产品名称：**HA15**
产品别名：**HA15**

生物活性：		
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 IC50 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].	
	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)
	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].	

<table>
<tr><td rowspan="4">In Vivo</td><td>Animal Model:</td><td>6-weeks female BALB/c nu/nu (nude) mice with A375 melanoma cells xenograft[1]</td></tr>
<tr><td>Dosage:</td><td>0.7 mg/mouse/day</td></tr>
<tr><td>Administration:</td><td>Subcutaneous injection; over a period of 2 weeks</td></tr>
<tr><td>Result:</td><td>Attenuated the development of tumors.</td></tr>
<tr><td>Solvent&Solubility</td><td colspan="2">
In Vitro:
DMSO : ≥ 50 mg/mL (107.16 mM)
H_2O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.
<table>
<tr><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>2.1433 mL</td><td>10.7163 mL</td><td>21.4326 mL</td></tr>
<tr><td>5 mM</td><td>0.4287 mL</td><td>2.1433 mL</td><td>4.2865 mL</td></tr>
<tr><td>10 mM</td><td>0.2143 mL</td><td>1.0716 mL</td><td>2.1433 mL</td></tr>
</table>
*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。
储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。
In Vivo:
请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：
——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶
1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline
Solubility: ≥ 2.5 mg/mL (5.36 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (5.36 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。
</td></tr>
<tr><td>References</td><td colspan="2">
[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.
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