上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

# 产品名称：米贝拉地尔
# 产品别名：Mibefradil dihydrochloride；盐酸米贝拉地尔；Ro 40-5967 (dihydrochloride)

## 生物活性：

| | |
|---|---|
| **Description** | Mibefradil dihydrochloride (Ro 40-5967 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** | IC50: 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 $Ca_V3.2$ expression in the spinal cord and DRG[4]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**$H_2O$ : ≥ 125 mg/mL (219.86 mM)**<br>* "≥" means soluble, but saturation unknown. |

**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 |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

**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. |

**实验参考：**

| | |
|---|---|
| **Animal Administration** | Mice[3]<br>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.<br>Rats[4]<br>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 $Ca_V3.2$. Hematoxylin-eosin and toluidine blue staining are used to evaluate the neurotoxicity of tested agents. |
| **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.<br>[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.<br>[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.<br>[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. |