Homoharringtonine

Cat. No.: HY-14944

CAS No.: 26833-87-4

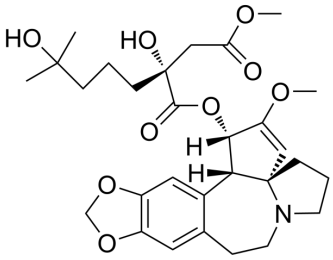
Molecular Formula: $C_{29}H_{39}NO_9$

Molecular Weight: 545.62

Target: STAT

Pathway: JAK/STAT Signaling; Stem Cell/Wnt

Storage: 4°C, protect from light
* In solvent : -80°C, 1 years; -20°C, 6 months (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (91.64 mM)

H_2O : 1.4 mg/mL (2.57 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8328 mL	9.1639 mL	18.3278 mL
	5 mM	0.3666 mL	1.8328 mL	3.6656 mL
	10 mM	0.1833 mL	0.9164 mL	1.8328 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 (4.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.58 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.58 mM); Clear solution
4. Add each solvent one by one: PBS
   Solubility: 1.67 mg/mL (3.06 mM); Clear solution; Need ultrasonic and warming and heat to 60°C

BIOLOGICAL ACTIVITY

Description

Homoharringtonine (Omacetaxine mepesuccinate;HHT) is a cytotoxic alkaloid with antitumor properties which acts by inhibiting translation elongation.

IC_{50} & Target

STAT3

In Vitro	Homoharringtonine inhibits IL-6-induced STAT3 phosphorylation in a dose- and time-dependent manner. Homoharringtonine (HHT) inhibits cells growth, cell viability and colony formation, as well as induced cell apoptosis through mitochondria pathway. The cytotoxicity of Homoharringtonine on human NSCLC cell lines is investigated, A549 (wild type EGFR) and NCI-H1975 (H1975, mutant EGFR with L858R and T790M), Gefitinib is used as a control. By MTT assay, Homoharringtonine has moderate cytotoxicity to A549 with an IC_{50} of 3.7 μM and H1975 cells are more sensitive to Homoharringtonine with an IC_{50} of 0.7 μM. Homoharringtonine inhibits the cell proliferation and growth of A549 cells and H1975 cells in a time- and dose-dependent manner through MTT assay. By trypan blue exclusion assay, Homoharringtonine rapidly reduces viable A549 and H1975 cells in a dose- and time-dependent manner. Homoharringtonine significantly inhibits the clonogenic ability of A549 and H1975 cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Homoharringtonine (10 mg/kg) efficiently represses tumor growth compared to vehicle control or Gefitinib ($P<0.05$). Additionally, Homoharringtonine (HHT) treatment does not reduce the mice body weight, which suggests that Homoharringtonine has no apparent side effect. All the mice are euthanized, the tumors are isolated and imaged and the tumor sample cells are harvested to extract protein for determination if Homoharringtonine inhibits STAT3 phosphorylation via western blot. The level of STAT3 phosphorylation and MCL1 from Homoharringtonine treatment group is significantly decreased compared to vehicle control or Gefitinib treatment. Meanwhile, consistant with the results in the above, AKT1/2/3 and ERK1/2 phosphorylation is not inhibited with Homoharringtonine treatment. To further examine the STAT3 phosphorylation in the xenograft tumor samples with different treatments, the tumor samples are frozen and cutted into 10 μm sections for fluorescent immunohistochemistry. Homoharringtonine treatment inhibits STAT3 phosphorylation compared to vehicle control or Gefitinib treatment[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Human NSCLC cell lines MCF-10A, A549 and H1975 cells are seeded into 96-well plate and precultured for 24 h, then treated with Homoharringtonine for 24 h or 48 h. Cell cytotoxicity is determined by MTT assay. The absorbance is measured at 570 nm by Varioskan Flash Multimode Reader, and the cell death rate is calculated. Cell viability is estimated by trypan blue dye exclusion assay. The cells which exclude the dye are viable. Place 0.5 mL of a suitable cell suspension (dilute cells in complete medium without serum to 1×10^6 cells per mL) following adding 0.1 mL of 0.4% trypan blue dye and mixing thoroughly, and then incubate at room temperature for 3 min and load into a hemacytometer to count cells in three separate fields (nonviable, deep blue cells as well as viable, clear cells). The cell viability rate is calculated. After staining with Hoechst 33258 at 10 mg/mL for 10 min, cell death is observed by a fluorescence microscope[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Equal amounts of female and male nude immunodeficient mice (nu/nu), 6-8 weeks old, are injected subcutaneously with NSCLC H1975 cells (2.5×10^6) suspended in 100 μL RPMI-1640 medium into the rightflank of each mouse. Treatments are started when the tumors reached a palpablesize. Mice are randomly divided into three groups (n=10) and treated with Homoharringtonine (10 mg/kg), Gefitinib (30 mg/kg) or vehicle control for 3 weeks. Vernier caliper measurements of the longest perpendicular tumor diameters are conducted along with the mice treatment to estimate the tumor volume, using the following formula: $4\pi/3\times(\text{width}/2)^2\times(\text{length}/2)$, representing the 3-dimensional volume of an ellipse tumor tissue. Animals are sacrificed when tumors reached to 2 cm or if the mice appeared moribund to prevent unnecessary morbidity to the mice. At the time of the animals' death, tumors are excised; cells are separatedand lyzed for western blot using anti-STAT3 antibody, anti-pSTAT3, anti-MCL1 and anti-GAPDH antibodies and immunohistochemistry. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2023 Jan 19;186(2):346-362.e17.

- Cell Discov. 2022 Jul 19;8(1):68.
- Nat Commun. 2021 Jun 23;12(1):3907.
- J Med Virol. 2019 Sep;91(9):1595-1601.
- Pharmacol Res. 2020 May;155:104751.

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REFERENCES

[1]. Cao W, et al. Homoharringtonine induces apoptosis and inhibits STAT3 via IL-6/JAK1/STAT3 signal pathway in Gefitinib-resistant lung cancer cells. Sci Rep. 2015 Jul 13;5:8477

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