Asunaprevir

Cat. No.: HY-14434

CAS No.: 630420-16-5

Molecular Formula: $C_{35}H_{46}ClN_5O_9S$

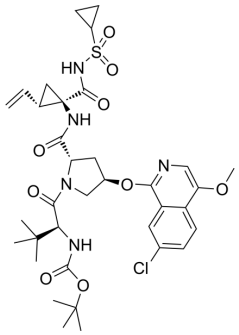
Molecular Weight: 748.29

Target: HCV; HCV Protease; SARS-CoV

Pathway: Anti-infection; Metabolic Enzyme/Protease

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 : ≥ 100 mg/mL (133.64 mM)

Ethanol : 20 mg/mL (26.73 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.3364 mL	6.6819 mL	13.3638 mL
5 mM	0.2673 mL	1.3364 mL	2.6728 mL
10 mM	0.1336 mL	0.6682 mL	1.3364 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (3.34 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.34 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.34 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (3.34 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2 mg/mL (2.67 mM); Clear solution; Need ultrasonic
6. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 2 mg/mL (2.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Asunaprevir (BMS-650032) is a potent and orally bioavailable hepatitis C virus (HCV) NS3 protease inhibitor, with IC_{50} of 0.2 nM-3.5 nM[1]. Asunaprevir inhibits SARS-CoV-2 $3CL^{pro}$ activity[5].
IC_{50} & Target	IC50: 0.2 nM-3.5 nM (HCV NS3 protease)
In Vitro	In multiple experiments, populations of resistant colonies are markedly reduced when cells are treated with a combination of DCV and Asunaprevir[1]. Asunaprevir (ASV) inhibits the NS3 proteolytic activity of genotype 1a (H77 strain) and genotype 1b (J4L6S strain), with IC_{50}s of 0.7 and 0.3 nM, respectively. The EC_{50}s of ASV against replicons encoding the NS3 protease domains representing genotypes 1a, 1b, and 4a, range from 1.2 to 4.0 nM[2]. Replicon cells are maintained under selective pressure with asunaprevir at concentrations of 10 and 30 times the EC_{50} values (50 or 150 nM final concentrations, respectively). For genotype 1b resistance selection, replicon cells are maintained in the presence of asunaprevir at 10 or 30 times the EC_{50} values (30 or 90 nM final concentrations, respectively)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Asunaprevir (ASV, 3-15 mg/kg, p.o.) displays a hepatotropic disposition (liver-to-plasma ratios ranging from 40- to 359-fold across species) in several animal species. Twenty-four hours postdose, liver exposures across all species tested are ≥110-fold above the inhibitor EC_{50} observed with HCV genotype-1 replicons[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cytotoxicity is determined by incubating cells (3,000 to 10,000 cells/well) with serially diluted test compounds or DMSO for 5 days (MT-2 cells) or 4 days (all other cell types). Cell viability is quantitated using an MTS assay for MT-2 or a Cell-Titer Blue reagent assay for HEK-293, HuH-7, HepG2, and MRC5 cells, and 50% cytotoxic concentrations (CC_{50}s) are calculated. For the HCV and BVDV replicon assays, CC_{50}s are determined from the same wells that are later used to determine EC_{50}s. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice (n=9 per group; overnight fast) receive Asunaprevir (ASV) by oral gavage (5 mg/kg; vehicle of PEG-400-ethanol, 9:1). Blood samples (-0.2 mL) are obtained by retro-orbital bleeding at 0.25, 0.5, 1, 3, 6, 8, and 24 h after dosing. Within each group, three animals are bled at 0.25, 3, and 24 h, three at 0.5 and 6 h, and three at 1 and 8 h, resulting in a composite pharmacokinetic profile. Livers and brains are also removed from mice at the terminal sampling points. Rats (n=3 per group; overnight fast) receive ASV (amorphous free acid) by oral gavage (3, 5, 10, and 15 mg/kg) in PEG-400-ethanol (9:1). Serial blood samples (-0.3 mL) are obtained from the jugular vein predosing (0 h) and at 0.25, 0.5, 0.75, 1, 2, 4, 6, 8, 24, and 48 h postdosing. To assess tissue exposure, rats are orally administered ASV (5 or 15 mg/kg, same vehicle as above), and blood, liver, and heart samples from two rats/group are obtained at 0.17, 0.5, 1, 2, 4, 6, 8, 24, 48, and 72 h after dosing. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2020 Oct;586(7829):407-411.
- Cell. 2019 Aug 22;178(5):1145-1158.e20.
- Nat Methods. 2018 Jul;15(7):519-522.
- Signal Transduct Target Ther. 2021 May 29;6(1):212.
- Nat Neurosci. 2020 Feb;23(2):281-292.

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REFERENCES

[1]. Pelosi LA, et al. Effect on HCV Replication by Combinations of Direct Acting Antivirals Including NS5A Inhibitor BMS-790052. Antimicrob Agents Chemother. 2012 Jul 30.

[2]. McPhee F, et al. Preclinical Profile and Characterization of the Hepatitis C Virus NS3 Protease Inhibitor Asunaprevir (BMS-650032).Antimicrob Agents Chemother. 2012 Aug 6.

[3]. McPhee F, et al. Resistance analysis of the hepatitis C virus NS3 protease inhibitor asunaprevir.Antimicrob Agents Chemother. 2012 Jul;56(7):3670-81.

[4]. Pasquinelli C, et al. Single- and multiple-ascending-dose studies of the NS3 protease inhibitor asunaprevir in subjects with or without chronic hepatitis C. Antimicrob Agents Chemother. 2012 Apr;56(4):1838-44.

[5]. Qi Sun, et al. Bardoxolone and bardoxolone methyl, two Nrf2 activators in clinical trials, inhibit SARS-CoV-2 replication and its 3C-like protease. Signal Transduct Target Ther. 2021 May 29;6(1):212.

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