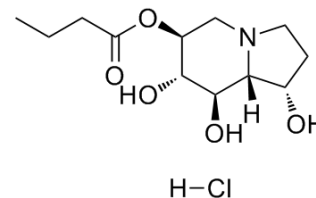


Celgosivir hydrochloride

Cat. No.:	HY-16134A		
CAS No.:	141117-12-6		
Molecular Formula:	C ₁₂ H ₂₂ ClNO ₅		
Molecular Weight:	295.76		
Target:	Glucosidase; HCV; HIV		
Pathway:	Metabolic Enzyme/Protease; 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

H₂O : ≥ 100 mg/mL (338.11 mM)
 DMSO : 100 mg/mL (338.11 mM; Need ultrasonic)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	3.3811 mL	16.9056 mL	33.8112 mL
	5 mM	0.6762 mL	3.3811 mL	6.7622 mL
	10 mM	0.3381 mL	1.6906 mL	3.3811 mL

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

In Vivo

- Add each solvent one by one: PBS
Solubility: 100 mg/mL (338.11 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 (8.45 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (8.45 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (8.45 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Celgosivir hydrochloride (MBI 3253 hydrochloride; MDL 28574 hydrochloride; MX3253 hydrochloride) is an α-glucosidase I inhibitor; inhibits bovine viral diarrhoea virus (BVDV) with an IC₅₀ of 1.27 μM in in vitro assay.

IC₅₀ & Target	IC ₅₀ : 1.27 μM (α-glucosidase I) ^[1]
In Vitro	<p>Celgosivir is more effective (IC₅₀=20 μM) than the parent molecule (IC₅₀=254 μM) at causing the accumulation of glucosylated oligosaccharides in HIV-infected cells by inhibition of glycoprotein processing. Celgosivir exhibits potent antiviral activity against HIV-1 with an IC₅₀ of 2.0±2.3 μM^[1]. Bovine viral diarrhoea virus (BVDV) is a closely related virus of hepatitis C virus (HCV). Celgosivir inhibits BVDV with IC₅₀ values of 16 and 47 μM in plaque assay and cytopathic effect assay, respectively^[2]. Celgosivir inhibits DENV2 replication with an EC₅₀ of 0.2 μM. The EC₅₀ values against DENV1, 3 and 4 are less than 0.7 μM^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>Celgosivir fully protects AG129 mice from lethal infection with a mouse adapted dengue virus at a dose of 50 mg/kg twice daily (BID) for 5 days and is effective even after 48 h delayed treatment. The protection by celgosivir is dose- and schedule-dependent and that a twice-a-day regimen of 50, 25 or 10 mg/kg is more protective than a single daily dose of 100 mg/kg. Pharmacokinetics studies of celgosivir in mice shows that it rapidly metabolizes to castanospermine^[4]. During primary infection with a mouse-adapted DENV strain S221, mice shows increased viremia on day 3, yet 80% survived day 10 with virus completely cleared by day 8^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Cell Assay ^[3]	<p>The cytotoxicity of Celgosivir is measured by the Cell titer-Glo Luminescent cell viability assay. The luminescence signals for cells treated with the test compounds are compared to those for cells treated with the maximum tolerated DMSO to determine the 50% cytotoxic concentration^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[3]	<p>Mice: To model ADE, mice are injected i.p. with 20 μg /mouse of mouse monoclonal antibody against DENV E protein one day prior to infection. For treatment during infection, celgosivir (50 mg/kg) is injected i.p. twice daily for 5 days, starting from day 0, 1 or 2. Blood is collected at days 1, 3 and 7 by submandibular bleeding. Survival of mice is followed until day 10 and survival curves are plotted^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

REFERENCES

- [1]. Taylor DL, et al. Inhibition of alpha-glucosidase I of the glycoprotein-processing enzymes by 6-O-butanoylcastanospermine (MDL 28,574) and its consequences in human immunodeficiency virus-infected T cells. *Antimicrob Agents Chemother.* 1994 Aug;38(8):1780-7.
- [2]. Whitby K, et al. Action of celgosivir (6 O-butanoyl castanospermine) against the pestivirus BVDV: implications for the treatment of hepatitis C. *Antivir Chem Chemother.* 2004 May;15(3):141-51.
- [3]. Watanabe S, et al. Dose- and schedule-dependent protective efficacy of celgosivir in a lethal mouse model for dengue virus infection informs dosing regimen for a proof of concept clinical trial. *Antiviral Res.* 2012 Oct;96(1):32-5.
- [4]. Rathore AP, et al. Celgosivir treatment misfolds dengue virus NS1 protein, induces cellular pro-survival genes and protects against lethal challenge mouse model. *Antiviral Res.* 2011 Dec;92(3):453-60.

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

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