Roflumilast N-oxide

Cat. No.: HY-100639
CAS No.: 292135-78-5
Molecular Formula: C₁₇H₁₄Cl₂F₂N₂O₄
Molecular Weight: 419.21
Target: Phosphodiesterase (PDE)
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: 250 mg/mL (596.36 mM; Need ultrasonic)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.3854 mL</td>
<td>11.9272 mL</td>
<td>23.8544 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4771 mL</td>
<td>2.3854 mL</td>
<td>4.7709 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2385 mL</td>
<td>1.1927 mL</td>
<td>2.3854 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 >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.96 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Roflumilast N-oxide is a PDE type 4 inhibitor.

IC₅₀ & Target
PDE type 4[^1]

In Vitro
Roflumilast N-oxide at 2 nM partly mitigates the cigarette smoke extract (CSE)-induced epithelial to mesenchymal transition (EMT) in WD-HBEC in vitro. Roflumilast N-oxide (2 nM) reverses the compromised expression of E-cadherin transcripts following CSE by 45%. The expression of collagen type I is abrogated by Roflumilast N-oxide (2 nM). The epithelial cell phenotype appears protected when cells are co-incubated with Roflumilast N-oxide (2 nM). Pre-incubation with Roflumilast N-oxide (2 nM) also partly attenuates the nuclear translocation of β-catenin[^2].

[^1]: MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo

Single treatment of db/db mice with 10 mg/kg Roflumilast N-oxide enhances plasma glucagon-like peptide-1 (GLP-1) 4-fold. Chronic treatment of db/db mice with Roflumilast N-oxide at 3 mg/kg shows prevention of disease progression. Roflumilast-N-oxide abolishes the increase in blood glucose, reduces the increment in HbA1c by 50% and doubles fasted serum insulin compare with vehicle, concomitants with preservation of pancreatic islet morphology. Furthermore, Roflumilast-N-oxide amplifies forskolin-induced insulin release in primary islets. Roflumilast-N-oxide also shows stronger glucose-lowering effects than its parent compound\(^3\).

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

---

PROTOCOL

**Cell Assay**\(^1\)

A549 cells are washed and cultured overnight in serum-free F-12 K medium supplemented with antibiotics, L-glutamine and HEPES. The starved cells are incubated with Neutrophil elastase (NE) for 30 min or vehicle (PBS), washed with PBS and then cultured in serum free F-12 K. After stimulation, cell supernatants are collected at 24 h (for cytokine measurements) and cell pellets are collected after 2 h (for mRNA expression analysis). Alternatively, A549 cells are pre-incubated for 2 h with Roflumilast N-oxide (RNO) (at 0.1 \(\mu\)M, 0.3 \(\mu\)M and 1 \(\mu\)M), vehicle (DMSO 0.01%) prior to the addition of NE. All experiments are performed in serum-free medium in triplicate and are repeated at least three times. At the end of the incubation period, culture supernatants are harvested and stored at -80°C until further analysis\(^1\).

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

**Animal Administration**\(^3\)

At 7 weeks of age, 16 h fasting mice receive a single oral dose of vehicle (4% methocel) or 10 mg/kg Roflumilast-N-oxide, and a glucose bolus of 2 g/kg body weight is co-administered as a physiological initiator for glucagon-like peptide-1 (GLP-1) secretion. Plasma GLP-1 is analyzed 60 min before, and 10 and 60 min after administration of Roflumilast-N-oxide and glucose. The effect of Roflumilast-N-oxide on plasma GLP-1 is also investigated in the absence of the glucose bolus\(^3\).

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

---

REFERENCES


---

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA

www.MedChemExpress.com