Vesatolimod

Cat. No.: HY-15601

CAS No.: 1228585-88-3

Molecular Formula: $C_{22}H_{30}N_6O_2$

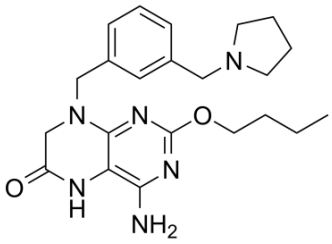
Molecular Weight: 410.51

Target: Toll-like Receptor (TLR); Apoptosis; HBV; HCV; HIV

Pathway: Immunology/Inflammation; Apoptosis; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 16.67 mg/mL (40.61 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4360 mL	12.1800 mL	24.3599 mL
5 mM	0.4872 mL	2.4360 mL	4.8720 mL
10 mM	0.2436 mL	1.2180 mL	2.4360 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: ≥ 1.67 mg/mL (4.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.67 mg/mL (4.07 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (4.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vesatolimod (GS-9620) is a potent, selective and orally active agonist of Toll-Like Receptor (TLR7) with an EC_{50} of 291 nM.

IC_{50} & Target

EC50: 291 nM (TLR7), 9 μM (TLR8)[3]

In Vitro

Vesatolimod (GS-9620) rapidly internalizes into cells and preferentially localizes to and signals from endo-lysosomal compartments. To test this hypothesis, the kinetics of cellular uptake of the compound in Daudi cells using tritiated

	Vesatolimod (^{3}H-GS-9620) is measured. The kinetics of ^{3}H-GS-9620 accumulation is rapid, reaching concentration-dependent steady-state equilibrium in approximately thirty minutes. Measured intracellular concentration of ^{3}H-Vesatolimod is 5-fold higher than the extracellular concentration of ^{3}H-GS-9620 used to treat cells. Increases in intracellular ^{3}H-Vesatolimod concentrations are roughly proportional with increasing concentrations of ^{3}H-GS-9620[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Single oral doses of Vesatolimod (GS-9620) at 0.3 and 1 mg/kg in uninfected chimpanzees demonstrates a dose- and exposure-related induction of serum IFN-α, select cytokines/chemokines, and IFN-stimulated genes (ISG) in the peripheral blood and liver. Following oral administration at 0.3 (n=3), and 1 mg/kg (n=3 and n=4), Vesatolimod (GS-9620) C_{max} is 3.6±3.5, 36.8±34.5, and 55.4±81.0 nM, respectively. Peak serum IFN responses occur at 8 h post-dose. The mean peak levels of induced serum IFN-α are 66 and 479 pg/mL at doses of 0.3 and 1 mg/kg, respectively. Vesatolimod (GS-9620) treatment induces ISG transcripts including ISG15, OAS-1, MX1, IP-10 (CXCL10), and I-TAC (CXCL11) in peripheral blood mononuclear cells (PBMC) at 0.3 mg/kg and in both PBMC and the liver at 1 mg/kg[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Daudi cells are incubated for indicated times with varying concentrations [^{3}H]Vesatolimod (GS-9620) (0.7μCi/mL). Cell associated radioactivity is extracted with ice cold 80% ethanol and measured using liquid scintillation counting. The total amount of Vesatolimod in cells is calculated from a calibration curve for Vesatolimod (GS-9620) mass versus radioactivity. Cell volume is measured[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Chimpanzee[2] Chimpanzees are used. The trial design includes 4 weeks of pre-study evaluation (Day-28, -13 and just prior to first dose) and two cycles of oral Vesatolimod (GS-9620) treatment every other day three times per week for 4 weeks with one cycle at 1 mg/kg, and, after a one week rest, a second cycle at 2 mg/kg. Animals are also intensely monitored for 14 weeks after treatment to assess tolerability and durability of response. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Front Microbiol. 2018 Sep 19;9:2022.
- Antiviral Res. 2018 May;153:39-48.
- Vaccine. 2018 Feb 1;36(6):794-801.
- Drug Test Anal. 2019 Feb;11(2):240-249.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Rebbapragada I, et al. Molecular Determinants of GS-9620-Dependent TLR7 Activation. PLoS One. 2016 Jan 19;11(1):e0146835.

[2]. Lanford RE, et al. GS-9620, an Oral Agonist of Toll-Like Receptor-7, Induces Prolonged Suppression of Hepatitis B Virus in Chronically Infected Chimpanzees. Gastroenterology. 2013 Feb 13. pii: S0016-5085(13)00169-8.

[3]. D Tumas, et al. Preclinical Characterization of GS-9620, A Potent and Selective Oral TLR7 Agonist.

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