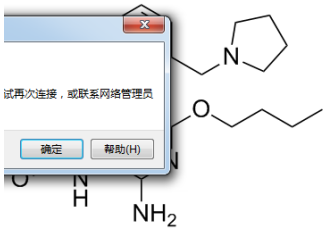
GS-9620

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)
Pathway:	Immunology/Inflammation
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 : 4.8 mg/mL (11.69 mM; Need ultrasonic)

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.

BIOLOGICAL ACTIVITY

Description	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	TLR7[1]
In Vitro	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 GS-9620 (^{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-GS-9620 is 5-fold higher than the extracellular concentration of ^{3}H-GS-9620 used to treat cells. Increases in intracellular ^{3}H-GS-9620 concentrations are roughly proportional with increasing concentrations of ^{3}H-GS-9620[1].
In Vivo	Single oral doses of 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 interferon-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), GS-9620 C_{max} is

	3.6±3.5, 36.8±34.5, and 55.4±81.0 nM, respectively. Peak serum interferon 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. 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].

PROTOCOL

Cell Assay [1]	Daudi cells are incubated for indicated times with varying concentrations [^{3}H]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 GS-9620 in cells is calculated from a calibration curve for 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 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

- **Antiviral Res**. 2018 Feb 6;153:39-48.
- **Front Microbiol**. 2018 Sep 19;9:2022.
- **Vaccine**. 2018 Feb 1;36(6):794-801.
- **Drug Test Anal**. 2018 Aug 20.
- **Nat Biomed Eng**. 2018;2:578-588.

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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.

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