

Product Data Sheet

Product Name: A2AR-agonist-1

Cat. No.: GC30987

Chemical Properties

Cas. No. 41552-95-8

SMILES OC[C@H]1[C@H]([C@H]([C@H](N2C=NC3=C2N=CN=C3NCCC4=CNC5=C4C=CC=C5)O1)O)O

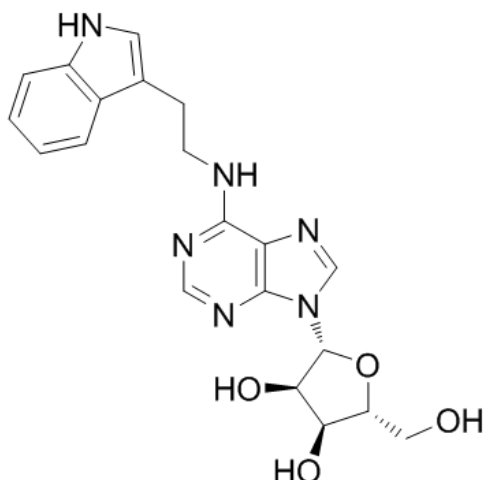
Formula $C_{20}H_{22}N_6O_4$ M.Wt 410.43

Solubility DMSO: 10 mM Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines RAW264.7

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Preparation Method 1×10^6 macrophage cells per well were treated by the A2AR-agonist-1 (1.0 μ M) or antagonist SCH58261 (1.0 μ M) for 30 min and transferred to the low-glucose DMEM and cultured under a hypoxic condition (1% O₂, 5% CO₂, and 94% N₂, 37°C) for 2, 6, 12, or 24h. The protein expression of inflammatory cytokines from macrophages cultured under low-glucose and hypoxic conditions was examined by ELISA. Mouse Quantikine ELISA kits for TNF- α , IL-1 β , and IL-10 were used in the study. Working reagents were prepared and 50 μ L of standard controls and cell supernatants from each group were added to the wells of a plate according to manufactures instructions. The antibody was added and incubated for two hours at room temperature, followed by incubation with the substrate solution for 30 minutes. The absorbance was read using a FLvostar Omega microplate reader at 450nm and 540nm.

Reaction Conditions 1 μ M; 37°C for 2, 6, 12, or 24h

Applications Under conditions of low glucose and low oxygen, A2AR-agonist-1 inhibits the expression of inflammatory and anti-inflammatory cytokines in macrophages.

Animal experiment [2]:

Animal models C57BL/6N male mice

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Twenty-four 57BL/6N mice were randomly divided into four groups. After isoflurane gas anesthesia, 0.1mL (50mg/mL) of silica suspension was given intravenously in the SiO₂ group, the SiO₂+Vehicle group and the SiO₂+ A2AR-agonist-1 group, while the control group mice were given the same volume of normal saline group. In addition, mice in the SiO₂+A2AR-agonist-1 group were

Preparation Method intraperitoneally injected with 0.2mL of A2AR-agonist-1 solution. Mice in the SiO₂+Vehicle group were injected with 0.2mL of A2AR-agonist-1 free vehicle every day. Last for 28 days. Take the left lung of the mouse, soak it in 10% formalin for 48 hours, and then coat it with wax. Subsequently, it was cut into 5µm sections. Hematoxylin and eosin (H&E) staining and Masson staining were used to analyze the pathological changes of mouse lung tissue.

Dosage form 0.25mg/kg; once a day for 28 consecutive days.

Applications A2AR-agonist-1 reduces the infiltration of inflammatory cells in lung tissue and the degree of pulmonary fibrosis.

References:

- [1] Mou K-J, Shen K-F, Li Y-L, et al. Adenosine A2A Receptor in Bone Marrow-Derived Cells Mediated Macrophages M2 Polarization via PPAR γ -P65 Pathway in Chronic Hypoperfusion Situation. *Frontiers in Aging Neuroscience* 2022, Volume 13 - 2021.
- [2] Tian Y, Xia J, Yang G, et al. A2aR inhibits fibrosis and the EMT process in silicosis by regulating Wnt/ β -catenin pathway. *Ecotoxicol Environ Saf* 2023, 249:114410.

Background

A2AR-agonist-1 is a potent agonist of adenosine A2A receptor (A2AR) and equilibrative nucleoside transporter1 (ENT1), with K_i values of 4.39 and 3.47, respectively^[1]. By activating A2AR, it regulates the downstream cAMP signaling pathway, while inhibiting ENT1 to reduce cellular adenosine uptake and increase extracellular adenosine concentration, synergistically enhancing the activation effect of

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A2AR^[2]. As an important ligand for the G protein-coupled receptor family, its dual mechanism of action can effectively regulate intracellular signal transduction, thereby exerting multiple physiological effects such as anti-inflammation, neuroprotection, and improvement of cardiovascular function^[3].

In vitro, treatment of macrophages with A2AR-agonist-1 (1 μ M) for 2-24 hours induced M2 polarization of macrophages, increased the expression of the anti-inflammatory cytokine IL-10 through the PPAR γ -P65 pathway, and inhibited the expression of tumor necrosis factor- α (TNF- α) and interleukin-1 β (IL-1 β)^[4]. Treatment of human corneal epithelial cells with A2AR-agonist-1 (0.001-1 μ M) for 12 hours significantly promoted corneal epithelial cell proliferation and migration and accelerated wound healing through a biphasic regulatory mechanism of short-term phosphorylation inhibition of YAP activity and long-term activation of YAP nuclear translocation^[5].

In vivo, silicosis model mice were treated with intraperitoneal injection of A2AR-Agonist-1 (0.25mg/kg) for 28 days. By activating A2AR to inhibit the Wnt/ β -catenin signaling pathway, the inflammation, fibrosis and epithelial-mesenchymal transition of lung tissue were alleviated^[6]. Intraperitoneal injection of A2AR-agonist-1 (1mg/kg) reduced the expression of E-selectin and ICAM-1 proteins in the aorta, heart, and pulmonary blood vessels of LPS-challenged mice, alleviating corresponding cardiac inflammatory damage^[7].

References:

- [1] Chen JB, Liu EM, Chern TR, et al. Design and synthesis of novel dual-action compounds targeting the adenosine A(2A) receptor and adenosine transporter for neuroprotection. ChemMedChem 2011, 6(8):1390-1400.
- [2] Cristalli G, Lambertucci C, Marucci G, et al. A2A adenosine receptor and its modulators: overview on a druggable GPCR and on structure-activity relationship analysis and binding requirements of agonists and antagonists. Curr Pharm Des 2008, 14(15):1525-1552.
- [3] Al-Attraqchi OHA, Attimarad M, Venugopala KN, et al. Adenosine A2A Receptor as a Potential Drug Target - Current Status and Future Perspectives. Curr Pharm Des 2019, 25(25):2716-2740.
- [4] Mou K-J, Shen K-F, Li Y-L, et al. Adenosine A2A Receptor in Bone Marrow-Derived Cells Mediated Macrophages M2 Polarization via PPAR γ -P65 Pathway in Chronic Hypoperfusion Situation. Frontiers in Aging Neuroscience 2022, Volume 13 - 2021.
- [5] Sun Q, Jiang N, Yao R, et al. An agonist of the adenosine A(2A) receptor, CGS21680, promotes corneal epithelial wound healing via the YAP signalling pathway. Br J Pharmacol 2024,

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181(19):3779-3795.

[6] Tian Y, Xia J, Yang G, et al. A2aR inhibits fibrosis and the EMT process in silicosis by regulating Wnt/ β -catenin pathway. *Ecotoxicol Environ Saf* 2023, 249:114410.

[7] Li Y, Chen T, Cheang I, et al. Macrophage A2aR Alleviates LPS-Induced Vascular Endothelial Injury and Inflammation via Inhibiting M1 Polarisation and Oxidative Stress. *J Cell Mol Med* 2025, 29(5):e70458.

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