Acalisib

Cat. No.: HY-12644

CAS No.: 870281-34-8

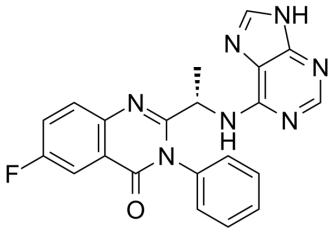
Molecular Formula: $C_{21}H_{16}FN_7O$

Molecular Weight: 401.4

Target: PI3K

Pathway: PI3K/Akt/mTOR

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (311.41 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4913 mL	12.4564 mL	24.9128 mL
	5 mM	0.4983 mL	2.4913 mL	4.9826 mL
	10 mM	0.2491 mL	1.2456 mL	2.4913 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 (6.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Acalisib is a potent and selective PI3Kδ inhibitor with an IC_{50} of 12.7 nM.

IC_{50} & Target

p110δ 12.7 nM (IC_{50})	p110γ 1389 nM (IC_{50})	p110β 3377 nM (IC_{50})	p110α 5441 nM (IC_{50})
hVps34 12682 nM (IC_{50})	DNA-PK 18749 nM (IC_{50})		

In Vitro

Acalisib (GS-9820) is more selective for PI3Kδ (IC_{50}=12.7 nM) relative to other PI3K class I enzymes (IC_{50}: PI3Kα, 5,441 nM;

	PI3Kβ, 3,377 nM; PI3Kγ, 1,389 nM). Acalisib is also 10^3-fold more selective against PI3Kδ than against related kinases, such as PI3KCIIβ (IC_{50}>10 nM), hVPS34 (IC_{50}=12.7 μM), DNA-PK (IC_{50}=18.7 μM), and mTOR (IC_{50}>10 nM). In fibroblasts, the PDGF receptor signals through PI3Kα and the GPCR for lysophosphatidic acid (LPA) signals through PI3Kβ. Acalisib reduces PDGF-induced pAkt by only 50% at 11,585 nM, and LPA-induced pAkt by 50% at 2,069 nM. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To dissect the relative contribution of PI3Kα and PI3Kδ inhibition in the reduction of obesity, obese hyperphagic ob/ob mice are treated with a selective PI3Kα inhibitor, BYL-719, or with a selective PI3Kδ inhibitor, Acalisib (GS-9820). Remarkably, BYL-719 reduces body weight after 15 days of treatment to a similar extent as CNIO-PI3Ki, whereas Acalisib has no significant effect at the same doses as BYL-719. It should be noted that 10 mg/kg of Acalisib is sufficient to reduce the growth of multiple myeloma xenografts in mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Biochemical in vitro lipid kinase assays are performed. A stock solution of Acalisib (GS-9820) is prepared in DMSO at a concentration of 10 mM. Ten-point kinase inhibitory activities are measured over a concentration range (5 to 10^4 nM) with ATP at a concentration consistent with the K_m of each of the enzymes[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	The effect of inhibitors on RAW264.7 cell survival is evaluated using the MTT assay. RAW264.7 cells are seeded in Falcon flat bottom 96-well plates at a density of 2.5-3×10^4 cells/cm^2 in 100 μL of DMEM with 10% FBS and 1% antibiotic solution. After seeding, the cells are allowed to attach for 24 h then exposed to control or Acalisib (GS-9820) (100 pM to 10 μM) for 24 h. After incubation at 37°C in 5% CO_2, MTT substrate is added at a final concentration of 0.5 mg/mL for 4 h. Following a 4-h incubation, 100 μL of solubilization solution is added to each well to dissolve the formazan crystals and samples are analyzed after 24 h. Absorbance of the samples is assessed using a plate reader using a wavelength of 550 nm and a reference wavelength of 700 nm[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Ob/ob C57BL6J mice and Wild-type C57BL6J/Ola.Hsd mice are housed under specific pathogen free (SPF) conditions, at 22°C, and with 12 hours dark/light cycles (light cycle from 8 am to 8 pm). All mice used are males of 20 weeks of age. Mice are fed with standard chow diet (18% of fat-based caloric content). PI3K inhibitors are administered daily by oral gavage during 15 or 16 days as follows, BYL-719 (5 and 10 mg/kg) and Acalisib (5 and 10 mg/kg), CNIO-PI3Ki (1 and 5 mg/kg), dissolved in PEG-300 and 10% N-methyl-2-pyrrolidone. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Shugg RP, et al. Effects of isoform-selective phosphatidylinositol 3-kinase inhibitors on osteoclasts: actions on cytoskeletal organization, survival, and resorption. J Biol Chem. 2013 Dec 6;288(49):35346-57.

[2]. Lopez-Guadamillas E, et al. PI3Kα inhibition reduces obesity in mice. Aging (Albany NY). 2016 Nov 4;8(11):2747-2753.

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