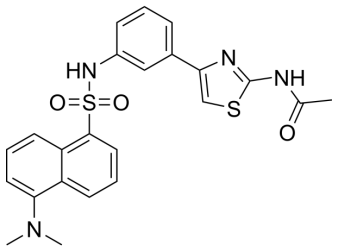
HA15

Cat. No.:	HY-100437
CAS No.:	1609402-14-3
Molecular Formula:	$C_{23}H_{22}N_4O_3S_2$
Molecular Weight:	466.58
Target:	HSP; Autophagy; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Autophagy; Apoptosis
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 (107.16 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1433 mL	10.7163 mL	21.4326 mL
5 mM	0.4287 mL	2.1433 mL	4.2865 mL
10 mM	0.2143 mL	1.0716 mL	2.1433 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 (5.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

HA15 is a potent and specific inhibitor of ER chaperone BiP/GRP78/HSPA5, inhibits the ATPase activity of BiP, with anti-cancerous activity[1].

IC_{50} & Target

BiP/GRP78/HSPA5[1]

In Vitro

HA15 (10 μM; 1-24 hours) induces an early endoplasmic reticulum stress (ER Stress)[1].
?HA15 (0-10μM; 24 hours) decreases melanoma cell viability in a dose-dependent manner compared with control conditions (DMSO), with an IC_{50} of 1-2.5 μM in? A375 cells[1].
?HA15 (1-10 μM; 24 hours) induces apoptosis in A375 cells[1].
?HA15 (1-24 μM; 24 hours) induces autophagy[1].
?HA15 (10 μM; 48 hours) has high efficiency in inducing cell death and ER stress in BRAF-inhibitor-resistant melanoma cells.

And HA15 inhibits tumor growth through autophagic and apoptotic mechanisms initiated by ER stress[1].
?No deleterious effects on the viability of normal human melanocytes or human fibroblasts were observed with low or high doses of HA15[1].

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

Cell Viability Assay[1]

Cell Line:	A375 cells
Concentration:	1 μM,2.5 μM,5 μM,7.5 μM,10 μM
Incubation Time:	24 hours
Result:	Decreased melanoma cell viability in a dose-dependent manner compared with control conditions (DMSO) in A375 cells.

Apoptosis Analysis[1]

Cell Line:	A375 cells
Concentration:	1 μM, 5 μM, 10 μM
Incubation Time:	24 hours
Result:	Induces apoptosis.

Cell Autophagy Assay[1]

Cell Line:	A375 cells
Concentration:	1 μM, 4 μM, 10 μM, 24 μM
Incubation Time:	24 hours
Result:	Increased LC3B-II expression after 1 hour and persisted after 24 hours, enhanced the expression level of Beclin 1, clearly be indicated that induces autophagy.

Western Blot Analysis[1]

Cell Line:	A375 cells
Concentration:	10 μM
Incubation Time:	1 hour, 4 hours, 10 hours, 24 hours
Result:	Exhibited a rapid induction within 1 hour of the ER stress markers (phosphorylation of PERK and eIF2α and a weak increase in ATF4 and CHOP expression)

In Vivo

HA15 (0.7 mg/mouse/day; i.h.; over 2 weeks) inhibits melanoma tumor development in mice, induces no apparent toxicity and no change in their behavior, body mass, or liver mass, suggesting an absence of hepatomegaly[1].
?HA15 (0.7 mg/mouse; i.p.; 5 days/week) suppresses MPM tumor growth in vivo[3].

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

Animal Model:	6-weeks female BALB/c nu/nu (nude) mice with A375 melanoma cells xenograft[1]
Dosage:	0.7 mg/mouse/day
Administration:	Subcutaneous injection; over a period of 2 weeks

Result:	Attenuated the development of tumors.

Animal Model:	Mouse, NSG (NOD-scid IL2Rγnull)[3]
Dosage:	0.7 mg/mouse
Administration:	Intraperitoneal injection, 5 days/week, for 5 weeks
Result:	Suppressed MPM tumor growth.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2023 Mar 15;8(1):107.
- J Am Chem Soc. 2022 Jun 15;144(23):10407-10416.
- Leukemia. 2023 Feb 22.
- EMBO Mol Med. 2023 Oct 9:e17761.
- Adv Healthc Mater. 2023 Apr 29;e2300913.

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REFERENCES

[1]. Cerezo M et al. Compounds Triggering ER Stress Exert Anti-Melanoma Effects and Overcome BRAF Inhibitor Resistance. Cancer Cell. 2016 Jun 13;29(6):805-19.

[2]. Ruggiero C, et al. The GRP78/BiP inhibitor HA15 synergizes with mitotane action against adrenocortical carcinoma cells through convergent activation of ER stress pathways. Mol Cell Endocrinol. 2018 Oct 15;474:57-64.

[3]. Duo Xu, et al. Endoplasmic Reticulum Stress Signaling as a Therapeutic Target in Malignant Pleural Mesothelioma. Cancers (Basel). 2019 Oct; 11(10): 1502.

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