

Product Data Sheet

Product Name: JZL184
Cat. No.: GC14390

Chemical Properties

Cas. No. 1101854-58-3

Chemical Name (4-nitrophenyl) 4-[bis(1,3-benzodioxol-5-yl)-hydroxymethyl]piperidine-1-carboxylate

SMILES C1CN(CCC1C(C2=CC3=C(C=C2)OCO3)(C4=CC5=C(C=C4)OCO5)O)C(=O)OC6=CC=C(C=C6)[N+](=O)[O-]

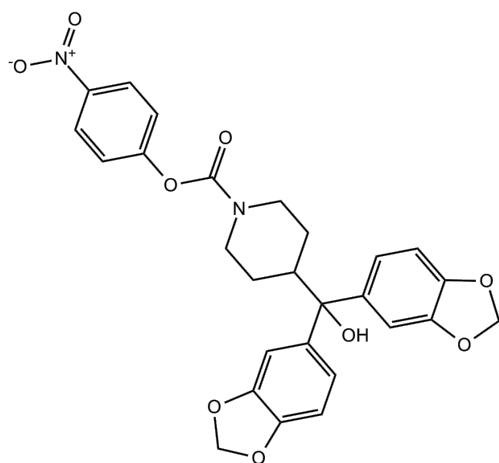
Formula $C_{27}H_{24}N_2O_9$ M.Wt 520.49

Solubility $\geq 20.35\text{mg/mL}$ in DMSO 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 A549, H358 cells

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

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Under hypoxic conditions, A549 and H358 cells were incubated with vehicle or Preparation Method JZL184 (0.01, 0.1, 1μM) for 6h. Western blot was used to detect the expression of HIF-1α and HIF-2α proteins.

Reaction Conditions 0.01, 0.1, 1μM; 6h

Applications JZL184 induced a concentration-dependent partial decrease in HIF-1α protein in hypoxic A549 cells. In H358 cells, however, no significant inhibitory effect of JZL184 on HIF-1α could be detected.

Animal experiment [2]:

Animal models Athymic nude mice、 C57BL/6j mice

Preparation Method Sixteen female NMRI athymic nude mice 5-week-old mice received para-tibial injection of human MNNG/HOS osteosarcoma cancer cells (2×10^6 cells) and 16 female C57BL/6j 6-week old mice received para-tibial injection of mouse MOSJ osteosarcoma cancer cells (2×10^6 cells) or a sham injection of PBS into their right leg. Animals were divided into two groups (n=8) and received intraperitoneal injection of either vehicle (water) or JZL184 (16mg/kg, thrice weekly). Animals were euthanized 35 days post injection and bones were analyzed by microCT (Skyscan 1172 scanner).

Dosage form 16mg/kg; thrice weekly; i.p.

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Applications JZL184 reduces skeletal tumour growth, metastasis and cachexia and improves survival in mice.

References:

- [1] Wittig F, Pannenberg L, Schwarz R, et al. Antiangiogenic Action of JZL184 on Endothelial Cells via Inhibition of VEGF Expression in Hypoxic Lung Cancer Cells[J]. Cells, 2023, 12(19): 2332.
- [2] Marino S, de Ridder D, Bishop R T, et al. Paradoxical effects of JZL184, an inhibitor of monoacylglycerol lipase, on bone remodelling in healthy and cancer-bearing mice[J]. EBioMedicine, 2019, 44: 452-466.

Background

JZL184 is a potent, selective and irreversible inhibitor of monoacylglycerol lipase (MAGL), which blocks the hydrolysis of 2-arachidonoylglycerol (2-AG) in the brain membrane with an IC₅₀ value of 8nM^[1]. JZL184 displays >300-fold selectivity for MAGL than fatty acid amide hydrolase (FAAH) ^[2]. JZL184 can alleviate neurological impairment after cardiac arrest by regulating mitochondrial transport and lipid droplet accumulation^[3].

In vitro, JZL184 (0.01, 0.1, 1μM) treated A549 and H358 cells cultured under hypoxia for 6h inhibited HIF-1α protein expression in hypoxic A549 cells in a dose-dependent manner, but no significant decrease in HIF-1α protein expression was detected in H358 cells^[4].

In vivo, JZL184 (16mg/kg) was intraperitoneally injected into mice with cancer-induced bone disease for 35 days, which significantly inhibited cancer-related bone damage, reduced bone tumor growth, reduced the migration and osteolytic characteristics of bone-tropic cancer cells, and prolonged the survival of mice^[5]. JZL184 (10mg/kg) was intraperitoneally injected into rats with acute immune stress induced by lipopolysaccharide (LPS) and attenuated the increase of IL-1β, IL-6, TNF-α, and IL-10 in the frontal cortex of rats, but did not attenuate the expression of NFκB inhibitor (IκBa)^[6]. JZL184 (40mg/kg) was intraperitoneally injected into transgenic APdE9 mice and significantly reduced the proinflammatory response of microglia in the hippocampus, temporal lobe, and parietal cortex of mice, and reduced the total load of Aβ and its precursors^[7].

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- [1] Long J Z, Li W, Booker L, et al. Selective blockade of 2-arachidonoylglycerol hydrolysis produces cannabinoid behavioral effects[J]. Nature chemical biology, 2009, 5(1): 37-44.
- [2] Pan B, Wang W, Long J Z, et al. Blockade of 2-arachidonoylglycerol hydrolysis by selective monoacylglycerol lipase inhibitor 4-nitrophenyl 4-(dibenzo [d][1, 3] dioxol-5-yl (hydroxy) methyl) piperidine-1-carboxylate (JZL184) Enhances retrograde endocannabinoid signaling[J]. The Journal of pharmacology and experimental therapeutics, 2009, 331(2): 591-597.
- [3] Zhang Q, Zhang C, Lu Y, et al. JZL-184 Alleviate Neurological Impairment through Regulation of Mitochondrial Transfer and Lipid Droplet Accumulation after Cardiac Arrest[J]. Molecular Neurobiology, 2024: 1-17.
- [4] Wittig F, Pannenberg L, Schwarz R, et al. Antiangiogenic Action of JZL184 on Endothelial Cells via Inhibition of VEGF Expression in Hypoxic Lung Cancer Cells[J]. Cells, 2023, 12(19): 2332.
- [5] Marino S, de Ridder D, Bishop R T, et al. Paradoxical effects of JZL184, an inhibitor of monoacylglycerol lipase, on bone remodelling in healthy and cancer-bearing mice[J]. EBioMedicine, 2019, 44: 452-466.
- [6] Kerr D M, Harhen B, Okine B N, et al. The monoacylglycerol lipase inhibitor JZL 184 attenuates LPS-induced increases in cytokine expression in the rat frontal cortex and plasma: differential mechanisms of action[J]. British journal of pharmacology, 2013, 169(4): 808-819.
- [7] Pihlaja R, Takkinen J, Eskola O, et al. Monoacylglycerol lipase inhibitor JZL184 reduces neuroinflammatory response in APdE9 mice and in adult mouse glial cells[J]. Journal of Neuroinflammation, 2015, 12: 1-6.

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