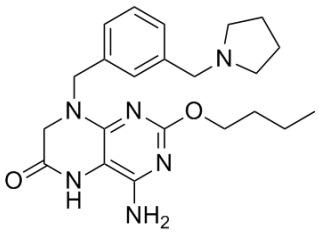
Data Sheet

Product Name:	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
Solubility:	DMSO: 4.8 mg/mL (Need ultrasonic)



BIOLOGICAL ACTIVITY:

GS-9620 is a potent and selective orally active agonist of **Toll-Like Receptor (TLR)7**.
IC50 & 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 (Extracted from published papers and Only for reference)

Cell Assay: GS-9620 is dissolved in DMSO and stored, and then diluted with appropriate medium before use[1]. [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]. **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.

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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