

PKI-179 hydrochloride

Chemical Properties

CAS No. :	1463510-35-1
Formula:	C ₂₅ H ₂₉ ClN ₈ O ₃
Molecular Weight:	525.00
Storage:	Keep away from moisture Powder: -20°C for 3 years In solvent: -80°C for 1 year <small>Actual storage temperature shall be subject to the COA.</small>

Biological Description

Description	PKI-179 hydrochloride is a potent and orally available dual PI3K/mTOR inhibitor. Its IC ₅₀ values against PI3K- α , PI3K- β , PI3K- γ , PI3K- δ and mTOR are 8 nM, 24 nM, 74 nM, 77 nM and 0.42 nM respectively. It also exerts inhibitory activity against E545K and H1047R mutants with IC ₅₀ values of 14 nM and 11 nM, and exhibits significant antitumor effects in in vivo models.
In vitro	<p>Methods: In vitro cell proliferation assays and kinase/ion channel/metabolic enzyme screening systems were used to evaluate the antitumor activity and selectivity of PKI-179 hydrochloride.</p> <p>Results: :</p> <ol style="list-style-type: none"> 1. PKI-179 hydrochloride significantly inhibited tumor cell proliferation, with IC₅₀ values of 22 nM and 29 nM for MDA361 and PC3 cells, respectively. 2. At concentrations higher than 30 μM, PKI-179 hydrochloride showed no obvious inhibitory effect on 361 other kinases, hERG, and multiple cytochrome P450 (CYP) isoforms, but exhibited certain inhibitory activity against CYP2C8 with an IC₅₀ of 3 μM [1].
In vivo	<p>Methods: Nude mice bearing MDA-361 human breast cancer xenografts were treated with oral administration to evaluate the in vivo antitumor activity, target inhibition and tolerability of PKI-179 hydrochloride. The oral bioavailability and half-life of PKI-179 hydrochloride were determined in multiple animal models including nude mice, rats, monkeys and dogs.</p> <p>Results: :</p> <ol style="list-style-type: none"> 1. In vivo antitumor activity and tolerability: PKI-179 hydrochloride (5-50 mg/kg, oral administration once daily for 40 days) could significantly inhibit the growth of MDA-361 human breast cancer xenografts and exhibited good tolerability in nude mice. 2. In vivo target signaling inhibition: PKI-179 hydrochloride (50 mg/kg, oral administration) effectively suppressed PI3K signaling in nude mice bearing MDA-361 tumor xenografts. 3. Oral bioavailability and half-life: PKI-179 hydrochloride displayed favorable oral bioavailability (98% in nude mice, 46% in rats, 38% in monkeys, 61% in dogs) with a long half-life (>60 minutes) [1].

Solubility Information

A DRUG SCREENING EXPERT

Solubility	Ethanol: Slightly soluble DMF: 2.00 mg/mL (3.81 mM), Sonication is recommended. DMSO:PBS(pH 7.2) (1:3): 0.25 mg/mL (0.48 mM), Sonication is recommended. DMSO: 16.00 mg/mL (30.48 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9048 mL	9.5238 mL	19.0476 mL
5 mM	0.381 mL	1.9048 mL	3.8095 mL
10 mM	0.1905 mL	0.9524 mL	1.9048 mL
50 mM	0.0381 mL	0.1905 mL	0.381 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

Venkatesan AM, et, al. PKI-179: an orally efficacious dual phosphatidylinositol-3-kinase (PI3K)/mammalian target of rapamycin (mTOR) inhibitor. *Bioorg Med Chem Lett*. 2010 Oct 1;20(19):5869-73.

Rehan M. A structural insight into the inhibitory mechanism of an orally active PI3K/mTOR dual inhibitor, PKI-179 using computational approaches. *J Mol Graph Model*. 2015 Nov;62:226-234.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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