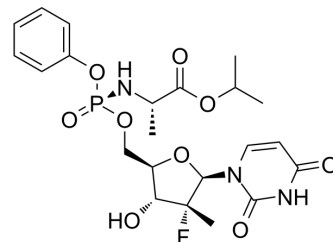


Sofosbuvir

Cat. No.:	HY-15005		
CAS No.:	1190307-88-0		
Molecular Formula:	C ₂₂ H ₂₉ FN ₃ O ₉ P		
Molecular Weight:	529.45		
Target:	HCV		
Pathway:	Anti-infection		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (188.88 mM; Need ultrasonic)
 H₂O : 25 mg/mL (47.22 mM; ultrasonic and warming and heat to 50°C)

Concentration	Mass		
	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

- Add each solvent one by one: PBS
Solubility: 4.55 mg/mL (8.59 mM); Clear solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (4.72 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (4.72 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (4.72 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sofosbuvir (GS-7977) is an HCV RNA replication inhibitor with an EC₅₀ of 92 nM^[1].

IC₅₀ & 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 EC₅₀s (between 16 and 48 nM), and is especially active against the chimeric replicon containing the J6 NS5B (EC₅₀=4.7 nM). Sofosbuvir (PSI-7977) inhibits clone A (GT 1b) wild-type and S282T replicons with EC₉₀ values of 0.42 and 7.8 μM, respectively^[2]. In the clone A replicon assay, Sofosbuvir (PSI-7977) produces anti-HCV activity with EC₉₀ 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 5×10⁶ 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 5×10⁶ 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% CO₂ atmosphere. The same procedures are applied when radiolabeled PSI-7851 is used in the study except that 1×10⁶ cells per well are seeded into a 6-well plate, and the cells are incubated with 5 μM [³H]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.
- Nat Immunol. 2017 Dec;18(12):1299-1309.
- Gastroenterology. 2015 Feb;148(2):392-402.e13.
- Nat Microbiol. 2019 Jul;4(7):1096-1104.
- Nucleic Acids Res. 2019 Jul 9;47(12):6411-6424.

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- [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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