Istaroxime hydrochloride

Cat. No.: HY-15718A

CAS No.: 374559-48-5

Molecular Formula: $C_{21}H_{33}ClN_2O_3$

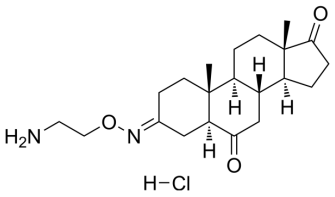
Molecular Weight: 396.95

Target: Na+/K+ ATPase; Calcium Channel

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 45 mg/mL (113.36 mM)

H_2O : 25 mg/mL (62.98 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5192 mL	12.5960 mL	25.1921 mL
5 mM	0.5038 mL	2.5192 mL	5.0384 mL
10 mM	0.2519 mL	1.2596 mL	2.5192 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 12.5 mg/mL (31.49 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.30 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.30 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Istaroxime hydrochloride is a Na^+/K^+-ATPase inhibitor (IC_{50}=0.11 μM) and a sarcoplasmic/endoplasmic reticulum calcium ATPase 2 (SERCA 2) activator.

IC_{50} & Target

IC50: 0.11 μM (Na^+,K^+-ATPase)[1]

In Vitro	Istaroxime hydrochloride acting as a positive inotropic compound through the inhibition of the Na^+,K^+-ATPase[2]. Istaroxime (PST2744) inhibits the Na^+/K^+-ATPase activity from dog kidney with an IC_{50} value of 0.43 ± 0.15 μM. Inhibition of Na^+/K^+-ATPase activity in preparations from guinea pig kidney yielded potencies of 8.5 μM for PST2744[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Istaroxime (PST2744) induces a progressive increase in $+dP/dt_{max}$ throughout the infusion that reaches 80% (ED_{80}) at the cumulative dose of 1.89±0.37 mg/kg and a peak of 140±3.5% at the dose (ED_{max}) of 4.88±0.6 mg/kg[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [3]	Dog or guinea pig kidney outer medulla is homogenized with a Polytron in 250 mM sucrose and 30 mM histidine, at pH 7.2. The homogenate is centrifuged at 6,000g for 15 min at 4°C and the supernatant at 48,000g for 30 min at 20°C with SDS and then layered onto a discontinuous sucrose density gradient (10, 15, and 29%) and centrifuged at 60,000 rpm for 115 min at 4°C. The pellet is resuspended in 25 mM imidazole and 1 mM EDTA, pH 7.5. Protein content is measured. Na^+/K^+-ATPase activity is measured after the release of ^{32}P from [^{32}P]ATP. Increasing concentrations of compounds are preincubated with purified enzyme for 10 min at 37°C in 120 μL of final volume of medium containing 140 mM NaCl, 3 mM $MgCl_2$, 50 mM HEPES-Tris, and 3 mM ATP, pH 7.5. After preincubation, 10 μL of incubation solution containing 10 mM KCl and 20 nCi of [^{32}P]ATP (0.5-3 Ci/mmol) is added, and the reaction is carried out for 15 min at 37°C before being stopped by acidification with 30% (v/v) perchloric acid. ^{32}P is separated by centrifugation with activated charcoal and radioactivity measured by liquid scintillation counting. Inhibitory activity is expressed as percentage of control sample, carried out in the absence of standard compound. IC_{50} is calculated by weighed nonlinear regression curve fitting to the mass-action equilibrium[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Pigs[3] Male guinea Pigs (350-450 g) are used. Istaroxime (300 μg/kg) or Digoxin (75 μg/kg) are given by i.v. bolus 10 and 20 min before starting the exercise, respectively, and compared with vehicle. The following variables, HR, ECG, LVP, and aortic pressures, are recorded through a computerized acquisition system, which calculated the left ventricular rates of pressure changes. Data are analyzed from the real-time digitized recordings. Control values are obtained before compound administration. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biochem Pharmacol. 2023 Mar 24;211:115516.
- Biochem Pharmacol. 2020 Oct;180:114122.
- Front Pharmacol. 2020 Dec 14.
- J Am Heart Assoc. 2021 Jul 3;e018833.

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REFERENCES

[1]. Gobbini M, et al. Novel analogues of istaroxime, a potent inhibitor of Na+,K+-ATPase: synthesis and structure-activity relationship. J Med Chem. 2008 Aug 14;51(15):4601-8.

[2]. Gobbini M, et al. Novel analogues of Istaroxime, a potent inhibitor of Na(+),K(+)-ATPase: Synthesis, structure-activity relationship and 3D-quantitative structure-activity relationship of derivatives at position 6 on the androstane scaffold. Bioorg Med Ch

[3]. Micheletti R, et al. Pharmacological profile of the novel inotropic agent (E,Z)-3-((2-aminoethoxy)imino)androstane-6,17-dione hydrochloride (PST2744). J Pharmacol Exp Ther. 2002 Nov;303(2):592-600.

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