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产品名称: **Istaroxime (hydrochloride)**  
产品别名: **PST2744 hydrochloride**

<b>生物活性:</b>				
<b>Description</b>	Istaroxime hydrochloride is a Na <sup>+</sup> /K <sup>+</sup> -ATPase inhibitor (IC <sub>50</sub> =0.11 μM) and a sarcoplasmic/endoplasmic reticulum calcium ATPase 2 (SERCA 2) activator.			
<b>IC<sub>50</sub> &amp; Target</b>	IC <sub>50</sub> : 0.11 μM (Na <sup>+</sup> ,K <sup>+</sup> -ATPase)[1]			
<b>In Vitro</b>	Istaroxime hydrochloride acting as a positive inotropic compound through the inhibition of the Na <sup>+</sup> ,K <sup>+</sup> -ATPase[2]. Istaroxime (PST2744) inhibits the Na <sup>+</sup> /K <sup>+</sup> -ATPase activity from dog kidney with an IC <sub>50</sub> value of 0.43 ± 0.15 μM. Inhibition of Na <sup>+</sup> /K <sup>+</sup> -ATPase activity in preparations from guinea pig kidney yielded potencies of 8.5 μM for PST2744[3].			
<b>In Vivo</b>	Istaroxime (PST2744) induces a progressive increase in +dP/dt <sub>max</sub> throughout the infusion that reaches 80% (ED <sub>80</sub> ) at the cumulative dose of 1.89±0.37 mg/kg and a peak of 140±3.5% at the dose (ED <sub>max</sub> ) of 4.88±0.6 mg/kg[3].			
<b>Solvent&amp;Solubility</b>	<b>In Vitro:</b> <b>DMSO : ≥ 45 mg/mL (113.36 mM)</b>  * "≥" means soluble, but saturation unknown.			
	<b>Preparing Stock Solutions</b>	<b>Solvent</b>	<b>Mass</b>	
		<b>Concentration</b>		
			<b>1 mg</b>	<b>5 mg</b>
				<b>10 mg</b>
		1 mM	2.5192 mL	12.5960 mL
		5 mM	0.5038 mL	2.5192 mL
		10 mM	0.2519 mL	1.2596 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℃，6 months；-20℃，1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。  <b>In Vivo:</b>  请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：  ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶  1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline  Solubility: ≥ 2.5 mg/mL (6.30 mM); Clear solution  此方案可获得 ≥ 2.5 mg/mL (6.30 mM，饱和度未知) 的澄清溶液。  以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀，向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。  2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)  Solubility: ≥ 2.5 mg/mL (6.30 mM); Clear solution  此方案可获得 ≥ 2.5 mg/mL (6.30 mM，饱和度未知) 的澄清溶液。			



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	<p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水溶液中, 混合均匀。</p> <p>3.请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% corn oil</p> <p>Solubility: <math>\geq</math> 2.5 mg/mL (6.30 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 2.5 mg/mL (6.30 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p>
References	<p>[1]. Gobbini M, et al. Novel analogues of istaroxime, a potent inhibitor of Na<sup>+</sup>,K<sup>+</sup>-ATPase: synthesis and structure-activity relationship. J Med Chem. 2008 Aug 14;51(15):4601-8.</p> <p>[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</p> <p>[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.</p>
实验参考:	
Animal Administration	<p>Pigs[3]</p> <p>Male guinea Pigs (350-450 g) are used. Istaroxime (300 <math>\mu</math>g/kg) or Digoxin (75 <math>\mu</math>g/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.</p>
Kinase Assay	<p>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.</p> <p>Na<sup>+</sup>/K<sup>+</sup>-ATPase activity is measured after the release of <sup>32</sup>P from [<sup>32</sup>P]ATP. Increasing concentrations of compounds are preincubated with purified enzyme for 10 min at 37°C in 120 <math>\mu</math>L of final volume of medium containing 140 mM NaCl, 3 mM MgCl<sub>2</sub>, 50 mM HEPES-Tris, and 3 mM ATP, pH 7.5. After preincubation, 10 <math>\mu</math>L of incubation solution containing 10 mM KCl and 20 nCi of [<sup>32</sup>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. <sup>32</sup>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.</p> <p>IC<sub>50</sub> is calculated by weighed nonlinear regression curve fitting to the mass-action equilibrium[3].</p>
	<p>[1]. Gobbini M, et al. Novel analogues of istaroxime, a potent inhibitor of Na<sup>+</sup>,K<sup>+</sup>-ATPase: synthesis and structure-activity relationship. J Med Chem. 2008 Aug 14;51(15):4601-8.</p>



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#### References

- [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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