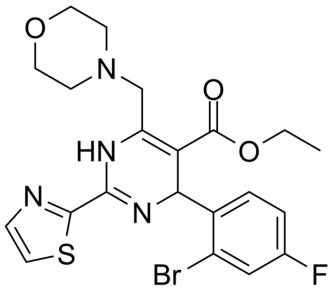
Morphothiadin

Cat. No.:	HY-108917
CAS No.:	1092970-12-1
Molecular Formula:	$C_{21}H_{22}BrFN_4O_3S$
Molecular Weight:	509.39
Target:	HBV
Pathway:	Anti-infection
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 : 62.5 mg/mL (122.70 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9631 mL	9.8157 mL	19.6313 mL
	5 mM	0.3926 mL	1.9631 mL	3.9263 mL
	10 mM	0.1963 mL	0.9816 mL	1.9631 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: ≥ 3 mg/mL (5.89 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3 mg/mL (5.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Morphothiadin is a potent inhibitor on the replication of both wild-type and adefovir-resistant HBV with an IC_{50} of 12 nM.

IC_{50} & Target

IC50: 12 nM (HBV)[1]

In Vitro

Morphothiadin is a potent inhibitor on the replication of both wild-type and adefovir-resistant HBV with an IC_{50} of 12 nM. Morphothiadin (GLS4) shows no toxicity up to 25 μM. The cytotoxic dose whereby 50% of cells die (CC_{50}) for primary hepatocytes is 115 μM for Morphothiadin (P<0.001). The CC_{90} is 190 μM for Morphothiadin (P<0.01) in HepAD38 cells. Morphothiadin strongly inhibits virus accumulation in the supernatant of HepAD38 cells at 25 nM to 100 nM (P<0.02). Results show a concentration-dependent decrease of core protein in cells treated with Morphothiadin[2].

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

In Vivo	The area under the concentration-time curve from 0 to 24 h (AUC_{0-24}) of Morphothiadin (GLS4) is 556 h•ng/mL. After intravenous administration of 10 mg/kg Morphothiadin, the total plasma clearance and apparent volume distribution are 4.2 liters/h/kg and 7.38 liters/kg, respectively. The bioavailability of Morphothiadin is 25.5%. It is found that virus titers have increased 83.5-fold in mice treated with 3.75 mg/kg per day of Morphothiadin, 28.3-fold among mice treated with 7.5 mg/kg per day, but only 3- to 6-fold among mice treated with the higher doses of Morphothiadin. There is generally an inverse relationship between Morphothiadin dose and virus titer, with the greatest rebound seen in mice treated with 3.75 mg/kg per day of Morphothiadin (540-fold) and the smallest rebound in mice treated with 60 mg/kg per day (23-fold) (P<0.001). The Morphothiadin doses of >7.5 mg/kg per day significantly suppresses the virus replication cycle throughout the treatment period, while Morphothiadin doses of >15 mg/kg per day suppresses virus for up to 2 weeks after the end of treatment[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	HepAD38 cells are grown to about 80% confluence in 0.3 μg/mL of tetracycline (TET). After the removal of TET, the cells are treated with different doses of Morphothiadin (GLS4), or no drug. Cell viability is monitored by 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	ICR mice are used to evaluate the pharmacokinetic (PK) properties of Morphothiadin (GLS4). Following oral administration of 10 mg/kg (of body weight) of Morphothiadin to male mice, the concentration of Morphothiadin in plasma is determined using liquid chromatography-tandem mass spectrometry (LC/MS/MS). For toxicity studies, ICR mice are given Morphothiadin by gavage over a 4-week period and then kept off drug for another 2 weeks. Groups consisting of 20 male plus 20 female mice are administered a vehicle (1% methyl-2-hydroxyethyl cellulose), 35.7, 118.9, or 356.6 mg/kg per day in a volume corresponding to 20 mL/kg. Ten mice per dose group are euthanized 2 weeks after the end of drug treatment. Body weight, food consumption, serum albumin levels, and adverse effects are determined[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Emerg Microbes Infect. 2020 Dec 9;1-22.
- Cell Mol Gastroenterol Hepatol. 2021 Dec 8;S2352-345X(21)00249-6.
- PLoS Pathog. 2021 Aug 9;17(8):e1009838.
- J Virol. 2022 Oct 13;e0136222.
- Anal Methods. 2021 Dec 17.

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REFERENCES

[1]. Zhou X, et al. Effects of ketoconazole and rifampicin on the pharmacokinetics of GLS4, a novel anti-hepatitis B virus compound, in dogs. Acta Pharmacol Sin. 2013 Nov;34(11):1420-6.

[2]. Wu G, et al. Preclinical characterization of GLS4, an inhibitor of hepatitis B virus core particle assembly. Antimicrob Agents Chemother. 2013 Nov;57(11):5344-54.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA