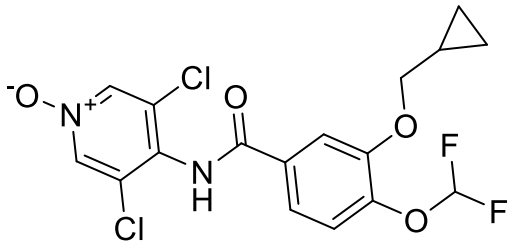
Product data sheet

MedKoo Cat#: 329998 Name: Roflumilast N-oxide CAS#: 292135-78-5 Chemical Formula: $C_{17}H_{14}Cl_2F_2N_2O_4$ Exact Mass: 418.0299 Molecular Weight: 419.21	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Roflumilast N-oxide is a PDE-4 inhibitor. Roflumilast N-oxide is the active metabolite of roflumilast. Roflumilast (also known as Daxas and Daliresp) acts as a selective, long-acting inhibitor of PDE-4. It has anti-inflammatory effects and is under development as an orally administered drug for the treatment of inflammatory conditions of the lungs.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMF	30	71.56
DMSO	30	71.56
Ethanol	5	11.93

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.39 mL	11.93 mL	23.86 mL
5 mM	0.48 mL	2.39 mL	4.77 mL
10 mM	0.24 mL	1.19 mL	2.39 mL
50 mM	0.05 mL	0.24 mL	0.48 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Abdel-Wahab BA, Walbi IA, Albarqi HA, Ali FEM, Hassanein EHM. Roflumilast protects from cisplatin-induced testicular toxicity in male rats and enhances its cytotoxicity in prostate cancer cell line. Role of NF-κB-p65, cAMP/PKA and Nrf2/HO-1, NQO1 signaling. Food Chem Toxicol. 2021 May;151:112133. doi: 10.1016/j.fct.2021.112133. Epub 2021 Mar 20. PMID: 33757793.
2. Gong S, Chen Y, Meng F, Zhang Y, Li C, Zhang G, Huan W, Wu F. Roflumilast enhances cisplatin-sensitivity and reverses cisplatin-resistance of ovarian cancer cells via cAMP/PKA/CREB-FtMt signalling axis. Cell Prolif. 2018 Oct;51(5):e12474. doi: 10.1111/cpr.12474. Epub 2018 Aug 2. PMID: 30069985; PMCID: PMC6528923.

In vivo study

1. Farid HA, Sayed RH, El-Shamarka ME, Abdel-Salam OME, El Sayed NS. PI3K/AKT signaling activation by roflumilast ameliorates rotenone-induced Parkinson's disease in rats. Inflammopharmacology. 2023 Aug 4. doi: 10.1007/s10787-023-01305-x. Epub ahead of print. PMID: 37541971.

2. Patel P, Patel S, Chudasama P, Soni S, Raval M. Roflumilast ameliorates diabetic nephropathy in rats through down-regulation of JAK/STAT signaling pathway. Naunyn Schmiedebergs Arch Pharmacol. 2023 Jun 15. doi: 10.1007/s00210-023-02535-0. Epub ahead of print. PMID: 37318524.

7. Bioactivity

Biological target:

Roflumilast N-oxide is an inhibitor of phosphodiesterase 4 (PDE4; IC50 = 2 nM). It is selective for PDE4 over PDE1-3 and PDE5 (IC50s = >10,000 nM for all). It reduces TNF-α-induced ICAM-1 and eotaxin levels when used in combination with PGE2 in GM06114 human fetal lung fibroblasts (IC50s = 0.9 and 0.5 nM, respectively). It also reduces bFGF-induced and IL-1β augmented proliferation in the same cells.

In vitro activity

In the PC3 cell line, roflumilast reversed cisplatin (CIS)-induced abnormalities in sperm characteristics, normalized serum testosterone level, ameliorated CIS-induced alterations in testicular and epididymal weights, and restored normal testicular structure. Roflumilast increased intracellular cAMP levels, PKA, and HO-1 activities; Nrf2, NQO-1 and HO-1 gene expression; improved testicular oxidative stress parameters and inflammatory mediators; and reduced the proapoptotic proteins, caspase-3, Bax and increased Bcl-2.

Reference: Food Chem Toxicol. 2021 May;151:112133. https://pubmed.ncbi.nlm.nih.gov/33757793/

In vivo activity

This study revealed that roflumilast exerted neuroprotective effects in rotenone-induced neurotoxicity in a model of Parkinson's disease in rats. Rats treated with roflumilast showed an improvement in motor activity and coordination and preservation of dopaminergic neurons in the striatum. Roflumilast increased cAMP level and activated the PI3K/AKT axis via stimulation of CREB/BDNF/TrkB and SIRT1/PTP1B/IGF1 signaling cascades. Roflumilast caused an upsurge in mTOR and Nrf2, halted GSK-3β and NF-κB, and suppressed FoxO1 and caspase-3.

Reference: Inflammopharmacology. 2023 Aug 4. https://pubmed.ncbi.nlm.nih.gov/37541971/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.