Pirmenol hydrochloride

Cat. No.: HY-100795A
CAS No.: 61477-94-9
Molecular Formula: C₂₂H₃₁ClN₂O
Molecular Weight: 374.95
Target: mAChR; Potassium Channel
Pathway: GPCR/G Protein; Neuronal Signaling; Membrane Transporter/Ion Channel
Storage: 4°C, stored under nitrogen
* In solvent: -80°C, 6 months; -20°C, 1 month (stored under nitrogen)

SOLVENT & SOLUBILITY

In Vitro
DMSO: ≥ 28 mg/mL (74.68 mM)
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass (1 mg)</th>
<th>Mass (5 mg)</th>
<th>Mass (10 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.6670 mL</td>
<td>13.3351 mL</td>
<td>26.6702 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.5334 mL</td>
<td>2.6670 mL</td>
<td>5.3340 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2667 mL</td>
<td>1.3335 mL</td>
<td>2.6670 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
Pirmenol hydrochloride inhibits Iₖ,ACH by blocking muscarinic receptors. The IC₅₀ of Pirmenol for inhibition of Carbachol-induced Iₖ,ACH is 0.1 μM.

IC₅₀ & Target
IC₅₀: 0.1 μM (Iₖ,ACH)¹

In Vitro
Pirmenol inhibits the carbachol-induced Iₖ,ACH in a concentration-dependent manner. Pirmenol also inhibits the GTPγS-induced current although the concentrations of Pirmenol needed to inhibit the GTPγS-induced current are much higher than those to inhibit the carbachol-induced Iₖ,ACH. The IC₅₀ of Pirmenol for inhibition of the GTPγS-induced currents is 30 μM. The inhibitory effect of Pirmenol on these Iₖ,ACH is almost completely reversible and the outward current reappeared upon washout of Pirmenol. Pirmenol on the muscarinic acetylcholine receptor-operated K⁺ current (Iₖ,ACH) in atrial cells and on experimental atrial fibrillation in isolated guinea-pig hearts. In isolated atrial myocytes, Pirmenol concentration dependently inhibits the Iₖ,ACH induced by carbachol or intracellular loading of GTPγS. In Langendorff-perfused hearts Pirmenol reverses the carbachol-induced decreases in effective refractory periods and atrial fibrillation threshold⁰. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo
The pyridine-methanol derivative Pirmenol hydrochloride is a new antiarrhythmic agent. Single-dose studies in rodents
demonstrate a 10- to 15-fold difference between the po and iv LD\(_{50}\) values. In rats, the po LD\(_{50}\) is 359.9 mg/kg and the iv LD\(_{50}\) is 23.6 mg/kg. Mice LD\(_{50}\) values are 215.5 and 20.8 mg/kg for po and iv routes, respectively. Short-term subacute iv toxicity studies in rats (2.5, 5.0, and 7.5 mg/kg) and dogs (2.5, 5, and 10 mg/kg) for 4 weeks elicit minimal reactions. Cardiac effects in dogs include drug related increases in heart rate, increases QRS duration, shortening of ST interval without evidence of cardiac tissue damage and mild local reaction at the injection site. Orally, Pirmeol is well tolerated for 13 weeks in rats receiving 25, 50, and 100 mg/kg/day while dogs given 5, 10, and 15 mg/kg/day shows anticholinergic effects at high levels (dryness of mucosae, body tremors). Heart rates are significantly accelerated only at the beginning of the study and QRS changes are seen with wide individual variations. No drug-related tissue changes are elicited in these species. Teratology studies in rats (50, 100, and 150 mg/kg) and in rabbits (10, 25, and 50 mg/kg) show no overt effect on organogenesis but embryotoxicity is seen at 150 mg/kg in rats\(^2\).

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**PROTOCOL**

**Animal Administration**\(^2\)

Mice and Rats\(^2\)

The species and strains used in these studies are: male mice, 21-29 g; rats, 116-261 g; purebred beagle dogs, 6.8-12.4 kg; and rabbits, 2.9 kg average. For acute oral and intravenous studies and subacute oral studies, Pirmeol hydrochloride, hereafter referred to as Pirmeol, is supplied as bulk white crystalline compound of approximately 89% purity. Doses are calculated on the basis of base content. In acute studies, Pirmeol is given by gavage as 2 (mice) or 2.5% (rats) in aqueous solution; for iv administration, as 0.5 (mice) or 1% (rats) aqueous solution. In oral subacute studies in dogs, it is given in gelatin capsules, and in rats, it is mixed with the diet to yield the intended dose concentrations. Rabbits received the drug in a 5% aqueous solution by intragastric intubation. For subacute iv studies, Pirmeol is supplied in sterile vials as a 1% solution. In rats, iv injection approximated 0.6 mL/min, and in dogs, the drug is administered via an infusion pump at the rate of 1 mg/kg/min. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**
