

Product Data Sheet

Product Name: SK-124
Cat. No.: GC79425

Chemical Properties

Cas. No. 2760404-50-8

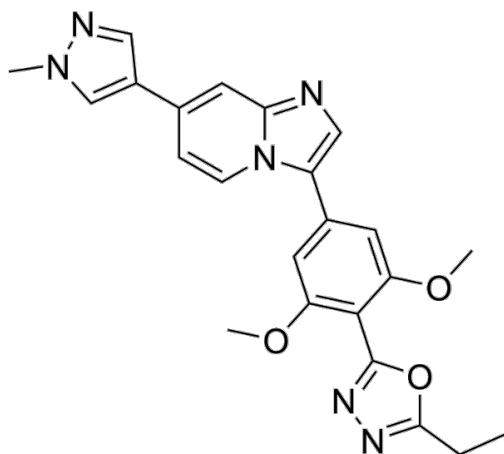
Formula $C_{23}H_{22}N_6O_3$ M.Wt 430.46

Solubility DMSO: 100 mg/mL (232.31 mM; Need ultrasonic) Storage Store at 4°C, away from moisture

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



Background

SK-124 is an orally active salt-inducible kinase (SIK) inhibitor with an IC_{50} of 230 nM against SIK1,

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4.1 nM against SIK2, and 21 nM against SIK3, exhibiting excellent kinome selectivity [1] [2] [4]. SK-124 blocks SIK-mediated CRTC2 phosphorylation, promotes CRTC2 nuclear translocation, and regulates vitamin D metabolism by upregulating renal Cyp27b1 and downregulating Cyp24a1 [1] [4]. SK-124 upregulates the expression of bone-related genes, increases serum Ca²⁺, 1,25-vitamin D and intact FGF23 levels, and suppresses endogenous PTH levels [1] [2] [3] [4]. SK-124 can be used in studies related to osteoporosis, male osteoporosis, and chronic kidney disease-mineral and bone disorder [2] [3] [4].

In Vivo, SK-124 (40-120 mg/kg; i.p.; single injection) induces renal Cyp27b1 expression, increases skeletal Fgf23 and Tnfsf11 expression, and modulates genomic coactivator occupancy near Cyp27b1 and Cyp24a1 in wild-type C57BL/6 mice, with maximal renal Cyp27b1 activity observed at 40 mg/kg at 3 h post-injection^[1]. SK-124 (40 mg/kg; i.p.; single dose) significantly increases renal Cyp27b1 expression, decreases renal Cyp24a1 expression, and elevates serum 1,25-vitamin D levels in healthy male C57BL/6 mice^[4]. SK-124 (40 mg/kg; i.p.; single dose) significantly increases renal Cyp27b1 expression, decreases renal Cyp24a1 expression, and stimulates 1,25-vitamin D production in both healthy mice and mice with CKD-MBD^[4]. SK-124 (2.5-40 mg/kg; p.o.; daily; 21 days) induces PTH-like effects on bone and mineral metabolism in male C57BL/6J mice, with the 40 mg/kg dose increasing trabecular bone volume fraction to ~60% and boosting bone formation rate per bone surface to ~0.008 $\mu\text{m}^3/\mu\text{m}^2/\text{d}$ ^[2]. SK-124 (40 mg/kg; p.o.; once daily; 4 weeks) restores trabecular and cortical bone mass, improves structural bone strength, stimulates bone formation via PTH-like mechanisms, and attenuates immune-related gene expression changes in hypogonadal ORX male BALB/cJ mice^[3].

In Vitro, SK-124 potently inhibits recombinant SIK2 (IC_{50} = 4.1 nM) and SIK3 (IC_{50} = 21 nM), with corresponding IC_{50} values in single-digit and low double-digit nanomolar range, respectively; in an in vitro radioisotope kinase assay, it exhibits 15-fold selectivity for SIK1 (IC_{50} = 230 nM)^[2]. SK-124 (0.5 μM) exhibits superior kinome selectivity compared to non-selective SIK inhibitors. Only 9 out of 300 human kinases tested at 0.5 μM are inhibited by more than 80%, and it displays primary activity against SIK2 and SIK3^[2]. SK-124 (0.5 μM) binds to intracellular SIK2 and SIK3 in HEK293T cells; in NanoBRET target binding assays, its corresponding IC_{50} values are 8.8 nM and 11.3 nM^[2]. SK-124 (1.25-20 μM ; 1 h) binds to endogenous SIK2 in murine osteocyte-like Ocy454 cells, which is

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confirmed by the increased thermal stability of SIK2 in cellular thermal shift assay^[2]. SK-124 (78 nM-20 μ M; 1 h) for immunoblotting, 90 min for nuclear translocation assay) inhibits the SIK signaling pathway in mouse osteocyte-like Ocy454 cells and human Saos2 cells by reducing the phosphorylation levels of HDAC4/HDAC5 and CRTC2 and promoting CRTC2 nuclear translocation, with an EC₅₀ of 128 nM^[2]. SK-124 (0.01-10 μ M; 4 h) regulates the expression of SIK target genes in mouse osteocyte-like Ocy454 cells, reducing SOST expression and increasing TNFSF11 expression in a PTH-like manner^[2]. SK-124 (10 μ M; 3 h) induces nuclear translocation of CRTC2 in proximal tubule cells of H9 human embryonic stem cell-derived kidney organoids^[4]. SK-124 (20 μ M) reduces the phosphorylation level of CRTC2 and induces nuclear translocation of CRTC2 in opossum kidney cells^[4]. SK-124 promotes the nuclear translocation of CRTC in a heterologous cell system, with an EC₅₀ of 32 nM^[4]. SK-124 (20 μ M; 2-48 h) upregulates Cyp27b1 expression and increases 1,25-vitamin D production in a time-dependent manner in kidney organoids derived from H9 human embryonic stem cells^[4].

References:

- [1]. Meyer MB, et al. Rapid genomic changes by mineralotropic hormones and kinase SIK inhibition drive coordinated renal Cyp27b1 and Cyp24a1 expression via CREB modules. The Journal of biological chemistry. 2022 Nov;298(11):102559.
- [2]. Sato T, et al. Structure-based design of selective, orally available salt-inducible kinase inhibitors that stimulate bone formation in mice. Proceedings of the National Academy of Sciences of the United States of America. 2022 Dec 13;119(50):e2214396119.
- [3]. Choi RB, et al. The orally available SIK2/SIK3 inhibitor SK-124 increases bone mass in hypogonadal male mice. JBMR plus. 2026 Apr;10(4):ziag032.
- [4]. Yoon SH, et al. A parathyroid hormone/salt-inducible kinase signaling axis controls renal vitamin D activation and organismal calcium homeostasis. The Journal of clinical investigation. 2023 May 01;133(9):e163627.

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