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产品名称：罗氟司特氧化物
产品别名：Roflumilast N-oxide；罗氟司特 N-氧化物

生物活性：

Description	Roflumilast N-oxide is a PDE type 4 inhibitor.
IC_{50} & 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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : 320 mg/mL** (**763.34 mM;** Need ultrasonic and warming)

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

*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°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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.

实验参考：

	A549 cells are washed and cultured overnight in serum-free F-12 K medium supplemented with

Cell Assay	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 μM, 0.3 μM and 1 μM), 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].
Animal Administration	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].
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.