Mibefradil dihydrochloride

Cat. No.: HY-15553A

CAS No.: 116666-63-8

Molecular Formula: $C_{29}H_{40}Cl_2FN_3O_3$

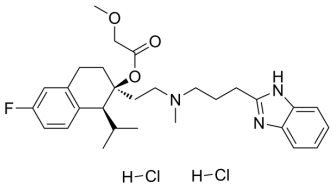
Molecular Weight: 568.55

Target: Calcium Channel

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: -20°C, stored under nitrogen

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



SOLVENT & SOLUBILITY

In Vitro

H_2O : 150 mg/mL (263.83 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7589 mL	8.7943 mL	17.5886 mL
	5 mM	0.3518 mL	1.7589 mL	3.5177 mL
	10 mM	0.1759 mL	0.8794 mL	1.7589 mL

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

BIOLOGICAL ACTIVITY

Description

Mibefradil dihydrochloride (Ro 40-5967 dihydrochloride) is a calcium channel blocker with moderate selectivity for T-type Ca^{2+} channels (IC_{50}s of 2.7 μM and 18.6 μM for T-type and L-type currents, respectively)[1].

IC_{50} & Target	L-type calcium channel	T-type calcium channel

In Vitro

Mibefradil dihydrochloride inhibits reversibly the T- and L-type currents with IC_{50} values of 2.7 and 18.6 μM, respectively. The inhibition of the L-type current is voltage-dependent, whereas that of the T-type current is not. Ro 40-5967 blocks T-type current already at a holding potential of -100 mV[1] At a higher concentration (20 μM), Mibefradil reduces the amplitude of excitatory junction potentials (by 37±10 %), slows the rate of repolarisation (by 44±16 %) and causes a significant membrane potential depolarisation (from 83±1 mV to 71±5 mV). At a higher Mibefradil concentration (20 μM) there is significant membrane potential depolarisation and a slowing of repolarisation. These actions of Mibefradil are consistent with K^+ channel inhibition, which has been shown to occur in human myoblasts and other cells[2].

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

In Vivo

The hearing thresholds of the 24-26 week old C57BL/6J mice differ following the 4-week treatment period. The hearing threshold at 24 kHz is significantly decreased in the Mibefradil-treated and benidipine-treated groups compared with the saline-treated group ($P<0.05$)[3]. Compared with the saline-treated group, rats receiving Mibefradil or NSC 64013 show

significant lower $Ca_V3.2$ expression in the spinal cord and DRG[4].

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

PROTOCOL

Animal Administration [3][4]

Mice[3]

A total of 30 male C57BL/6J mice (age, 6-8 weeks) are randomized into three groups for the detection of three calcium channel receptor subunits α1G, α1H and α1I, using reverse transcription-quantitative polymerase chain reaction (RT-qPCR). In addition, a further 30 C57BL/6J male mice (age, 24-26 weeks) are allocated at random into three treatment groups: Saline, Mibefradil and benidipine. Each group is subjected to auditory brainstem recording (ABR) and distortion product otoacoustic emission (DPOAE) tests following treatment. Mibefradil and benidipine are dissolved in physiological saline solution. A preliminary experiment led to the selection of dosages of 30 mg/kg/day Mibefradil and 10 mg/kg/day Benidipine. The drugs are administered to the mice by gavage for four consecutive weeks.

Rats[4]

Male Sprague-Dawley rats (200-250 g) are used for right L5/6 SNL to induce neuropathic pain. Intrathecal infusion of saline or TCC blockers [Mibefradil (0.7 μg/h) or NSC 64013 (60 μg/h)] is started after surgery for 7 days. Fluorescent immunohistochemistry and Western blotting are used to determine the expression pattern and protein level of $Ca_V3.2$. Hematoxylin-eosin and toluidine blue staining are used to evaluate the neurotoxicity of tested agents.

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

CUSTOMER VALIDATION

- Br J Pharmacol. 2021 Jan;178(2):346-362.
- Front Pharmacol. 2022 Feb 23;13:816133.
- Front Pharmacol. 23 February 2022.
- J Cell Physiol. 2021 Mar 11.
- Eur J Pharmacol. 2021 Feb 5;892:173782.

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REFERENCES

[1]. Mehrke G, et al. The Ca(++)-channel blocker Ro 40-5967 blocks differently T-type and L-type Ca++ channels. J Pharmacol Exp Ther. 1994 Dec;271(3):1483-8.

[2]. Brain KL, et al. The sources and sequestration of Ca(2+) contributing to neuroeffector Ca(2+) transients in the mouse vas deferens. J Physiol. 2003 Dec 1;553(Pt 2):627-35.

[3]. Yu YF, et al. Protection of the cochlear hair cells in adult C57BL/6J mice by T-type calcium channel blockers. Exp Ther Med. 2016 Mar;11(3):1039-1044.

[4]. Shiue SJ, et al. Chronic intrathecal infusion of T-type calcium channel blockers attenuates CaV3.2 upregulation in nerve-ligated rats. Acta Anaesthesiol Taiwan. 2016 Oct 17. pii: S1875-4597(16)30071-6.

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