EMD638683

Cat. No.: HY-15193
CAS No.: 1181770-72-8
Molecular Formula: C₁₈H₁₈F₂N₂O₄
Molecular Weight: 364.34
Target: SGK
Pathway: Metabolic Enzyme/Protease
Storage:
- Powder: -20°C, 3 years; 4°C, 2 years; In solvent: -80°C, 6 months; -20°C, 1 month

SOLVENT & SOLUBILITY

In Vitro
DMSO: ≥ 50 mg/mL (137.23 mM)
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass for 1 mg</th>
<th>Mass for 5 mg</th>
<th>Mass for 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<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>
</tbody>
</table>

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

In Vivo
1. 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
2. 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
3. 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
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) compared to vehicle-dosed controls\(^3\).

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% CO\(_2\)). 10\(^5\) 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\(^2\).

Animal Administration\(^3\)

Rats and Mice

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.

CUSTOMER VALIDATION

- FASEB J. 2015 Sep;29(9):3737-49.
REFERENCES


Caution: Product has not been fully validated for medical applications. For research use only.

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