GSK 650394

Cat. No.: HY-15192

CAS No.: 890842-28-1

Molecular Formula: $C_{25}H_{22}N_2O_2$

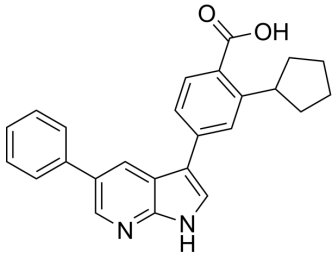
Molecular Weight: 382.45

Target: SGK; Influenza Virus

Pathway: Metabolic Enzyme/Protease; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 40.7 mg/mL (106.42 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6147 mL	13.0736 mL	26.1472 mL
5 mM	0.5229 mL	2.6147 mL	5.2294 mL
10 mM	0.2615 mL	1.3074 mL	2.6147 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (6.54 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.54 mM); Suspended solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK 650394 is a novel SGK inhibitor with IC_{50} of 62 nM and 103 nM for SGK1 and SGK2 in the SPA assay respectively. GSK 650394 also inhibits influenza virus replication.

IC_{50} & Target

SGK1

In Vitro

GSK650394 is relatively non-toxic, with LC_{50} values of 41 μM in M1 cells (68 times its activity IC_{50}) and a LC_{50} greater than 100

	μM in HeLa cells. GSK650394 inhibits SGK1-mediated epithelial transport with an IC_{50} of 0.6 μM in the SCC assay. GSK650394 inhibits the growth of LNCaP cells with IC_{50} of approximately 1 μM[1]. GSK650394A inhibits the insulin-induced phosphorylation of PKB-Ser^{473} at 3 μM, and essentially abolishes this response at 10 μM. GSK650394A (1-10 μM) does not alter the phosphorylation of PRAS40-Ser246 in hormone-deprived cells or prevent the insulin-induced phosphorylation of this residue[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GSK650394 (1, 10, and 30 μM, 10 μL/rat, intrathecally) dose-dependently prevents CFA-induced pain behavior and the associates SGK1 phosphorylation, GluR1 trafficking, and protein-protein interactions at 1 day after CFA administration[3]. GSK650394 at concentrations of 10, 30, and 100 nM (10 μL), but not vehicle solution (SNL 3D+Veh and SNL 7D+Veh, respectively), dose-dependently increases the withdrawal latency of the ipsilateral hindpaw at 1-3 and 1-5 h after injection at days 3 and 7 postsurgery (SNL 3D+GSK and SNL 7D+GSK, respectively). GSK650394 (from day 0 to 6 postsurgery; 100 nM, 10 μL, i.t.) administration alleviates SNL-induced allodynia at days 3, 5, and 7 postsurgery in SNL animals[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The toxicity of GSK650394 to M-1 and HeLa cells is assessed using the Cell Proliferation Kit (XTT) following manufacturer's instructions. Briefly, 10,000 HeLa or M-1 cells/well are plated into 96-well plates in 100μL of the appropriate maintenance media. After 48 h, media is removed and replaced with 100 μL of EMEM with Earle's salts containing 2 mM L-glutamine and 1% antibiotic-antimycotic overnight. M-1 cells are also supplemented with 1 μg/mL insulin, 6.25 μg/mL sodium selenite, and 6.25 μg/mL transferrin. After 24 h, the media is removed and replaced with 100 μL media alone or media containing increasing concentrations of GSK650394. For HeLa cells, 50 μL of activated XTT solution is added after 4 h. For M-1 cells, 50 μL of activated XTT solution is added after 24 h. Following a 2 h incubation, absorbance is measured at 490 nm using a SpectraMAX PLUS spectrophotometer and the data analyzed to obtain IC_{50} values using GraphPad Prism 3 software. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Briefly, the rats are anesthetized under isoflurane anesthesia (induction 5%, maintenance 2% in oxygen). An incision is made, and the left L5 spinal nerves are carefully isolated and tightly ligated with 6-0 silk sutures 2-5 mm distal to the dorsal root ganglia. GSK650394 (10, 30, and 100 nM, 10 μL) is administered by bolus injection at 3 or 7 d or by daily injection for 7 d (day 0-6) postspinal nerve ligation. A vehicle solution of a volume identical to that of the tested agents is dispensed to serve as a control. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Int J Biol Sci. 2023; 19(1): 204-224.
- Oncogene. 2021 Sep;40(35):5367-5378.
- J Transl Med. 2023 Aug 14;21(1):544.
- Br J Pharmacol. 2020 Apr;177(7):1666-1676.

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REFERENCES

[1]. Sherk AB, et al. Development of a small-molecule serum- and glucocorticoid-regulated kinase-1 antagonist and its evaluation as a prostate cancer therapeutic. Cancer

Res. 2008 Sep 15;68(18):7475-83.

[2]. Mansley MK, et al. Effects of nominally selective inhibitors of the kinases PI3K, SGK1 and PKB on the insulin-dependent control of epithelial Na+ absorption. Br J Pharmacol. 2010 Oct;161(3):571-88.

[3]. Peng HY, et al. Spinal SGK1/GRASP-1/Rab4 is involved in complete Freund's adjuvant-induced inflammatory pain via regulating dorsal horn GluR1-containing AMPA receptor trafficking in rats. Pain. 2012 Dec;153(12):2380-92.

[4]. Peng HY, et al. Spinal serum-inducible and glucocorticoid-inducible kinase 1 mediates neuropathic pain via kalirin and downstream PSD-95-dependent NR2B phosphorylation in rats. J Neurosci. 2013 Mar 20;33(12):5227-40.

[5]. Alamares-Sapuay JG, et al. Serum- and glucocorticoid-regulated kinase 1 is required for nuclear export of the ribonucleoprotein of influenza A virus. J Virol. 2013 May;87(10):6020-6.

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