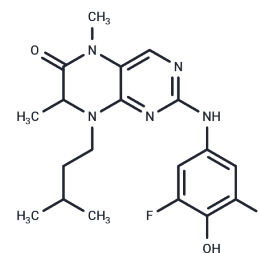


BI-D1870

Chemical Properties

CAS No. : 501437-28-1
 Formula: C₁₉H₂₃F₂N₅O₂
 Molecular Weight: 391.42
 Storage: 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	BI-D1870 is a highly specific, blood-brain-permeable, and ATP-competitive inhibitor of the N-terminal AGC kinase domain of RSK, with IC ₅₀ values of 31 nM, 24 nM, 18 nM, and 15 nM for RSK1, RSK2, RSK3, and RSK4.
Targets(IC ₅₀)	Autophagy,S6 Kinase
In vitro	<p>METHODS: HEK-293 cells were incubated with BI-D1870 (10 μM, 15 min, 4 h total) To examine whether BI-D1870 could inhibit RSK activity in cells, the effect of BI-D1870 on RSK-catalyzed phosphorylation of its known substrates in HEK-293 cells was investigated using PMA as an agonist to activate ERK1/ERK2 and RSK isoforms.</p> <p>RESULTS Incubation of cells with BI-D1870 significantly inhibited PMA-induced phosphorylation of GSK3α and GSK3β. In contrast, BI-D1870 had little effect on PMA-induced activation of ERK1/ERK2 (catalyzed by Raf and MKK1) or phosphorylation of CREB at Ser at any time point. [1]</p> <p>METHODS: Oral cancer cell lines (SCC2095, SCC4, SCC9, Ca922 and HSC-3) and NHOK cells were treated with BI-D1870 (1, 2, 3, 4, 5.28 or 48 hours), and the growth of these cells was detected by MTT.</p> <p>RESULTS BI-D1870 showed a dose-responsive antiproliferative effect on OSCC cells. [3]</p> <p>METHODS: Cells transfected with immunofluorescent GFP-LC3 were treated with BI-D1870 (0.5, 2 μM) for 48 hours and observed under a confocal microscope; DAPI staining was used to locate the nucleus, and Western blot of LC3B was observed in cells treated with BI-D1870 for 48 hours.</p> <p>RESULTS BI-D1870 induced autophagy, and Western blot of LC3B-II showed that this induction was dose-dependent. [3]</p>
In vivo	<p>METHODS: Two days after immunization with MOG peptide, BI-D1870 (0.5 mg/kg) was injected intraperitoneally into mice and repeated every other day for 11 days.</p> <p>RESULTS Mice showed delayed neurological deficits; BI-D1870 treatment had a moderate protective effect against weight loss. [4]</p>
Kinase Assay	Purified His6-RSK1, His6-RSK2 or GST-RSK21-389:S381E (1-2 units/ml) were assayed for 10 min at 30 °C in a 50 μl assay mixture in Buffer A containing 30 μM substrate peptide (KEAKEKRQEIQIAKRRRLSSLRASTSKSGGSQK), 10 mM magnesium acetate and 100 μM of [γ- ³² P]ATP. Reactions were terminated and analyzed as described previously. The amount of enzyme that catalyzed the phosphorylation of 1 nmol of substrate peptide in 1 min was termed one unit. In order to assay RSK and MSK1 in HEK-293 or Rat-2 cell lysates, these kinases were immunoprecipitated from the cell lysates (0.1 mg of lysate protein

Kinase Assay	for RSK and 0.3 mg for MSK1) and assayed as described previously, except that for RSK assays the immunoprecipitates were washed twice with Buffer A containing 1 mM ATP and twice with Buffer A prior to the assay, as a precaution to ensure dissociation of BI-D1870 from the RSK isoforms [1].
Cell Research	The rat embryo fibroblast cell line, Rat-2 cells were cultured on 10 cm-diameter dishes in Dulbecco's Modified Eagle's medium supplemented with 10% (v/v) FBS. HEK-293 cells were cultured on 10 cm-diameter dishes in Dulbecco's Modified Eagle's medium supplemented with 10% FBS and 1xantimycotic/antibiotic solution. Prior to stimulation, cells were cultured in the absence of serum for 16 h. Inhibitors were dissolved in DMSO at a 1000-fold higher concentration than they were used at. These inhibitors, or the equivalent volume of DMSO as a control, were added to the tissue culture medium 30 min prior to stimulation unless indicated otherwise. The final concentration of DMSO in the culture medium was 0.1% and had no effect on agonist-induced activation or phosphorylation of any of the substrates examined. The cells were stimulated with the indicated agonists and lysed in 1 ml of ice-cold Lysis Buffer and centrifuged at 16000 g at 4 °C for 5 min. The supernatants were frozen in liquid nitrogen and stored at -80 °C until use. Protein concentrations were determined using the Bradford method with BSA as the standard [1].
Animal Research	Myelin oligodendrocyte glycoprotein (MOG) peptide 35-55. (MEVGWYRSPFSRVVHLYRNGK) (BEX) was used to induce EAE in C57/BL6J mice. Mice were injected s.c. with 200 µg of MOG peptide in 100 µL of PBS emulsified in 100 µL complete Freund's adjuvant (CFA) that was further supplemented with five mg mL ⁻¹ Mycobacterium tuberculosis (H37Ra). In addition, 500 ng pertussis toxin was injected i.p. on days zero and two. The RSK inhibitor (BI-D1870; 0.5 mg kg ⁻¹) was injected i.p. into mice two days after immunization with MOG peptide, and injection was repeated every other day for 11 days. Mice that received only dimethyl sulfoxide (DMSO) solution were used as controls. Paralysis was evaluated according to the following scale: zero, no disease; one, tail limpness; two, hind limb weakness; three, hind limb paralysis; four, forelimb weakness; five, quadriplegia; six, death. For histological analysis, CNS samples were fixed with 4% paraformaldehyde and sliced at 4 µm, and then hematoxylin & eosin (H & E) staining was performed [4].

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H ₂ O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 16.9 mg/mL (43.18 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: 7.2 mg/mL (18.39 mM), Suspension. 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	2.5548 mL	12.774 mL	25.548 mL
5 mM	0.511 mL	2.5548 mL	5.1096 mL
10 mM	0.2555 mL	1.2774 mL	2.5548 mL
50 mM	0.0511 mL	0.2555 mL	0.511 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

- Sapkota GP, et al. BI-D1870 is a specific inhibitor of the p90 RSK (ribosomal S6 kinase) isoforms in vitro and in vivo. *Biochem J.* 2007 Jan 1;401(1):29-38.
- He S, Lu M, Zhang L, et al. RSK4 promotes the macrophage recruitment and M2 polarization in esophageal squamous cell carcinoma. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease.* 2023: 166996.
- Roffé M, et al. Two widely used RSK inhibitors, BI-D1870 and SL0101, alter mTORC1 signaling in a RSK-independent manner. *Cell Signal.* 2015 Aug;27(8):1630-42.
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