

Product Data Sheet

Product Name: HG-9-91-01

Cat. No.: GC11719

Chemical Properties

Cas. No. 1456858-58-4

Chemical Name (Z)-N-(2,4-dimethoxyphenyl)-N'-(2,6-dimethylphenyl)-N-(6-((4-(4-methylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)carbamimidic acid

SMILES CC1=C(/N=C(O)/N(C2=NC=NC(NC3=CC=C(N4CCN(CC4)C)C=C3)=C2)C5=C(OC)C=C(OC)C=C5)C(C)=CC=C1

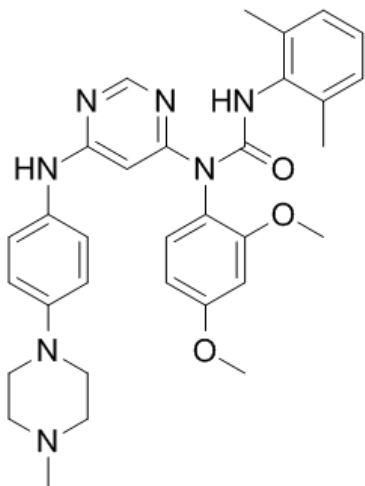
Formula $C_{32}H_{37}N_7O_3$ M.Wt 567.68

Solubility $\geq 56.8\text{mg/mL}$ 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 Bone marrow-derived macrophages

Preparation Method Powder was dissolved in DMSO as 10 mM stock solutions and stored at -20°C until use. BMM cells were plated at concentration of 160×10^3 cells/well in 24 wells osteo assay plates coated with bone biomimetic synthetic surface and cultured with rmM-CSF (30ng/ml) and rmRANKL (50ng/ml) for 3 days in absence or presence of different concentrations of HG-9-91-01.

Reaction Conditions 0, 0.1, 0.3, 0.5 μ M for 72 days

Applications No significant toxicity was observed at the concentrations tested. Pre-treatment with 0.5 μ M HG-9-91-01 significantly reduced the formation of resorption lacunae compared to RANKL alone.

Animal experiment [2]:

Animal models TNBS-induced colitis in female BALB/c mice, C57BL/6J mice

Preparation Method The TNBS-challenged mice were treated with different doses of HG-9-91-01 (3, 10, 30 mg/kg/day intraperitoneally (i.p.), dissolved in 100 μ L olive oil).

Dosage form Intraperitoneal injection, 3, 10, 30 mg/kg/day for 8 days.

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

Applications TNBS-treated mice given HG-9-91-01 at 3, 10, or 30 mg/kg rapidly recovered their lost body weight. The macroscopic inflammatory signs (gross bleeding, ulceration) and the shortening of colon length typically caused by TNBS were also improved by treatment with 3, 10, or 30 mg/kg HG-9-91-01

References:

- [1]: Lombardi M S, GilliÉron C, Berkelaar M, et al. Salt-inducible kinases (SIK) inhibition reduces RANKL-induced osteoclastogenesis[J]. PloS one, 2017, 12(10): e0185426.
- [2]: Fu Y, Ma G, Zhang Y, et al. HG-9-91-01 Attenuates murine experimental colitis by promoting interleukin-10 production in colonic macrophages through the SIK/CRTC3 pathway[J]. Inflammatory Bowel Diseases, 2021, 27(11): 1821-1831.

Background

HG-9-91-01 is a salt-inducible kinases (SIK) inhibitor, inhibited SIK1, SIK2, SIK3 with IC50 values of 0.92nM, 6.5nM and 19.4nM, respectively [1].

HG-9-91-01 potently inhibited the SIKs and did not inhibit any other member of the AMPK-related kinase subfamily. HG-9-91-01 increased LPS-stimulated IL-10 production and suppressed proinflammatory cytokine secretion [2]. 0.5 µM HG-9-91-01 pretreated RAW264.7 for 30 min before RANKL stimulation resulted in reduction of multinucleated cell formation and of TRAP staining, and significantly reduced the mRNA of osteoclast differentiation markers in a concentration dependent manner. Pre-treatment with 0.5 µM HG-9-91-01 significantly reduced the formation of resorption lacunae compared to RANKL alone [3].

HG-9-91-01 (3, 10, or 30 mg/kg) enhanced the expression of IL-10 whereas downregulated the levels of IL-12 and TNF-α in the colon tissue of the TNBS mice [4].

References:

- [1]. Sundberg T B, Choi H G, Song J H, et al. Small-molecule screening identifies inhibition of salt-inducible kinases as a therapeutic strategy to enhance immunoregulatory functions of dendritic cells[J]. Proceedings of the National Academy of Sciences, 2014, 111(34): 12468-12473.

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

- [2]. Clark K, MacKenzie K F, Petkevicius K, et al. Phosphorylation of CRT3 by the salt-inducible kinases controls the interconversion of classically activated and regulatory macrophages[J]. Proceedings of the National Academy of Sciences, 2012, 109(42): 16986-16991.
- [3]. Lombardi M S, GilliÉron C, Berkelaar M, et al. Salt-inducible kinases (SIK) inhibition reduces RANKL-induced osteoclastogenesis[J]. PloS one, 2017, 12(10): e0185426.
- [4]. Fu Y, Ma G, Zhang Y, et al. HG-9-91-01 Attenuates murine experimental colitis by promoting interleukin-10 production in colonic macrophages through the SIK/CRT3 pathway[J]. Inflammatory Bowel Diseases, 2021, 27(11): 1821-1831.

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