# Product data sheet

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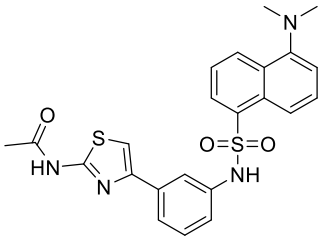
|---|---|
| MedKoo Cat#: 406823<br>Name: HA-15 free base<br>CAS#: 1609402-14-3<br>Chemical Formula: $C_{23}H_{22}N_4O_3S_2$<br>Exact Mass: 466.1133<br>Molecular Weight: 466.574 | |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |




**1. Product description:**
HA15 is a specifc inhibitor of the chaperone BiP (Binding immunoglobulin protein, GRP78 or HSPA5). HA15 displayed anti-cancerous activity on all melanoma cells tested, including cells isolated from patients and cells that developed resistance to BRAF inhibitors. HA15 also exhibited strong efficacy in xenograft mouse models with melanoma cells either sensitive or resistant to BRAF inhibitors. Transcriptomic, proteomic, and biochemical studies identified the chaperone BiP/GRP78/HSPA5 as the specific target of HA15 and demonstrated that the interaction increases ER stress, leading to melanoma cell death by concomitant induction of autophagic and apoptotic mechanisms.

**2. CoA, QC data, SDS, and handling instruction**
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

**3. Solubility data**

| Solvent | Max Conc. mg/mL | Max Conc. mM |
|---|---|---|
| DMSO | 71.5 | 153.24 |
| Ethanol | 45.0 | 96.45 |

**4. Stock solution preparation table:**

| **Concentration / Solvent Volume / Mass** | **1 mg** | **5 mg** | **10 mg** |
|---|---|---|---|
| 1 mM | 2.14 mL | 10.72 mL | 21.43 mL |
| 5 mM | 0.43 mL | 2.14 mL | 4.29 mL |
| 10 mM | 0.21 mL | 1.07 mL | 2.14 mL |
| 50 mM | 0.04 mL | 0.21 mL | 0.43 mL |

**5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator**
Please refer the product web page under section of "Calculator"

**6. Recommended literature which reported protocols for in vitro and in vivo study**

In vitro study

1. Barrera MD, Callahan V, Akhrymuk I, Bhalla N, Zhou W, Campbell C, Narayanan A, Kehn-Hall K. Proteomic Discovery of VEEV E2-Host Partner Interactions Identifies GRP78 Inhibitor HA15 as a Potential Therapeutic for Alphavirus Infections. Pathogens. 2021 Mar 2;10(3):283. doi: 10.3390/pathogens10030283. PMID: 33801554; PMCID: PMC8000471.
2. Wu J, Wu Y, Lian X. Targeted inhibition of GRP78 by HA15 promotes apoptosis of lung cancer cells accompanied by ER stress and autophagy. Biol Open. 2020 Nov 12;9(11):bio053298. doi: 10.1242/bio.053298. PMID: 33115703; PMCID: PMC7673357.

In vivo study

1. Fu D, Li P, Sheng Q, Lv Z. β-arrestin-2 enhances intestinal epithelial apoptosis in necrotizing enterocolitis. Aging (Albany NY). 2019 Oct 14;11(19):8294-8312. doi: 10.18632/aging.102320. Epub 2019 Oct 14. PMID: 31612867; PMCID: PMC6814604.
2. Xu D, Yang H, Yang Z, Berezowska S, Gao Y, Liang SQ, Marti TM, Hall SRR, Dorn P, Kocher GJ, Schmid RA, Peng RW. Endoplasmic Reticulum Stress Signaling as a Therapeutic Target in Malignant Pleural Mesothelioma. Cancers (Basel). 2019 Oct 8;11(10):1502. doi: 10.3390/cancers11101502. PMID: 31597321; PMCID: PMC6827154.

# Product data sheet

**7. Bioactivity**

Biological target:

HA15 is an inhibitor of ER chaperone BiP/GRP78/HSPA5, and inhibits the ATPase activity of BiP.

In vitro activity

Both VEEV TrD and EEEV infectious viral titers were significantly impacted by HA15 treatment with a 3 $\log_{10}$ reduction observed in cells treated with 50 µM of HA15 (Figure 3A,B). HA15 treatment of SINV infected Vero cells at 50 µM and 25 µM reduced the viral titers from $2.18 \times 10^7$ PFU/mL (DMSO treated cells) to $1.00 \times 10^4$ PFU/mL and $1.43 \times 10^6$ PFU/mL, respectively (Figure 3C). Likewise, HA15 treatment impacted CHIKV infectious viral titers, reducing them from $4.4 \times 10^7$ PFU/mL (DMSO treated cells) to $3.33 \times 10^4$ PFU/mL (HA15 50 µM) and $3.13 \times 10^6$ PFU/mL (HA15 25µM) (Figure 3D). These results agree with the data demonstrating the ability of HA15 to inhibit VEEV TC-83 infectious titers (Figure 2E), indicating that HA15 inhibition of GRP78 impacts multiple alphaviruses.

Reference: Pathogens. 2021 Mar; 10(3): 283. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8000471/

In vivo activity

Another interesting finding was that HA15-induced apoptosis was maintained at a high level in LPS-treated cells, regardless of whether or not β-arrestin-2 was overexpressed (Figure 5D). In this study's animal models, KO+NEC and WT+NEC mice pretreated with HA15 exhibited almost the same degree of intestinal damage (Figure 5E), further confirming the involvement of BiP in β-arrestin-2-induced ER stress and apoptotic signaling.

Reference: Aging (Albany NY). 2019 Oct 15; 11(19): 8294–8312. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6814604/

*Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.*