Milrinone

Cat. No.: HY-14252

CAS No.: 78415-72-2

Molecular Formula: $C_{12}H_9N_3O$

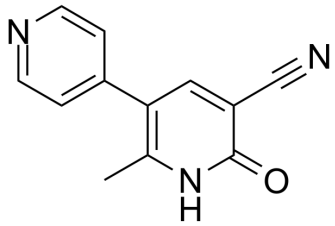
Molecular Weight: 211.22

Target: Phosphodiesterase (PDE)

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (236.72 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.7344 mL	23.6720 mL	47.3440 mL
5 mM	0.9469 mL	4.7344 mL	9.4688 mL
10 mM	0.4734 mL	2.3672 mL	4.7344 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.75 mg/mL (13.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (13.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Milrinone is a PDE3 inhibitor, and also an inotrope and vasodilator.

IC_{50} & Target

PDE3

In Vitro

Milrinone (1 μM) increases PKA activity in hypoxic myocytes to normoxic levels. Milrinone (50 nM) normalizes TP receptor sensitivity in hypoxic myocytes by restoring PKA-mediated regulatory TP receptor phosphorylation[1]. Milrinone significantly reduces NE-induced vasoconstriction, attenuating both NE sensitivity and maximal tension generation. Inhibition of ATP-sensitive K^+ channels or voltage-gated K^+ channels do not prevent the milrinone-induced attenuation of NE responses[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	Milrinone (1 μg/kg/min, i.v.) significantly reduces PAP, PVR (−18.96 ± 1.7%), and LAP (−26.03 ± 2.3%) in congestive heart failure (CHF) rats. Milrinone (1 mg/mL, inhalation) results in a near-maximal reduction of PAP without significant effects on AP, decreases pulmonary artery pressure similarly in a larger collective of CHF rats. Milrinone inhalation selectively increases cAMP but not cGMP plasma concentrations in both groups. Repeated milrinone inhalations even reduce lung wet/dry weight ratio[2]. Milrinone (49.5 μg) largely shifts the ESPVR upwards and significantly increases end-systolic pressure (ESP(0.08)) and the systolic pressure-volume area (PVA(0.08)) at a mid-range LV volume (0.08 mL/g myocardium). Milrinone also slightly decreases LV ESP(ESV) and decreased Ea[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	In juvenile rats of 100 ± 8 g body weight (bw), CHF is induced by supracoronary aortic banding. In brief, rats are anesthetized by intraperitoneal injection of ketamine (87 mg/kg bw) and xylazine (13 mg/kg bw). Rats are placed in the supine position, the chest wall is shaved, and a left thoracotomy is performed in the third intercostal space during ventilation with 100% O_2. The ascending aorta is freed from connective tissue and partially occluded by implantation of a titanium clip with a defined internal diameter of 0.8 mm. After surgical closure of the thorax, the rats are allowed to recover from anesthesia. For postoperative analgesia, rats receive 250 mg/kg bw of metamizole intramuscularly immediately after the operation and on the first postoperative day. Sham-operated rats serve as controls. After recovery from anesthesia, the animals are placed in cages with free access to water and standard laboratory diet. For inhalation, milrinone (0.2-5 mg/mL) or NaCl (0.9%) are nebulized using an ultrasonic nebulizer and inhaled for 3 min at identical peak inspiratory pressures as used throughout the experiment. A 3-min nebulization of 1 mg/mL milrinone results in vaporization of 14 μg of the phosphodiesterase-3 inhibitor as determined by microgravimetry. Therefore, the respective dose of 39 μg/kg is analog to inhaled doses in human studies. For intravenous delivery, milrinone (initial bolus of 2-10 μg/kg, followed by 0.2-1 μg/kg/min) or equivalent volumes of NaCl (0.9%; initial bolus of 1.6 mL/kg, followed by 10 μL/kg/h) are administered by an infusion pump for 10 min. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2022 Nov 18;378(6621):eabq7361.
- EMBO Mol Med. 2021 Dec 7;13(12):e14887.
- Sci Total Environ. 2021, 147792.
- Cell Rep. 2023 Dec 6;42(12):113531.
- Ecotoxicol Environ Saf. 2022 Jul 28;242:113921.

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REFERENCES

[1]. Santhosh KT, et al. Milrinone attenuates thromboxane receptor-mediated hyperresponsiveness in hypoxic pulmonary arterial myocytes. Br J Pharmacol. 2011 Jul;163(6):1223-36.

[2]. Hentschel T, et al. Inhalation of the phosphodiesterase-3 inhibitor milrinone attenuates pulmonary hypertension in a rat model of congestive heart failure. Anesthesiology. 2007 Jan;106(1):124-31.

[3]. Kishi T, et al. Effects of milrinone on left ventricular end-systolic pressure-volume relationship of rat hearts in situ. Clin Exp Pharmacol Physiol. 2001 Sep;28(9):737-42.

[4]. Taylor MS, et al. Effect of milrinone on small mesenteric artery vasoconstriction: role of K(+) channels. Am J Physiol. 1999 Jul;277(1 Pt 1):G69-78.

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

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