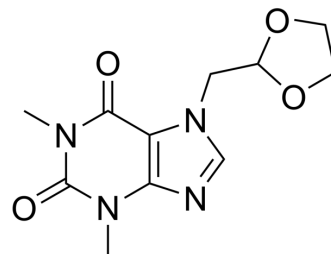


## Doxofylline

<b>Cat. No.:</b>	HY-B0004		
<b>CAS No.:</b>	69975-86-6		
<b>Molecular Formula:</b>	C <sub>11</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub>		
<b>Molecular Weight:</b>	266.25		
<b>Target:</b>	Adenosine Receptor; Phosphodiesterase (PDE); Reactive Oxygen Species		
<b>Pathway:</b>	GPCR/G Protein; Metabolic Enzyme/Protease; Immunology/Inflammation; NF-κB		
<b>Storage:</b>	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<sub>2</sub>O : 25 mg/mL (93.90 mM; Need ultrasonic)

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

- 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
- 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
- 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
- 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). Doxofylline can be used in studies of asthma, chronic obstructive pulmonary disease, and bronchospasm<sup>[1][2][3]</sup>.

<b>IC<sub>50</sub> &amp; Target</b>	Adenosine A1 receptor, phosphodiesterase IV <sup>[1][2][3]</sup> .																
<b>In Vitro</b>	<p>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<sup>[1]</sup>.</p> <p>Doxofylline (5, 10 μM; 48 h) suppresses LPS-induced expression of NADPH oxidase subunits and TXNIP 16HBE cells<sup>[1]</sup>.</p> <p>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<sup>[1]</sup>.</p> <p>Doxofylline (0.1-10 μM; 15 min) significantly reduces fMLP-induced leukocyte migration in BM cells (fMLP: Formyl-Methionyl-Leucyl-Phenylalanine)<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Cell Viability Assay<sup>[1]</sup></p> <table border="1" data-bbox="347 520 1516 919"> <tr> <td>Cell Line:</td> <td>16HBE cells</td> </tr> <tr> <td>Concentration:</td> <td>5, 10 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>48 h</td> </tr> <tr> <td>Result:</td> <td> <p>Weakened LPS-induced NO and PGE2 in a dose-dependent manner.</p> <p>Exerted dose-dependent inhibition on LPS-induced mitochondrial ROS production and NADPH oxidase subunits expression.</p> <p>Suppressed LPS-induced TXNIP expression and NLRP3 inflammasome activation at the protein level in a dose-dependent manner.</p> <p>Inhibited LPS-induced secretion of IL-1b and IL-18.</p> </td> </tr> </table> <p>Cell Viability Assay<sup>[2]</sup></p> <table border="1" data-bbox="347 995 1516 1226"> <tr> <td>Cell Line:</td> <td>BM cells (from naive mice)</td> </tr> <tr> <td>Concentration:</td> <td>0.1-10 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>15 min (pretreat)</td> </tr> <tr> <td>Result:</td> <td>Notably suppressed positive migration of BM cells in response to fMLP.</td> </tr> </table>	Cell Line:	16HBE cells	Concentration:	5, 10 μM	Incubation Time:	48 h	Result:	<p>Weakened LPS-induced NO and PGE2 in a dose-dependent manner.</p> <p>Exerted dose-dependent inhibition on LPS-induced mitochondrial ROS production and NADPH oxidase subunits expression.</p> <p>Suppressed LPS-induced TXNIP expression and NLRP3 inflammasome activation at the protein level in a dose-dependent manner.</p> <p>Inhibited LPS-induced secretion of IL-1b and IL-18.</p>	Cell Line:	BM cells (from naive mice)	Concentration:	0.1-10 μM	Incubation Time:	15 min (pretreat)	Result:	Notably suppressed positive migration of BM cells in response to fMLP.
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<b>In Vivo</b>	<p>Doxofylline (0.3, 1 mg/kg; i.p.; single) inhibits LPS-induced inflammation in the lungs of mice<sup>[2]</sup>.</p> <p>Doxofylline (0.3 mg/kg; i.p.; pre-treat; single) notably reduces the adhesion of cells to the vascular tissue and suppresses the expression of LPS-induced ICAM-1 in vivo<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1" data-bbox="347 1423 1516 1835"> <tr> <td>Animal Model:</td> <td>Male BALB/c mice (6 to 8-week-old)<sup>[2]</sup>.</td> </tr> <tr> <td>Dosage:</td> <td>0.3, 1 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Intraperitoneal injection; single.</td> </tr> <tr> <td>Result:</td> <td> <p>Significantly inhibited the migration of neutrophils and the release of IL-6 and TNF-α into the lung lumen.</p> <p>Increased the bone marrow leukocyte numbers to levels similar to those seen in the saline-treated group.</p> <p>Notably reduced the number of circulating leukocytes in comparison to LPS-treated mice.</p> <p>Significantly reduced accumulation of neutrophils in the peribronchial area.</p> </td> </tr> </table> <table border="1" data-bbox="347 1877 1516 1940"> <tr> <td>Animal Model:</td> <td>Male BALB/c mice (6 to 8-week-old)<sup>[2]</sup>.</td> </tr> </table>	Animal Model:	Male BALB/c mice (6 to 8-week-old) <sup>[2]</sup> .	Dosage:	0.3, 1 mg/kg	Administration:	Intraperitoneal injection; single.	Result:	<p>Significantly inhibited the migration of neutrophils and the release of IL-6 and TNF-α into the lung lumen.</p> <p>Increased the bone marrow leukocyte numbers to levels similar to those seen in the saline-treated group.</p> <p>Notably reduced the number of circulating leukocytes in comparison to LPS-treated mice.</p> <p>Significantly reduced accumulation of neutrophils in the peribronchial area.</p>	Animal Model:	Male BALB/c mice (6 to 8-week-old) <sup>[2]</sup> .						
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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]. Rifo-Vasquez Y, et al. Doxofylline, a novofylline inhibits lung inflammation induced by lipopolysaccharide 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.

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

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