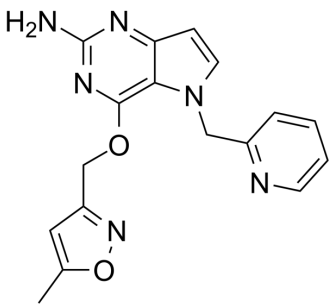
TLR7 agonist 2

Cat. No.:	HY-103039
CAS No.:	1642857-69-9
Molecular Formula:	$C_{17}H_{16}N_6O_2$
Molecular Weight:	336.35
Target:	Toll-like Receptor (TLR)
Pathway:	Immunology/Inflammation
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 : 160 mg/mL (475.69 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.9731 mL	14.8655 mL	29.7309 mL
	5 mM	0.5946 mL	2.9731 mL	5.9462 mL
	10 mM	0.2973 mL	1.4865 mL	2.9731 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

TLR7 agonist 2 is a potent and selective Toll-like Receptor 7 (TLR7) agonist with a LEC of 0.4 μM.

IC_{50} & Target

LEC: 0.4 μM (TLR7)[1]

In Vitro

TLR7 agonist 2 is a potent and selective Toll-like Receptor 7 (TLR7) agonist with a lowest effective concentration (LEC) of 0.4 μM in HEK293 cell. TLR7 agonist 2 is found to be selective for TLR7 over TLR8 with LEC of >100 μM for human TLR8. TLR7 agonist 2 demonstrates low inhibition across five CYP450 isozymes (IC_{50} >10 μM) and is also not a time dependent inhibitor of CYP450 3A4. TLR7 agonist 2 has limited inhibition of the hERG potassium ion channel ^{3}H-dofetilide binding in vitro (IC_{50} >50 μM)[1].

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

In Vivo

TLR7 agonist 2 is found to be rapidly cleared in conjunction with our target profile. Both C_{max} and AUC increase less than dose proportionally between 0.3 and 3 mg/kg and more than dose-proportionally between 3 and 10 mg/kg. TLR7 agonist 2 can induce an antiviral interferon stimulated gene (ISG) response without inducing an IFNα response at a low dose. TLR7 agonist 2 also induces a 2.7 log decrease in serum HBV viral load from 0.3 mg/kg, and a maximum 3.1 log decrease is

observed for doses between 1 and 5 mg/kg[1].

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

PROTOCOL

Cell Assay [1]

The ability of TLR7 agonist 2 to activate human TLR7 and/or TLR8 is assessed by using HEK293 cells. Briefly, HEK293 cells are grown in culture medium (DMEM supplemented with 10% FCS and 2 mM Glutamine). Transfected cells are then detached with Trypsin-EDTA, washed in PBS and resuspended in medium to a density of 1.67×10^5 cells/mL. Thirty microliters of cells are then dispensed into each well in 384-well plates, where 10 µL of TLR7-agonist-1 in 4% DMSO is already present. Following 6 hours incubation at 37°C, 5% CO_2, the luciferase activity is determined by adding 15 µL of Steady Lite Plus substrate to each well and readout performed on a microplate imager. Lowest effective concentrations (LEC) values are determined for TLR7-agonist-1[1].

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

Animal Administration [1]

A mouse in vivo model is used to demonstrate the initial proof of concept to induce endogenous IFNα. Single oral administration of 0.3, 1, 3, and 10 mg/kg doses of TLR7 agonist 2 is given to healthy, female, fasted C57Bl/6 mice. Concentrations of TLR7 agonist 2 and mouse-IFN via ELISA are measured from the plasma and compare to vehicle[1].

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

CUSTOMER VALIDATION

- Research Square Print. 2023 Feb 1.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. McGowan DC, et al. Identification and Optimization of Pyrrolo[3,2-d]pyrimidine Toll-like Receptor 7 (TLR7) Selective Agonists for the Treatment of Hepatitis B. J Med Chem. 2017 Jul 27;60(14):6137-6151.

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