

Product Data Sheet

Product Name: BMS 309403

Cat. No.: GC11894

Chemical Properties

Cas. No. 300657-03-8

Chemical Name 2-((2'-(5-ethyl-3,4-diphenyl-1H-pyrazol-1-yl)-[1,1'-biphenyl]-3-yl)oxy)acetic acid

SMILES OC(COC1=CC(C2=CC=CC=C2N3N=C(C4=CC=CC=C4)C(C5=CC=CC=C5)=C3CC)=CC=C1)=O

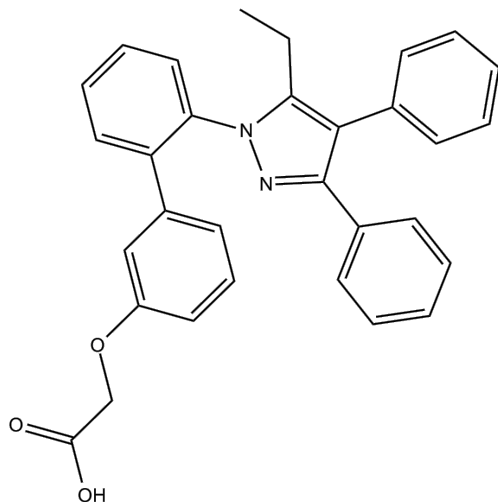
Formula $C_{31}H_{26}N_2O_3$ M.Wt 474.55

Solubility $\geq 18.15\text{mg/mL}$ 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]:

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell lines A2780 cells

The A2780 cells were cultured in a medium containing 10% fetal bovine serum (FBS), 100IU/ml penicillin-streptomycin and 2mM glutamine, with the culture conditions set at 37°C, 5% CO₂ and 95% humidity. A2780 cells were seeded at

Preparation Method a density of 2.35×10^4 cells/ml in 96-well plates and cultured in a medium containing 5% FBS overnight. Then, different concentrations of BMS 309403 (0, 20, 40, 60, 80, and 100µM) were added and the cells were treated for 72 hours. Finally, the number of viable cells was determined.

Reaction
Conditions 0, 20, 40, 60, 80, and 100µM; 72h

Applications BMS 309403 treatment reduced cell viability of A2780 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models Male C57BL/6J mice

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Male C57BL/6J mice (9-10 weeks old, weighing 25-27g) were housed in an environment with a temperature controlled at $23\pm 2^{\circ}\text{C}$ and a 12-hour light/12-hour dark cycle. Mice had free access to food and water. After an adaptation period of 1 week, the mice were randomly divided into 4 groups ($n \geq 6$ in each group): control group, hyperuricemic nephropathy (HN) group, allopurinol group, and FABP4i group. The HN mouse model was established by intragastric Preparation Method administration. A 200 μl solution of adenine (160mg/kg/day) and potassium oxonate (2400mg/kg/day) dissolved in double-distilled water was administered intragastrically daily for 3 weeks. The control group was given the same volume of double-distilled water. 3 hours after intragastric administration, the mice were given allopurinol (10mg/kg/day) or BMS 309403 (40mg/kg/day) daily. After 3 weeks, the mice were sacrificed and kidney samples were collected for subsequent analysis.

Dosage form 40mg/kg/day for 3 weeks; p.o.

Applications BMS 309403 treatment suppressed kidney inflammation and fibrosis in hyperuricemic mice.

References:

- [1] Lemberger L, Wagner R, Heller G, et al. Pharmacological inhibition of lipid import and transport proteins in ovarian cancer[J]. *Cancers*, 2022, 14(23): 6004.
- [2] Shi M, Guo F, Liao D, et al. Pharmacological inhibition of fatty acid-binding protein 4 alleviated kidney inflammation and fibrosis in hyperuricemic nephropathy[J]. *European journal of pharmacology*, 2020, 887: 173570.

Background

BMS 309403 is a potent, orally active and selective inhibitor of adipocyte fatty acid binding protein (FABP4), with an IC_{50} value of $0.71\mu\text{M}$ [1]. The pyrazole core and the 4-position aromatic ring of BMS 309403 can respectively be inserted into two different hydrophobic pockets of the lipid transporter domain of FABP4 to exhibit inhibitory effect and reduce lipid accumulation[2]. BMS

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

309403 has been widely used to attenuate a systemic inflammatory damage in mice [3].

In vitro, BMS 309403 treatment for 72 hours significantly inhibited the proliferation of A2780 cells, SKOV3 cells and OVCAR3 cells, with IC₅₀ values of 48.1μM, 71.2μM and 60.5μM, respectively [4]. 5μM dose of BMS 309403 pretreatment for 2 hours significantly inhibited the DNA synthesis and cell migration of rat vascular smooth muscle cells (VSMCs) induced by PDGF-BB (10ng/ml; 24 hours) [5]. Treatment with 50μM BMS 309403 for 24 hours can alleviate endoplasmic reticulum stress in H9c2 cardiomyocytes under hypoxic conditions and reduce cell apoptosis [6].

In vivo, BMS 309403 treatment via oral administration at a dose of 40mg/kg/day for 6 consecutive weeks could lead to a reduction in liver fat infiltration in ob/ob mice, a significant decrease in total liver triglyceride content, and alleviation of atherosclerosis [7]. For three consecutive weeks, intragastric administration of 40mg/kg/day dose of BMS 309403 significantly inhibited renal inflammation and fibrosis in mice with hyperuricemia, improved renal dysfunction, suppressed the mRNA levels of KIM-1 and NGAL, and reduced the expression of pro-inflammatory cytokines and fibrotic proteins in the damaged kidneys [8].

References:

- [1] Okada T, Hiromura M, Otsuka M, et al. Synthesis of BMS-309403-related compounds, including [14C] BMS-309403, a radioligand for adipocyte fatty acid binding protein[J]. Chemical and Pharmaceutical Bulletin, 2012, 60(1): 164-168.
- [2] Chen S, Pan Z, Liu M, et al. Recent Advances on Small-Molecule Inhibitors of Lipocalin-like Proteins[J]. Journal of Medicinal Chemistry, 2024, 67(7): 5144-5167.
- [3] Su H, Zou Y, Chen G, et al. Exploration of fragment binding poses leading to efficient discovery of highly potent and orally effective inhibitors of FABP4 for anti-inflammation[J]. Journal of Medicinal Chemistry, 2020, 63(8): 4090-4106.
- [4] Lemberger L, Wagner R, Heller G, et al. Pharmacological inhibition of lipid import and transport proteins in ovarian cancer[J]. Cancers, 2022, 14(23): 6004.
- [5] Okamura Y, Otani K, Sekiguchi A, et al. Vasculo-protective effect of BMS-309403 is independent of its specific inhibition of fatty acid-binding protein 4[J]. Pflügers Archiv-European Journal of Physiology, 2017, 469(9): 1177-1188.
- [6] Sun F, Du J, Li H, et al. FABP4 inhibitor BMS309403 protects against hypoxia-induced H9c2 cardiomyocyte apoptosis through attenuating endoplasmic reticulum stress[J]. Journal of Cellular and

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Molecular Medicine, 2020, 24(19): 11188-11197.

[7] Furuhashi M, Tuncman G, Görgün C Z, et al. Treatment of diabetes and atherosclerosis by inhibiting fatty-acid-binding protein aP2[J]. Nature, 2007, 447(7147): 959-965.

[8] Shi M, Guo F, Liao D, et al. Pharmacological inhibition of fatty acid-binding protein 4 alleviated kidney inflammation and fibrosis in hyperuricemic nephropathy[J]. European journal of pharmacology, 2020, 887: 173570.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA