

Product Data Sheet

Product Name: JZL 195
Cat. No.: GC12693

Chemical Properties

Cas. No. 1210004-12-8

Chemical Name 4-nitrophenyl 4-(3-phenoxybenzyl)piperazine-1-carboxylate

SMILES O=C(N1CCN(CC2=CC=CC(OC3=CC=CC=C3)=C2)CC1)OC(C=C4)=CC=C4[N+](O-)=O

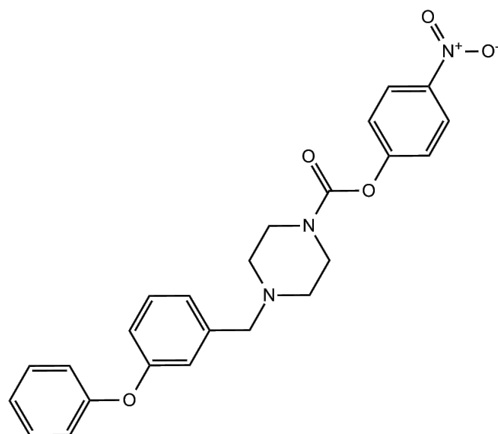
Formula $C_{24}H_{23}N_3O_5$ M.Wt 433.46

Solubility DMF: 5 mg/ml, DMSO: 1.25 mg/ml 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 HK-2 cells (Human immortalized renal proximal tubular cells)

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HK-2 cells were treated with 250nM JZL 195 for 24h, after which EPO mRNA Preparation Method and protein expression levels were analyzed by real-time PCR and Western blotting, respectively.

Reaction
Conditions 250nM; 24h

Applications Treatment of JZL 195 can significantly enhance the mRNA and protein expression levels of EPO.

Animal experiment [2]:

Animal models Sprague-Dawley rat

Preparation Method Male Sprague-Dawley rats were intraperitoneally injected with 3mg/kg JZL 195 2h after NTG administration. Following behavioral testing, blood samples were collected via decapitation, and serum levels of CGRP were quantified using ELISA.

Dosage form 3mg/kg; i.p.

Applications Treatment of JZL 195 significantly reduced the increase in CGRP levels caused by NTG.

References:

[1] BARAGHITHY S, SOAE Y, ASSAF D, et al. Renal proximal tubule cell cannabinoid-1 receptor regulates bone remodeling and mass via a kidney-to-bone axis[J]. Cells, 2021, 10(2): 414.

[2] GRECO R, DEMARTINI C, FRANCAVILLA M, et al. Dual inhibition of FAAH and MAGL counteracts migraine-like pain and behavior in an animal model of migraine[J]. Cells, 2021, 10(10): 2543.

Background

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JZL 195 is a highly selective and irreversible dual inhibitor of fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL), with IC₅₀ values of 2nM and 4nM, respectively^[1]. In vivo, JZL 195 elevates the levels of endogenous cannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG)^[2]. JZL 195 is commonly used to alleviate neuropathic and inflammatory pain, manage chemotherapy-induced peripheral neuropathy, and investigate potential antihypertensive effects, among other applications^[3,4].

In vitro, pretreatment of immortalized human renal proximal tubular HK-2 cells with 250nM JZL 195 for 24h indirectly activated CB₁R and significantly increased the mRNA and protein expression levels of erythropoietin (EPO)^[5].

In vivo, oral administration of JZL 195 (20mg/kg) for 15 days in a streptozotocin-induced sporadic Alzheimer's disease mouse model significantly reversed the elevated levels of Aβ₁₋₄₂ in hippocampal tissue^[6]. Intraperitoneal injection of JZL 195 (3mg/kg) 2h after nitroglycerin (NTG) administration in Sprague-Dawley rats, with tissue sampling following behavioral tests, significantly reduced the NTG-induced increase in calcitonin gene-related peptide (CGRP) levels^[7]. Intraperitoneal administration of JZL 195 (10mg/kg) 45min before bilateral carotid artery occlusion surgery in C3H mice significantly ameliorated ischemia-induced neurological deficits^[8].

References:

- [1] LONG J Z, NOMURA D K, VANN R E, et al. Dual blockade of FAAH and MAGL identifies behavioral processes regulated by endocannabinoid crosstalk in vivo[J]. Proceedings of the National Academy of Sciences, 2009, 106(48): 20270-20275.
- [2] MANDUCA A, MORENA M, CAMPOLONGO P, et al. Distinct roles of the endocannabinoids anandamide and 2-arachidonoylglycerol in social behavior and emotionality at different developmental ages in rats[J]. European Neuropsychopharmacology, 2015, 25(8): 1362-1374.
- [3] ANDERSON W B, GOULD M J, TORRES R D, et al. Actions of the dual FAAH/MAGL inhibitor JZL195 in a murine inflammatory pain model[J]. Neuropharmacology, 2014, 81: 224-230.
- [4] TOCZEK M, RYSZKIEWICZ P, REMISZEWSKI P, et al. Weak hypotensive effect of chronic administration of the dual FAAH/MAGL inhibitor JZL195 in spontaneously hypertensive rats as revealed by area under the curve analysis[J]. International Journal of Molecular Sciences, 2023, 24(13): 10942.
- [5] BARAGHITHY S, SOAE Y, ASSAF D, et al. Renal proximal tubule cell cannabinoid-1 receptor

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regulates bone remodeling and mass via a kidney-to-bone axis[J]. Cells, 2021, 10(2): 414.

[6] BAJAJ S, ZAMEER S, JAIN S, et al. Effect of the MAGL/FAAH dual inhibitor JZL-195 on streptozotocin-induced Alzheimer's disease-like sporadic dementia in mice with an emphasis on A β , HSP-70, neuroinflammation, and oxidative stress[J]. ACS Chemical Neuroscience, 2022, 13(7): 920-932.

[7] GRECO R, DEMARTINI C, FRANCAVILLA M, et al. Dual inhibition of FAAH and MAGL counteracts migraine-like pain and behavior in an animal model of migraine[J]. Cells, 2021, 10(10): 2543.

[8] MITROSHINA E V, ABOGESSIMENGANE B Z, URAZOV M D, et al. The influence of Glial cell line-derived neurotrophic factor and modulated activity of endocannabinoid system on c3h mice sustainability to ischemic brain injury in vivo[J]. Opera Medica et Physiologica, 2016(S1): 83-84.

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