

产品名称: Omecamtiv mecarbil(CK-1827452)
产品别名: Omecamtiv mecarbil

生物活性:				
Description	Omecamtiv mecarbil is a selective cardiac myosin activator.			
In Vitro	Omecamtiv mecarbil (10 μM) reduces the maximal ATPase (k_{cat}) 4.5-fold and dramatically reduces the actin concentration at which ATPase is half-maximal (K_{ATPase}) 30-fold. The Omecamtiv mecarbil-induced inhibition of the actin-activated ATPase is evaluated in a concentration-dependent manner to determine the EC_{50} ($0.52 \pm 0.10 \mu M$). Omecamtiv mecarbil does not change the overall actin affinity. Omecamtiv mecarbil traps a population of myosin heads in a weak actin affinity state with slow product release. Omecamtiv mecarbil can reduce the actin sliding velocity more than 100-fold in the in vitro motility assay[3].			
In Vivo	Omecamtiv mecarbil (100-1000 ng/mL) demonstrates concentration-dependent increases in FS in Sprague-Dawley rats model. Omecamtiv mecarbil demonstrates good PK parameters in both rats (Sprague-Dawley) and dogs (Beagle) with clearances of 22 and 7.2 mL/min/kg, volumes of 3.5 and 3.6 L/kg, and bioavailabilities (F%) of 100 and 80%, respectively[1]. Omecamtiv mecarbil does not affect the phosphorylation status of myofilament proteins in both WT and KO hearts as shown by the absence of significant differences between pre and post Omecamtiv mecarbil samples within WT and KO groups, or affect the force generation at maximal Ca^{2+} activation (pCa 4.5) in any of the groups. Omecamtiv mecarbil increases the responsiveness of the cardiac myofilaments to Ca^{2+} at submaximal Ca^{2+} -activations[2].			
Solvent&Solubility	In Vitro: DMSO : 50 mg/mL (124.55 mM; Need ultrasonic)			
	Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg
		1 mM	2.4911 mL	12.4555 mL
		5 mM	0.4982 mL	2.4911 mL
		10 mM	0.2491 mL	1.2455 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。			
	In Vivo: 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 (6.23 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.23 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 (6.23 mM); Clear solution			

	此方案可获得 ≥ 2.5 mg/mL (6.23 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中, 混合均匀。 3.请依序添加每种溶剂: 10% DMSO $\rightarrow$90% corn oil Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.23 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。 以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。
References	[1]. <u>Morgan BP, et al. Discovery of omecamtiv mecarbil the first, selective, small molecule activator of cardiac Myosin. ACS Med Chem Lett. 2010 Aug 20;1(9):472-7.</u> [2]. <u>Mamidi R, et al. Molecular effects of the myosin activator omecamtiv mecarbil on contractile properties of skinned myocardium lacking cardiac myosin binding protein-C. J Mol Cell Cardiol. 2015 Aug;85:262-72.</u> [3]. <u>Swenson AM, et al. Omecamtiv Mecarbil Enhances the Duty Ratio of Human β-Cardiac Myosin Resulting in Increased Calcium Sensitivity and Slowed Force Development in Cardiac Muscle. J Biol Chem. 2017 Mar 3;292(9):3768-3778.</u>

源叶生物