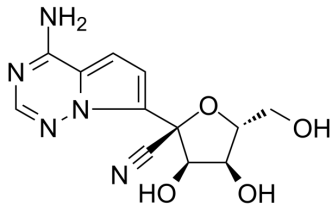
GS-441524

Cat. No.:	HY-103586
CAS No.:	1191237-69-0
Molecular Formula:	$C_{12}H_{13}N_5O_4$
Molecular Weight:	291
Target:	DNA/RNA Synthesis; SARS-CoV
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 : 83.33 mg/mL (286.36 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4364 mL	17.1821 mL	34.3643 mL
	5 mM	0.6873 mL	3.4364 mL	6.8729 mL
	10 mM	0.3436 mL	1.7182 mL	3.4364 mL

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

In Vivo

1. Add each solvent one by one: 5% ethanol, 30% propylene glycol, 45% PEG 400, 20% water (pH 1.5 with HCl)
   Solubility: 10 mg/mL (34.36 mM); Clear solution; Need ultrasonic and adjust pH to 2 with HCl
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.75 mg/mL (9.45 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.15 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.15 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GS-441524, predominant metabolite of Remdesivir and superior to Remdesivir against Covid-19 , shows comparable efficacy in cell-based models of primary human lung and cat cells infected with coronavirus. GS-441524 could strongly inhibits feline infectious peritonitis virus (FIPV), with an EC_{50} of 0.78 μM[1][2][3].

IC_{50} & Target	EC50: 0.78 μM (FIPV)[1].
In Vitro	The cells appear and grow normally at all concentrations of GS-441524 and fail to uptake the fluorescent dye CellTox Green at 24 h. The cytotoxic concentration-50% (CC50) is therefore>100 μM. The effective concentration-50% (EC_{50}) of GS-441524 is calculated to be 0.78 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	All 10 treated cats have a rapid response to treatment and lymphocyte levels and rectal temperatures return to pre-infection levels and levels of the two asymptomatic cats. All ten of the once or twice treated cats have remained normal to date (more than eight months post infection). Injections cause a transient "stinging" reaction in some cats within 10 s of compound administration. Localized and transient pain is evidenced by unusual posturing, licking at the injection site and/or vocalizations that last for approximately 30-60 s after injection. Injection reactions are more pronounced in some animals relative to others and reactions are inconsistent from one injection to the next and decreas over time[1]. Remdesivi (IV injection) in NHP results in GS-441524 being present in serum at concentrations 1000-fold higher than Remdesivir throughout a 7-day treatment course[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay	To determine the toxicity of GS-441524 to CRFK cells n, CRFK cells are treated with 100, 33.3, 11.1, 3.7 or 1.2 μM GS-441524 for 24 h[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Cats[1] The 10 cats that developed disease signs are divided into two groups and treated with either 5 mg/kg (Group A; n=5) or 2 mg/kg (Group B; n=5) GS-441524 SC q24 h starting three days after unequivocal clinical evidence of FIP (days 12-19 post infection). The two cats that do not develop disease signs serve as controls for normal blood lymphocyte counts and rectal temperature[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2021 Nov 5;12(1):6415.
- Nucleic Acids Res. 2021 Jan 8;49(D1):D1113-D1121.
- J Med Virol. 2021 Mar 5.
- Nano Lett. 2023 Oct 25;23(20):9437-9444.
- Biomed Pharmacother. 2022 Nov 22;157:114037.

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REFERENCES

[1]. Murphy BG, et al. The nucleoside analog GS-441524 strongly inhibits feline infectious peritonitis (FIP) virus in tissue culture and experimental cat infection studies. Vet Microbiol. 2018 Jun;219:226-233.

[2]. Katherine Yang, et al. What Do We Know About Remdesivir Drug Interactions? Clin Transl Sci. 2020 May 13;10.1111/cts.12815.

[3]. Victoria C. Yan, et al. Advantages of the Parent Nucleoside GS-441524 over Remdesivir for Covid-19 Treatment. ACS Med. Chem. Lett. 2020.

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