# Celgosivir

**Cat. No.:** HY-16134

**CAS No.:** 121104-96-9

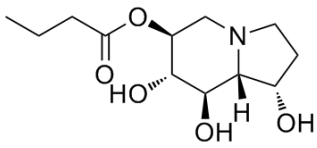
**Molecular Formula:** $C_{12}H_{21}NO_5$

**Molecular Weight:** 259.3

**Target:** Glucosidase; HCV; HIV

**Pathway:** Metabolic Enzyme/Protease; Anti-infection

**Storage:** Please store the product under the recommended conditions in the Certificate of Analysis.



## BIOLOGICAL ACTIVITY

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| **Description** | Celgosivir (MBI 3253; MDL 28574; MX3253) is an α-glucosidase I inhibitor; inhibits bovine viral diarrhoea virus (BVDV) with an $IC_{50}$ of 1.27 μM in in vitro assay. |
| **$IC_{50}$ & Target** | IC50: 1.27 μM (α-glucosidase I)[1] |
| **In Vitro** | Celgosivir is more effective ($IC_{50}$=20 μM) than the parent molecule ($IC_{50}$=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 $IC_{50}$ 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 $IC_{50}$ values of 16 and 47 μM in plaque assay and cytopathic effect assay, respectively[2]. Celgosivir inhibits DENV2 replication with an $EC_{50}$ of 0.2 μM. The $EC_{50}$ values against DENV1, 3 and 4 are less than 0.7 μM[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | 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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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| **Cell Assay** [3] | 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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [3] | 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].

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

## 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 andprotects against lethal challenge mouse model. Antiviral Res. 2011 Dec;92(3):453-60.





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