PSI-7409 tetrasodium

Cat. No.: HY-15745A

CAS No.: 1621884-22-7

Molecular Formula: $C_{10}H_{12}FN_2Na_4O_{14}P_3$

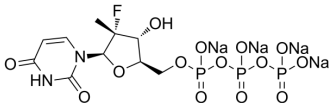
Molecular Weight: 588.09

Target: HCV

Pathway: Anti-infection

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : ≥ 100 mg/mL (170.04 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.7004 mL	8.5021 mL	17.0042 mL
5 mM	0.3401 mL	1.7004 mL	3.4008 mL
10 mM	0.1700 mL	0.8502 mL	1.7004 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (170.04 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

PSI-7409 tetrasodium is an active 5'-triphosphate metabolite of sofosbuvir (PSI-7977), inhibiting HCV NS5B polymerases, with IC_{50}s of 1.6, 2.8, 0.7 and 2.6 μM for GT 1b_Con1, GT 2a_JFH1, GT 3a, and GT 4a NS5B polymerases, respectively.

IC_{50} & Target

IC50: 1.6 μM (GT 1b_Con1), 2.8 μM (GT 2a_JFH1), 0.7 μM (GT 3a), 2.6 μM (GT 4a)[1]

In Vitro

PSI-7409 tetrasodium is an active 5'-triphosphate metabolite, inhibiting HCV NS5B polymerases, with IC_{50}s of 1.6, 2.8, 0.7 and 2.6 μM for GT 1b_Con1, GT 2a_JFH1, GT 3a, and GT 4a NS5B polymerases, respectively. PSI-7409 also weakly inhibits human DNA polymerase α, with an IC_{50} of 550 μM, but shows no inhibition on DNA Pol β and γ[1]. In clone A cells, the levels of PSI-7409 gradually increases to a maximum concentration of about 25 μM over a period of 48 h. PSI-7409 forms at a much faster rate in primary human hepatocytes, achieving a maximum intracellular concentration of ⊠100 μM at 4 h and remains at that concentration for 48 h[2].

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

PROTOCOL

Kinase Assay [1]

Human DNA polymerase α, β, or γ is assayed in a 10-μL reaction mixture containing 50 mM Tris (pH 7.5), 50 mM NaCl, 3 mU/μL activated calf thymus DNA, a 20 μM concentration of all four natural deoxynucleoside triphosphates, 4 μCi [α-^{32}P]dCTP, 5 mM $MgCl_2$, and increasing concentrations of PSI-7409 (up to 1 mM), D-ddFCTP, or aphidicolin. DNA polymerase α, β, or γ is added to the reaction mixture to give final concentrations of 20, 18, and, 50 μg/mL, respectively. All reactions are run at 37°C and quenched at 30 min by mixing with 1 μL of 0.5 M EDTA. The radiolabeled products are quantified. A nonlinear fit is performed to determine the IC_{50}. The activity of RNA polymerase II is determined in a 25-μL in vitro transcription reaction mixture containing 100 ng of cytomegalovirus (CMV) immediate-early promoter DNA, 400 μM ATP, CTP, and UTP, 16 μM GTP, 10 μCi [α-^{32}P]GTP, 3 mM $MgCl_2$, and various concentrations of PSI-7409 (up to 1 mM), 3'-dCTP, or α-amanitin in transcription buffer (20 mM HEPES [pH 7.9], 100 mM KCl, 0.2 mM EDTA, 0.5 mM DTT, and 20% glycerol). All reactions are run at 30°C and quenched at 60 min by mixing with 125 μL of stop solution (0.3 M Tris-HCl [pH 7.4], 0.3 M sodium acetate, 0.5% SDS, 2 mM EDTA, and 3 μg/mL tRNA). The RNA product is purified. The resulting samples contains 12 μL and the same volume of gel loading dye (98% formamide, 10 mM EDTA, 0.1% xylene cyanol, and 0.1% bromophenol blue) is added. The samples are heated at 90°C for 5 min and loaded onto a 6% polyacrylamide sequencing gel. After running, the gel is exposed to a phosphorscreen, and the product is visualized and quantified by using a phosphorimager[1].

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.
- Asian J Pharm Sci. 21 October 2021.
- Antiviral Res. 2020 Mar;175:104708.
- Microbiol Spectr. 2022 Aug 18;e0272922.
- Biochem Biophys Res Commun. 2022 Dec 8;641:50-56.

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REFERENCES

[1]. Lam AM, et al. PSI-7851, a pronucleotide of beta-D-2'-deoxy-2'-fluoro-2'-C-methyluridine monophosphate, is a potent and pan-genotype inhibitor of hepatitis C virus replication. Antimicrob Agents Chemother. 2010 Aug;54(8):3187-96.

[2]. Murakami E, et al. Mechanism of activation of PSI-7851 and its diastereoisomer PSI-7977. J Biol Chem. 2010 Nov 5;285(45):34337-47.

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