

Product Data Sheet

Product Name: K145
Cat. No.: GC12581

Chemical Properties

Cas. No. 1309444-75-4

Chemical Name (Z)-3-(2-aminoethyl)-5-(3-(4-butoxyphenyl)propylidene)thiazolidine-2,4-dione

SMILES CCCCOC1=CC=C(C=C1)CC/C([H])=C(S2)/C(N(C2=O)CCN)=O

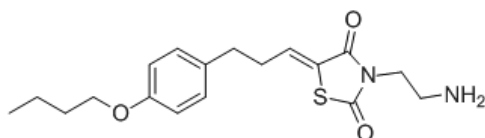
Formula $C_{18}H_{24}N_2O_3S$ M.Wt 348.46

Solubility Soluble 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



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

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Protocol

Cell experiment [1]:

Cell lines MCF-7、MDA-MB-231、LM2-4 cells

Cells were maintained in 1-2% serum containing medium for 18h. The monolayers were carefully scratched using a 20- μ l or 200- μ l pipette tip. The cellular debris was subsequently removed by washing with PBS, and the cells Preparation Method were incubated in medium with 1-2% serum. Cells were pre-treated with 2 μ M PF543 (SphK1 inhibitor), and K145 (SphK2 inhibitor before treatment of epidermal growth factor (EGF) (100ng/ml) for 8 to 24h. Migrating cells into the wounded area were photographed under a phase contrast microscope.

Reaction
Conditions 2 μ M; 8, 24h

Applications Inhibiting SphK2 with compound K145 not only suppresses EGF-mediated migration of MCF-7 and MDA-MB-231 cells, but also significantly inhibits EGF-mediated migration of the lung metastatic breast cancer cell line LM2-4.

Animal experiment [2]:

Animal models Male C57BL/6, leptin deficient ob/ob mice, db/db mice

13 weeks male C57BL/6, leptin deficient ob/ob mice and db/db mice were maintained in a room of 12-h light-dark cycle with temperature-controlled at 25°C. Six mice were used in each group and received i.p. injection of SphK2 Preparation Method inhibitor K145 at dosage of 5mg/kg and 10mg/kg (dissolved in DMSO) everyday as experimental group. For control group, mice received equivalent DMSO i.p. injection. After injection for 10 days, their blood and liver samples were collected.

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Dosage form 5, 10mg/kg; 10 days; i.p.

Applications K145 ameliorated fatty liver of ob/ob mice. K145 ameliorated hepatic lipid accumulation and fasting blood glucose of db/db mice. Hepatic mRNA levels for Lipid metabolism related genes were regulated by K145 treatment of ob/ob mice.

References:

- [1] Maiti A, Takabe K, Hait N C. Metastatic triple-negative breast cancer is dependent on SphKs/S1P signaling for growth and survival[J]. Cellular signalling, 2017, 32: 85-92.
[2] Shi Y, Wei Q, Liu Y, et al. The alleviating effect of sphingosine kinases 2 inhibitor K145 on nonalcoholic fatty liver[J]. Biochemical and biophysical research communications, 2021, 580: 1-6.

Background

K145 is a selective sphingosine kinase 2 (SphK2) inhibitor with an IC₅₀ value of 4.3μM and a K_i value of 6.4μM, exhibiting anticancer activity^[1, 2]. K145 inhibits SphK2 activity by competitively binding to it, without affecting the homologous enzyme SphK1^[3]. K145 can inhibit the growth of solitary plasmacytoma (SP) cells^[4].

In vitro, pretreatment of breast cancer cells (MCF-7, MDA-MB-231, and LM2-4 cells) with K145 (2μM) significantly inhibited epidermal growth factor (EGF)-mediated cell migration and significantly reduced sphingosine-1-phosphate (S1P) levels in LM2-4 cells^[5].

In vivo, K145 (5, 10mg/kg) administered via intraperitoneal injection for 10 days in ob/ob and db/db mice reduced hepatic lipid accumulation and lowered fasting blood glucose levels in db/db mice, and regulated the mRNA levels of lipid metabolism-related genes in the liver of ob/ob mice^[6]. K145 (50mg/kg/day) administered via intraperitoneal injection for 30 days in glioblastoma (GBM) cell xenograft mice slowed tumor growth and increased mouse survival rate^[7].

References:

- [1] Liu K, Guo T L, Hait N C, et al. Biological characterization of 3-(2-amino-ethyl)-5-[3-(4-butoxyl-

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phenyl)-propylidene]-thiazolidine-2, 4-dione (K145) as a selective sphingosine kinase-2 inhibitor and anticancer agent[J]. PloS one, 2013, 8(2): e56471.

[2] Lewis A C, Wallington-Beddoe C T, Powell J A, et al. Targeting sphingolipid metabolism as an approach for combination therapies in haematological malignancies[J]. Cell Death Discovery, 2018, 4(1): 72.

[3] Worrell B L, Brown A M, Santos W L, et al. In silico characterization of structural distinctions between isoforms of human and mouse sphingosine kinases for accelerating drug discovery[J]. Journal of chemical information and modeling, 2019, 59(5): 2339-2351.

[4] Li J, Li X J, Zhao D, et al. K145, a sphingosine kinase 2 inhibitor, inhibits solitary plasmacytoma cell growth[J]. The FASEB Journal, 2018, 32: 836.14-836.14.

[5] Maiti A, Takabe K, Hait N C. Metastatic triple-negative breast cancer is dependent on SphKs/S1P signaling for growth and survival[J]. Cellular signalling, 2017, 32: 85-92.

[6] Shi Y, Wei Q, Liu Y, et al. The alleviating effect of sphingosine kinases 2 inhibitor K145 on nonalcoholic fatty liver[J]. Biochemical and biophysical research communications, 2021, 580: 1-6.

[7] Fei X, Dou Y, Sun K, et al. TRIM22 promotes the proliferation of glioblastoma cells by activating MAPK signaling and accelerating the degradation of Raf-1[J]. Experimental & molecular medicine, 2023, 55(6): 1203-1217.

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