

Product Data Sheet

Product Name: SC 26196

Cat. No.: GC13772

Chemical Properties

Cas. No. 218136-59-5

Chemical Name (E)-2,2-diphenyl-5-(4-((pyridin-3-ylmethylene)amino)piperazin-1-yl)pentanenitrile

SMILES N#CC(C1=CC=CC=C1)(C2=CC=CC=C2)CCCN(CCN3)N=C/C4=CC=CN=C4

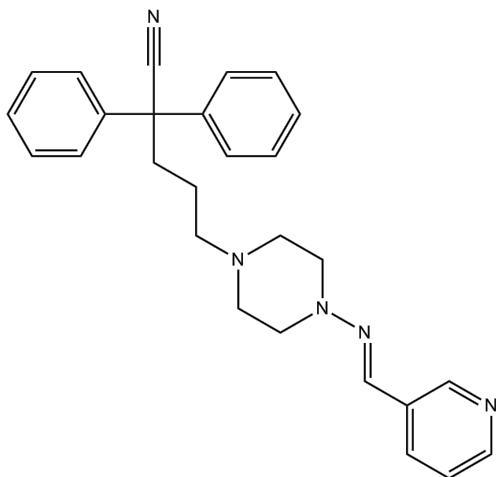
Formula C27H29N5 M.Wt 423.55

Solubility DMF: 12 mg/mL, DMF:PBS (pH 7.2) (1:4): 0.2 mg/mL, DMSO: 5 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]:

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Cell lines 3T3-L1 adipocytes (murine preadipocyte cell line)

Preparation Method 3T3-L1 pre-adipocytes were differentiated in high-glucose DMEM supplemented with 10% FBS, a standard differentiation cocktail (IBMX, DEX, insulin), and treated with the Δ -6 desaturase (D6D) inhibitor SC 26196 (5 μ M) throughout the 8-day differentiation process, either in the presence or absence of α -linolenic acid (ALA, 50 μ M) or eicosapentaenoic acid (EPA, 50 μ M).

Reaction
Conditions 5 μ M; treatment throughout differentiation (8 days).

Applications SC 26196 treatment significantly reduced triacylglycerol (TAG) accumulation in differentiated 3T3-L1 adipocytes. SC 26196 inhibited the conversion of ALA to EPA and docosapentaenoic acid (DPA_n-3). SC 26196 increased the release of non-esterified fatty acids (NEFA) and glycerol into the medium, elevated the NEFA/glycerol ratio, and decreased the expression of fatty acid re-esterification markers PEPCK and CD36 at both mRNA and protein levels. These effects on TAG accumulation and fatty acid re-esterification were observed independently of changes in cellular n-3 polyunsaturated fatty acid (PUFA) content.

Animal experiment [2]:

Animal models ApcMin/+ mice (intestinal tumorigenesis model) and nude mice bearing HT-29 human colon cancer cell xenografts.

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Preparation Method	ApcMin/+ mice were fed SC 26196 mixed into their diet (AIN-93G diet or US17 diet) at a dosage of 100mg/kg/day for 7 weeks. In a separate xenograft study, nude mice were inoculated with HT-29 cells, maintained on the US17 diet, and then fed SC 26196 mixed into the same diet (100mg/kg/day) starting 5 days after tumor cell implantation. Primary tumor growth in the xenograft model was monitored.
Dosage form	100mg/kg/day; Administered in the diet; Daily for 7 weeks (ApcMin/+ mice) and for the study duration post-implantation (xenograft mice).
Applications	SC 26196 treatment resulted fewer intestinal tumors in ApcMin/+ mice and reduced average primary tumor size. In nude mice bearing HT-29 xenografts, SC 26196 treatment inhibited tumor growth at 4 weeks. The anti-tumorigenic effects on ApcMin/+ mice were nullified by concomitant dietary supplementation of arachidonic acid (AA), which bypassed the SC 26196-mediated inhibition of Δ -6 desaturase.

References:

- [1] Wang C, MacIntyre B, Mutch DM. Inhibition of Δ -6 desaturase reduces fatty acid re-esterification in 3T3-L1 adipocytes independent of changes in n3-PUFA cellular content. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2022 Jul;1867(7):159160.
- [2] Hansen-Petrik MB, McEntee MF, Johnson BT, et al. Selective inhibition of Delta-6 desaturase impedes intestinal tumorigenesis. *Cancer Lett*. 2002 Jan 25;175(2):157-63.

Background

SC 26196 is an orally active Delta6 desaturase (D6D, FADS2) inhibitor that regulates lipid metabolism by inhibiting the conversion of linoleic acid and α -linolenic acid into long-chain unsaturated fatty acids^[1-2]. SC 26196 is applicable for research related to inflammatory diseases and lipid metabolism disorders^[3-4].

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In vitro, in skin fibroblasts, coronary artery smooth muscle cells, and astrocytes, SC 26196 (2 μ M; 24 hours) inhibited the desaturation of 2 μ M [1-14C]18:2n-6 and significantly reduced the synthesis of arachidonic acid, EPA, and DHA^[5]. During the differentiation of 3T3-L1 adipocytes, SC 26196 (5 μ M; 8 days) blocked the conversion of α -linolenic acid (ALA) to eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA_n-3), and reduced triacylglycerol accumulation in adipocytes. SC 26196 treatment increased the release of non-esterified fatty acids and glycerol into the culture medium and decreased the expression of the fatty acid re-esterification markers PEPCCK and CD36^[6].

In vivo, in athymic mice bearing U-87 MG cell xenografts, SC 26196 (30mg/kg) administered via intraperitoneal injection (every three days for four weeks). SC 26196 synergistically inhibited the growth of U-87 MG xenograft tumors when combined with radiation therapy (5Gy local X-ray irradiation, every three days)^[7]. In ApcMin/+ mice bearing HT-29 colon cancer cell xenografts, dietary administration of SC 26196 (100mg/kg) for seven weeks. SC 26196 reduced number of intestinal tumors and a significant decrease in tumor size^[8].

References:

- [1] Sibbons CM, Irvine NA, Pérez-Mojica JE, et al. Polyunsaturated Fatty Acid Biosynthesis Involving Δ 8 Desaturation and Differential DNA Methylation of FADS2 Regulates Proliferation of Human Peripheral Blood Mononuclear Cells. *Front Immunol*. 2018 Mar 5;9:432.
- [2] Hargrave-Barnes KM, Azain MJ, Miner JL. Conjugated linoleic acid-induced fat loss dependence on Delta6-desaturase or cyclooxygenase. *Obesity (Silver Spring)*. 2008 Oct;16(10):2245-52.
- [3] Duffin KL, Obukowicz MG, Salsgiver WJ, et al. Lipid remodeling in mouse liver and plasma resulting from delta6 fatty acid desaturase inhibition. *Lipids*. 2001 Nov;36(11):1203-8.
- [4] Obukowicz MG, Welsch DJ, Salsgiver WJ, et al. Novel, selective delta6 or delta5 fatty acid desaturase inhibitors as antiinflammatory agents in mice. *J Pharmacol Exp Ther*. 1998 Oct;287(1):157-66.
- [5] Harmon SD, Kaduce TL, Manuel TD, et al. Effect of the delta6-desaturase inhibitor SC-26196 on PUFA metabolism in human cells. *Lipids*. 2003 Apr;38(4):469-76.
- [6] Wang C, MacIntyre B, Mutch DM. Inhibition of Δ -6 desaturase reduces fatty acid re-esterification in 3T3-L1 adipocytes independent of changes in n3-PUFA cellular content. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2022 Jul;1867(7):159160.
- [7] Wang J, Liang H, Sun M, et al. Delta-6-desaturase inhibitor enhances radiation therapy in glioblastoma in vitro and in vivo. *Cancer Manag Res*. 2018 Dec 7;10:6779-6790.
- [8] Hansen-Petrik MB, McEntee MF, Johnson BT, et al. Selective inhibition of Delta-6 desaturase

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