**Inhibitors, Agonists, Screening Libraries**

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**Data Sheet**

**Product Name:** Mibefradil (dihydrochloride)

**Cat. No.:** HY-15553A

**CAS No.:** 116666-63-8

**Molecular Formula:** C29H40Cl2FN3O3

**Molecular Weight:** 568.55

**Target:** Calcium Channel

**Pathway:** Membrane Transporter/Ion Channel

**Solubility:** 10 mM in DMSO

**BIOLOGICAL ACTIVITY:**

Mibefradil dihydrochloride is a **calcium channel** blocker with moderate selectivity for T–type Ca\(^{2+}\) channels displaying IC\(_{50}\)s of 2.7 μM and 18.6 μM for T–type and L–type currents, respectively.

**IC\(_{50}\) & Target:** IC\(_{50}\): 2.7 μM (T–type calcium channel), 18.6 μM (L–type calcium channel)\(^{[1]}\)

**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\(^{[2]}\).

**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 Ethosuximide show significant lower Cav3.2 expression in the spinal cord and DRG\(^{[4]}\).

**PROTOCOL** (Extracted from published papers and Only for reference)

**Animal Administration:** Mibefradil is dissolved in physiological saline solution\(^{[3]}\). 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.

**Rat**\(^{[4]}\)

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 Ethosuximide (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 Cav3.2. Hematoxylin–eosin and toluidine blue staining are used to evaluate the neurotoxicity of tested agents.

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References:


