Sofosbuvir

Cat. No.: HY-15005

CAS No.: 1190307-88-0

Molecular Formula: $C_{22}H_{29}FN_3O_9P$

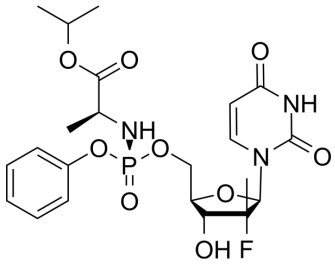
Molecular Weight: 529.45

Target: HCV

Pathway: 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 : 50 mg/mL (94.44 mM; Need ultrasonic)

H_2O : 25 mg/mL (47.22 mM; ultrasonic and warming and heat to 50°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8888 mL	9.4438 mL	18.8875 mL
5 mM	0.3778 mL	1.8888 mL	3.7775 mL
10 mM	0.1889 mL	0.9444 mL	1.8888 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 4.55 mg/mL (8.59 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (3.15 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (3.15 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sofosbuvir (GS-7977) is an HCV RNA replication inhibitor with an EC_{50} of 92 nM[1].

IC_{50} & Target

EC50: 92±5 nM (HCV)[1]

In Vitro

When cathepsin A (CatA) is incubated with PSI-7977 or Sofosbuvir (PSI-7977) for 150 min, ~18-fold more PSI-352707 is formed when Sofosbuvir (PSI-7977) is the substrate compared with PSI-7976. Moreover, the catalytic efficiency for Sofosbuvir (PSI-7977) with CatA is ~30-fold higher than that for PSI-7976[1]. The genotype coverage of Sofosbuvir (PSI-7977) by using GT 1b (Con1)-, 1a (H77)-, and 2a (JFH-1)-derived replicons and GT 1b chimeric replicons containing the NS5B region from the J6 GT 2a isolate and from GT 2b and GT 3a patient isolates is evaluated, Sofosbuvir (PSI-7977) inhibits the replication of these replicons with similar EC_{50}s (between 16 and 48 nM), and is especially active against the chimeric replicon containing the J6 NS5B (EC_{50}=4.7 nM). Sofosbuvir (PSI-7977) inhibits clone A (GT 1b) wild-type and S282T replicons with EC_{90} values of 0.42 and 7.8 μM, respectively[2]. In the clone A replicon assay, Sofosbuvir (PSI-7977) produces anti-HCV activity with EC_{90} values 0.42 μM[3].

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

PROTOCOL

Cell Assay [1]

Clone A cells are seeded into T75 flasks at about 5×10^6 cells/flask in Dulbecco's modified Eagle's medium (DMEM) containing 100 IU/mL Penicillin/100 μg/mL streptomycin and 10% fetal bovine serum. Similarly, human primary hepatocytes are seeded in cell plating medium into T75 flasks at about 5×10^6 cells/flask. After overnight incubation to allow the cells to attach, cells are incubated with 50 μM PSI-7851, PSI-7976, or Sofosbuvir (PSI-7977) in fresh medium for clone A cells or in cell maintenance medium for primary hepatocytes for up to 24 h at 37°C in a 5% CO_2 atmosphere. The same procedures are applied when radiolabeled PSI-7851 is used in the study except that 1×10^6 cells per well are seeded into a 6-well plate, and the cells are incubated with 5 μM [^{3}H]PSI-7851. At selected times, the medium is removed, and the cell layer is washed with cold phosphate-buffered saline (PBS). After trypsinization, cells are counted and centrifuged at 1,200 rpm for 5 min. The cell pellets are suspended in 1 mL of cold 60% methanol and incubated overnight at −20°C. The samples are centrifuged at 14,000 rpm for 5 min, and the supernatants are collected and dried using a SpeedVac concentrator and stored at −20°C until they are analyzed by high performance liquid chromatography (HPLC). Residues are suspended in 100 μL of water, and 50-μL aliquots are injected into HPLC[1].

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CUSTOMER VALIDATION

- Nat Med. 2014 Aug;20(8):927-35.
- Cell. 2023 Nov 22;186(24):5363-5374.e16.
- Cell. 2022 Dec 8;185(25):4801-4810.e13.
- Nat Immunol. 2017 Dec;18(12):1299-1309.
- Gastroenterology. 2015 Feb;148(2):392-402.e13.

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REFERENCES

[1]. 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.

[2]. Lam AM, et al. Genotype and subtype profiling of PSI-7977 as a nucleotide inhibitor of hepatitis C virus. Antimicrob Agents Chemother. 2012 Jun;56(6):3359-68.

[3]. Sofia MJ, et al. Discovery of a β-d-2'-deoxy-2'-α-fluoro-2'-β-C-methyluridine nucleotide prodrug (PSI-7977) for the treatment of hepatitis C virus. J Med Chem. 2010 Oct 14;53(19):7202-18.

[4]. Zhang X, et al. Discovery and evolution of aloperine derivatives as a new family of HCV inhibitors with novel mechanism. Eur J Med Chem. 2018 Jan 1;143:1053-1065.

Caution: Product has not been fully validated for medical applications. For research use only.

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