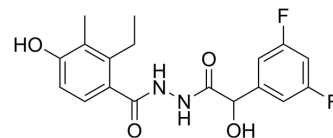


EMD638683

Cat. No.:	HY-15193		
CAS No.:	1181770-72-8		
Molecular Formula:	C ₁₈ H ₁₈ F ₂ N ₂ O ₄		
Molecular Weight:	364.34		
Target:	SGK		
Pathway:	Metabolic Enzyme/Protease		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (137.23 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent		Mass		
	Concentration		1 mg	5 mg	10 mg
	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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
 Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

EMD638683 is a highly selective SGK1 inhibitor, with an IC₅₀ value of 3 μM.

IC₅₀ & Target

SGK1

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[3]

Rats and Mice^[3]

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 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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2022 Jul 27;7(1):255.
- J Infection. 2022 Nov 2;S0163-4453(22)00635-1.
- Adv Sci (Weinh). 2021 Nov 10;e2101485.
- J Autoimmun. 2016 Feb;67:90-101.
- Int J Biol Sci. 2024 Jan 12;20(3):968-986.

REFERENCES

- [1]. Ackermann TF, et al. EMD638683, a novel SGK inhibitor with antihypertensive potency. *Cell Physiol Biochem*. 2011;28(1):137-46.
- [2]. Towhid ST, et al. Inhibition of colonic tumor growth by the selective SGK inhibitor EMD638683. *Cell Physiol Biochem*. 2013;32(4):838-48.
- [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.
- [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.
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Caution: Product has not been fully validated for medical applications. For research use only.

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