

Product Data Sheet

Product Name: NH125
Cat. No.: GC13793

Chemical Properties

Cas. No. 278603-08-0

Chemical Name 1-benzyl-3-hexadecyl-2-methylimidazol-1-ium;iodide

SMILES CCCCCCCCCCCCCCCCN1C=C[N+](=C1C)CC2=CC=CC=C2.[I-]

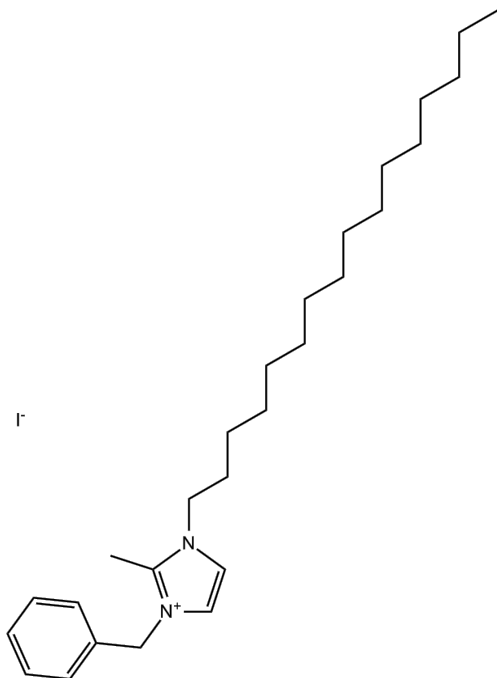
Formula $C_{27}H_{45}IN_2$ M.Wt 524.56

Solubility $\geq 25.9\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment [1]:

Cell lines	T98G and LN-229 cells (human glioblastoma cell lines)
Preparation Method	T98G, LN-229 cells were cultured in Ham's F-DMEM (10:1) medium supplemented with 10% fetal bovine serum at 37°C, 5% CO ₂ . Cells were treated with of NH125 (0.25μM) and Curcumin (5-50μM) or Velcade (25-800nM) for 48 hours.
Reaction Conditions	0.25μM; 48h
Applications	NH125 significantly increased the cytotoxicity of Curcumin and Velcade against T98G and LN-229 cells. This suggests that NH125 can enhance the efficacy of these ER stress-inducing anticancer drugs by inhibiting EEF2K-mediated autophagy.

Animal experiment [2]:

Animal models	C57BL/6J male mice
Preparation Method	Mice were treated with lipopolysaccharide (LPS) (2mg/kg, intraperitoneally) to induce depression-like behavior. Some mice were also treated with the HDAC1 inhibitor NH125 (1mg/kg, intraperitoneally) to investigate its effects on LPS-induced neuroinflammation and depression.
Dosage form	1mg/kg; i.p.

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Applications

NH125 treatment significantly reduced LPS-induced depressive-like behaviors, as evidenced by decreased immobility time in the forced swimming test and increased sucrose preference in the sucrose preference test. NH125 also attenuated LPS-induced neuroinflammation by reducing the expression of pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6) and NLRP3 inflammasome components.

References:

- [1] Cheng Y, Ren X, Zhang Y, et al. Integrated regulation of autophagy and apoptosis by EEF2K controls cellular fate and modulates the efficacy of curcumin and velcade against tumor cells. *Autophagy*. 2013 Feb 1;9(2):208-19.
- [2] Li W, Ali T, Zheng C, et al. Fluoxetine regulates eEF2 activity (phosphorylation) via HDAC1 inhibitory mechanism in an LPS-induced mouse model of depression. *J Neuroinflammation*. 2021 Feb 1;18(1):38.

Background

NH125 is a multitarget active substance and an inhibitor of several members of the histidine protein kinase family^[1]. NH125 can inhibit the activity of eukaryotic elongation factor-2 kinase (eEF-2K) with an IC₅₀ of 60nM ^[2]. NH125 can also target and inhibit the two-component signal transduction system in bacteria, exerting antibacterial effects^[3]. NH125 can reduce the expression of the RNA-binding protein CPEB3 to increase the level of synaptic GluA2^[4].

In vitro, pre-treatment of *Staphylococcus aureus* strain Newman with NH125 (41–298 μ M) for 1 hour, followed by cultivation for 24 hours in the presence of sub-lethal doses of cell wall-targeting antibiotics (Oxacillin at 0.5MIC or Vancomycin at 0.5MIC), significantly enhanced the inhibitory effects of the antibiotics on bacterial growth and reduced the expression levels of antibiotic resistance-related genes (vraSR, pbpB, and blaZ)^[5]. Co-treatment of tumor cells with NH125 (0.25 μ M) and endoplasmic reticulum (ER) stress inducers (Curcumin at 5-50 μ M or Velcade at 25-800nM) for 48 hours significantly enhanced the cytotoxicity of the ER stress inducers against tumor cells and promoted apoptosis compared to treatment with the ER stress inducers alone^[6].

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In vivo, NH125 (1mg/kg) was administered intraperitoneally once daily to mice with LPS-induced depression. NH125 reduced the levels of pro-inflammatory cytokines and increased the immobility time of the mice^[7]. NH125 (1mg/kg) was also administered intraperitoneally once daily to SARM1 knockout (SARM1KO) mice for 3 consecutive days. NH125 significantly improved depressive-like behaviors in SARM1KO mice, reducing immobility time, increasing sucrose preference, and restoring synaptic protein levels while increasing dendritic spine density^[8].

References:

- [1] Devkota AK, Tavares CD, Warthaka M, et al. Investigating the kinetic mechanism of inhibition of elongation factor 2 kinase by NH125: evidence of a common in vitro artifact. *Biochemistry*. 2012 Mar 13;51(10):2100-12.
- [2] Arora S, Yang JM, Kinzy TG, et al. Identification and characterization of an inhibitor of eukaryotic elongation factor 2 kinase against human cancer cell lines. *Cancer Res*. 2003 Oct 15;63(20):6894-9.
- [3] Yamamoto K, Kitayama T, Ishida N, et al. Identification and characterization of a potent antibacterial agent, NH125 against drug-resistant bacteria. *Biosci Biotechnol Biochem*. 2000 Apr;64(4):919-23.
- [4] Bender CL, Yang Q, Sun L, et al. NH125 reduces the level of CPEB3, an RNA binding protein, to promote synaptic GluA2 expression. *Neuropharmacology*. 2016 Feb;101:531-7.
- [5] Bhattarai S, Marsh L, Knight K, et al. NH125 Sensitizes Staphylococcus aureus to Cell Wall-Targeting Antibiotics through the Inhibition of the VraS Sensor Histidine Kinase. *Microbiol Spectr*. 2023 Jun 15;11(3):e0486122.
- [6] Cheng Y, Ren X, Zhang Y, et al. Integrated regulation of autophagy and apoptosis by EEF2K controls cellular fate and modulates the efficacy of curcumin and velcade against tumor cells. *Autophagy*. 2013 Feb 1;9(2):208-19.
- [7] Li W, Ali T, Zheng C, et al. Fluoxetine regulates eEF2 activity (phosphorylation) via HDAC1 inhibitory mechanism in an LPS-induced mouse model of depression. *J Neuroinflammation*. 2021 Feb 1;18(1):38.
- [8] Li W, Zhu W, Chen J, et al. SARM1 deficiency induced depressive-like behavior via AMPK α /p-eEF2 axis to synapse dysfunction. *Neuropharmacology*. 2025 Jan 1;262:110206.

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