



# SZABO SCANDIC

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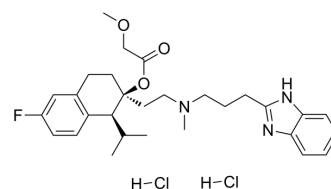
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## Mibefradil dihydrochloride

|                    |  |
|--------------------|--|
| Cat. No.:          | HY-15553A  |
| CAS No.:           | 116666-63-8  |
| Molecular Formula: | C <sub>29</sub> H <sub>40</sub> Cl <sub>2</sub> FN <sub>3</sub> O <sub>3</sub>                         |
| Molecular Weight:  | 568.55   |
| Target:            | Calcium Channel  |
| Pathway:           | Membrane Transporter/Ion Channel; Neuronal Signaling   |
| Storage:           | -20°C, stored under nitrogen<br>* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen) |



### SOLVENT & SOLUBILITY

In Vitro H<sub>2</sub>O : 150 mg/mL (263.83 mM; Need ultrasonic)

| Solvent                   | Mass Concentration | Mass      |           |            |
|---------------------------|--------------------|-----------|-----------|------------|
|                           |                    | 1 mg      | 5 mg      | 10 mg      |
| Preparing Stock Solutions | 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<sup>2+</sup> channels (IC<sub>50</sub>s of 2.7 μM and 18.6 μM for T-type and L-type currents, respectively)<sup>[1]</sup>.

**IC<sub>50</sub> & Target** L-type calcium channel T-type calcium channel

**In Vitro** Mibefradil dihydrochloride inhibits reversibly the T- and L-type currents with IC<sub>50</sub> 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<sup>[1]</sup>. 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<sup>+</sup> channel inhibition, which has been shown to occur in human myoblasts and other cells<sup>[2]</sup>.  
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)<sup>[3]</sup>. Compared with the saline-treated group, rats receiving Mibefradil or NSC 64013 show

significant lower  $\text{Ca}_v3.2$  expression in the spinal cord and DRG<sup>[4]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Animal

#### Administration <sup>[3][4]</sup>

#### Mice<sup>[3]</sup>

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  $\alpha1G$ ,  $\alpha1H$  and  $\alpha1I$ , 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<sup>[4]</sup>

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  $\mu\text{g}/\text{h}$ ) or NSC 64013 (60  $\mu\text{g}/\text{h}$ )] is started after surgery for 7 days. Fluorescent immunohistochemistry and Western blotting are used to determine the expression pattern and protein level of  $\text{Ca}_v3.2$ . 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  $\text{Ca}^{++}$ -channel blocker Ro 40-5967 blocks differently T-type and L-type  $\text{Ca}^{++}$  channels. J Pharmacol Exp Ther. 1994 Dec;271(3):1483-8.
- [2]. Brain KL, et al. The sources and sequestration of  $\text{Ca}^{(2+)}$  contributing to neuroeffector  $\text{Ca}^{(2+)}$  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  $\text{Ca}_v3.2$  upregulation in nerve-ligated rats. Acta Anaesthesiol Taiwan. 2016 Oct 17. pii: S1875-4597(16)30071-6.

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

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