Doxofylline

Cat. No.: HY-B0004

CAS No.: 69975-86-6

Molecular Formula: $C_{11}H_{14}N_4O_4$

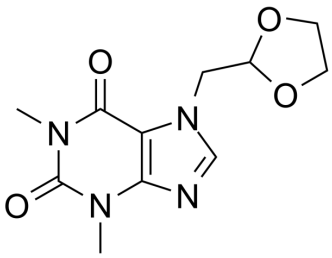
Molecular Weight: 266.25

Target: Adenosine Receptor; Phosphodiesterase (PDE); Reactive Oxygen Species

Pathway: GPCR/G Protein; Metabolic Enzyme/Protease; Immunology/Inflammation; NF-κB

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 : 50 mg/mL (187.79 mM; Need ultrasonic)

H_2O : 25 mg/mL (93.90 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.7559 mL	18.7793 mL	37.5587 mL
5 mM	0.7512 mL	3.7559 mL	7.5117 mL
10 mM	0.3756 mL	1.8779 mL	3.7559 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 65 mg/mL (244.13 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (9.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (9.39 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (9.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Doxofylline is an orally active PDE IV inhibitor and A1AR antagonist. Doxofylline reduces inflammation in epithelial cells via inhibiting mitochondrial ROS production and amelioration of multiple cellular pathways (NLRP3-TXNIP inflammasome activation). Doxophylline can be used in studies of asthma, chronic obstructive pulmonary disease, and bronchospasm[1][2][3].

IC_{50} & Target	Adenosine A1 receptor, phosphodiesterase IV[1][2][3].

In Vitro

Doxofylline (5, 10 μM; 48 h) shows potent protection against LPS-induced epithelial inflammation by reducing PGE2, NO release, and decreasing mitochondrial ROS generation in 16HBE cells[1].
Doxofylline (5, 10 μM; 48 h) suppresses LPS-induced expression of NADPH oxidase subunits and TXNIP 16HBE cells[1].
Doxofylline (5, 10 μM; 48 h) inhibits LPS-induced NLRP3 inflammasome activation and secretion of IL-1b and IL-18, as well as mitigates LPS-mediated SIRT1 reduction[1].
Doxofylline (0.1-10 μM; 15 min) significantly reduces fMLP-induced leukocyte migration in BM cells (fMLP: Formyl-Methionyl-Leucyl-Phenylalanine)[2].

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

Cell Viability Assay[1]

Cell Line:	16HBE cells
Concentration:	5, 10 μM
Incubation Time:	48 h
Result:	Weakened LPS-induced NO and PGE2 in a dose-dependent manner. Exerted dose-dependent inhibition on LPS-induced mitochondrial ROS production and NADPH oxidase subunits expression. Suppressed LPS-induced TXNIP expression and NLRP3 inflammasome activation at the protein level in a dose-dependent manner. Inhibited LPS-induced secretion of IL-1b and IL-18.

Cell Viability Assay[2]

Cell Line:	BM cells (from naive mice)
Concentration:	0.1-10 μM
Incubation Time:	15 min (pretreat)
Result:	Notably surpressed positive migration of BM cells in response to fMLP.

In Vivo

Doxofylline (0.3, 1 mg/kg; i.p.; single) inhibits LPS-induced inflammation in the lungs of mice[2].
Doxofylline (0.3 mg/kg; i.p.; pre-treat; single) notably reduces the adhesion of cells to the vascular tissue and surpresses the expression of LPS-induced ICAM-1 in vivo[2].

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

Animal Model:	Male BALB/c mice (6 to 8-week-old)[2].
Dosage:	0.3, 1 mg/kg
Administration:	Intraperitoneal injection; single.
Result:	Significantly inhibited the migration of neutrophils and the release of IL-6 and TNF-a into the lung lumen. Increased the bone marrow leukocyte numbers to levels similar to those seen in the saline-treated group. Notably reduced the number of circulating leukocytes in comparison to LPS-treated mice. Significantly reduced accumulation of neutrophils in the peribronchial area.

Animal Model:	Male BALB/c mice (6 to 8-week-old)[2].

Dosage:	0.3 mg/kg
Administration:	Intraperitoneal injection; pre-treat; single.
Result:	Significantly reduced the adhesion of cells to the vascular tissue, but not the rolling of cells along the vessel wall in mice. Significantly reduced the expression of ICAM-1 induced by LPS.

REFERENCES

[1]. Jiao P, et al. The protective effect of doxofylline against lipopolysaccharides (LPS)-induced activation of NLRP3 inflammasome is mediated by SIRT1 in human pulmonary bronchial epithelial cells. Artif Cells Nanomed Biotechnol. 2020 Dec;48(1):687-694.

[2]. Riffo-Vasquez Y, et al. Doxofylline, a novofylline inhibits lung inflammation induced by lipopolysacharide in the mouse. Pulm Pharmacol Ther. 2014 Apr;27(2):170-8.

[3]. Shukla D, et al. Doxofylline: a promising methylxanthine derivative for the treatment of asthma and chronic obstructive pulmonary disease. Expert Opin Pharmacother. 2009 Oct;10(14):2343-56.

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