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产品名称: **BIX 02565**
产品别名: **BIX 02565**

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| 生物活性: | | | | |
| Description | BIX 02565 is a potent ribosomal S6 kinase 2 (RSK2) inhibitor with IC ₅₀ of 1.1 nM. | | | |
| IC₅₀ & Target | IC ₅₀ : 1.1 nM (RSK2)[1] | | | |
| In Vitro | BIX 02565, a potent RSK2 inhibitor (IC ₅₀ =1.1 nM) targets for the treatment of heart failure secondary to myocardial infarction through indirect NHE inhibition ^[1] . BIX 02565, a second Rsk inhibitor, protects enzyme active sites from reaction with biotinylated nucleotide acyl phosphates ^[2] . | | | |
| In Vivo | In telemetry-instrumented rats, BIX 02565 (30, 100, and 300 mg/kg p.o. QD for 4 days) elicits concentration-dependent decreases in MAP after each dose (to -39±4 mm Hg on day 4 at T _{max}). BIX 02565 produces concentration-dependent relaxation ex vivo in the phenylephrine-constricted rat aortic ring at concentrations above 0.03 µM with a calculated EC ₅₀ of 3.1 µM. Subsequently, BIX 02565 is infused in the anesthetized rat in a low-dose (0.1, 0.3, and 1.0 mg/kg per 20 min) and high-dose (1.0, 3.0, and 10.0 mg/kg per 20 min) series of continuous infusions to test the effect of compound on hemodynamics in vivo ^[1] . | | | |
| Solvent&Solubility | In Vitro: DMSO : 20.75 mg/mL (45.25 mM; Need ultrasonic and warming) | | | |
| | | Solvent | Mass | |
| | | Concentration | | |
| | Preparing | 1 mM | 2.1807 mL | 10.9037 mL |
| | Stock Solutions | 5 mM | 0.4361 mL | 2.1807 mL |
| | | 10 mM | 0.2181 mL | 1.0904 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: ≥ 1.67 mg/mL (3.64 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.64 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 µL 16.699999 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: ≥ 1.67 mg/mL (3.64 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.64 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 | | | | |



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| | <p>的实验。</p> <p>以 1 mL 工作液为例, 取 100 μL 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p> |
| References | <p>[1]. Fryer RM, et al. Mitigation of off-target adrenergic binding and effects on cardiovascular function in the discovery of novel ribosomal S6 kinase 2 inhibitors. Journal of Pharmacology and Experimental Therapeutics (2012), 340(3), 492-500.</p> <p>[2]. Edgar AJ, et al. A combination of SILAC and nucleotide acyl phosphate labelling reveals unexpected targets of the Rsk inhibitor BI-D1870. Biosci Rep. 2013 Dec 17.</p> |
| 实验参考: | |
| Animal Administration | <p>Rats^[1]</p> <p>Mean arterial pressure is assessed in conscious, freely moving male Sprague-Dawley rats (n=6/group) instrumented with telemetry transmitters. BIX 02565 (30, 100, and 300 mg/kg p.o. QD) is administered as a solution (10 mL/kg) in a 20% hydroxy-propyl-β-cyclodextran vehicle. Mean arterial pressure is reported from 2 h before (baseline) and 90 h after the first dose; compound is administered at 0, 24, 48, and 72 h. A blood sample is collected from satellite rats (n=3/group) at 1-h after dose (T_{max}) on days 1 and 4 for analysis of plasma drug concentrations by mass spectrometry.</p> |
| Kinase Assay | <p>Radioligand binding studies are performed at MDS Pharma Services. Mean percentage inhibition of specific binding or activity is shown for each assay tested, and in selected assays (for BIX 02565) when inhibition of adrenergic binding generally exceeded 50%, an IC₅₀ is determined by a nonlinear least-squares regression analysis. In brief, human RSK2 protein is used to measure kinase activity utilizing Kinase GloPlus that uses a luciferin-luciferase based detection reagent to quantify residual ATP. The relative light unit signal is measured on an LJL Analyst in luminescence mode using 384 aperture; relative light unit signals are converted to percentage of control; the IC₅₀ is fitted to a standard four-parameter logistic equation[1].</p> |
| References | <p>[1]. Fryer RM, et al. Mitigation of off-target adrenergic binding and effects on cardiovascular function in the discovery of novel ribosomal S6 kinase 2 inhibitors. Journal of Pharmacology and Experimental Therapeutics (2012), 340(3), 492-500.</p> <p>[2]. Edgar AJ, et al. A combination of SILAC and nucleotide acyl phosphate labelling reveals unexpected targets of the Rsk inhibitor BI-D1870. Biosci Rep. 2013 Dec 17.</p> |