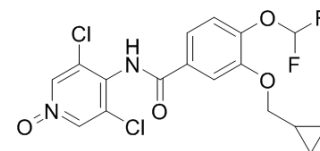


Roflumilast N-oxide

Cat. No.:	HY-100639		
CAS No.:	292135-78-5		
Molecular Formula:	C ₁₇ H ₁₄ Cl ₂ F ₂ N ₂ O ₄		
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	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 320 mg/mL (763.34 mM; Need ultrasonic and warming)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.3854 mL	11.9272 mL	23.8544 mL
	5 mM	0.4771 mL	2.3854 mL	4.7709 mL
	10 mM	0.2385 mL	1.1927 mL	2.3854 mL

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

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].

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 HbA_{1c} 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 μ M, 0.3 μ M and 1 μ 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

- [1]. Victoni T, et al. Roflumilast n-oxide associated with PGE2 prevents the neutrophil elastase-induced production of chemokines by epithelial cells. *Int Immunopharmacol.* 2016 Jan;30:1-8.
- [2]. Milara J, et al. Simvastatin Increases the Ability of Roflumilast N-oxide to Inhibit Cigarette Smoke-Induced Epithelial to Mesenchymal Transition in Well-differentiated Human Bronchial Epithelial Cells in vitro. *COPD.* 2015 Jun;12(3):320-31.
- [3]. Vollert S, et al. The glucose-lowering effects of the PDE4 inhibitors roflumilast and roflumilast-N-oxide in db/db mice. *Diabetologia.* 2012 Oct;55(10):2779-2788.

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

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