



上海源叶生物科技有限公司
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产品名称: **EMD638683**
产品别名: **EMD638683**

生物活性:

Description	EMD638683 is a highly selective SGK1 inhibitor, with an IC ₅₀ value of 3 μM.																								
IC ₅₀ & Target	IC50: 3 μM (SGK1)[1]																								
In Vitro	EMD638683 is a SGK1 inhibitor. EMD638683 inhibits the NDRG1 (N-Myc downstream-regulated gene 1) phosphorylation, an effect requiring 3.35±0.32 μM EMD638683 in the cell culture medium for half maximal effect (IC50). EMD638683 has also an inhibitory effect on cAMP-dependent protein kinase (PKA), mitogen- and stress-activated protein kinase 1 (MSK1), protein kinase C-related kinase 2 (PKR2), and the SGK isoforms SGK2 and SGK3[1]. In both, control and EMD638683 (50 μM)-treated CaCo-2 cells, radiation significantly increases the percentage of CaCo-2 cells undergoing late apoptosis. EMD638683 treatment alone tends to enhance the percentage of apoptotic CaCo-2 cells. Following radiation the percentage of apoptotic EMD638683-treated CaCo-2 cells is significantly higher than the percentage of apoptotic control cells. Thus, EMD638683 treatment significantly augments the apoptosis following radiation[2].																								
In Vivo	The colon is significantly longer and the colon weight significantly lower in EMD638683-treated mice than in placebo-treated mice, a finding pointing to an influence of EMD638683 on tumor growth following chemical carcinogenesis. In addition, the stomach weight is significantly lower in the EMD treated group. Most importantly, the number of developing tumors following carcinogenic treatment is significantly blunted by EMD638683 treatment[2]. EMD638683 (20 mg/kg, intragastrically) prevents progression of monocrotaline (MCT)-induced pulmonary vascular remodeling in rats. Hemodynamic characteristics show that EMD638683 treatment attenuates right ventricular systolic pressure (RVSP) (15.8±2.5 vs. 28.2±3.1 mmHg; P<0.05; n=6) and right ventricular hypertrophy index (RVHI) (0.27±0.02 vs. 0.41±0.06;P<0.05; n=6) compare to vehicle-dosed controls[3].																								
Solvent&Solubility	In Vitro: DMSO : ≥ 50 mg/mL (137.23 mM) * "≥" means soluble, but saturation unknown.																								
	<table><tr><td rowspan="2">Preparing</td><td>Solvent</td><td>Mass</td><td rowspan="2">1 mg</td><td rowspan="2">5 mg</td><td rowspan="2">10 mg</td></tr><tr><td colspan="2">Concentration</td></tr><tr><td rowspan="3">Stock Solutions</td><td></td><td>1 mM</td><td>2.7447 mL</td><td>13.7234 mL</td><td>27.4469 mL</td></tr><tr><td></td><td>5 mM</td><td>0.5489 mL</td><td>2.7447 mL</td><td>5.4894 mL</td></tr><tr><td></td><td>10 mM</td><td>0.2745 mL</td><td>1.3723 mL</td><td>2.7447 mL</td></tr></table>	Preparing	Solvent	Mass	1 mg	5 mg	10 mg	Concentration		Stock Solutions		1 mM	2.7447 mL	13.7234 mL	27.4469 mL		5 mM	0.5489 mL	2.7447 mL	5.4894 mL		10 mM	0.2745 mL	1.3723 mL	2.7447 mL
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*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																									



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	<p>现沉淀、析出现象，可以通过加热和/或超声的方式助溶</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (6.86 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (6.86 mM, 饱和度未知) 的澄清溶液。</p> <p>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 生理盐水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (6.86 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 μL 25.0 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]. Ackermann TF, et al. EMD638683, a novel SGK inhibitor with antihypertensive potency. Cell Physiol Biochem. 2011;28(1):137-46.</p> <p>[2]. Towhid ST, et al. Inhibition of colonic tumor growth by the selective SGK inhibitor EMD638683. Cell Physiol Biochem. 2013;32(4):838-48.</p> <p>[3]. Xi X, et al. Serum-glucocorticoid regulated kinase 1 regulates macrophage recruitment and activation contributing to monocrotaline-induced pulmonary arterial hypertension. Cardiovasc Toxicol. 2014 Dec;14(4):368-78.</p> <p>[4]. Zhou H, et al. Inhibition of serum- and glucocorticoid-inducible kinase 1 enhances TLR-mediated inflammation and promotes endotoxin-driven organ failure. FASEB J. 2015 Sep;29(9):3737-49.</p>
实验参考:	
Cell Assay	<p>Colon carcinoma (CaCo-2) cells are grown in complete DMEM medium containing 10% fetal calf serum, 1% sodium pyruvate, 1% penicillin-streptomycin and 1% non-essential amino acids under standard culture conditions (37°C, 5% CO₂). 10⁵ cells are seeded in 6 well plates and cultured with fresh culture medium for 24 h, after which EMD638683 (50 μM) is applied for 24 hours. For comparison, the cells are treated with the solvent (0.2 μL DMSO) and one solvent control is analysed with each set of experiments. The cells are subsequently exposed to 3.18 min radiation (3 Gray). After further incubation for 72 h in the presence or absence of EMD638683 (50 μM) the cells are analyzed utilizing flow cytometry[2].</p>
	<p>Rats and Mice[3]</p> <p>PAH is induced in 2-month-old male Sprague-Dawley rats by administering a single subcutaneous injection of MCT (60 mg/kg, n=12). Rats in the control group are given the vehicle saline (0.5 mL, subcutaneously, n=12). Six rats in each group are given EMD638683 (20 mg/kg) intragastrically</p>



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Animal Administration	once daily starting 2 days prior to MCT treatment. Rats are anesthetized with sodium pentobarbital (50 mg/kg intraperitoneally). Right ventricular systolic pressure (RVSP), right ventricular hypertrophy, and pulmonary vascular remodeling are evaluated 21 days after MCT injection. At the age of 10-12 weeks, male SGK1 ^{-/-} mice and their wild-type (WT) littermates are given MCT in doses of 60 mg/100 g body weight once a week for 8 consecutive weeks by subcutaneous injection to induce PAH. There are eight mice per group. Mice are anesthetized with sodium pentobarbital (50 mg/kg intraperitoneally) on day 8 after the last MCT administration. Then RVSP, right ventricular hypertrophy, and pulmonary vascular remodeling are evaluated.
References	<p>[1]. Ackermann TF, et al. EMD638683, a novel SGK inhibitor with antihypertensive potency. <i>Cell Physiol Biochem.</i> 2011;28(1):137-46.</p> <p>[2]. Towhid ST, et al. Inhibition of colonic tumor growth by the selective SGK inhibitor EMD638683. <i>Cell Physiol Biochem.</i> 2013;32(4):838-48.</p> <p>[3]. Xi X, et al. Serum-glucocorticoid regulated kinase 1 regulates macrophage recruitment and activation contributing to monocrotaline-induced pulmonary arterial hypertension. <i>Cardiovasc Toxicol.</i> 2014 Dec;14(4):368-78.</p> <p>[4]. Zhou H, et al. Inhibition of serum- and glucocorticoid-inducible kinase 1 enhances TLR-mediated inflammation and promotes endotoxin-driven organ failure. <i>FASEB J.</i> 2015 Sep;29(9):3737-49.</p>

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