Manidipine dihydrochloride

Cat. No.: HY-17403

CAS No.: 89226-75-5

Molecular Formula: $C_{35}H_{40}Cl_2N_4O_6$

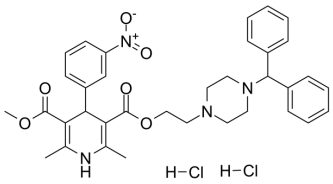
Molecular Weight: 683.62

Target: Calcium Channel; NF-κB

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling; NF-κB

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (73.14 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Concentration \ Solvent / Mass	1 mg	5 mg	10 mg
1 mM	1.4628 mL	7.3140 mL	14.6280 mL
5 mM	0.2926 mL	1.4628 mL	2.9256 mL
10 mM	0.1463 mL	0.7314 mL	1.4628 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 (3.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Manidipine dihydrochloride is a third-generation, lipophilic, orally active and highly vasoselective calcium channel antagonist (IC_{50} = 2.6 nM in guinea-pig ventricular cells) and acts as an antihypertensive agent. Manidipine effectively reduces blood pressure as well as improving insulin sensitivity, renal protection, and antiatherosclerotic activity. Manidipine also exerts anti-inflammatory activity mediated by NF-κB and antiviral activity against many flavivirus and negative-strand RNA viruses through the inhibition of calcium channel. Manidipine is widely applied to research of cardiovascular, metabolic disease and infection[1][2][3][4][5][6].

IC_{50} & Target

T-type calcium channel

In Vitro

Manidipine dihydrochloride (1 μM, 42 h) suppresses IL-6 secretion in lipoproteins-induced HUVEC[3].

Manidipine dihydrochloride (1 μM, 16 h) suppresses IL-6 secretion in 10 ng/mL IL-1, 10 ng/mL IFN-γ, and 25 ng/mL TNFα treated THP-I [3].
Manidipine dihydrochloride (20 mg/mL, 48/20 h) inhibits propagation/genome replication of SFTSV (a negative-strand RNA virus) in SW13 cells[4].
Manidipine dihydrochloride (20 mg/mL, 48 h) interferes SFTSV N-induced inclusion body formation in Huh-7 cells[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Manidipine dihydrochloride (10 mg/kg, i.p., b.i.d. at day 4, day 5) prolongs survival in SFTSV-infected mice[4].
Manidipine dihydrochloride (25 mg/kg, i.p., b.i.d. for 2 d, then daily for 19 d) protects mice from JEV infection[5].
Manidipine dihydrochloride (3 mg/kg, i.g., once per day, 7 d) prevents isoproterenol-induced left ventricular hypertrophy in rats[7].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	IFNAR$^{-/-}$ mice[4]
Dosage:	10 mg/kg
Administration:	Intraperitoneal injection (i.p.), b.i.d. at day 4, day 5
Result:	Exhibited a modest, but statistically significant increase in the survival rate of lethal animal model with SFTSV infection, significantly reduced viral titers in the spleen and kidney.

Animal Model:	Adult female BALB/c mice (age, 4 weeks) [5]
Dosage:	25 mg/kg
Administration:	Intraperitoneal injection (i.p.), b.i.d. for 2 days, then daily for 19 days
Result:	Reduced the mortality rate from 73% to 20%, significantly reduced the viral load in infected mice while remarkably alleviated brain damage phenomena. Had little effect on peripheral JEV infection, which indicated that manidipine protected the mice against JEV-induced lethality by decreasing the viral load in the brain.

Animal Model:	8-week-old male Wistar rats[7]
Dosage:	3 mg/kg
Administration:	Intragastric gavage (i.g.), once per day for 7 d
Result:	Prevented isoproterenol-induced left ventricular hypertrophy (2.26±0.02 g/kg; p<0.01) as isoproterenol increased left ventricular weight (2.40±0.04 g/kg; p<0.01). Inhibited expression of mRNA of ANP (0.9-fold of the control value; p<0.01), collagen types I (1.1-fold; p<0.01) and type III (1.6-fold; p<0.01), and fibronectin (1.1-fold; p<0.01).

REFERENCES

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[4]. Urata S, et al. Calcium Influx Regulates the Replication of Several Negative-Strand RNA Viruses Including Severe Fever with Thrombocytopenia Syndrome Virus. J Virol.

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[7]. Yoshiyama M, et al. Effect of manidipine hydrochloride, a calcium antagonist, on isoproterenol-induced left ventricular hypertrophy. Pharmacol Res. 2010Jpn Circ J. 1998;62(1):47-52.

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