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产品名称：GS967
产品别名：GS967

生物活性：

Description	GS967 (GS-458967) is a potent, and selective inhibitor of cardiac late sodium current (late I_{Na}) with IC_{50} values of 0.13 and 0.21 μM for ventricular myocytes and isolated hearts, respectively.
IC_{50} & Target	IC50: 0.13 μM (late I_{Na}, ventricular myocytes)and 0.21 μM (late I_{Na}, isolated hearts)[1]
In Vitro	GS967 (10, 100, 300 nM) completely attenuates the effect of ATX-II (10 nM) to increase action potential duration (APD) and APD variability in ventricular myocytes, with an apparent IC50 value of ~10 nM and decreased the beat-to-beat variability of APD[1].
In Vivo	GS967 prevents and reverses proarrhythmic effects of the late I_{Na} enhancer ATX-II and the I_{Kr} inhibitor E-4031. GS967 significantly attenuates the proarrhythmic effects of methoxamine 1 clofilium and suppressed ischemia-induced arrhythmias[1]. GS967 causes a reduction of I_{NaP} in a frequency-dependent manner, consistent with use-dependent block (UDB). GS967 evokes more potent UDB of I_{NaP} (IC_{50}=0.07 μM) than ranolazine (16 μM) and lidocaine (17 μM). GS967 is found to exert these same effects on a prototypical long QT syndromemutation (delKPQ)[2]. GS967 prevents ischemia-induced increases in alternans in the left atrium and left ventricle. GS967 reduces ischemia-induced increases in depolarization heterogeneity and repolarizationheterogeneity. GS967 does not alter heart rate, arterial blood pressure, PR and QT intervals, or QRS duration, but it mildly decreased contractility during ischemia, which was consistent with late INa inhibition[3].

Solvent&Solubility

In Vitro:

DMSO : 50 mg/mL (144.00 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8800 mL	14.4001 mL	28.8002 mL
	5 mM	0.5760 mL	2.8800 mL	5.7600 mL
	10 mM	0.2880 mL	1.4400 mL	2.8800 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°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 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 (7.20 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (7.20 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

	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% corn oil Solubility: ≥ 2.5 mg/mL (7.20 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.20 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]. Belardinelli L, et al. A novel, potent, and selective inhibitor of cardiac late sodium current suppresses experimental arrhythmias. J Pharmacol Exp Ther. 2013 Jan;344(1):23-32. [2]. Wei X, et al. Pre- and Delayed Treatments With Ranolazine Ameliorate Ventricular Arrhythmias and Nav1.5 Downregulation in Ischemic/Reperfused Rat Hearts. J Cardiovasc Pharmacol. 2016 Oct;68(4):269-279. [3]. Potet F, et al. Use-Dependent Block of Human Cardiac Sodium Channels by GS967. Mol Pharmacol. 2016 Jul;90(1):52-60. [4]. Bonatti R, et al. Selective late sodium current blockade with GS-458967 markedly reduces ischemia-induced atrial and ventricular repolarization alternans and ECG heterogeneity. Heart Rhythm. 2014 Oct;11(10):1827-35.

实验参考：

Animal Administration	Rats: Ventricular tachycardia or fibrillation are induced either by local aconitine injection (50 μg) in the left ventricular muscle of adult male rats or by arterial perfusion of 0.1 mM hydrogen peroxide in aged male rats. The left ventricular epicardial surface of the isolated-perfused hearts is optically mapped using fluorescent voltage-sensitive dye, and microelectrode recordings of action potentials are made adjacent to the aconitine injection site. The suppressive and preventive effects of GS967 (1 μM) against EAD/DAD-mediated ventricular tachycardia or fibrillation are then determined[2]. Rabbits: To determine the effect of GS967 on the inducibility of TdP by clofilium in the presence of methoxamine, rabbits are first treated with either vehicle or GS967 (in randomized manner) given as a 60 μg/kg bolus, followed by a 16 μg/kg/min infusion that is maintained for the duration of an experiment. After 10 minutes, methoxamine is infused intravenously at 15 μg/kg/min, followed 10 minutes later by clofilium at 100 nmol/kg/min. The incidences of premature ventricular contractions (PVCs), ventricular tachycardia (VT; defined as three or more consecutive abnormal beats), and TdP are determined from the ECG recordings[1].
References	[1]. Belardinelli L, et al. A novel, potent, and selective inhibitor of cardiac late sodium current suppresses experimental arrhythmias. J Pharmacol Exp Ther. 2013 Jan;344(1):23-32. [2]. Wei X, et al. Pre- and Delayed Treatments With Ranolazine Ameliorate Ventricular Arrhythmias and Nav1.5 Downregulation in Ischemic/Reperfused Rat Hearts. J Cardiovasc Pharmacol. 2016 Oct;68(4):269-279. [3]. Potet F, et al. Use-Dependent Block of Human Cardiac Sodium Channels by GS967. Mol

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