Dronedarone Hydrochloride

Cat. No.: HY-75839

CAS No.: 141625-93-6

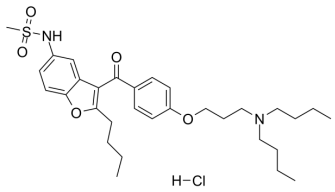
Molecular Formula: $C_{31}H_{45}ClN_2O_5S$

Molecular Weight: 593.22

Target: Potassium Channel; Autophagy

Pathway: Membrane Transporter/Ion Channel; Autophagy

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (42.14 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.6857 mL	8.4286 mL	16.8572 mL
5 mM	0.3371 mL	1.6857 mL	3.3714 mL
10 mM	0.1686 mL	0.8429 mL	1.6857 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: ≥ 2.5 mg/mL (4.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Dronedarone Hydrochloride is a non-iodinated amiodarone derivative that inhibits Na^+, K^+ and Ca^{2+} currents.

In Vitro

Dronedarone (SR-33589) is a multichannel blocker for atrial fibrillation . It is a potent inhibitor of the acetylcholine-activated K^+ current from atrial and sinoatrial nodal tissue, and inhibits the rapid delayed rectifier more potently than slow and inward rectifier K+ currents and inhibits L-type calcium current. Under whole-cell patch clamp, it blocks I_{Kr} (IC_{50}=3 μM) and $I_{Ca\text{-}L}$ (IC_{50}=0.18 μM). The effects on $I_{Ca\text{-}L}$ are use- and frequency-dependent. Dronedarone inhibits current carried by human ether-a-go-go gene (HERG)-expressing oocytes (analagous to I_{Kr}) with an IC_{50} of 9 μM[1]. In guinea pig ventricular myocytes, dronedarone exhibits a state dependent inhibition of the fast Na^+ channel current with an IC_{50} of 0.7±0.1 μM, when the

	holding potential is −80 mV[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Dronedarone (Hydrochloride) reduces significantly the incidence of ventricular fibrillation (VF) from 80 to 30% ($p < 0.05$) at 3 mg/kg i.v. and eliminated VF and mortality at 10 mg/kg i.v. [3]. Dronedarone inhibited carotid artery thrombus formation in vivo. Thrombin- and collagen-induced platelet aggregation is impaired indronedarone-treated mice (P\0.05), and expression ofplasminogen activator inhibitor-1 (PAI1), an inhibitor of the fibrinolytic system, is reduced in the arterial wall[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3][4]	Rats: Rats are anesthetized, artificially ventilated, and the thorax opened by a left thoracotomy. Ischemia is induced by left coronary artery ligation, and reperfusion is achieved (after a 5-min period of ischemia) in a separate group of rats by removing the ligature. Agents are given intravenously 5 min before occlusion or orally 4 h before study[3]. Mice: Twelve-week-old C57Bl/6 mice are divided into two groups: dronedarone (200 mg/kg body weight with a once daily oral gavage for 14 days) or control (1.4 % methylcellulose). Twenty-four hours after the last application, mice are anesthetized by intraperitoneal injection of 87 mg/kg sodium pentobarbital. Rose bengal is diluted to 12 mg/mL in phosphate-buffered saline and then injected into the tail vein at a concentration of 63 mg/kg[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bogdan R, et al. Effect of?dronedarone?on Na+, Ca2+ and HCN channels. Naunyn Schmiedebergs Arch Pharmacol.?2011 Apr;383(4):347-56.?

[2]. Doggrell SA, et al. Dronedarone: an amiodarone analogue. Expert Opin Investig Drugs. 2004 Apr;13(4):415-26.

[3]. Manning AS, et al. SR 33589, a new amiodarone-like agent: effect on ischemia- and reperfusion-induced arrhythmias in anesthetized rats. J Cardiovasc Pharmacol. 1995 Sep;26(3):453-61.

[4]. Breitenstein A, et al. Dronedarone reduces arterial thrombus formation. Basic Res Cardiol. 2012 Nov;107(6):302.

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