Oseltamivir acid

Cat. No.: HY-13318

CAS No.: 187227-45-8

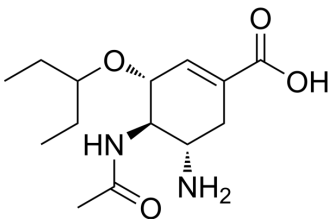
Molecular Formula: $C_{14}H_{24}N_2O_4$

Molecular Weight: 284.35

Target: Influenza Virus; Drug Metabolite

Pathway: Anti-infection; Metabolic Enzyme/Protease

Storage: 4°C, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 230 mg/mL (808.86 mM)

H_2O : 100 mg/mL (351.68 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.5168 mL	17.5840 mL	35.1679 mL
	5 mM	0.7034 mL	3.5168 mL	7.0336 mL
	10 mM	0.3517 mL	1.7584 mL	3.5168 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (351.68 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5.75 mg/mL (20.22 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5.75 mg/mL (20.22 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5.75 mg/mL (20.22 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Oseltamivir acid (GS 4071), the active metabolite of Oseltamivir phosphate, is an orally bioavailable, potent and selective inhibitor of influenza virus neuraminidase (IC_{50}=2 nM) with activity against both influenza A and B viruses[1][2].

IC_{50} & Target

IC50: 2 nM (influenza virus neuraminidase)

In Vitro	Oseltamivir acid inhibits virus replication in vitro and in vivo. Influenza B and A/H1N1 viruses appeare to be sensitive to Oseltamivir (mean B IC_{50} value: 13 nM; mean H1N1 IC_{50} value: 1.34 nM), while A/H1N2 and A/H3N2 viruses are more sensitive to Oseltamivir (mean H3N2 IC_{50} value: 0.67 nM; mean H1N2 IC_{50} value: 0.9 nM)[3]. ?In neuraminidases inhibition assays with influenza A viruses, the IC_{50} of RWJ-270201 (approximately 0.34 nM) is comparable to that of Oseltamivir carboxylate (0.45 nM) For influenza B virus isolates, the IC_{50} of RWJ-270201 (1.36 nM) is comparable to that of Zanamivir (2.7 nM) and less than that of Oseltamivir carboxylate (8.5 nM)[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oseltamivir acid (0.1, 1, or 10 mg/kg/day, twice daily by oral gavage) produces a dose-dependent antiviral effect against Vietnam/1203/04 (VN1203/04) virus. The 5-day regimen at 10 mg/kg/day protects 50% of mice; deaths in this treatment group are delayed and indicated the replication of residual virus after the completion of treatment. Dosages of 1 and 10 mg/kg/day significantly reduced virus titers in organs and provided 60% and 80% survival rates, respectively[5]. ? MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3][4]	Mice[3] Female 6-week-old BALB/c mice are anesthetized with isofluorane and intranasally inoculated with 50 µL of 10-fold serial dilutions of VN1203/04 virus in PBS. The mouse lethal dose (MLD_{50}) is calculated after a 16-day observation period. Oseltamivir is administered by oral gavage twice daily for 5 or 8 days to groups of 10 mice at dosages of 0.1, 1, and 10 mg/kg/day. Control (infected but untreated) mice received sterile PBS (placebo) on the same schedule. Four hours after the first dose of Oseltamivir, the mice are inoculated intranasally with 5 MLD_{50} of VN1203/04 virus in 50 µL of PBS. Survival and weight change are observed for 24 days. Virus titers in the mouse organs are determined on days 3, 6, and 9 after inoculation. Three mice from each experimental and placebo group are killed, and the lungs and brains are removed. The organs are homogenized and suspended in 1 mL of PBS. The cellular debris is cleared by centrifugation at 2000 g for 5 min. The limit of virus detection is 0.75 $\log_{10}$ EID_{50}. For calculation of the mean, samples with a virus titer <0.75 $\log_{10}$ EID_{50}/mL are assigned a value of 0. Virus titers in each organ are calculated by use of the method of Reed and Muench and are expressed as mean $\log_{10}$ EID_{50}/mL±SE. Rats[4] Several studies are performed to characterize the pharmacokinetics of Oseltamivir and OC in the plasma, cerebrospinal fluid (CSF), and brain of Sprague-Dawley rats following single-dose bolus administration of Oseltamivir (intravenous [i.v.] and oral) and OC (i.v.). In the i.v. studies, nonfasted adult rats (two groups of 35 animals for each test substance) received a dose of 30 mg/kg body weight of either Oseltamivir or Oseltamivir carboxylate (OC) in aqueous solution with sodium chloride (0.9%; pH 4.0) via slow injection into the tail vein over 20 to 30 s. In both i.v. studies, pharmacokinetic sampling took place at 5 min and at 0.25, 0.5, 1, 2, 4, and 8 h postdose (four or five rats/time point). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2023 Jun;618(7965):590-597.
- ACS Nano. 2014 Jun 24;8(6):5468-77.
- Small. 2020 Apr 24:e2000556.
- J Med Virol. 2023 Jul;95(7):e28968.
- J Med Virol. 2020 Jul 4.

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REFERENCES

[1]. Li W, et al. Identification of GS 4104 as an orally bioavailable prodrug of the influenza virus neuraminidase inhibitor GS 4071. Antimicrob Agents Chemother. 1998 Mar;42(3):647-53.

[2]. Ghosh GC, et al. Oseltamivir carboxylate, the active metabolite of oseltamivir phosphate (Tamiflu), detected in sewage discharge and river water in Japan. Environ Health Perspect. 2010 Jan;118(1):103-7.

[3]. Ferraris O, et al. Sensitivity of influenza viruses to zanamivir and oseltamivir: a study performed on viruses circulating in France prior to the introduction of neuraminidase inhibitors in clinical practice. Antiviral Res. 2005 Oct;68(1):43-8.

[4]. Gubareva LV, et al. Comparison of the activities of zanamivir, oseltamivir, and RWJ-270201 against clinical isolates of influenza virus and neuraminidase inhibitor-resistant variants.Antimicrob Agents Chemother. 2001 Dec;45(12):3403-8.

[5]. Yen HL, et al. Virulence may determine the necessary duration and dosage of oseltamivir treatment for highly pathogenic A/Vietnam/1203/04 influenza virus in mice. J Infect Dis. 2005 Aug 15;192(4):665-72.

[6]. Hoffmann G, et al. Nonclinical pharmacokinetics of oseltamivir and oseltamivir carboxylate in the central nervous system. Antimicrob Agents Chemother. 2009 Nov;53(11):4753-61.

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