Proteins

Product Data Sheet

AB-423

Cat. No.: HY-112142 CAS No.: 1572510-80-5 Molecular Formula: $C_{17}H_{17}F_3N_2O_3S$

Molecular Weight: 386.39 Target: HBV

Pathway: Anti-infection

Storage: Powder -20°C 3 years

 $4^{\circ}C$ 2 years

In solvent -80°C 2 years

> -20°C 1 year

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SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (258.81 mM)

* "≥" means soluble, but saturation unknown.

Solve Concentration Preparing 1 mM Stock Solutions 5 mM	Solvent Mass Concentration	1 mg	5 mg	10 mg
	1 mM	2.5881 mL	12.9403 mL	25.8806 mL
	5 mM	0.5176 mL	2.5881 mL	5.1761 mL
	10 mM	0.2588 mL	1.2940 mL	2.5881 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 (6.47 mM); Clear solution
- 2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (6.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	AB-423 is an inhibitor of HBV capsid assembly, and potent inhibits HBV replication with EC $_{50}$ /EC $_{90}$ of 0.08-0.27 μ M/0.33-1.32 μ M in cells.
IC ₅₀ & Target	$HBVcapsid^{[1]}$
In Vitro	AB-423 is an inhibitor of HBV capsid assembly. AB-423 shows inhibitory effect on rcDNA production in AML12-HBV10 and HepDE19 cells with EC $_{50}$ s of -0.260 μ M. AB-423 also suppresses cccDNA formation-dependent HBeAg production in the HepBHAe82 assay with an EC $_{50}$ of 0.267 μ M and inhibits HBV DNA levels in culture supernatants of HepG 2.2.15 cells with an EC $_{50}$ of 0.134 μ M. However, AB-423 has no cytotoxicity in any of the three cell lines $^{[1]}$.

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

In Vivo

AB-423 (30 and 100 mg/kg, p.o. bid) blocks HBV replication in a mouse model of HBV. AB-423 (100 mg/kg, p.o. bid) with entecavir (ETV, 100 ng/mg, qd, p.o.) or 0.1 mg/kg dose of ARB-1467 potently inhibits serum HBV DNA in an HDI model of HBV in immunodeficient NOD-SCID mice^[1].

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PROTOCOL

Cell Assay [1]

To test the compound combinations, HepBHAe82 (50,000 cells/well) are plated in 96-well tissue-culture treated microtiter plates in DMEM/F12 medium supplemented with 10% fetal bovine serum, 1% penicillin-streptomycin and tetracycline (1 μ g/mL), and incubated in a humidified incubator at 37°C and 5% CO₂ overnight. On the next day, the cells are switched to fresh medium and treated with inhibitor A and inhibitor B, at concentration range in the vicinity of their respective EC₅₀ values. The inhibitors are either diluted in 100% DMSO (ETV, TDF and AB-423) or growth medium (ARB-1467 and ARB-1740) and the final DMSO concentration in the assay is \leq 0.5%. The two inhibitors are tested both singly as well as in combinations determine their effects on inhibition of rcDNA production. The final DMSO concentration in the assay is 0.5%. The plates are incubated for 9 days in a humidified incubator at 37°C and 5% CO₂. Following a 9 day-incubation, medium is removed, and cells are subjected to RNA extraction to measure the cccDNA-dependent precore mRNA level^[1].

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Animal Administration [1]

Mice^[1]

Prior to start of treatment, 10 micrograms of the plasmid pHBV1.3 is administered to NOD.CB17-Prkdcscid/J mice via hydrodynamic injection (HDI; rapid high volume injection into the tail vein; n = 6 to 8 animals per group). This plasmid carries a 1.3-fold overlength copy of a HBV genotype D genome which, when expressed, generates hepatitis B viral particles and other HBV products. AB-423 is administered via oral gavage at 30 or 100 mg/kg twice-daily for 7 consecutive days, starting on Day 0. Entecavir (ETV) at 100 ng/kg once-daily for 7 consecutive days, starting on Day 0. ARB-1467 is administered as a single intravenous bolus tail vein injection at 0.1 mg/kg on Day 0. Blood is collected on Days 0 (pre-dose), 4 and 7 for HBV biomarker analysis. Serum HBV DNA concentration in mice is measured from total extracted DNA using a quantitative PCR assay using primer/probe sequences^[1].

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

CUSTOMER VALIDATION

- Nat Commun. 2021 Apr 9;12(1):2114.
- · Virus Res. 2019 Oct 2;271:197677.
- Viruses. 2023 May 18, 15(5), 1195.

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REFERENCES

[1]. Mani N, et al. Preclinical profile of AB-423, an inhibitor of Hepatitis B virus pgRNA encapsidation. Antimicrob Agents Chemother. 2018 Mar 19.

 $\label{lem:caution:Product} \textbf{Caution: Product has not been fully validated for medical applications. For research use only.}$

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Page 3 of 3 www.MedChemExpress.com