motorneuron protection[3].

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

CUSTOMER VALIDATION

- J Virol. 2021 Oct 13;JVI0169521.
- Environ Toxicol. 2023 May 6.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Rosarda JD, et al. Metabolically Activated Proteostasis Regulators Protect against Glutamate Toxicity by Activating NRF2. ACS Chem Biol. 2021 Dec 17;16(12):2852-2863.

[2]. Kubra KT, et al. Activating transcription factor 6 protects against endothelial barrier dysfunction. Cell Signal. 2022 Aug 4;99:110432.

[3]. D'Amico D, et al. Activating ATF6 in spinal muscular atrophy promotes SMN expression and motor neuron survival through the IRE1α-XBP1 pathway. Neuropathol Appl Neurobiol. 2022 Aug;48(5):e12816.

[4]. Christina COOLEY, et al. Regulators of the endoplasmic reticulum proteostasis network. WO2017117430A1.

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