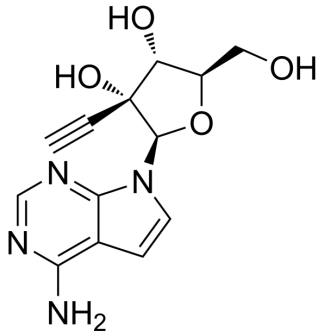
NITD008



Cat. No.:	HY-12957
CAS No.:	1044589-82-3
Molecular Formula:	$C_{13}H_{14}N_4O_4$
Molecular Weight:	290.27
Target:	DNA/RNA Synthesis; Flavivirus; Dengue virus
Pathway:	Cell Cycle/DNA Damage; 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 : ≥ 50 mg/mL (172.25 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4451 mL	17.2253 mL	34.4507 mL
	5 mM	0.6890 mL	3.4451 mL	6.8901 mL
	10 mM	0.3445 mL	1.7225 mL	3.4451 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 (8.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.61 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NITD008 is a potent and selective flaviviruse inhibitor which can inhibit Dengue Virus Type 2 (DENV-2) with an EC_{50} of 0.64 μM. NITD008 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

EC50: 0.64 μM (DENV-2)[1]

In Vitro	NITD008 potently inhibits other, including Dengue virus (DENV), West Nile virus, yellow fever virus, and Poissan virus. NITD008 inhibits DENV-2 in a dose-responsive manner, with an EC_{50} value of 0.64 μM; treatment with 9 μM compound reduces viral titer by >104-fold[1]. NITD008 also inhibits a luciferase-reporting replicon of hepatitis C virus (HCV, genotype 1b), a member from the genus Hepacivirus, with an EC_{50} value of 0.11 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	NITD008 is orally bioavailable and has good pharmacokinetic properties. NITD008 exhibits the best pharmacokinetic parameters when formulated using 6 N of HCl (1.5 equimolar amount), 1 N of NaOH (pH adjusted to 3.5), and 100 mM citrate buffer (pH 3.5). Following i.v. injection, NITD008 has a high volume of distribution (3.71 L/kg) and a low systemic clearance (31.11 mL/min per kg), resulting in a long elimination half-life ($t_{1/2}$=4.99 h). After p.o. dosing, NITD008 is rapidly absorbed (time of peak plasma concentration=0.5 h), with a maximal plasma concentration of 3 μM and bioavailability of 48%. Treatment of the mice immediately after viral infection with 1 mg/kg of NITD008 does not reduce mortality, but treatment with 3 mg/kg partially protects and treatment with ≥10 mg/kg completely protects the infected mice from death. NITD008 can suppress peak viremia, decrease cytokine elevation, and prevent death[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For measurement of compound cytotoxicity, Vero cells (10000 cells per well of a 96-well plate) are incubated with various concentrations of NITD008 (3, 6, 12, 25, 50 μM) for 48 h; cell viability is quantified using a MTT assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] The in vivo efficacy of NITD008 is evaluated in a dengue viremia model and a lethal model in mice. Both models use AG129 mice (with knockout IFN-α/β and IFN-γ receptors). DENV-2 strains TSV01and D2S10, respectively, are used in the 2 models and are propagated in C6/36 mosquito cells grown in RPMI-1640 medium with 5% FBS (vol/vol) at 28°C. The evaluation in the lethal model is performed by injecting mice i.v. with 0.2 mL of RPMI-1640 medium containing 3×10^7 pfu/mL DENV-2 strain D2S10; the infected mice are then subjected to different treatment regimens, as indicated in each experiment. NITD008 (1, 3, 10, 25, 50 mg/kg) in 0.2-0.25 mL of formulation solution is administered by p.o. gavage. The mice (6 or 8 mice per group) are monitored twice a day[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Antiviral Res. 2022 Jun;202:105325.
- Eur J Med Chem. 2023 Oct 1:261:115852.
- Viruses. 2022 Jun 5;14(6):1228.
- Viruses. 2022 May 25;14(6):1142.
- Virology. 2023 Nov 11, 109939.

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REFERENCES

[1]. Yin Z, et al. An adenosine nucleoside inhibitor of dengue virus. Proc Natl Acad Sci U S A. 2009 Dec 1;106(48):20435-9.

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