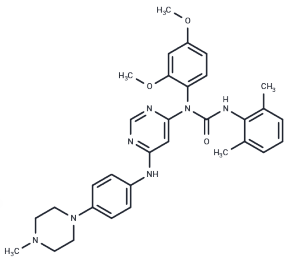
Data Sheet (Cat.No.T4599)

TargetMol

HG-9-91-01

Chemical Properties



CAS No. : 1456858-58-4

Formula: C32H37N7O3

Molecular Weight: 567.68

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	HG-9-91-01 (SIK inhibitor 1) is a potent and highly selective salt-inducible kinase (SIKs) inhibitor with IC50s of 0.92 nM, 6.6 nM and 9.6 nM for SIK1, SIK2 and SIK3respectively.
Targets(IC50)	SIK
In vitro	HG-9-91-01, a recently identified inhibitor of SIK1-3 and various other kinases, targets numerous protein tyrosine kinases with a threonine residue at their gatekeeper site, including members of the Src family (Src, Lck, and Yes), BTK, and the FGF and Ephrin receptors. This compound has been shown to significantly inhibit SIK2, thereby enhancing IL-10 production, with effects akin to those observed with PGE2 treatment–demonstrating potentiation of zymosan-induced IL-10 production in a concentration-dependent manner with an EC50 of approximately 200 nM. Moreover, HG-9-91-01 exhibits over 100-fold greater potency against SIKs compared to AMPK in cell-free assays (IC50=4.5 μM). Additionally, treatment with HG-9-91-01 leads to a dose-dependent increase in mRNA expression of Pck1 and G6pc, paralleling the effects of 0.1 μM glucagon, and consequently results in elevated glucose production.
Cell Research	Bone marrow is harvested from femurs and tibias of C57BL/6 mice. Bone-marrow-derived dendritic cells (BMDCs) are differentiated DMEM supplemented with 2 mM GlutaMAX, 10% (vol/vol) FBS, Penicillin, Streptomycin, and 2% mouse granulocyte-macrophage colony-stimulating factor (GM-CSF)-conditioned media derived from murine L cells. Cultures are differentiated for 7 d and routinely analyzed for >90% CD11c (allophycocyanin (APC) anti-CD11c clone HL3) positivity by flow cytometry before use in experiments. Lentiviral transduction of bone marrow cultures is conducted by addition of 293T culture supernatants containing lentiviral particles encoding the CREB-dependent luciferase reporter construct or CRTC3 targeting or control shRNAs 1 d postisolation. Stable integration of lentiviral shRNA constructs is selected by addition of puromycin (3 μg/mL) on day 4 posttransduction. After 2 d, stably transduced BMDCs are released from selection and used in subsequent assays. Unless otherwise indicated, cells are treated for 2 d with PGE2 (5 μM) or HG-9-91-01 (0.5 μM) or an equivalent concentration of DMSO (≤0.5%) and then stimulated for 18 h with LPS (100 ng/mL), R848 (10 μg/mL), or Zymosan (4 μg/mL)[2].

Solubility Information

Solubility	30% propylene glycol plus 70% ethanol: Soluble, DMSO: 250 mg/mL (440.39 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.52 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7616 mL	8.8078 mL	17.6156 mL
5 mM	0.3523 mL	1.7616 mL	3.5231 mL
10 mM	0.1762 mL	0.8808 mL	1.7616 mL
50 mM	0.0352 mL	0.1762 mL	0.3523 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Clark K, et al. Phosphorylation of CRTC3 by the salt-inducible kinases controls the interconversion of classically activated andregulatory macrophages. Proc Natl Acad Sci U S A. 2012 Oct 16;109(42):16986-91.
Huang J, Fan H, Chen Y M, et al.The salt-inducible kinases inhibitor HG-9-91-01 exhibits antidepressant-like actions in mice exposed to chronic unpredictable mild stress.Neuropharmacology.2023: 109437.
Li X W, Yuan S C, Wang M, et al.Rosmarinic acid ameliorates autoimmune responses through suppression of intracellular nucleic acid-mediated type I interferon expression.Biochemical and Biophysical Research Communications.2023
Sundberg TB, et al. Small-molecule screening identifies inhibition of salt-inducible kinases as a therapeutic strategy to enhance immunoregulatory functions of dendritic cells. Proc Natl Acad Sci U S A. 2014 Aug 26;111(34): 12468-73.
Patel K, et al.The LKB1-salt-inducible kinase pathway functions as a key gluconeogenic suppressor in the liver. Nat Commun. 2014 Aug 4;5:4535.
Mujahid N, et al. A UV-Independent Topical Small-Molecule Approach for Melanin Production in Human Skin. Cell Rep. 2017 Jun 13;19(11):2177-2184.