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：
4-[(2R,6S)-2,6-dimethyl-1-piperidyl]-1-phenyl-1-pyridin-2-yl-butan-1-o l hydrochloride

产品别名：Pirmenol hydrochloride；盐酸吡美诺；CI-845; (±)-Pirmenol hydrochlorid

生物活性：

Description	Pirmenol hydrochloride inhibits $I_{K.ACh}$ by blocking muscarinic receptors. The IC_{50} of Pirmenol for inhibition of Carbachol-induced $I_{K.ACh}$ is 0.1 μM.
IC_{50} & Target	IC50: 0.1 μM ($I_{K.ACh}$)[1]
In Vitro	Pirmenol inhibits the carbachol-induced $I_{K.ACh}$ 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 $I_{K.ACh}$. The IC_{50} of Pirmenol for inhibition of the GTPγS-induced currents is 30 μM. The inhibitory effect of Pirmenol on these $I_{K.ACh}$ is almost completely reversible and the outward current reappeared upon washout of Pirmenol. Pirmenol on the muscarinic acetylcholine receptor-operated K^+ current ($I_{K.ACh}$) in atrial cells and on experimental atrial fibrillation in isolated guinea-pig hearts. In isolated atrial myocytes, Pirmenol concentration dependently inhibits the $I_{K.ACh}$ 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 threshold[1].
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 elicite 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, Pirmenol 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].

Solvent&Solubility

In Vitro:

DMSO : ≥ 28 mg/mL (74.68 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6670 mL	13.3351 mL	26.6702 mL
5 mM	0.5334 mL	2.6670 mL	5.3340 mL
10 mM	0.2667 mL	1.3335 mL	2.6670 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]. Watanabe Y, et al. Pirmenol inhibits muscarinic acetylcholine receptor-operated K+ current in the guinea pig heart. Eur J Pharmacol. 1997 Oct 29;338(1):71-4. [2]. Schardein JL, et al. Preclinical toxicology studies with a new antiarrhythmic agent: Pirmenol hydrochloride (CI-845). Toxicol Appl Pharmacol. 1980 Nov;56(2):294-301.

实验参考：

Animal Administration	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, Pirmenol hydrochloride, hereafter referred to as Pirmenol, is supplied as bulk white crystalline compound of approximately 89% purity. Doses are calculated on the basis of base content. In acute studies, Pirmenol 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, Pirmenol 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.
References	[1]. Watanabe Y, et al. Pirmenol inhibits muscarinic acetylcholine receptor-operated K+ current in the guinea pig heart. Eur J Pharmacol. 1997 Oct 29;338(1):71-4. [2]. Schardein JL, et al. Preclinical toxicology studies with a new antiarrhythmic agent: Pirmenol hydrochloride (CI-845). Toxicol Appl Pharmacol. 1980 Nov;56(2):294-301.