GS-443902 trisodium

Cat. No.: HY-126303C

CAS No.: 1355050-21-3

Molecular Formula: $C_{12}H_{13}N_5Na_3O_{13}P_3$

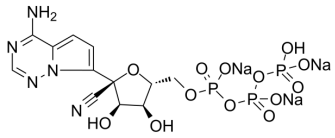
Molecular Weight: 597.15

Target: DNA/RNA Synthesis; SARS-CoV; RSV; HCV; Drug Metabolite

Pathway: Cell Cycle/DNA Damage; Anti-infection; Metabolic Enzyme/Protease

Storage: -80°C, protect from light, stored under nitrogen

* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

H_2O : 33.33 mg/mL (55.82 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.6746 mL	8.3731 mL	16.7462 mL
	5 mM	0.3349 mL	1.6746 mL	3.3492 mL
	10 mM	0.1675 mL	0.8373 mL	1.6746 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (83.73 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GS-443902 trisodium (GS-441524 triphosphate trisodium) is a potent viral RNA-dependent RNA-polymerases (RdRp) inhibitor with IC_{50}s of 1.1 μM, 5 μM for RSV RdRp and HCV RdRp, respectively. GS-443902 trisodium is the active triphosphate metabolite of Remdesivir (GS-5734)[1][2].

IC_{50} & Target

IC50: 1.1 μM (RSV RdRp) and 5 μM (HCV RdRp)[1][2]

In Vitro

In a continuous 72 h incubation of 1 μM Remdesivir (GS-5734), the GS-443902 trisodium (GS-441524 triphosphate trisodium; Remdesivir metabolite trisodium) level is measured at 2, 24, 48 and 72 h, and reaches a C_{max} of 300, 110, and 90 pmol/million cells in macrophages, HMVEC, and HeLa cells lines respectively[1].

GS-443902 trisodium (compound 8a) is a triphosphates (TP) derivative[2].

GS-443902 trisodium (NTP; 0.01, 0.1, 1, 10, 100 μM) inhibits RSV RdRp-catalysed RNA synthesis by incorporating into the nascent viral RNA transcript and causing its premature termination. GS-5734 selectively inhibits EBOV replication by targeting its RdRp and inhibiting viral RNA synthesis following efficient intracellular conversion to GS-443902 sodium[3].

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

In Vivo	Remdesivir (GS-5734; 10 mg kg; i.v.) rapidly distributes into peripheral blood mononuclear cells (PBMCs), and efficient conversion to GS-443902 trisodium (Remdesivir metabolite trisodium; NTP) is apparent within 2 h of dose administration in rhesus monkeys. In PBMCs, GS-443902 trisodium represents the predominant metabolite and is persistent with a $t_{1/2}$ of 14 h and levels required for >50% virus inhibition for 24 hours[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2022 Nov 10;185(23):4347-4360.e17.
- Nat Commun. 2021 Oct 4;12(1):5811.
- Acta Pharm Sin B. 2021 Mar 22.
- Int J Mol Sci. 2022, 23(15), 8302.
- Chem Biol Interact. 2021 Apr 19;109480.

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REFERENCES

[1]. Warren TK, et al. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature. 2016 Mar 17;531(7594):381-5.

[2]. Siegel D, et al. Discovery and Synthesis of a Phosphoramidate Prodrug of a Pyrrolo[2,1-f][triazin-4-amino] Adenine C-Nucleoside (GS-5734) for the Treatment of Ebola and Emerging Viruses. Med Chem. 2017 Mar 9;60(5):1648-1661.

[3]. Cho A, et al. Synthesis and antiviral activity of a series of 1'-substituted 4-aza-7,9-dideazaadenosine C-nucleosides. Bioorg Med Chem Lett. 2012 Apr 15;22(8):2705-7.

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